MOrphogenesis Simulation and Analysis
In siliCo

IN COLLABORATION WITH: Réproduction et Développement des Plantes

DOMAIN
Digital Health, Biology and Earth

THEME
Computational Biology
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Project-Team MOSAIC

Creation of the Project-Team: 2019 July 01

Keywords

Computer sciences and digital sciences
- A3.4. – Machine learning and statistics
- A6.1. – Methods in mathematical modeling
- A6.2. – Scientific computing, Numerical Analysis & Optimization
- A6.3. – Computation-data interaction
- A6.5. – Mathematical modeling for physical sciences
- A7.1. – Algorithms
- A8.1. – Discrete mathematics, combinatorics
- A8.2. – Optimization
- A8.3. – Geometry, Topology
- A8.7. – Graph theory
- A9.2. – Machine learning
- A9.5. – Robotics

Other research topics and application domains
- B1.1.2. – Molecular and cellular biology
- B1.1.3. – Developmental biology
- B1.1.7. – Bioinformatics
- B1.1.8. – Mathematical biology
- B1.1.9. – Biomechanics and anatomy
- B1.1.10. – Systems and synthetic biology
- B1.1.11. – Plant Biology
- B3.5. – Agronomy
- B9.1.2. – Serious games
- B9.5.1. – Computer science
- B9.5.2. – Mathematics
- B9.5.5. – Mechanics
- B9.5.6. – Data science
1 Team members, visitors, external collaborators

Research Scientists

- Christophe Godin [Team leader, INRIA, Senior Researcher, HDR]
- Olivier Ali [INRIA, Researcher]
- Romain Azais [INRIA, Researcher, HDR]

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- Ibrahim Cheddadi [UGA, Associate Professor]
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Post-Doctoral Fellow

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- Elsa Gascon [INRIA, from Oct 2022]
- Florian INGELS [INRIA, until Aug 2022]
- Katia Mirande [INRIA, until Dec 2022]
- Manuel Petit [INRIA, from May 2021]
- Lucie Poupardin [INRIA, from Oct 2022]

Technical Staff

- Guillaume Cerutti [INRAE, Engineer]
- Andre-Claude Clapson [Inria, Engineer, from Apr 2022, CDD]
- Annamaria Kiss [INRAE, Engineer, from Sep 2022]
- Jonathan Legrand [CNRS, Engineer]
- Arthur Luciani [INRIA, from Dec 2021, Engineer, CDD]
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Interns and Apprentices

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Administrative Assistant

- Sylvie Boyer [INRIA]
Project MOSAIC

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- Arezki Boudaoud [ENS DE LYON, HDR]
- Frédéric Boudon [CIRAD]
- Emmanuel Faure [CNRS]
- Franck Hétroy [UNIV STRASBOURG, HDR]
- Patrick Lemaire [CNRS, HDR]
- François Parcy [CNRS, HDR]
- Jan Traas [INRAE, HDR]
- Samuel Vernoux [CNRS, HDR]

2 Overall objectives

Our general aim in MOSAIC is to identify key principles of organism development in close collaboration with biologists by constructing a new generation of models based on explicit mathematical and computational representations of forms. For this we will develop a dual modeling approach where conceptual models will be used to identify self-organizing principles and realistic models will be used to test non-trivial genetic and physical hypotheses in silico and assess them against observations. This will contribute to extend the domain of systems biology to developmental systems and help interpret where possible the vast amount of geometric, molecular and physical data collected on growing forms.

The main originality of the project lies in its integrated approach: we want to face the complexity of living organisms by developing an integrated view of form development, relying on the study of the interaction between coupled processes.

While our approach will mainly focus on plant development at different scales, the MOSAIC project will also consider the morphogenesis of model animal systems, such as ascidians, to cross-fertilize the approaches and to open the possibility to identify abstractions and principles that are relevant to morphogenesis of living forms in general. Our work will focus on how physical and chemical processes interact within the medium defined by the form and feedback on its development. We will seek to integrate both mechanistic and stochastic components in our models to account for biological variability in shape development. In the long run, the team’s results are expected to contribute to set up a new vision of morphogenesis in biology, at the origin of a new physics of living matter, and based on a more mechanistic understanding of the link between genes, forms and their environment.

To achieve the team’s objectives, we will develop over the next 12 years a project focused on the definition of a consistent mathematical framework to formalize form growth and on the development of corresponding computational algorithms. The mathematical framework will extend classical dynamical systems to dynamical systems with a dynamical state-structure, i.e. to dynamical systems whose state is represented as a graph of components that may change in time. A similar approach was successfully developed in the last two decades in the restricted context of branching organisms and plant development. We now want to extend it to more general forms, and address the diversity of associated new and stimulating computational challenges. For this, we will organize our research program into three main research axes.

3 Research program

3.1 Axis 1: Representation of biological organisms and their forms in silico

The modeling of organism development requires a formalization of the concept of form, i.e. a mathematical definition of what is a form and how it can change in time, together with the development of efficient

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1 A large class of marine animals (also called sea-squirt) in the phylum of Tunicates that is close to vertebrates, shares a particularly well conserved developmental program and that is a good model to study the development of chordates.
algorithms to construct corresponding computational representations from observations, to manipulate them and associate local molecular and physical information with them. Our aim is threefold. First, we will develop new computational structures that make it possible to represent complex forms efficiently in space and time. For branching forms, the challenge will be to reduce the computational burden of the current tree-like representations that usually stems from their exponential increase in size during growth. For tissue structures, we will seek to develop models that integrate seamlessly continuous representations of the cell geometry and discrete representations of their adjacency network in dynamical and adaptive framework. Second, we will explore the use of machine learning strategies to set up robust and adaptive strategies to construct form representations in computers from imaging protocols. Finally, we will develop the notion of digital atlases of development, by mapping patterns of molecular (gene activity, hormones concentrations, cell polarity, ...) and physical (stress, mechanical properties, turgidity, ...) expressions observed at different stages of development on models representing average form development and by providing tools to manipulate and explore these digital atlases.

3.2 Axis 2: Data-driven models of form development

Our aim in this second research axis will be to develop models of physiological patterning and bio-physical growth to simulate the development of 3D biological forms in a realistic way. Models of key processes participating to different aspects of morphogenesis (signaling, transport, molecular regulation, cell division, etc.) will be developed and tested in silico on 3D data structures reconstructed from digitized forms. The way these component-based models scale-up at more abstract levels where forms can be considered as continuums will also be investigated. Altogether, this will lead us to design first highly integrated models of form development, combining models of different processes in one computational structure representing the form, and to analyze how these processes interact in the course of development to build up the form. The simulation results will be assessed by quantitative comparison with actual form development. From a computational point of view, as branching or organ forms are often represented by large and complex data-structures, we aim to develop optimized data structures and algorithms to achieve satisfactory compromises between accuracy and efficiency.

3.3 Axis 3: Plasticity and robustness of forms

In this research axis, building on the insights gained from axes 1 and 2 on the mechanisms driving form development, we aim to explore the mechanistic origin of form plasticity and robustness. At the ontogenetic scale, we will study the ability of specific developmental mechanisms to buffer, or even to exploit, biological noise during morphogenesis. For plants, we will develop models capturing morphogenetic reactions to specific environmental changes (such as water stress or pruning), and their ability to modulate or even to reallocate growth in an opportunistic manner.

At the phylogenetic scale, we will investigate new connections that can be drawn from the use of a better understanding of form development mechanisms in the evolution of forms. In animals, we will use ascidians as a model organism to investigate how the variability of certain genomes relates to the variability of their forms. In plants, models of the genetic regulation of form development will be used to test hypotheses on the evolution of regulatory gene networks of key morphogenetic mechanisms such as branching. We believe that a better mechanistic understanding of developmental processes should shed new light on old evo-devo questions related to the evolution of biological forms, such as understanding the origin of developmental constraints how the internal rules that govern form development, such as chemical interactions and physical constraints, may channel form changes so that selection is limited in the phenotype it can achieve?

3.4 Key modeling challenges

During the project lifetime, we will address several computational challenges related to the modeling of living forms and transversal to our main research axes. During the first phase of the project, we concentrate on 4 key challenges.

3.4.1 A new paradigm for modeling tree structures in biology

There is an ubiquitous presence of tree data in biology: plant structures, tree-like organs in animals (lungs, kidney vasculature), corals, sponges, but also phylogenetic trees, cell lineage trees, etc. To represent, analyze and simulate these data, a huge variety of algorithms have been developed. For a majority, their computational time and space complexity is proportional to the size of the trees. In dealing with massive amounts of data, like trees in a plant orchard or cell lineages in tissues containing several thousands of cells, this level of complexity is often intractable. Here, our idea is to make use of a new class of tree structures, that can be efficiently compressed and that can be used to approximate any tree, to cut-down the complexity of usual algorithms on trees.

3.4.2 Efficient computational mechanical models of growing tissues

The ability to simulate efficiently physical forces that drive form development and their consequences in biological tissues is a critical issue of the MOSAIC project. Our aim is thus to design efficient algorithms to compute mechanical stresses within data-structures representing forms as the growth simulation proceeds. The challenge consists of computing the distribution of stresses and corresponding tissue deformations throughout data-structures containing thousands of 3D cells in close to interactive time. For this we will develop new strategies to simulate mechanics based on approaches originally developed in computer graphics to simulate in real time the deformation of natural objects. In particular, we will study how meshless and isogeometric variational methods can be adapted to the simulation of a population of growing and dividing cells.

3.4.3 Realistic integrated digital models

Most of the models developed in MOSAIC correspond to specific parts of real morphogenetic systems, avoiding the overwhelming complexity of real systems. However, as these models will be developed on computational structures representing the detailed geometry of an organ or an organism, it will be possible to assemble several of these sub-models within one single model, to figure out missing components, and to test potential interactions between the model sub-components as the form develops.

Throughout the project, we will thus develop two digital models, one plant and one animal, aimed at integrating various aspects of form development in a single simulation system. The development of these digital models will be made using an agile development strategy, in which the models are created and get functional at a very early stage, and become subsequently refined progressively.

3.4.4 Development of a computational environment for the simulation of biological form development

To support and integrate the software components of the team, we aim to develop a computational environment dedicated to the interactive simulation of biological form development. This environment will be built to support the paradigm of dynamical systems with dynamical structures. In brief, the form is represented at any time by a central data-structure that contains any topological, geometric, genetic and physiological information. The computational environment will provide in a user-friendly manner tools to upload forms, to create them, to program their development, to analyze, visualize them and interact with them in 3D+time.

4 Application domains

Our application domain is developmental biology (see overall objectives, research program above).

5 Highlights of the year

- Romain Azais defended his Habilitation in December 2022 on "Algorithmic approaches for statistics: piece-wise deterministic processes and random trees".
Following the departure of Arezki Boudaoud to Ecole Polytechnique, Annamaria Kiss who was a former member of Arezki’s group at RDP, joint the Mosaic team in June 2022. Annamaria is a research engineer at Inrae.

Following the work on cauliflower development carried out in the Mosaic team in collaboration with François Parcy’s group, and published in 2021 in the journal Science [2], Eugenio Azpeitia (former post-doc of the team and first author of the paper) was awarded the prize "Les Grandes Avancées Françaises en Biologie présentées par leurs auteurs 2022" from the French Académie des Sciences. The work was presented on June 28th 2022 at the Academy of sciences in Paris by Christophe Godin and Eugenio Azpeitia, (see program here).

6 New software and platforms

6.1 New software

6.1.1 Gnomon

Name: Gnomon

Keywords: 4D, Modelization and numerical simulations, Finite element modelling, Computational biology, Data visualization

Scientific Description: Gnomon is a user-friendly computer platform developed by the Mosaic team for seamless simulation of form development in silico. It is intended to be a major tool for the team members to develop, integrate and share their models, algorithms and tools. In Gnomon, a developing form is represented at any time by a central data-structure that contains topological, geometric, genetic and physiological information and that represents the state of the growing form. Flexible components (plugins) make it possible to upload or to create such data-structures, to program their development, to analyze, visualize them and interact with them in 3D+time.

Functional Description: Gnomon is a plugin-based computational platform for the analysis and simulation of morphogenesis. It relies on a scalable software architecture based on the dtk kernel developed by the group of software engineers (SED) from the Sophia-Antipolis Inria Center. The development of Gnomon aims at answering four main challenges:

* Provide an easily accessible computational tool for the exploration of morphogenesis, by focusing on the deployability of the software (using conda), on the ergonomics of the user interface and the availability of the documentation.

* Give access to powerful tools for the exploration of dynamical forms, through an interactive visualization framework allowing the exploration in space in time and the access to algorithmic resources developed by the team for image sequences of multicellular tissues or collections of branching forms.

* Ensure the interoperability of computational libraries within the platform and its extensibility by a generalized plugin-based architecture (facilitated by the dtk framework) for algorithms, visualizations and data structures, enabling the members of the team and future users to feed the platform with their own C++ and Python libraries.

* Bridge the gap between experimental data and computational simulations by offering the possibility to go from one to the other in the same platform in a nearly transparent way, thanks to a common dynamical system framework integrated to the core of the platform.

Gnomon project organization: * Project leader: Christophe Godin * Software development coordinator: Guillaume Cerutti * DTK coordinators: Julien Wintz, Thibaud Kloczko * Plugin coordinators: Jonathan Legrand, Romain Azais, Olivier Ali, Frédéric Boudon. * Diffusion coordinator: Teva Vernoux

This work is part of the Gnomon ADT project supported by the Inria centers of Grenoble Rhône-Alpes and Sophia-Antipolis Méditerranée.
Release Contributions: This version comes with a major GUI redesign through the migration to Qt6/QML, giving rise to a more fluid and user-friendly interface and a unified styling. The layout and action flow has been revised to provide a more intuitive user experience. Regarding functionalities, it focuses on the possibility to save the current session as a .json file, to reload it in the main application and run the same pipeline again, or to replay it directly through a command-line interface. Developments have been made to support cell-tracking in multicellular tissue images, and to provide a connection with the web-based 4 browser Morphonet.

News of the Year: The ADT project, started in 12/2021 with the recruitment of 2 software development engineers in the team, provides significant momentum to the Gnomon project. It allowed to address wide-ranging technical challenges (Qt6/QML migration) but most importantly to ensure a steady development pace, under the supervision of a project manager (T. Cabel). The focus features of this first year (GUI, session reloading, 3D image analysis) have made it possible to pass on the Gnomon application to beta-testers, picked among close collaborators, and to include user feedback in the development process.

Contact: Christophe Godin

Participants: Olivier Ali, Frédéric Boudon, Tristan Cabel, Guillaume Cerutti, Christophe Godin, Jonathan Legrand, Arthur Luciani, Grégoire Malandain, Karamoko Samassa

6.1.2 MorphoNet

Name: MorphoNet

Keywords: 3D web, Morphogenesis, Big data, 3D reconstruction

Functional Description: MorphiNet is an open-source web-based morphological browser. It consists of a web application, exploiting the Unity3D gaming engine, which offers the user a comprehensive palette of interactions with the data, in order to explore the structure, the dynamics and the variability of biological systems. Users can also project quantitative and genetic properties onto the morphological scaffold, allowing for instance to easily explore the correlation between shape dynamics and gene expression patterns. On top of that, datasets and associated information can be shared with other selected users or with entire groups. This possibility of directly sharing results within and between research communities, together with the use of a unified, human readable format, makes MorphoNet a unique tool for multidisciplinary research. Its web-based, user-friendly and open-source structure is also ideal for science dissemination and teaching.

URL: http://www.morphonet.org

Contact: Emmanuel Faure

Partner: CRBM - Centre de Recherche en Biologie cellulaire de Montpellier

6.1.3 TimageTK

Name: Tissue Image ToolKit

Keywords: 3D, Image segmentation, Fluorescence microscopy, Image registration, Image processing, Image filter

Scientific Description: TimageTK (Tissue Image Toolkit) is a Python package dedicated to image processing of multicellular architectures such as plants or animals and is intended for biologists, modellers and computer scientists.

Functional Description: TimageTK (Tissue Image Toolkit) is a Python package dedicated to image processing of multicellular architectures such as plants or animals and is intended for biologists and modelers. It provides grayscale or labeled image filtering and mathematical morphology algorithms, as well as image registration and segmentation methods.
**Release Contributions:** - Improve CLI tools - Improve data model - IO fixes - Add physical axes management for image-like data - Improve algorithms module - Improve components module - Improve logging - Improve documentation & docstrings - Better notebooks - Add cluster matching methods - Add analysis reporting tools - Add synthetic data generation algorithms - Add seed detection & signal quantification algorithms - Better conda packaging

**URL:** [https://mosaic.gitlabpages.inria.fr/timagetk/index.html](https://mosaic.gitlabpages.inria.fr/timagetk/index.html)

**Contact:** Jonathan Legrand

**Participants:** Guillaume Cerutti, Jonathan Legrand, Grégoire Malandain

### 6.1.4 treex

**Name:** treex

**Keywords:** Graph algorithmics, Data structures, Combinatorics, Machine learning

**Scientific Description:** Trees form an expanded family of combinatorial objects that offers a wide range of application fields, especially in biology, from plant modeling to blood vessels network analysis through study of lineages. Consequently, it is crucial for the team to develop numerical tools and algorithms for processing tree data, in particular to answer questions about the representation of biological organisms and their forms in silico.

treex is a Python 3 library dedicated to the manipulation of tree objects, whatever they are ordered or not, with or without quantitative or qualitative labels.

**Functional Description:** The package provides a data structure for rooted trees as well as the following main functionalities: - Random generation algorithms - DAG compression for ordered or not, labeled or not, trees - Approximation algorithms for unordered trees - Edit distance for unordered labeled trees - Kernels for ordered or not, labeled or not, trees - Computation of coding processes (Harris path, Lukasiewicz walk and height process) - Visualization algorithms in Matplotlib or in LaTeX

**Release Contributions:** In 2019, treex has been published in JOSS (Journal of Open Source Software). In 2021, the architecture of treex has been deeply modified. In the new version, treex is made of a main module implementing the data structure and of several self-contained application modules: analysis, simulation, lossy or lossless compression, etc.

**URL:** [https://gitlab.inria.fr/azais/treex](https://gitlab.inria.fr/azais/treex)

**Publication:** [hal-02164364](https://hal.archives-ouvertes.fr/hal-02164364)

**Contact:** Romain Azais

**Participants:** Romain Azais, Guillaume Cerutti, Didier Gemmerle, Florian Ingels

### 6.1.5 ctrl

**Name:** Cell Tracking and Robust Lineaging

**Keywords:** Image registration, Fluorescence microscopy, 3D, Multi-Object Tracking

**Scientific Description:** The package provides several robust automatic or semi-automatic cell lineage methods in order to handle different ranges of deformations. All rely on the estimation of a non-linear transformation between consecutive images of a time-lapse sequence obtained using the blockmatching algorithm (provided in the TimageTK library). The choice of the method depends on the quality of the tissue alignment obtained after the registration procedure.

When tissues are correctly aligned, which usually happens in the case of small deformations, a “one-shot” approach was developed that uses an overlap measure between daughter cells and their
transformed candidate mother cells to determine the best cell pairings. This decision can be made either locally (maximum overlap) or through a global flow-graph optimization approach.

If only a partially correct alignment is observed, a situation commonly related to large deformation cases, this simple tracking method can be embedded in an iterative procedure. More precisely, high-confidence pairings are selected at each iteration to improve the estimated non-linear transformation at each step.

In the case where no correct alignment is obtained, it is possible to define manually a set of pairings used to initialize the registration procedure. Depending on the quality of resulting alignment, either the “one-shot” or the iterative approach can then be applied.

The package also provides an intrinsic metric to estimate the quality of a cell lineage based on the preservation of the geometric cell context between a mother cell and its daughter cells. This quality map can be visualized to easily identify the tissue areas where there might be errors in the computed lineage.

In the case where errors are observed in the computed lineage, we allow the user to specify manually “nudge” pairings, that are used to re-estimate the transformation and subsequently the lineage. This effectively provides a tool to locally correct a cell lineage in a semi-automatic way.

**Functional Description**: Python package providing tracking methods to compute cell lineages in 3D+T images of growing plant tissues

**URL**: [https://gitlab.inria.fr/mosaic/work-in-progress/ctrl/-/tree/develop](https://gitlab.inria.fr/mosaic/work-in-progress/ctrl/-/tree/develop)

**Publication**: [hal-03683119](https://hal.archives-ouvertes.fr/hal-03683119)

**Contact**: Jonathan Legrand

**Participants**: Manuel Petit, Jonathan Legrand, Guillaume Cerutti, Grégoire Malandain, Christophe Godin

### 7 New results

#### 7.1 Dynamical characterization of morphogenesis at cellular scale

**Participants**: Guillaume Cerutti, Julien Derr, Emmanuel Faure, Christophe Godin, Jonathan Legrand, Grégoire Malandain, Manuel Petit, Jan Traas.

- Related Research Axes: RA1 (Representation of biological organisms and their forms in silico) & RA3 (Plasticity & robustness of forms)

- Related Key Modeling Challenges: KMC3 (Realistic integrated digital models)

The modeling of morphogenesis requires to explore the interconnection of different spatial and temporal scales of developing organisms. Non-trivial questions such as whether the observed robustness of morphogenesis is rooted in some highly conserved properties at the cellular level or whether it emerges as a macroscopic phenomenon, necessitates precise, quantitative analyses of complex 3D dynamic structures. The study of dynamical properties at the cellular scale poses at the same time key technical challenges and fundamental theoretical questions such as: how to characterize and follow the change of shape of cells within tissues? or of tissues within organs, how to couple this change with gene expression dynamics or how to define cell-scale variability of morphogenesis within and between species?

Our team has produced this year several results in this context:
Comparison of image segmentation methods for cell identification

Accurately identifying cell regions in 3D images is a crucial first step in many biological analysis methods. For a long time, cell segmentation has been performed using techniques that required significant manual parameter tuning. Recently, a new class of algorithms based on deep learning have been proposed which have been shown to achieve high accuracy in identifying objects from images automatically and requiring minimum human intervention. These deep learning based algorithms usually have the structure of a sequential pipeline consisting of a deep learning model which can be trained for prediction of the segmented regions along with set of pre and post processing steps.

To compare the relative performances of deep learning segmentation algorithms and identify their strengths and weaknesses, we proposed a global evaluation strategy that consisted in:

- Selecting several deep learning based pipelines from the literature which could be trained for 3D cell instance segmentation task.
- Using a common expertized dataset of 3D cellular images (confocal images of floral or shoot apical meristems) to train and test the pipelines.
- Modifying raw images by adding artificial artefacts (over/under-exposition, noise, blur) encountered in image acquisition to evaluate the robustness of the pipelines.
- Applying the same set of metrics and visualisation tools to compare the performances of the pipelines and in depth evaluation of their segmentation quality.
- Comparing the performance of the deep learning based pipelines with an established watershed based non-deep learning segmentation method [31].

By evaluating segmentation accuracy, rates of and under and over-segmentation in the whole tissue or in individual cellular layers (L1, L2, inner), this analysis provides a deeper insight into the robustness of each of the segmentation pipelines and helps to test their sensitivity to different image artifacts.

A Gitlab repository has been created to make this segmentation evaluation framework publicly available and a paper was published in Plos Computational Biology [15].

Robust extraction and characterization of cellular lineages

The quantitative study of developing tissues is mainly based on the analysis of time-lapse image acquisitions, from which cell-level temporal properties such as volumetric growth rate or cell cycle duration can be recovered through the identification of cell lineages. In plant tissues, accurate and automatic construction of cell lineages remains a real challenge because of the large deformations taking place between consecutive time-points, especially during the post-embryonic morphogenesis processes. In contrast with animal embryogenesis [6], these constraints impose the use of a two-stage procedure where image segmentation and cell lineaging are done separately.

Building on previous tracking methods published by the team [31, 38] and on the TimageTK computational library (developed in collaboration with the Inria team Morpheme), we implemented several robust fully-automatic cell lineage methods in order to handle different range of non-linear deformations. For small deformations, an overlap-based tracking method was implemented and tested on synthetic data and expertized experimental data. We embedded this method in an iterative procedure where cell lineage and registration transformation are alternatively improved. Based on geometric cell context preservation, a cell lineage quality map can be automatically inferred and used later on to select appropriate anchor points that will improve registration transformation. The validation on experimental data showed a significant improvement of the tracking accuracy in the regions presenting larger deformations.

On top of our iterative automatic tracking method we developed a nudge approach for fast and semi-automatic lineage curation. Given a proposed cell lineage, the cell lineage quality map can be used to detect visually low lineage quality areas. Then, in these areas, the user can manually provide a small set of correct cell lineages. This additional information is then used to improve the registration transformation and automatically correct the lineage locally.

These methods have been presented at the IEEE-ISBI 2022 conference [18] and are included in a new Python library called ctrl (Cell Tracking & Robust Lineaging) 6.1.5, built upon the TimageTK package. This work is part of the Inria Défi Naviscope.
Cells spatio-temporal properties and population statistics

Over the past few years, we have developed algorithms and libraries to achieve quantitative characterization of various spatio-temporal properties of the cells, such as volume, volumetric growth rate or strain pattern. A recent addition to this collection of quantification tools is the estimation of the cell heights in a multi-layered tissue, as their maximal extent in the local normal direction to the tissue surface [16].

To structure this rich spatio-temporal data, we have implemented a spatio-temporal graph structure, formalizing the cell tissue network and its dynamics in a dedicated computational object. For practical use, such as statistical analysis and data interaction, we implemented biologically relevant methods to explore the tissues through an API with a biological semantics. In addition, we proposed a simple data structure model and implemented CLI tools to allow for batch processing of biological tissues. As the biological objects to study may contain several thousands of cells and/or can be observed at a high temporal frequency, the obtained spatio-temporal graph structures can become very large. Therefore we also developed specific 3D visualization tools to manipulate and explore these structures. This work is implemented in the long-term supported Python library TimageTK 6.1.3.

The latest development for this project was mostly improvements or fixes of existing features as we are now making use of this library to tackle broader biological problems than those envisioned in the initial developments. Originally, we aimed at the characterization of Arabidopsis thaliana Floral Meristem cellular patterns by means of clustering. On that topic, we implemented methods to automatically generate analysis reports and easily compare clusters.

Part of these tools and methodology is now also used in a collaborative work aiming at the characterization of the early developmental stages of the moss Physcomitrium patens. The switch to this new species is challenging as, instead of the large and dense tissues of Arabidopsis thaliana Floral Meristem, it presents filamentous structures with emerging young buds composed of just a few cells. The change of biological object and the necessity to have non-computer scientists working with our tools is a great driving force for this project.

Finally, the integration of TimageTK software components as plugins in the Gnomon platform 6.1.1 is still ongoing, and its use in the beta-testing phase has given helpful insight on possible improvements.

Atlases of development: construction and update

Developing digital atlases of organism or organ development is a complex challenge for tissues that do not present a stereotyped cellular layout, as it is the case for most plant organs. For instance, to generate a cell-based atlas representing the development of a floral meristem of Arabidopsis thaliana we had to chose a single representative flower template, on which the spatio-temporal binary expression patterns of 27 genes was then introduced manually [8].

To proceed further, as the manual building of a cellular template remains a bottleneck of the method, we aim to automatize the construction of genetic atlases from time-lapse image acquisitions displaying both cell interface markers and genetic reporters. In such case, we need to consider a pipeline where (1) time-lapse sequences can be spatio-temporally registered and (2) genetic information can be projected from one sequence to another in a quantitative manner. Methods have been developed on these two aspects.

A previous work addressing the spatio-temporal registration of floral meristem time-lapses sequences [38] relied on the meristem size to perform the temporal alignment. This metric is not fully adapted to accurately compare developmental states, since important size variations can be observed from one individual to another. To overcome this limitation, we developed a method based on the surface curvature, a metric that captures all the morphological changes of the floral development. More precisely, curvature profiles are extracted from each image along the lateral symmetry plane of floral meristems, and then compared 2-by-2 to obtain a temporal alignment of the sequences. The method was evaluated on floral meristem datasets against the previous approach and showed improvement on the temporal alignment quality. Moreover, the comparison method naturally provides a spatial alignment between individuals that can be used to initialize an automatic spatial registration procedure.

Superimposing organs with a similar developmental state allows to propagate genetic information across different individuals. Because floral development is not stereotyped at the cell scale, projection can not be performed through a 1-to-1 cell mapping, but has to be considered at the tissue level. We developed
methods to transfer gene expression information in various ways (quantity/concentration losses transfer). The main rationale behind these methods is to rely on the overlap of cells after registration to distribute the genetic information across individuals. The validation of this approach is currently performed on a larger set of experimental data, and should be published in 2023. This work is part of the Inria Défi Naviscope.

**Extraction of biological landmarks using Machine Learning**

In order to superimpose similar organs coming from different individuals, it is possible to map biological landmarks to compute a geometrical transformation, instead of relying only on image-based registration. For instance, in the case of the shoot apical meristem (SAM), detecting the centers of the central zone (CZ) and of the youngest organ primordium allows to align a population with a great precision [4].

However, locating such landmarks often requires to acquire images with an additional biological marker, which adds experimental constraints. Focusing on the detection of the CZ center, we used a Machine Learning approach trained on existing data of SAMs imaged with both a geometry and a CZ marker (CLV3) to predict the position of the CZ center.

The chosen model is an adaptation of the deep learning model U-Net to downsampled 2D projections of confocal microscopy SAM images. The model trained on 69 SAM images, augmented with random geometrical and intensity transformations, was able to detect the CZ center with an error of less than 1 cell on an independent set of SAM images, even imaged with a different geometry marker. This work, initially carried out in the context of a M2 internship in 2021, was presented in a conference this year [23] and will be applied to biological questions in the coming year in the context of the HydroField ANR project.

**Experimental characterization of tissues during morphogenesis**

Spanning from tissue to organ scales, we have started to investigate the structure of the tendrils of climbing plants, and their evolution during growth. We aim at monitoring the underlying 3D structure of the tendril as a function of time by destructive and non-destructive technics.

- We started by characterizing the time evolution of tendrils geometry using time-lapse photography. This enabled us to identify the stereotyped stages of tendril evolution at a macroscopic scale: first attachment to the support, then onset of writhing, then formation of helicoidal loops and a so-called perversion which connects two helices of opposite chiralities.

- To access 3D geometrical and histological information about the tendrils at the tissue scale, we have performed serial sectioning on different specimens at specific stages. Staining with appropriate chemicals have revealed cell walls, membranes and lignin, enabling to understand the microscopic organization of the tissue. The main result is the progressive lignification as a function of time and space. In particular lignification seems to evolve linearly with time and space, and does not depend on the geometry. This would indicate that the complex 3D geometry is the result of growth only.

- Preliminary non-destructive experiments have been performed. We plan to perform 3D time-lapse confocal microscopy imaging to follow the temporal evolution of the biological structure using natural auto-fluorescence or Propidium Iodide staining. These experiments will be complemented by X-ray microtomography experiments, which is more costly but should enable a full 3D reconstruction, while confocal imaging won't give access to the center of the samples.

This work has been carried out during the internship of Lénaelle Doualla in the framework of the Dynavine Emergence grant, and will be continued in 2023.

**7.2 Reconstruction of macroscopic forms from images and characterization of their variability**
**Participants:** Ayan Chaudhury, Christophe Godin, Julien Derr, Jonathan Legrand, Katia Mirande.

- Related Research Axes: RA1 (Representations of forms *in silico*) & RA3 (Plasticity & robustness of forms)
- Related Key Modeling Challenges: KMC3 (Realistic integrated digital models)

To study the variability of macroscopic forms resulting from organ or organism development, it is necessary to be able to measure phenotypic traits on a large population. Our strategy is to create digital clones to then be able to quantify traits of interest, therefore requiring to develop acquisition and reconstruction methods. These digital reconstructions enable the identification of organs, the quantification of macroscopic features as well as their distribution in space and, potentially, in time. The development of algorithms to analyse the structure of the organism or quantify traits and the creation of data structure adapted to future modeling is thus a key challenge. Furthermore, it is important to develop metrics and statistical tools to define notions of distance or average between these forms in order to be able to compare the obtained reconstructions and generated models.

The use of prior knowledge can be very beneficial, and indeed, realistic synthetic models of forms can guide the reconstruction algorithms and/or assess their performances. The automatic inference of computational representations of forms or organ traits from images is therefore an essential step.

Computational representations of forms can then be used to analyze how forms vary at the scale of a population, of a species or between species, with potential applications in species identification and genetic or environmental robustness estimation.

**Automatized characterization of 3D plant architecture.**

The digital reconstruction of branching forms and the quantification of phenotypic traits (lengths of inter-nodes, angles between organs, leaf shapes) is of great interest for the analysis of plant morphology at population scale.

The latest algorithmic development in the characterization of 3D plant architecture comes from the thesis of Katia Mirande who developed and published a graph-based approach for simultaneous semantic and instance segmentation of plant 3d point clouds [21]. This work has demonstrated the geometry-based methods can be efficient to tackle the problem at hand, even with a large and imperfect point-cloud. Moreover it has proven successful in identifying organs for different types of plants (tomato and chenopodium). This work was defended by Katia Mirande in December for her PhD thesis.

In the final year of the ROMI project, we aimed at making the Plant Imager (robot scanner) and the Plant 3D Vision tools (reconstruction and analysis pipeline) more than the initial proof of concept. To move towards a more mature technology, we notably had to improve its accessibility to standards users (human-readable messages, simplify commands, ...) and make it available on the web. For the Plant Imager, this meant to write a detailed documentation with the bill of materials and instructions to build the robot. For the Plant 3D Vision tools, this meant to release them on GitHub and the Inria GitLab and write a detailed documentation. We also provides Docker images to greatly simplify the installation procedure.

Another aspect that is required to propose a mature technology is the efficiency and robustness of the systems and processes. To that extent, we carried out experiments to determines the optimal set of acquisition parameters (like the number of images to acquire) or the reconstruction parameter to use to get the best digital clone possible. These experiments have been made with real plants and the automated measurements were compared to manual ones. This notably required to gain better and finer control over the used third-party libraries, especially for COLMAP. It also required new development in robotics as some of the original design shortcomings were too important to be ignored. This resulted in the development of a new camera arm for the Plant Imager and to re-think the communication across devices (now mostly wireless).

Altogether this lead to improve our acquisition setup and the software accessibility.
We are now moving to larger scale acquisitions to further test and improve our technology with an biology oriented experimental design that will lead us to publish our first biological paper using our technology.

Characterization of 3D plant shape and texture at the organ scale

Complementary to the full 3D reconstruction of plant architecture (ROMI project), we have developed a new platform to characterize plants in 3D at the organ scale coordinated by Julien Derr (typically at leaf scale). We can have access to the geometry and the texture of the leaf with high spatial (millimetric) and temporal (seconds) resolution. This will make it possible to quantify in 3D the rich spatio-temporal growth patterns of leaves observed during unfolding[40, 29, 39], where “fast” elastic phenomena (buckling) or ample (nutation) motions are occurring.

In collaboration with computer vision scientists from Université de Strasbourg (Franck Hetroy-Wheeler and collaborators), we built a multicamera setup[41]. The set up is installed at ENS de Lyon in the new M8 building dedicated to plant growth.

Lucie Poupardin started her PhD in October 2022. Lucie is now finishing to set up and calibrate the platform. Lucie is going to use this platform to research the kinematics of leaf unfolding.

7.3 Analysis and simulation of tree data

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<th>Participants: Romain Azaïs, Christophe Godin, Florian Ingels, Frédéric Boudon.</th>
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- Related Research Axes: RW1 (Representations of forms in silico)

- Related Key Modeling Challenges: KMC1 (A new paradigm for modeling tree structures in biology)

Tree-structured data naturally appear at different scales and in various fields of biology where plants as well as blood vessels for example may be described by trees. In the team, we aim to investigate a new paradigm for modeling tree structures in biology in particular to solve complex problems related to the representation of biological organisms and their forms in silico.

In previous years, we investigated the following questions linked to the analysis of tree data. (i) How to control the complexity of the algorithms used to solve queries on tree structures? For example, computing the edit distance matrix of a dataset of large trees is numerically expensive. (ii) How to estimate the parameters within a stochastic model of trees? And finally, (iii) how to develop statistical learning algorithms adapted to tree data? In general, trees do not admit a Euclidean representation, while most of classification algorithms are only adapted to Euclidean data. Consequently, we need to study methods that are specific to tree data.

Efficient algorithms on tree structures. Complex queries on tree structures (e.g., computation of edit distance, finding common substructures, compression) are required to handle tree objects. A critical question is to control the complexity of the algorithms implemented to solve these queries. This year, we have explored the following strategies to this end.

- We study how the edit distance algorithm developed by Zhang in the 1990s can be implemented in an incremental way when comparing trees along a random walk. Random walks form an important class of stochastic processes, which can be used to explore a combinatorial space. We have shown that the time-complexity of Zhang’s algorithm can be highly reduced using incremental computations. These very promising results, both in terms of theoretical and computational aspects, resulted in the paper [20] submitted this year (joint work with Farah Ben Naoum from the University of Sidi Bel Abbes, Algeria).

- One way to address the issue of the complexity of algorithms on tree structures is to approximate the original trees by simplified structures that achieve good algorithmic properties. One can expect good algorithmic properties from structures that present a high level of redundancy in their substructures. Indeed, one can take into account these repetitions to avoid redundant computations
on the whole structure. After developments on topological trees through the approximation class of self-nested trees in the past years [24, 25], we now work on approximation of trees with geometrical attributes on their vertices. With Farah Ben Naoum and Salah Habibeche (University of Sidi Bel Abbes, Algeria), we have exhibited a lossy compression algorithm for such trees, with a control on the information loss. In particular, it can be used to detect (imperfect) symmetries of plant architectures, which helps to characterize the production and growth mechanisms that generated them, at least on simulated plants. This piece of work has been submitted in an international conference and a longer version is in preparation.

• Recognizing when two trees are identical (isomorphic) is a crucial issue to reduce the complexity of algorithms and avoid repeating calculations. Assessing that two trees are topologically equal is a long-solved problem and can be done in linear time. When attributes (from a finite alphabet) are added to the nodes, two definitions exist for extending isomorphism definition: either attributes must be preserved through the topology, or it is rather their equivalence class that must be preserved, i.e., nodes with same labels in one tree are to be mapped to nodes with same labels on the other. The former can be solved easily by using the topological algorithm, but the latter can not. Actually, this problem is as difficult as graph isomorphism and seems to be open since the 1970s. In 2021, we published an algorithm that breaks the combinatorial complexity of the problem, reducing, on average from numerical simulations, the search space cardinality by an exponential factor within linear time [35]. This work has been published as a proceeding in an international conference [35]. Based on this previous work, we have developed a backtracking algorithm to explore the rest of the search space and either find an isomorphism if it exists, or certify that none exists. We use this technique to detect new types of patterns in tree data, namely subtrees with identical label distribution. A paper is in progress on this topic.

Kernel methods for tree data. Standard statistical techniques – such as SVMs for supervised learning – are usually designed to process Euclidean data. However, trees are typically non-Euclidean, thus preventing using these methods. Kernel methods allow this problem to be overcome by mapping trees in Hilbert spaces. However, the choice of kernel determines the feature space obtained, and thus greatly influences the performance of the different statistical algorithms. Our work is therefore focused on the question of how to build a good kernel.

We first looked in [1] at a kernel of the literature, the subtree kernel, and showed that the choice of the weight function (arbitrarily fixed so far) was crucial for prediction problems. By proposing a new framework to calculate this kernel, based on the DAG compression of trees, we were able to propose a new weight, learned from the data. In particular, on 8 data sets, we have empirically shown that this new weight improves prediction error in 7 cases, and with a relative improvement of more than 50% in 4 of these cases.

We then tried to generalize our framework by proposing a kernel that is no longer based on subtrees, but on more general structures. To this end, we have developed an algorithm for the exhaustive enumeration of such structures, namely the forests of subtrees. This makes us able to define a new feature extraction process from tree data, that, roughly speaking, brings the previous algorithm based on subtrees to any order. This piece of work has been published this year [14].

Simulating the growth of branching systems in curved spaces. The growth of biological structures or their functioning may occur on substrates that are not flat. This can be for example the case of molecules that diffuse between cells at the surface of organs, of teeth that migrate on curved epithelia in some animals during their lifetime (like sharks), of primordia outgrowth in plants, of organ vasculature that connects growing organs with the rest of the plant’s body following curved paths. Here, we extended the language of L-systems in order to model the growth of branching structures in curved spaces. The resulting language is called **Riemannian L-system**. The language makes it possible to define curved spaces using a variety of parametric models (sphere, torus, surface of revolution, nurbs patches, etc) and to simulated automatically the movements of the L-system’s turtle (move forward, turn some angle, etc.) in the underlying curved space. This makes it possible to simulate various dynamic phenomena in curved spaces: random walks and diffusion, movements on geodesics, parallel transport, fractals, growth of branching systems and their interaction with the substrate, phyllotaxis, etc. This year we used the possibility for L-systems to simulate the growth of branching structure in abstract Riemannian spaces with a user defined or procedurally defined metric field over the whole space. This made it
possible to implement different types of tropisms in a 2D space curved by external cues, such as a light source. We also implemented a generic algorithm to compute geodesics between two arbitrary points of a Riemannian space (solving a two point boundary value problem). A paper is in preparation about this work.

### 7.4 Mechanics of tissue morphogenesis

**Participants:** Olivier Ali, Elsa Gascon, Ibrahim Cheddadi, Andre-Claude Clapson, Christophe Godin, Guillaume Cerutti.

- Related Research Works: RW2 (Data-driven models) & RW3 (Plasticity & robustness of forms)
- Related Key Modeling Challenges: KMC2 (Efficient computational mechanical models of growing tissues) & KMC3 (Realistic integrated digital models)

Deformations supporting morphogenesis require the production of mechanical work within tissues. Such mechanical stresses cannot yet be experimentally quantified in living tissues; the ability to simulate accurately the mechanical behavior of growing multicellular structures is therefore a mere need in developmental biology and consequently a critical objective of the MOSAIC project.

From a macroscopic perspective, tissues mechanics can be formalized through the framework of continuum mechanics. However, the fact that they are composed, at the microscopic level, by mechano-sensitive elements out of equilibrium (namely cells) offers genuine modeling challenges and opportunities. Integrating cellular behaviors such as mechano-sensitivity and cell division into a macroscopic mechanical picture of plant tissue morphogenesis is the topic of this section.

**Antagonist cell responses to mechanical stress set organ size**

Organ size depends on complex biochemical and mechanical interactions between cells and tissues [30, 42]. In collaboration with biologists from the SEED-DEV team, we investigated the regulation of seed size, a key agronomic trait, by mechanical interactions between two compartments: the endosperm and the seed coat [34].

By combining experiments with computational modeling, we tested a mechanosensitive incoherent feedforward loop (ms-IFFL) hypothesis in which pressure-induced stresses play two antagonistic roles; directly driving seed growth, but indirectly inhibiting it through mechanosensitive stiffening of the seed coat. We showed that our ms-IFFL model can recapitulate wild type growth patterns and explain the counter-intuitive small seed phenotype of the haiku2 mutant. Our work further revealed that the developmental regulation of endosperm pressure is needed to prevent a precocious reduction of seed growth rate induced by force-dependent seed coat stiffening.

This work has been under review for publication during most of this year. The corresponding back and forth exchanges with reviewers generated multiple new investigations. We notably added a time dependence on the control variable (endosperm pressure) of our feedforward loop to account for observed phenotypes in some mutants of interest. With these add-ons, our manuscript has been accepted (dec. 9th 2022) for publication in Nature Communications [13].

**Mechanical stresses guide the formation of tricellular junction during cell division**

In most biological tissues, cells attach each other by forming stable tricellular junctions (3CJ) [36]. In plants, the emergence of these tricellular junctions during cell division remains poorly understood. However, the influence of mechanical stresses on cell division orientation has been recently highlighted [37, 26] and suggests that, as in animals [27], mechanical stresses could be central in defining such stable structures in plants.

Together with colleagues from the SICE team, we wondered how tissue topology produces mechanical patterns within cell walls leading to biochemical signaling involved in 3CJ formation. We focused our attention on a very specific tissue: The cortex layer of the root meristem in Arabidopsis thaliana. These
tissues have a very stereotypical organization (staged files of cells) that can be perturbed genetically and chemically, making them ideal structures for such studies.

To estimate pressure-induced stresses in the root cortex, we capitalized on its specific geometry (rotational symmetry around the root axis) and performed FEM-based simulations on 2D mechanical structures mimicking cortex cells, with subcellular resolution. These simulations were performed using the BVPy library [33], developed within the team. To characterize the influence of the cortex topology and cell geometry on the pressure-induced stress field, we conceived purely artificial structures where cell shapes, sizes and arrangements could be tuned. In parallel, to estimate accurately stress patterns in real tissues, we generated meshes directly from microscopic acquisitions of real tissues. Comparing both outputs enabled us to better understand how geometrical and topological features of the root cortex can be translated into mechanical signals at the subcellular scale. This project is a new collaboration between the MOSAIC & SICE teams. It has been mostly carried out by Elsa Gascon (now PhD student in the team) and supervised by Olivier Ali (MOSAIC) and Marie-Cecile Caillaud (SICE). A manuscript on this work is currently being written. Noteworthily, Olivier Ali & Marie-Cécile Caillaud have been invited to present this work in the context of the Inrae metaprogram Digit-Bio in October 2022.

**Multiscale modelling of growing plant tissues**

How morphogenesis depends on cell wall rheological properties is an active direction of research, and we are interested in mechanical models of growing plant tissues, where microscopic cellular structure or even subcellular structure is taken into account. In order to establish links between microscopic and macroscopic tissue properties, we perform a multiscale analysis of a model of growing plant tissue with subcellular resolution. We use homogeneisation to rigorously deduce the corresponding tissue scale continuous model. Tissue scale mechanical properties are computed from all microscopic structural and material properties, taking into account advection by the growth field. We then consider case studies and numerically compare the detailed microscopic model and the tissue-scale model, both implemented using finite element method in FreeFEM. We find that the macroscopic model can be used to efficiently make predictions about several configurations of interest. Our work will help making links between microscopic measurements and macroscopic observations in growing tissues. A paper is in preparation about these results.

This project is a collaboration between Annamaria Kiss, who freshly joined the MOSAIC team, Arezki Boudaoud (Ecole Polytechnique, Paris, France) and Mariya Ptashnyk (Heriot-Watt University, Edinburgh, UK).

**Force inference**

In the context of the HYDROFIELD ANR project and the postdoctoral contract of André-Claude Clapson, we are developing a force inference method in the SAM that derives wall stresses and cell turgor pressures from the geometry of the cells. Plant cells are inflating thanks to their turgor pressure, but this quantity cannot easily be measured. We have suggested a new indirect method inspired by foam mechanics: combining Laplace law (that relates pressure, wall curvature and stress) and the Gauss-Bonnet theorem (that expresses a geometrical constraint on cell shape), we develop a methodology to estimate stresses and pressures from observations of cells shapes in confocal images. We are finalizing this in 2D tissues and plan to extend the method to 3D tissues.

**Coupling wall mechanics and water fluxes**

Still in the context of Hydrofield and in collaboration with biologists from RDP (Olivier Hamant’s group), we showed that a model that we have previously developed [3] is able to explain a set of apparently contradictory experimental facts in the growth of primordia at the SAM. An article is being written with our colleagues biologists and could provide a seminal interpretation of the role of water in the SAM development.
Mechanics of tendrils

In the framework of the Dynavine project, we are investigating the force and torque generation of tendrils of climbing plants as a function of time and growth development. To do so, we have developed an experimental set up that we have been testing on synthetic rods.

- This preliminary work have lead us to discover a new and exciting result about rod mechanics: One can completely change the chirality of a helical rod by unwinding it. Doing so, the rod goes through a transition state involving two helices with opposite chiralities spatially connected by a so-called “perversion”. In our work, we reported an experimental demonstration of this phenomenon. We monitored the axial torque and load upon such a transformation and revealed a phase transition like behaviour. We proposed a biphasic expansion of the elastic energy and reproduced the encountered behaviours. Our experiments also displayed hysteresis upon helical unwinding but numerical simulations seems to indicate that it is due to specific properties of our material. A corresponding paper is beeing submited.

- Now that our set-up is ready, we are monitoring live plants. We are recording universal signatures of force and torque evolution as a function of writhing. Based on our experimental results, we are developing a phenomenological model of tendrils writhing.

7.5 Signaling and transport for tissue patterning and growth

Participants: Romain Azaïs, Guillaume Cerutti, Landry Duguet, Christophe Godin, Jonathan Legrand, Teva Vernoux (External Collaborator).

- Related Research Axes: RA1 (Representations of forms in silico) & RA2 (Data-driven models)
- Related Key Modeling Challenges: KMC3 (Realistic integrated digital models)

One central mechanism in the shaping of biological forms is the definition of regions with different genetic identities or physiological properties through bio-chemical processes operating at cellular level (see an introductory presentation in [19]). Such patterning of the tissue is often controlled by the action of molecular signals for which active or passive transport mechanisms determine the spatial precision of the targeting. The shoot apical meristem (SAM) of flowering plants is a remarkable example of such finely controlled system where the dynamic interplay between the hormone auxin and the polarization of efflux carriers PIN1 governs the rhythmic patterning of organs, and the consequent emergence of phyllotaxis.

Using Arabidopsis thaliana as a model system, we develop an integrated view of the meristem as a self-organizing dynamical form by reconstructing the dynamics of physiological processes from living tissues, and by proposing computational models to study tissue patterning and robustness of biological shapes in silico.

Transport of auxin in mosses.

Branching patterns are omnipresent in plant architecture. The molecular mechanisms that drive the emergence of such patterns during the development of the plant are being unravelled, but many questions are still open. It was first discovered in the 1930s, thanks to experiments on flowering plants, that the shoot apical meristem controls the plant architecture by inhibiting the initiation of new branches below it. This so-called apical dominance was later shown to be mediated by the phytohoromone auxin, which circulates from cell to cell thanks to polar membrane transporters, generating a basipetal bulk flow and acting as a morphogen gradient. It was recently discovered that apical dominance is a common mechanism in mosses [28], and that the responsible signal is auxin as well, which is surprising as axillary branching emerged independently in vascular plants and bryophytes, the two main groups of land plants, which respectively include flowering plants and mosses. However, there is no polar flux of auxin in mosses [32], and biological observation and computational modelling led to the hypothesis of a diffusive transport mechanism of auxin in mosses leafy shoots, through plasmodesmata, the channels that connect
neighbouring cells cytoplasms. In collaboration with Yoan Coudert (RDP Lab), we aim at modelling the moss development under the later hypothesis in order to test whether diffusion is sufficient to explain the branching patterns observed in our moss model Physcomitrium patens (PhD work of Jeanne Abitbol, year 1 in 2022).

Analysis of auxin transport at cellular level in the SAM from confocal images.

Macroscopic model of organ interactions in plants have been particularly successful in explaining phyllotaxis patterns at the SAM. However, the details of the molecular processes allowing the spatiotemporal coordination of the cells necessary to the maintenance of the regularity of the pattern is still a frontier question. Two main actors are thought to contribute to the emergence and maintenance of phyllotactic patterns. On the one hand, the plant hormone auxin accumulates at different sites of the SAM and triggers organ differentiation. On the other hand, polarized PIN1 proteins at the cell membranes directs auxin transport in the tissue. Recent experiments and methods developed in the team provided quantitative spatiotemporal data of auxin and PIN1 localization. These data have been analyzed at cell scale as discrete raw data, and at tissue scale as continuous data allowing to compare different individuals [4]. These observations question the mainly adopted interpretation of auxin transport in the SAM, saying that PIN1 are polarized in the cell membranes according to the gradients of auxin in the tissue. Our ongoing work consists of expanding the analysis of the mass of data collected in [4] and studying alternative auxin accumulation explanations [22]. In particular, we develop a continuous model to capture the essence of the interplay between the observed auxin scalar field and PIN1 vector field.

Phenotyping and modeling of root hydraulic architecture

Water uptake by roots is a key adaptation of plants to aerial life. Water uptake depends on root system architecture (RSA) and tissue hydraulic properties that, together, shape the root hydraulic architecture. This work investigates how the interplay between conductivities along radial (e.g. aquaporins) and axial (e.g. xylem vessels) pathways determines the water transport properties of highly branched RSAs as found in adult Arabidopsis (Arabidopsis thaliana) plants. A hydraulic model named HydroRoot was developed, based on multi-scale tree graph representations of RSAs. Root water flow was measured by the pressure chamber technique after successive cuts of a same root system from the tip toward the base. HydroRoot model inversion in corresponding RSAs allowed us to concomitantly determine radial and axial conductivities, providing evidence that the latter is often overestimated by classical evaluation based on the Hagen–Poiseuille law. Organizing principles of Arabidopsis primary and lateral root growth and branching were determined and used to apply the HydroRoot model to an extended set of simulated RSAs. Sensitivity analyses revealed that water transport can be co-limited by radial and axial conductances throughout the whole RSA. The number of roots that can be sectioned (intercepted) at a given distance from the base was defined as an accessible and informative indicator of RSA. The overall set of experimental and theoretical procedures was applied to plants mutated in ESKIMO1 and previously shown to have xylem collapse. This approach will be instrumental to dissect the root water transport phenotype of plants with intricate alterations in root growth or transport functions. This work, resulting from a collaboration with Christophe Maurel's group in Montpellier, has been published this year [12].

7.6 Regulation of branching mechanisms in plants

Participants: Christophe Godin, François Parcy (External Collaborator).

• Research Axes: RA2 (Data-driven models) & RA3 (Plasticity & robustness of forms)
• Key Modelling Challenges: KMC3 (Realistic integrated digital models)

Branching in plants results from the development of apical meristems that recursively produce lateral meristems. These meristems may be more or less differentiated with respect to the apical meristem from which they originate, potentially leading to different types of lateral branches or organs. They also can
undergo a more or less long period of inactivation, due to systemic regulation. The understanding of branching systems morphogenesis in plants thus relies on the analysis of the regulatory mechanisms that control both meristem differentiation and activation/inactivation.

The fractal nature of plants.

Inflorescence branching systems are complex and diverse. They result from the interaction between meristem growth and gene regulatory networks that control the flowering transition during morphogenesis. To study these systems, we focused on cauliflower mutants, in which the meristem repeatedly fails in making a complete transition to the flower and for which a complete mechanistic explanation was still lacking.

In collaboration with Eugenio Azpeitia (who started this project as a post-doc in the Virtual Plants team) and François Parcy's group in Grenoble, we have developed a model of the control of floral initiation by genes in Arabidopsis thaliana, refining previous networks from the literature so that they can integrate our hypotheses about the emergence of cauliflower phenotypes. The complete network was validated by multiple analyses, including sensitivity analyses, stable state analysis, mutant analysis, among others. It was then coupled with an architectural model of plant development using L-systems. The coupled model was used to study how changes in gene dynamics and expression could impact in different ways the architectural properties of plants. The model was then used to study how changes in certain parameters could generate different curd morphologies, including the fractal-like Romanesco. This work has been published in the Journal Science [2]. This year, we received a price from the French Academie des Sciences for this work (see Highlights of the year section) and we presented the work as invited presentations and in workshops and international conferences.

7.7 Miscellaneous

Participants: Romain Azaïs, Christophe Godin, Landry Duguet.

Goodness-of-fit tests in regression models.

Many goodness-of-fit tests have been developed to assess the different assumptions of a regression model. Most of them are “directional” in that they detect departures from a given assumption of the model. Other tests are said “global” because they assess whether a model fits a dataset on all its assumptions. In the paper [11] published this year, we focus on the task of choosing the structural part of the regression function because it contains easily interpretable information about the studied relationship. We consider 2 nonparametric “directional” tests and one nonparametric “global” test, all based on generalizations of the Cramér-von Mises statistic. To perform these goodness-of-fit tests, we have developed the R package cvmgof providing an easy-to-use tool for practitioners. A simulation study has been carried out in order to show how the package can be exploited to compare the 3 aforementioned tests.

Post-transcriptional regulation of transcription factor codes in immature Neurons in drosophila.

How the vast array of neuronal diversity is generated remains an unsolved problem. Here, we investigated how 29 morphologically distinct leg motoneurons are generated from a single stem cell in Drosophila. We contributed to a study where 19 transcription factor (TF) codes expressed in immature motoneurons just before their morphological differentiation were identified. We developed a novel computational analysis, based on peak detection in motorneuron expression data to show quantitatively that the TFs codes are progressively established in iMNs as a function of their birth order.

In this paper, comparison of RNA and protein expression patterns of multiple TFs revealed that post-transcriptional regulation plays an essential role in shaping these TF codes. We showed for the first time that two RNA binding proteins, Imp and Syp, are expressed in opposite gradients in immature post-mitotic motoneurons and control the translation of multiple TFs. The varying sensitivity of TF mRNAs to the opposite gradients of Imp and Syp in immature motoneurons decrypts these gradients.
into distinct TF codes, which in turn establish the connectome between motoneuron axons and their target muscles.

**A fast Dejittering approach for line scanning microscopy**

In an internship back in 2020 at Innopsys (a biomedical device designing and producing company) Landry Duguet focused on the image quality restoration of the InnoQuant device. This line-scanning microscope produces 2D images of 125 000 X 375 000 pixels of 200nm size in 3 hours. Its high precision makes it suffer from a jittering artifact where the odd and even lines of the image are shifted, significantly impacting the image analysis. We proposed two fast methods for dejittering, one is based on dynamic programming and is linear in time, the other rely on a convex relaxation designed for parallel architectures. Both provide better time and quality results than the literature. This work has been published this year [17]

# 8 Partnerships and cooperations

## 8.1 European initiatives

### 8.1.1 H2020 projects

**H2020 - ROMI (2017-2022)**

| Participants: | Romain Azaïs, Guillaume Cerutti, Christophe Godin, Florian Ingels, Jonathan Legrand, Katia Mirande, Franck Hetroy-Wheeler *(External Collaborator)*, Teva Vernoux *(External Collaborator)*. |

This project is aimed at understanding how molecular regulation integrates with mechanics to control overall plant shape, an unresolved problem with wide implications for both fundamental and applied biology. We will address this issue in the Arabidopsis flower, which, besides their obvious importance as reproductive structures, are amongst the best characterised systems in plant developmental biology. From a mechanistic point of view, it is widely accepted that regulatory molecular networks interfere with the properties of the structural cellular elements (cell wall, cytoskeleton) to induce particular growth patterns. How this occurs and how this is coordinated in space is not known. To obtain a mechanistic understanding of such a complex process, information from multiple scales, from molecular networks to physical properties and geometry have to be combined into a single picture. An integrated tool to do so is currently not available. Building on our complementary experience in interdisciplinary research on plant development, we will therefore develop a tool, called the “Computable Flower” that permits (i) integration of data on geometry, gene expression and biomechanics and (ii) the user to explore, interpret and generate hypotheses based on data supported by mechanistic modelling approaches. The tool therefore provides an integrated description in the form of a 3D dynamic template of the growing flower bud.

**Partners:**

- Sony-Paris(UK)
- Iaac(Spain)
- FEI(France)
- CNRS(France)
- UBER(Germany)
- Chatelain (France)
### 8.2 National initiatives

**Inria ADT - Gnomon / Naviscope (2021-2024)**


Gnomon is a user-friendly computer platform developed by the Mosaic team for the analysis and simulation of form development in silico. It is intended to be a major tool for the team members to develop, integrate and share their models, algorithms and tools. Flexible components (plugins) make it possible to load or to create such data-structures, to program their development, to analyze, visualize them and interact with them in 3D+time.

A first prototype 6.1.1 has been developed in collaboration with the software engineers (SED) from the Sophia-Antipolis Inria Center, relying on the *dtk* software kernel through the course of the previous ADT Gnomon (2018-2020). The current application is a highly interactive GUI that allows to manipulate 3D+t biological objects, and transform them using plugin-based algorithmic bricks, which implicitly composes a data processing pipeline.

The ambition of the new ADT project, designed in synergy with the partners from the Inria Défi Navicope, is to propose a complete ecosystem for the study of dynamical biological systems. It will focus on the possibility to conceive intuitively both analysis and modelling pipelines in the main Gnomon application, to use those pipelines to batch-process datasets with distributed computation, relying on the technical solutions developed in the BioImage-IT project, and to interact with the resulting objects through the web-based 3D+t browser MorphoNet, both projects being supported by Naviscope. The aim is to reach a software quality that will enable the diffusion of the platform, starting with the immediate collaborators of the partners.

**Partners:**

- SED Sophia Antipolis Inria Research Centre
- SED Rennes Inria Research Centre
- Serpico Inria project-team, Rennes, France
- Hybrid Inria project-team, Rennes, France
- Morpheme Inria project-team, Sophia Antipolis, France

**Inria IPL - Naviscope (2018-2022)**


In this project, we plan to develop 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. We will build Naviscope upon the strength of scientific visualization and machine learning methods in order to provide systems capable to assist the scientist to obtain a better understanding of massive amounts of information. Such systems will be able to recognize and highlight the most informative regions of the dataset by reducing the amount of information displayed and guiding the observer attention. Finally, we will overcome the technological challenge of gathering up the software developed in each team to provide a unique original tool for users in biological imaging, and potentially in medical imaging.
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 (switch-like) 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, in an original animal model organism, 3 major unanswered questions, each corresponding to a specific aim of the proposal:

• Aim 1: What is the spatio-temporal dynamic of intracellular signal transduction in response to FGF during embryogenesis?

• Aim 2: How is the switch-like response to graded extracellular signals controlled at the molecular level?

• Aim 3: Can the results be integrated into a predictive computational model of the pathway? Through this approach, in a simple model organism, we hope to gain an integrated molecular understanding of the spatio-temporal dynamics of this pathway and of its robustness to parameter variations.

Partners:

• UMR CRBM, CNRS Montpellier, France

• Morpheme Inria projec-team, Sophia Antipolis, France

The identification during the last decades of the molecular actors involved in guard cells signaling and ion transport highlights the fact that stomata opening or closure relies on the balanced control of ion fluxes across both plasma and vacuole membranes (PM and VM). However, how ion fluxes are coordinated between PM and VM membranes remains almost unknown. In this proposal, we hypothesize that the coupling between the ion transport at the PM and the VM is a major factor controlling stomatal aperture. Therefore, the main objective of the NetFlux project is to understand how cellular membranes are finely and tightly coordinated during cellular responses. For this purpose, we will use the guard cells from Arabidopsis thaliana as our cellular and biophysical model. To reach our goals the Netflux project will:

• characterize the ion flux across the PM and VM combining original genetic resources and highly resolutive techniques in living cells (refers to WP1 and WP2)

• develop mathematical and computational models of intracellular ion fluxes in GCs to quantitatively understand the coupling between ion transport across the PM and VM to control stomatal movements (refers to WP3)

• identify new regulators of ion transport in GCs using an original genetic screen based on a genetically encoded biosensor (refers to WP4).
Partners:

- BPMP Unit, Montpellier
- SAVE BIAM CEA, Cadarache

**ANR Hydrofield (2021 - 2024)**

**Participants:** Arezki Boudaoud *(External Collaborator)*, Christophe Godin, Ibrahim Cheddadi, Guillaume Cerutti.

Plant architecture continuously develop throughout their lifetime through the activity of the apical meristems located at the tip of growing axes. The genetic regulation of the shoot apical meristems (SAMs), which produces all plant aerial organs, has extensively been studied, various key molecular actors have been identified and their function in patterning the SAM has been mapped in space and time. In addition, recent work has established that these molecular actors not only regulate cell identities but also likely induce the physical deformation of tissues by modifying cell wall mechanical properties, in turn inducing leaf or flower primordia outgrowth. From these works progressively emerges a new mechanistic insight on the link connecting gene regulation, tissue deformation and organ growth in plants. However, despite these recent progresses, the contribution of turgor pressure and water fluxes regulation, that decisively contribute to tissue morphogenesis, is still elusive.

Partners:

- SIGNAL Team RDP, Lyon,
- Ecole Polytechnique, Saclay
- University of Singapour (Yuchen Long)

**AEx Discotik (2021 - 2025)**

**Participants:** Olivier Ali, Elsa Gascon.

Computational morphomechanics is the study of living tissue morphogenesis through the scope of physics-based computational modeling. It has become a forefront tool to study organogenesis, where mechanical stresses play a paramount regulating role. At macroscopic scale, smooth living tissues can be described as Riemannian manifolds, subject to continuous mechanics. Concomitantly, at the cellular scale, they appear as networks of discrete effectors, where mechanics should be expressed in a combinatorial manner. Current state-of-the-art models, based on “classic” Finite Element Methods, struggle to efficiently integrate this cellular (discrete) / tissular (continuous) dichotomy. The Discotik project aims to alleviate this difficulty through the use Discrete Exterior Calculus to express the laws of mechanics. While classic FEM rely solely on simplicial meshing of manifolds, “DEC” also exploits their dual structure, composed of cellular complexes. Strikingly, such cellular structures appear naturally in living tissues. Our goal is to assess this modeling approach on a specific, circumscribed problem: The morphomechanics of plant seed. We expect the “DEC” framework not only to enable faster computations but also to expose the deep connection between mechanical stress, tissue geometry and the corresponding cellular network topology.

Partners:

- Benoît Landrein, SEED team RDP, Lyon.
- Mathieu Desbrun, EPI Geomerix, Inria Saclay / Ecole Polytechnique.
Appel à projets blanc BAP INRAe : Biomove (2022-2023)

Participants: Julien Derr, Mohammed Bendahmane (External Collaborator).

In this proposal, we aim to combine 3D tracking and quantification of plant movements using biophysical modeling. Our ambition is to better understand the very process of plant growth, and to discover the processes that regulate posture in plant development. To reach these goals, we will use the model plant Arabidopsis thaliana. A. thaliana is more suitable for the planned experiments, as all required tools and lines are available in the participating teams. The key point of this project is that these rich movements associated with plant development are essentially in 3D, and therefore must be quantitatively tracked in 3D. Our scientific program is broken into 4 interconnected tasks. In Task 1, we will set-up an experimental apparatus for 3D reconstruction. Task 2 we be devoted to data processing, and to the development of a new methodology to obtain a precise and fine growth field. In Task 3, we will use and apply our newly developed system (above) to study and compare movements in wild-type A. thaliana and in mutant lines affected in mitotic growth (cell division and proliferation) or post-mitotic growth (cell expansion). The objective here is to assess the impact of slow or accelerated organ and plant growth on motion. In Task 4, we will use the above data and biophysical modeling to confront different mechanosensitivity scenarios in front of our experiments. By putting together three communities (physicist, computer scientists and biologists) we will achieve to quantify 3D plant motion to an extent which had never been done in the state of the art. Therefore, we expect the project to have strong scientific impact on plant biophysics. In particular, new mechanosensitivity lessons will be learned.

8.3 Regional initiatives

IXXI Grant: Emergent geometry in simplicial complexes inspired by plant tissues (2022 - 2024)

Participants: Olivier Ali.

During morphogenesis, plant tissues are developing macroscopic shapes based solely on two microscopic processes: cell growth and cell division. The regulation of morphogenesis through directional and differential cell expansion rate has been extensively studied but the influence of cell division on shape emergence remains far less understood. Concomitantly, the question of emergent geometry within dynamical networks is a very active field of research that draws inspirations from a wide spectrum of scientific question (neurosciences, social media, quantum gravity...). However, so far, only dynamical rule based on aggregation of new nodes at the network margin have been studied. In this project, we propose to implement a new class of dynamical networks where growth is inspired by plant cell division: pairs of nodes are substituting existing ones within the bulk of the network. We will address the question of emergent curvature within such dynamical systems.

IDEX Emergence Grant (Université de Paris): DynaVine (2021 - 2023)

Participants: Julien Derr, Dražen Zanchi (External Collaborator), Neukirch Sébastien (External Collaborator), Simoneau Thierry (External Collaborator).

The aim of DynaVine interdisciplinary emergence is to constitute a solid base for understanding and control of dynamics, growth and force generation by plant tendrils: soft organs with particularly strong mechanosensitivity including thigmotropism, by which the climbing plant can detect a rod-like support, attach to it and pull. Macroscopic mechanical growth patterns that will be deciphered will also help to reveal the microscopic cellular mechanisms of tendril growth under load. Once the growth and the force
onset/evolution are under control, we want to explore the possibility to create a tendril motor: a device in which the tendril differential growth is used to generate rapid mechanical action. In order to produce rapid force impulses by rather slow differential growth of the tendril we will use particular types of reversible snapping transition. Our proof of concept, small size and targeted competences of consortium guarantee the dynamism and success of proposed actions, including the application to more ambitious long-term research program. The proposers, J. Derr (now at ENS Lyon) and D. Zanchi (Université de Paris) with competences in plant morphogenesis, time-lapse monitoring and mechano-biophysics will carry out the experimental, time-lapse and data-analysis part of research, both in the laboratory and on the field. The INRA partner, coordinated by T. Simoneau, (UMR LEPSE, Montpellier) will provide necessary competences in agronomy (ampelography, plant ecophysiology) for on-the-field research. The partner S. Neukirch from Institut d’Alembert of the Sorbonne University will assume the theoretical part of the study, for his competences in theory and numerics of elastic structures.

**Fonds recherche ENS Lyon « attractivité nouveau professeur » (2022 - 2024)**

**Participants:** Julian Derr.

The active motions of plants observed during their development have never been seriously exploited yet. In this proposal, we aim for the first time, to combine 3D tracking and quantification of plant movements with physical modeling. Our ambition is to get insights about the very process of plant growth itself, and find out about the posture regulations. We will perform experiments on different kind of leaves. The experimental work will be to obtain kinematics and residual stresses. Thanks to the development of a new algorithm, the growth field will be extracted from kinematics. Finally, physical modeling aiming to reproduce the observations as well as chemical treatments will enable the discrimination between different mechanosensitivity hypotheses. We expect the project to have strong scientific impact both on plant biophysics but also in visual computing as new tools will be developed for the accurate reconstruction and tracking of geometrically non trivial shapes.

### 9 Dissemination

**Participants:** Jeanne Abitbol, Olivier Ali, Romain Azaïs, Guillaume Cerutti, Julien Derr, Landry Duguet, Elsa Gascon, Christophe Godin, Anna-maria Kiss.

#### 9.1 Promoting scientific activities

**General chair, scientific chair**

- Christophe Godin was co-Chair of the first international "From genes to plant architecture: the shoot apical meristem in all its states", Poitiers, France 28-30 Novembre 2022.

**Member of the conference program committees**

- Christophe Godin was a member of the Functional-Structural Plant Modeling international conference program committee.

#### 9.1.1 Journal

**Member of the editorial boards**

- Christophe Godin is associate editor of the journal Frontier in Plant Sciences, Section: Plant Biophysics and Modeling
Reviewer - reviewing activities

- Olivier Ali has conducted reviews for International Journal of Molecular Sciences (MDPI), PLOS Computational Biology and New Phytologist.
- Romain Azaïs has conducted reviews for ICLR 2023, Communications in Statistics, OpenMathematics, Journal of Open Source Software.
- Julien Derr has conducted reviews for European Physics Journals Plus and Physical Review Letters.
- Christophe Godin was a reviewer for the journals Science, Biochemical Society Transactions and the FSPM conference.

9.1.2 Invited talks

- Olivier Ali
  - The size of seed to come; How endosperm pressure both promotes and restricts seed growth and size (Cell wall and hormone meeting, 03/2022, Umeå, Sweden)
  - The mechanics behind fourway junction avoidance in Plants. (Webinaire Digit-Bio Concepts Math pour comprendre le vivant, 10/2022, online, hosted by Inrae)
- Guillaume Cerutti
  - Towards reproducible digital experimentation - The Gnomon Project (Plant Computational Biology Workshop, 09/2022, Lyon, France)
- Julien Derr
  - Plant morphogenesis: motions, growth and mechanics (mechanobio-lyon : Mechanobiology and Physics of Life in Lyon, 27/06/2022, Lyon, France)
  - Capturing plant movement at the macroscopic scale (5th LyMIC day, 22/11/2022, Lyon, France)
  - Plant morphogenesis: motions, growth and mechanics (Physics Department Colloquium, 05/12/2022, Lyon, France)
- Christophe Godin
  - International conference "PhysBio", June, Saclay, France, Juin 2022
  - International workshop on Multiscale Modeling of Plant Growth, Pattern Formation and Actuation (22w5179) BIRS Center in Oaxaca (Mexico), Oct 2022.
  - Departement of biology and ecology at the UNAM Université UNAM, Mexico city, Mexico, Oct 2022.
  - Max Planck Institute for Plant Breeding Research (MPIPZ), Cologne, Nov 2022.
- Annamaria Kiss
  - Structure and function of the morphing dandelion fruit (joint talk with Madeleine Seale, Theory of Living Matter Talks, 12/10/2022, Cambridge, UK)

9.1.3 Scientific expertise

- Christophe Godin
  - Review of a project for the Weismann Institute, Israel Science Fundation
  - Review of a project for the Indo–French Centre for the Promotion of Advanced Research.
  - Member of the International Scientific Advisory Committee of the Plant Phenotyping and Imaging Research Centre (P2IRC), Saskatchewan, Canada.
  - Member of the Scientific Committee of the Biology and Adaptation of plants of l’INRA, (43 units, 14 centres, 1150 permanent staff).
9.1.4 Research administration

- Olivier Ali
  - Member of the CAN (Conseil d’Analyse du Numérique) of the SFR Bioscience at ENS de Lyon.
  - Member of the RDP lab committee.

- Romain Azaïs
  - Member of the sustainability committee of the RDP lab at ENS de Lyon
  - Member of the Comité de Centre at Inria Lyon

- Christophe Godin
  - Member of the project-team committee of Lyon Inria Center
  - Member of the managing committee of the RDP Lab
  - President of the Jury of the Inria competition for positions of Chargés de Recherche Classe Normale in Grenoble, 2022.

- Annamaria Kiss
  - Leading the data management committee of the RDP lab
  - Webmaster of the RDP website

9.2 Teaching - Supervision - Juries

9.2.1 Teaching

- Olivier Ali
  - Master class 'The mechanics of growing Plants: Introduction to Plant morphomechanics', M2 SBCP Paris-Saclay University, visiting ENS Lyon (2h).

- Elsa Gascon
  - Techniques de microscopie et utilisation de Molécules Fluorescentes en Biologie Cellulaire, L3 Biosciences ENS Lyon, 10/2022 (2x2h).
  - Travaux pratiques de biologie moléculaire, option Physique et Chimie des systèmes Biologiques, L3 Sciences de la matière ENS de Lyon, 12/2022 (5h)

- Christophe Godin
  - Master Class (20h) in the context of the Romi project Creating Virtual Plants with L-systems, April 2022. Available on Youtube.
  - Master class 'Les plantes dans tous leurs états' for non-specialists, ENS de Lyon: Phyllotaxis. Coord A. Vialette (2h).

- Annamaria Kiss
  - in charge of the "Modelling in biology" L3 level course at the ENS de Lyon, Department of Biology (8h course, 8h practicals, exam).

- Julien Derr
  - in charge of the "Mathematics for biology" M1 level course at the ENS de Lyon, Department of Biology (8h course, exam). This teaching unit involves several members of our team : Jeanne Abitbol (8h tutorials), Guillaume Cerutti (5h lecture, tutorials), Landry Duguet (5h lecture, tutorials) and Romain Azaïs (6h lecture, tutorials, exam).
– in charge of the "Biostatistics" L3 level course at the ENS de Lyon, Department of Biology (16h tutorials, exam).
– "Biophysics" M2 level course at the ENS de Lyon, Department of Physics (8h lectures, 12h tutorials, exam).
– "Computational modeling for developmental biology” M1 level course at the ENS de Lyon, Department of Biology (10h projects, exam).
– "Bio-modeling " M2 level course at the ENS de Lyon, Department of Biology (18h projects, exam).
– participation in the "Developmental Biology" L3 level course at the ENS de Lyon, Department of Biology (4h).
– "Scientific Communications” M1 level course at the ENS de Lyon, Department of Biology (25h).
– in charge of the internship program for L3 level at the ENS de Lyon, Department of Biology (20h).
– "Modelling in biology” L3 level course at the ENS de Lyon, Department of Biology (exam).
– Master class 'Introduction to plant movements', M2 SBCP Paris-Saclay University, visiting ENS Lyon (<1h).

9.2.2 Supervision

• Olivier Ali
  – Co-supervisor of Elsa Gascon, as Research Engineer, from 09/2021 to 09/2022.
  – PhD Supervisor of Elsa Gascon, started 10/2022.

• Romain Azaïs
  – PhD co-supervisor (with Christophe Godin) of Florian Ingels (started 10/2019 and defended 09/2022)

• Julien Derr
  – PhD Supervisor of Paul Jeammet, started 10/2019. Co-supervision with S. Douady
  – PhD Supervisor of Camille Le Scao, started 10/2020. Co-supervision with S. Douady
  – PhD Supervisor of Émilien Dilly, started 10/2021. Co-supervision with D. Zanchi
  – PhD Supervisor of Lucie Poupardin, started 10/2022. Co-Supervision with M. Bendahmane

• Christophe Godin
  – PhD Advisor of Katia Mirande, started 10/2018, co-supervision with Franck Hetroy-Wheeler. (Defense held in December 2022)
  – PhD Advisor of Manuel Petit, started 10/2019, co-supervision with Grégoire Malandain. (Defense planned in May 2023)
  – PhD Supervisor of Florian Ingels, started 10/2019, co-supervision with Romain Azais.
  – PhD Supervisor of Jeanne Abitbol, started 10/2021, co-supervision with Yoan Coudert.
  – PhD Supervisor of Landry Duguet, started 10/2021, co-supervision with Teva Vernoux.
  – PhD Supervisor of Corentin Bisot, started 10/2021, co-supervision with Tom Shimizu.
  – Advisor for the Habilitation thesis at ENS de Lyon of Romain Azais (defense help in December 2022)
  – Advisor for the Habilitation thesis at ENS de Lyon of Olivier Ali
9.2.3 Juries

- Romain Azaïs and Christophe Godin were members of the PhD thesis jury of Florian Ingels as supervisors.
- Christophe Godin was
  - a member of Romain Azaïs Habilitation thesis jury as advisor (December 2022),
  - a member of the PhD thesis jury of Katia Mirande as supervisor.
- Julien Derr was member of the PhD Thesis jury of Baptiste Tesson as president.

9.3 Popularization

9.3.1 Articles and contents

Christophe Godin wrote in collaboration with François Parcy a paper "Les mystères biologiques de la formation des choux-fleurs." La Recherche, N 570, p 72.

10 Scientific production

10.1 Major publications


### 10.2 Publications of the year

#### International journals


#### International peer-reviewed conferences


#### Scientific book chapters

Reports & preprints


Other scientific publications


10.3 Cited publications


