RESEARCH CENTRE

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2024

ACTIVITY REPORT

Project-Team

MOSAIC

MOrphogenesis Simulation and Analysis In siliCo

IN COLLABORATION WITH: Réproduction et Développement des Plantes

DOMAIN

Digital Health, Biology and Earth

THEME

Computational Biology

Inria

Contents

Project-Team MOSAIC

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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]

Faculty Members

- Ibrahim Cheddadi [UGA, Associate Professor, until Aug 2024, Delegation at Inria]
- Julien Derr [ENS DE LYON, Professor]

Post-Doctoral Fellows

- Corentin Bisot [AMOLF, Post-Doctoral Fellow, from Sep 2024]
- Emilien Dilly [ENS DE LYON, Post-Doctoral Fellow, from Oct 2024]
- Guillaume Mestdagh [INRIA, Post-Doctoral Fellow]

PhD Students

- Jeanne Abitbol Spangaro [CNRS]
- Corentin Bisot [ENS DE LYON, until Aug 2024]
- Landry Duguet [INRIA]
- Elsa Gascon [INRIA]
- Natacha Javerzat [INRIA, until Jun 2024]
- Henri Pechoux [INRIA, from Sep 2024]
- Lucie Poupardin [INRIA]
- John Thampi [CNRS, from Aug 2024]

Technical Staff

- Guillaume Cerutti [INRAE, Engineer]
- Andre-Claude Clapson [INRIA, Engineer]
- Annamaria Kiss [INRAE, Engineer]
- Jonathan Legrand [CNRS, Engineer]
- Arthur Luciani [INRIA, Engineer, until Nov 2024]
- Manuel Petit [INRIA, Engineer, from Oct 2024]
- Manuel Petit [RDP, Engineer, until Sep 2024]
- Gonzalo Revilla Mut [INRIA, Engineer, from Oct 2024]
- Karamoko Samassa [INRIA, Engineer, until Jul 2024]
- John Thampi [INRIA, Engineer, until Jan 2024]

Interns and Apprentices

- Solune Denis [INRIA, Intern, from Apr 2024 until Jul 2024]
- Jorge Fernandez Villalba [ENS DE LYON, Intern, from May 2024 until Jul 2024]
- Henri Pechoux [UNIV LYON I, Intern, from Feb 2024 until Aug 2024]
- Nino Salomon [ENS DE LYON, Intern, from May 2024 until Jul 2024]

Administrative Assistant

- Leslie Dussollier [INRIA]

Visiting Scientist

- Mariana Yuste [UNAM, until Jan 2024]

External Collaborators

- Frédéric Boudon [CIRAD]
- Ali Farnudi [CIRC]
- Emmanuel Faure [LIRMM]
- Patrick Lemaire [CNRS]
- François Parcy [CNRS]
- Samuel Vernoux [CNRS]

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 [1], 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

[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.

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 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 biophysical 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* [2] 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 phylogenic 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

[2] Raff, R. A. (1996). The Shape of Life: Genes, Development, and the Evolution of Form. Univ. Chicago Press.

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 up-load 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

- The team published this year a work on pattern identification in tree-structured data in the journal Theoretical Computer Science [13]. Building upon Florian Ingels's thesis, this work advances the team's research on machine learning applied to structured data.
- The team released this year the version 1.0 of the *Gnomon* computational platform 6.1.1, providing an integrated pipeline design interface for the study of morphogenesis. This release concretizes the work achieved by Arthur Luciani, Karamoko Samassa and Guillaume Cerutti over the 3 years of the Gnomon/Naviscope ADT project, and marks a new step for the Gnomon project as the platform starts being used in autonomy by members of the RDP lab.
- In the context of the ANR Hydrofield project, and in collaboration with the RDP team mechanotransduction, the team published experiments and accompanying models confirming the prediction they made in 2019 that water could be considered as a morphogene in plant tissues, contributing to differential growth of tissue parts [12]. In particular, this paper explains how water flows deform primordia tissues in the growing meristem while preventing the growth of their boundary.

6 New software, platforms, open data

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 up-load 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 major version (v1.0) marks the release of a platform that can start to be used autonomously by non-computer scientists. The main new feature is the addition of a notion of project that gathers all the generated files (pipelines, plugins) in a shareable folder, while continuously saving the state of the user session so that no work is lost on shutdown. Other developments deriving from the alpha-testing phase include a more homogeneous behaviour of 2D and 3D views, a GUI component to replay pipelines on different input data, clearer and more abundant information in the interface, and a simplified command-line tool for installation and updates. Moreover, the documentation website was entirely redesigned to better guide the new users in their discovery of the platform.

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 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: - update third_party.plantseg version (1.8.1) & include multicut segmentation algorithm - include third_party.ctrl to remove crossed dependencies - update image IO tools - update vt & vt-python integration - include new image IO using pims library to externalize image format handling and increase flexibility - improve visualization tools - improve docstrings - use ‘pooch‘ library to access external dataset as test data - improved code clarity - improve multiangle fusion algorithm - improve test_coverage CI job - improve pyvista visualization tools - removed usage of Poetry, moved to standard ‘pyproject.toml‘

URL: https://mosaic.gitlabpages.inria.fr/timagetk/index.html

Contact: Jonathan Legrand

Participants: Jonathan Legrand, Guillaume Cerutti, Manuel Petit, Grégoire Malandain

6.1.3 dxtr

Name: dxtr

Keywords: Discrete exterior calculus, Computational geometry

Scientific Description: At the core of the dxtr library lie two main data structures implementing respectively the concepts of simplicial complex and cochain. The library also encompasses a collection of operators (differential, geometrical, topological) that can be applied to these data structures to simulate differential geometry problems, formalized through exterior calculus.

Functional Description: A Python library implementing data structures and algorithms to handle simplicial complexes and perform discrete exterior calculus.

Release Contributions: It is the beta version of the library at this stage, it is still in development and not open to the public.

News of the Year: This year we designed the major principles of the library: we implementation of the core data structures and algorithms and we set the general architecture. We wrote unit tests and proper documentation in parallel of this development. We also started to write detailed tutorials based on basic use cases.

Contact: Olivier Ali

Participants: Olivier Ali, Chao Huang

6.1.4 bvpy

Name: bvpy

Keywords: Finite element modelling, Python, Partial differential equation

Functional Description: Bvpy is a python library, based on FEniCS, Gmsh & Meshio, to easily implement and study numerically Boundary Value Problems and Initial Boundary Value Problems through the Finite Element Method.

News of the Year: bvpy ver 1.1 : The library has recently undergone updates to enhance its functionality and application range: (i) Integration of a PyVista-based module for advanced data visualization. (ii) Extension to support tetrahedral meshing for more complex geometries. (iii) Improved mesh import management from Gmsh, including integrity checks and enhanced labeling and naming of mesh entities. These enhancements make Bvpy more versatile and user-friendly for various scientific applications.

URL: https://gitlab.inria.fr/mosaic/bvpy

Contact: Olivier Ali

Participants: Olivier Ali, Florian Gacon, Elsa Gascon, Christophe Godin, Manuel Petit

6.1.5 geoinfer

Name: geometric force inference

Keywords: Geometric algorithms, Force inference, Image analysis, Biological tissue, Biomechanics

Functional Description: From cell geometries extracted from the segmentation image, cell wall tensions are estimated from the force equilibrium principle applied along the edges and internal cell pressures are derived from the Young-Laplace formalism.

Contact: Guillaume Cerutti

Participants: Andre-Claude Clapson, Ibrahim Cheddadi, Guillaume Cerutti

7 New results

7.1 Dynamical characterization of morphogenesis at cellular scale

Participants: Olivier Ali, Guillaume Cerutti, Julien Derr, Ali Farnudi, Emmanuel Faure *(External Collaborator)*, Elsa Gascon, Christophe Godin, Annamaria Kiss, Jonathan Legrand, Manuel Petit.

- 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? how to define cell-scale variability of morphogenesis within and between species?

Our team has produced this year several results in this context:

Measuring cell volumetric growth in the Shoot Apical Meristem

The peripheral zone of the Shoot Apical Meristem (SAM) of *Arabidopsis thaliana* is the place where organogenesis takes place, which implies contrasted cellular growth rates between nearby tissue areas. Relying on the tools provided by the *TimageTK* library 6.1.2, we developed a computational pipeline to segment and track cells in confocal time-lapse sequences of tissues where the cell membranes are marked by a fluorescent reporter. This pipeline has been used to generate a complete map of cell volumetric growth and deformation across the SAM.

One of the findings evidenced by this quantitative analysis is that, within the organ-meristem boundary, a subpopulation of cells next to fast-growing cells experiences volumetric shrinkage, indicating water outflow. In order to understand this observation and to test the role of water fluxes in the emergence of the new organ, a mechanohydraulic model of the growing tissue was then constructed 7.4.

This work has been carried out in collaboration with the Mechanodevo team of RDP, and is part of an article published this year [12]. It appears as a nice example of the interplay between data extraction and analysis on the one hand and testing hypothesis using a modelling approach on the other hand in order to understand the basic processes that can drive morphogenesis.

Impact of single-cell dynamics on moss phyllotaxis

While the Shoot Apical Meristem (SAM) of flowering plants such as *Arabidopsis thaliana* is a multicellular structure where complex cellular dynamics regulate the initiation of lateral organs - resulting in the establishment of phyllotaxis - in the moss model species *Physcomitrium patens*, this regulation is controlled by a single Apical Cell (AC) during leafy shoot development. Due to the simpler structure, in terms of the number of cells and layers involved in the process, the relationship between the division orientation of the AC and the resulting phyllotactic arrangement is more direct.

We investigate this process using time-lapse images of moss young leafy shoots, where cells have been segmented, lineaged, and labeled according to cell types. This cellular data allows us to study how the geometry of the AC and the surrounding primordia cells influences the establishment of phyllotaxis,

notably by monitoring specific cell shape descriptors (Guillaume Cerutti) and quantifying division angles in 3D (Jonathan Legrand) over time.

This work is conducted in collaboration with Laure Mancini, postdoctoral researcher, along with Yoan Coudert and Teva Vernoux from the Signal team of the RDP Lab.

Quantification and spatialization of cell wall signals in root cells

Cell walls play a central role in plant morphogenesis, serving as both structural and regulatory elements that mediate growth and development. Spatial variations in cell wall-related signals are particularly important to understand how plants coordinate morphogenesis at the cellular and tissue scale. To characterize precisely this spatialized information, we developed image processing pipelines using the *TimageTK* library 6.1.2 to enable the segmentation of cell walls and the quantification of fluorescent signals from high-resolution confocal microscopy images.

Focusing on *Arabiopsis* root cells, we are analyzing how cell wall signals vary depending on several factors. First, we investigated how the orientation of cell walls relatively to the root axis influences signal intensity, revealing potential anisotropies in their spatial distribution. Second, we analyzed how signals evolve with the age of a cell wall, relative to the timing of cell division, providing insights into the dynamic changes occurring in cell walls as they mature. Finally, we studied the distribution of signals at different distances from the cell wall, highlighting spatial patterns that may reflect local differences in wall composition or signaling activity.

This work is being conducted by Manuel Petit in collaboration with Antoine Chevallier, Ph.D. student, supervised by Charlotte Kirchhelle from the MechanoDevo team of RDP Lab. The tools developed during this work will be integrated into existing libraries to facilitate their use by other researchers. An article detailing these findings is currently in preparation for submission in 2025.

Constructing atlases of development at cellular scale: a practical usecase

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 choose a single representative flower template, on which the spatio-temporal binary expression patterns of 27 genes were then introduced manually [10].

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 several time-lapse image acquisitions displaying both cell interface markers and genetic reporters. This automation involves solving a series of key algorithmic challenges: (1) segmenting cells in 3D data, (2) tracking cells over time, and (3) integrating genetic information into the atlas. The integration of genetic data requires two essential substeps: (3.1) spatio-temporal alignment of time-lapse sequences from different individuals and (3.2) projection of genetic information onto a common template or between individuals.

Capitalizing on the Ph.D. work of Manuel Petit, where each of these algorithmic aspects has been methodically studied and addressed [38], we have been focusing on integrating the implementation of the developed methods into the *TimageTK* library 6.1.2. This library now centralizes the tools necessary to perform all the key algorithmic steps, hence enabling easier construction of complex pipelines. In the same spirit, the segmentation and tracking tools have also been made available as plugins in the *Gnomon* platform 6.1.1, to make these methods accessible to a broader audience.

A concrete application of these tools is currently being carried out in the context of a collaboration with Feng Zhao with the aim of constructing a genetic atlas of the *Arabidopsis thaliana* anther (tip of the stamen, the male reproductive organ). Starting from raw confocal time-lapse images, we are starting to combine the various integrated methods to build 3D+T cellularized templates with minimal recourse to hand-crafted, problem-specific code. The quality of the reconstructed templates could be conveniently assessed by collaborators through their upload on the MorphoNet web-based 4D browser [9] to provide feedback while developing the tools. By leveraging the automation brought by TimageTK and Gnomon, this collaboration demonstrates the practical benefits of these atlas construction methods for actual biological studies.

Numerical reconstruction of cellular layers of plant seeds.

During morphogenesis, plant organs acquire very stereotyped shapes through complex biological processes including cellular growth, an irreversible expansion of the cell wall leading to tissue deformation. However, the importance of the cellular organization of multi-layered tissues for the mechanical control of growth directions, and thus the emergence of anisotropic shapes, is not fully understood. Taking as a model organ the seed of *Arabidopsis thaliana*, where various external layers are known to control the growth across development, we propose to study the contribution of the different cell layers to morphogenesis.

To investigate this question, we aim to reconstruct numerically the full 3D layered structure of Arabidopsis seeds at cellular level. To do so, we are developing a pipeline combining experimental and computational techniques to go from confocal acquisition to FEM-ready meshes. We used the imaging protocol we developed for whole seed multi-angle acquisition, and performed a 3D segmentation of the entire seed coat using a seeded watershed algorithm provided by the *TimageTK* library 6.1.2. From a seed coat segmented image, successive 2D simplicial complexes of cell adjacency, which form a natural discretization of each layer of the tissue, are then extracted using tools from the *TimageTK-Geometry* library.

In order to represent in 3D the topology and geometry of the tissue and to perform 3D mechanical simulations within this structure, we are developing a new algorithm to iteratively reconstruct a 3D simplicial complex consistent with the 2D simplicial complexes of two consecutive layers. This optimization algorithm intends to make the resulting complex accurately represent the cell connectivity and tissue geometry, while building a tetrahedral mesh suitable for the resolution of boundary value problems using the finite element method (FEM) in *bvpy* 6.1.4. Moreover, the produced simplicial complexes will also serve as input for the *dxtr* library 6.1.3 currently in development within the team.

This work is being carried out by Elsa Gascon, whose Ph.D. started in 2022 under the supervision of Olivier Ali in the context of the Inria AEx Discotik 9.3. Guillaume Cerutti is providing technical expertise and guidance on this project.

Reconstruction of pollen tube trajectories on papilla surfaces

To fertilize the ovule during reproduction, the pollen grains of flowering plants first land on papillae, elongated cells located at the tip of the stigma, before "germinating" by forming a tube that will follow the surface of the papilla cell down to the ovule. Recent work mixing experimental and modelling approaches [22] showed that the geometry of the papilla cell has a major influence on the guidance of the pollen tube, and therefore on the reproductive success.

We want to refine the mechanical models of pollen tube guidance, and quantify deviation of pollen tube trajectories from geodesic curves by using more realistic papilla geometries, hence we are working with confocal images of *Arabidopsis* papilla cells fertilized with pollen grains. Relying on the *Gnomon* computational platform 6.1.1, we have been developing an image analysis pipeline that extracts the surface of a papilla cell as a 3D mesh, and the trajectory of the pollen tube, in order to estimate its landing point and initial direction on the papilla surface. This dataset will allow to simulate mechanical models on realistic papilla geometries and to compare quantitatively the predicted pollen tube trajectories directly with the experimental data.

This work is carried out in collaboration with Jonathas Pereira das Graças, Ingrid Revel and Isabelle Fobis-Loisy from the SiCE team of the RDP Lab.

7.2 Reconstruction of macroscopic forms from images and characterization of their variability

Participants: Julien Derr, Christophe Godin, Annamaria Kiss, Jonathan Legrand, Lucie Poupardin.

- 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 versions of these organs to 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 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 ROMI project ended in 2022, but the work carried by the MOSAIC team, notably on the development of the 3D plant phenotyping platform adapted to single potted plants with the *Plant Imager* (robot scanner) and the *Plant 3D Vision* tools (reconstruction and analysis pipeline) is still ongoing.

In 2024, the ROMI Plant Imager (scanning robot) and the Plant-3D-Vision library (reconstruction software) did not receive major updates, as we focused on validating our tools with the help of three biologist users who conducted approximately 250 acquisitions in total. Based on their feedback, we addressed minor issues and enhanced the overall usability and clarity of the tools.

Larger issues and improvements are planned for 2025, as we will begin a new project funded by the ANR, which aims to track plant development over time. To tackle these challenges, an engineer specializing in computer vision and robotics has been recruited.

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

Complementary to the full 3D reconstruction of plant architecture (ROMI project), we have developped 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[41, 28, 40], where “fast” elastic phenomena (buckling) or ample (nutation) motions are occuring.

In collaboration with computer vision scientists from Université de Strasbourg (Franck Hetroy-Wheeler and collaborators), we built a multicamera set up[42]. 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. During her first year, Lucie set up and calibrated the platform. During her second year, Lucie used this platform to research the kinematics of leaf unfolding. She evidenced leaf contraction synchronized to geometry changes in the leaf. These changes seem coherent with elastic contractions indicating that the growth of leaf is non stress free.

Additionnaly, we generated data (multi view time lapse photography) of leaf unfolding thanks to the set up. In 2024, Steve de Rose started a PhD in computer science in Unistra, under the supervision of Franck Hetroy-Wheeler, analysing these data.

7.3 Analysis and simulation of tree data

Participants: Romain Azaïs, Christophe Godin, Frédéric Boudon *(External Collaborator)*.

- 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.

Pattern recognition in tree data

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]. 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. This work continues our investigations conducted in recent years on other types of patterns (topological subtrees [1] followed by subforests [8]). The paper, which details our work on these questions, was published this year in Theoretical Computer Science [13].

Statistical inference: the case of Galton-Watson models

In the team, the question of statistical inference of probabilistic tree models has been explored in the context of Galton-Watson models. Spinal-structured trees are two-type Galton-Watson models parameterized by a birth distribution μ and a bias function f, generalizing the well-known Kesten's tree. These trees feature an infinite spine composed of special nodes, to which Galton-Watson trees of normal nodes (with birth distribution μ) are attached. The structure is defined by a biased offspring distribution for special nodes, derived from μ through f. This model offers a flexible framework for studying branching processes conditioned to survive. We investigate the statistical properties of spinal-structured trees, focusing on the problem of estimating μ, f, and the unobserved types of nodes from a single observation of the tree up to a fixed generation h. A maximum likelihood estimation framework is developed, enabling the estimation of μ without type observations, while estimation of f requires partial type information. Theoretical results establish the convergence of these estimators under various growth regimes of the tree, highlighting the influence of tree structure and growth rate on parameter recoverability.

The motivation for this work is twofold: to contribute to the theoretical understanding of type estimation in multi-type Galton-Watson processes and to provide a statistical framework for testing whether

population data have been conditioned to survive. By introducing the parameterization (μ, f), we generalize Kesten's tree and enable a rigorous comparison between survival-conditioned and unconditioned models. Our results demonstrate that spinal-structured trees are not only a powerful tool for analyzing survival-conditioned processes but also serve as a stepping stone toward solving broader challenges in multi-type Galton-Watson estimation with unobserved types. Through theoretical guarantees and practical algorithms, we hope that this study lays the groundwork for advancing the statistical analysis of complex branching processes. This work [18] is set to be published in 2025 in Advances in Applied Probability.

Hierarchical Timeline Warping (HTW): a generic method to design realistic plant architecture models

Virtual models of plant architecture are needed for diverse applications in developmental biology, agronomy, botany or computer graphics. They can be used for hypothesis testing, data annotation and augmentation associated with deep-learning training or for producing photorealistic rendering of plants. To match the increasing needs of these applications in precision and realism, virtual plants with increasing realistic details are required. However, the design of such detailed models remains a complex task and new techniques are required to ease this process.

To address this complexity, we developed a timeline-based approach, where the hierarchy of plant parts is described by a corresponding hierarchy of developmental timelines. For each simple or composed organ, a reference (normalized) timeline is defined [32]. Different stages of development of the organ are associated with different time-points of this reference timeline between 0 and 1. These stages are characteristic morphological steps, which can be easily and reproducibly defined across different individuals, genotypes, or even species, but do not occur at identical time points.

We tested our HDTW strategy in order to reproduce realistic virtual architectures of the model plant Arabidopsis thaliana. For this, we grew real plants in standard indoor conditions and manually collected various quantitative information on the plant at different scales, focusing on the relative and absolute developmental dynamics of many plant parts and organs. Depending on the trait, hierarchical timelines were either calibrated by measuring the same plants over days, or from snapshot pictures, taking advantage of the repetition of the same developmental sequences along the plant axis. Models constructed with this strategy can reproduce precisely plant architectural dynamics at different scales.

This year, in collaboration with Fabrice Besnard, we refined our Arabidopsis model by improving the calibration of the growth dynamics with additional experimental data, with the aime to publish the corresponding paper in 2025.

7.4 Mechanics of tissue morphogenesis

Participants: Olivier Ali, Ibrahim Cheddadi, Andre-Claude Clapson, Ali Farnudi, Elsa Gascon, Christophe Godin, Annamaria Kiss, Guillaume Cerutti, Patrick Lemaire *(External Collaborator)*.

- 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 team.

From a macroscopic perspective, tissues mechanics can be formalized within the framework of continuum mechanics. However, the fact that tissues 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.

Regulation of mechano-sensitive growth controls shape anisotropy of plant seed.

Organ morphogenesis depends on mechanical interactions between cells and tissues. These interactions generate forces that can be sensed by cells and affect key cellular processes. However,how mechanical forces, together with biochemical signals, contribute to the shaping of complex organs is still largely unclear.

Biologist colleagues addressed this question in the context of the Arabidopsis seed. Their quantitative observations of cortical microtubules (CMT) orientation, combined with our numerical simulations of stress patterns on pressurized shells, showed that seeds first experience a phase of rapid anisotropic growth along main stress directions in the outermost cell layer. However, at later stages of development, we also demonstrated that an isotropic growth phase happens, guided by the structural (isotropic) properties of an inner cell layer, independently of the orientation of surface stresses. Finally, we showed that this transition from anisotropic to isotropic growth is due to the loss of microtubule response to shape-driven stresses.

This work, a direct follow-up of [4] has been published this year [14].

Derivation of a formal expression of pressure-induced stresses.

In a growing tissue, mechano-sensitive cells relie on forces as guiding cues during morphogenesis [33]. From a signal processing perspective, one can wonder want kind of information can cells access to through mechanosensitivity? Within curved pressurized tissues, such as seeds for instance, experimental studies suggest that mechanical stresses could be a proxy for curvature, enableing growing cells to tune their expansion according to the shape of their embedding tissue.

As a follow-up question from our initial study on the regulation of seed growth [4], we wonder if a formal relationship between pressure-induced stresses and curvature could be established on closed surfaces. We derived such an expression in the case of symmetric and non-symmetric surfaces. In particular, we showed that pressure-induced stress fields eigendirections are tighly related to Killing vector fields in the case of symmetric surfaces and approximation of those in the case of non-symmetric ones.

In order to assess the validity of these developments, we also conducted a numerical simulation campaign on a familly of closed surfaces of varying symmetry. These simulations make use of the new *DEC*-based library currently in development within the team in the context of the Discotik project 9.3.

A manuscript is currently being written.

Mechanical stresses guide the formation of tricellular junction during cell division

In most biological tissues, cells attach each other by forming stable tricellular junctions [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 [25, 37] and suggests that, as in animals [26], mechanical stresses could be central in defining such stable structures in plants.

Together with colleagues from the SICE team, we wandered how tissue topology produces mechanical patterns within cell walls leading to biochemical signaling involved in 3WJ formation. We observed the existence of a process that guides the cell division site close to an adjacent tricellular junction. This mechanism appears under genetic control, as a mutant impaired in the metabolism of phospholipid produce ill-formed junctions.

We started by computing the elastic energy distribution on templates mimicking the geometry of root cortex cells. These simulations showed a depletion of elastic energy around an existing tricellular junction that could act as a characteristic hallmark preventing the cell plate attachment on this spot. To further strengthen our results, we extracted realistic finite element templates from root cortex confocal acquisitions and were able to retrieve similar hallmarks. These findings suggest that elastic energy distribution at the subcellular level within walls could act as positional cues revealing the positions of adjacent tricellular junctions. Moreover, perturbations of the root mechanical homeostasis as changes in the cellular turgor pressure partially disrupt four-way junction avoidance. This indicates that the biophysical properties of tricellular junctions play a significant role in guiding cell division orientation.

This project is a collaboration between the MOSAIC & SICE teams. It has been mostly carried out by Elsa Gascon, a PhD candidate supervised by Olivier Ali (MOSAIC) and with the strong support of Marie-Cecile Caillaud (SICE). A manuscript has been submitted in December 2024 in a top-tier biology journal and is currently under review.

Investigating the rôle of buckling in plant morphogenesis

Not only does heterogeneous growth in general, but buckling in particular, play a fundamental role in plant morphogenesis by mediating how tissues respond to growth-induced compressive stresses. As plant cells divide and expand, certain layers, such as the epidermis, may grow faster than underlying tissues. This differential growth generates mechanical instability, leading to buckling when the stress surpasses a critical threshold. The resulting deformation produces characteristic structures like folds, ridges, or wavy surfaces—a phenomenon we investigated using the sepal of Arabidopsis thaliana as a model organ.

In the 2024 version of the preprint https://hal.science/hal-04334525v1, we propose an analytical mechanical model that demonstrates how differential growth between the inner and outer epidermal layers surrounding the mesophyll leads to compressive stresses. These stresses trigger buckling on the one hand and curve the sepal on the other. In parallel, a finite element model of the transverse section of a growing sepal is presented, implemented using Fenics and BVPy . From a technical perspective, this work contributed to advancements in BVPy, particularly in simulating nonlinear elastic models and growth processes in heterogeneous tissues. A new release, incorporating these developments, is planned for early 2025.

The preprint further emphasizes the role of buckling in morphogenesis, highlighting that the deformation caused by buckling patterns the tissue, and that this patterning can regulate gene expression, creating feedback loops that reinforce specific growth patterns.

This work is made in collaboration with Arezki Boudaoud (Ecole Polytechnique, Paris, France) and Adrienne Roeder (Cornell University, Ithaca, USA).

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. Force inference is an active field of studies with recent publications [34], but mostly on animal tissues. Preliminary results with our method indicate that it compares well with the state of the art in the literature, while being more robust and better adapted to plant tissues. Our results will be compared to direct pressure measurements by our collaborators in Singapour (Yuchen Long team). Two publications are in preparation and the corresponding code will be provided to the community.

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 [12] written with our colleagues biologists has been published this year and provides a new interpretation of the role of water in the SAM development.

Hydromechanical Field Theory of Plant Morphogenesis

With Hadrien Oliveri (Max Plack Institute, Cologne), we have developed a new continuous formalism that couples water fluxes, wall mechanics and growth [21]. The model has the same phenomenology as the Lockhart model and its multicellular extension, in particular, the fact that pressure is not prescribed but

results from the coupling between fluxes and mechanics. The model couples poroelasticity to describe fluxes through the network of cells and morphoelasticity to describe growth.

Modelling of cambial growth

The vascular cambium is the meristem producing two tissues essential to trees: the phloem (inner-bark) and the xylem (wood). Wood fulfils numerous functions ensuring the functioning of trees: mechanical support and postural control, water transport and storage of reserves. For human uses, wood is a high performance composite cellular material whose new assets are constantly being discovered. While the impact of environmental variations on wood growth and microstructure is largely studied, a mechanistic approach is still missing to link these variations to cell growth mechanisms. In trees, several studies have shown that mechanical perturbations (tree bending or tilting) strongly modulate the cambial functioning (cell division rate, expansion and differentiation). However, contrary to apical meristem, no study investigated the possible role of mechanical constraints that may be crucial in the functioning of the cambium. We are part of the ANR project CEMACam coordinated by Eric Badel (INRAE Clermont-Ferrand, PIAF), that aims at unraveling fundamental aspects of wood formation with an interdisciplinary and integrated approach. In particular, we are developing a multicellular model of cambium based on a previously developed formalism [3].

A mechanohydraulic model for cotton fiber growth

The cotton fiber is among the plant cells with the highest growth rates. In cultivars, a single fiber cell generally reaches a few centimeters in length. In order to understand this highly efficent growth process, we built a comprehensive mathematical model of fiber elongation, considering cell mechanics and water entry into the cell.

More precisely, in this model plant cell growth depends on turgor pressure, the cell hydrodynamic pressure, which drives expansion of the cell wall. On the other hand, turgor pressure regulation depends on several physical, chemical and biological factors, including: vacuolar invertases, which modulate osmotic pressure of the cell, aquaporins, which determine the permeability of the plasma membrane, cell wall remodeling factors, which determine cell wall extensibility, and plasmodesmata, which are membrane-lined channels that allow free movement of water and solutes between cytoplasms of neighbouring cells. The volume, the turgor and the osmotic pressures are dynamical variables, while all other above mentioned factors are considered as parameters of the model.

In this context we performed a sensitivity analysis to changes in values of model parameters and found that plasmodesmal permeability is among the most important factors for building up turgor pressure and expanding cotton fibers. Moreover, we found that non-monotonic behaviors of turgor pressure that have been reported previously in cotton fibers cannot be recovered without accounting for dynamic changes of the parameters used in the model. Therefore, model predictions agree with experimental observations, provided that we take into account active opening and closure of plasmodesmata. Altogether, our results suggest an important role for plasmodesmal permeability in the regulation of turgor pressure.

The results of this work are presented in the article [16] and is the fruit of collaboration with Arezki Boudaoud (Ecole Polytechnique, Paris, France).

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. These results have been published in Physical Review Letters [30]

In 2024, we have pushed forward the analysis of the phase transition analogy. In particular we have looked with care at the behaviour of the perversion. These new results have been submitted for publication[19].

We have also used the set-up to monitor live plants. We are recording universal signatures of force and torque evolution as a function of writhing. Based on our experimental results, we have developed a phenomenological model of tendrils writhing. We found two distinct results : 1. A simple bilayer model where the dorsal side of the tendril is growing is enough to recapitulate all the experimental data. 2. The growth law of the ventral side can be completely understood in the framework of the Lockhart model ; it advocates for the fact that elastic stresses could have a major contribution in plant's autotropism. Two corresponding papers are in preparation.

Analysis of early pollen tube growth

Pollen grains are transported from flowers to flowers by wind or animals. They can germinate if they land on specific elongated cells, called papillae located at the tip of the stigma, the female organ of the flower. When they germinate, a pollen tube starts to grow out downward the papillae, and keeping at the papillae surface [39]. Papillae have roughly a pin-like structure, but may vary in shape within or between species and present either convex or non-convex forms. Biologists try to understand the possible physical or chemical clues that guide the growth of the pollen-tube downwards. One of the hypothesis is that the precise geometry of the papillae may play an important role in the guidance of the tube and that the tube could follow geodesics of the papillae surface.

To study this hypothesis, a mechanical model was constructed to explore how pollen tube growth is guided on the stigma geometry. We found that in mutants stigmas, the WT tube tip moves freely on the curved papilla surface and follows geodesics, while the pollen tube growth deviates from geodesic trajectories on WT, suggesting an additional guidance mechanism. Based on a computational analysis of the magnitude of possible mechanical forces acting on the pollen tube during its growth, we show that these deflections can be explained by a mechanism based on the geometry of the papilla, cell wall elasticity and turgor pressure.

This work is made in collaboration with Isabelle Fobis-Loisy (RDP Lab, Lyon) Karin John, and Catherine Quillet (LIP, Grenoble) and Lucie Riglet (Sainsbury Lab, Cambridge, UK) and is currently under review.

Theoretical and numerical investigations of cell division orientation during tissue deformation

Early-developed biological structures such as animal embryos are highly complex systems within which shape dynamics at different locations are tightly coordinated. One essential process during development is the regulation of cell division orientation. In simple cases, the cell division orientation can be predicted by studying their geometrical shapes. The orientation of a cell's division plane (the direction orthogonal to the plane) often aligns with the longer geometrical axis of the cell during interphase, famously known as Errera's rule (1886) for plant cells and Hertwig's rule (1893) for animals. Cell division is also oriented in response to mechanical forces propagating in tissue. Therefore, states of anisotropic tension in multicellular systems can emerge from both geometry and external tension, as often experimentally found in living tissues.

As a part of the ANR cell whisper project, we strive to create a minimalistic mechanical model for cell division orientation in developing biological systems. By characterising the different intracellular mechanisms at play through processes which minimise energy loss, we can investigate the trade-off between local and long-range mechanical signals. The consequences of this competition are explored in the epidermal morphogenesis of Ascidian embryos. As Ascidian embryos develop from the 64-cell stage (semi-oblate sphere) and go through gastrulation at ~ 200-cell stage (cup shape), they create a suitable canvas to study cell deformation and division orientation under various conditions.

Our efforts this year can be summarised as:

- Onboarded and trained the new team members on the theoretical background of the minimalistic mechanical model developed for the project. This was a model defined for flat geometrical

shapes representing the apical surface of cells in tissue. Through shape deformation energy cost calculations, the model predicts the cell division orientation for 2D hypothetical cells.

- Developed an image analysis pipeline to extract the apical surface shape of cells on 3D time series images of Ascidian embryos. Model (I) and previously studied models in the literature were used to predict the cell division orientation, and the results were compared to the actual observed division orientation as a function of time.
- An open-source Tissue Deformation Quantifier (TDQ) software package was developed in Python and placed on the team's Gitlab repository to generalise this study to time series images of any biological tissue of interest.
- A set of discrete differential geometry tools were put together and developed to enable the characterisation of the embryo surface deformation in time. The tools were extended and applied to triangulated meshes.

We have made significant progress in characterising the cell apical surface deformation and modelling the division orientation. The surface of the embryo is a sophisticated manifold that deforms in time. The tools we developed allow us and the scientific community to accurately study cells on an evolving manifold. A paper on our results is expected to be submitted next year.

7.5 Signaling and transport for tissue patterning and growth

Participants: Jeanne Abitbol Spangaro, Romain Azaïs, Guillaume Cerutti, Landry Duguet, Christophe Godin, Jonathan Legrand, John Thampi, 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. 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*.

We also consider other model systems, such as the moss *Physcomitrium patens* where different mechanisms need to be taken into account to understand the patterning of the organism.

Analysis and modelling of auxin transport at cellular level in the SAM.

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 [5].

These observations question the mainly adopted interpretation of auxin transport in the SAM, mainly 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 [5] and studying alternative explanations of the auxin accumulation patterns. In particular, we developed a rigorous analysis using discrete and continuous models to capture the essence of the interplay between the observed auxin and PIN1. We discovered a new correlation between the deflections in the PIN1 advection field and the auxin levels in the peripheral zone of the SAM, which could be a causality. We propose a new decomposition of PIN1 convergence into a change of direction and a change of intensity, and show that both components have equivalent significance. This highlights the importance of relying on quantitative data when analyzing PIN1 polarity patterns.

This work is part of a collaboration with Carlos Galvan-Ampudia and Teva Vernoux from the Signal team of the RDP. New experiments are currently being conducted to assess the conclusions of our analysis and modelling work, and the results will be gathered in an article to be submitted in the coming year.

Single-cell analysis of temporal responses to auxin signaling for organ initiation

Morphogenetic signals such as auxin define spatial distributions that are thought to control tissue patterning, but it has been proposed in animals that they also carry temporal information in their dynamics. Recent work provided evidence that organ initiation in the SAM is indeed dependent on the temporal integration of the auxin signal [5]. The duration of cell exposition to auxin is used to differentiate temporally sites of organ initiation, and provide robustness to the rhythmic organ patterning.

We are now studying more precisely at the level of single cells how the history of exposure to auxin might affect the transcriptional behaviour of auxin-responsive genes. To do so, we use time-lapses of SAMs imaged with both an auxin signaling sensor and an auxin-responsive transcriptional reporter, over long ranges of time (36 hours, i.e. 3 organ initiations on average). Relying on the *Gnomon* computational platform 6.1.1, we have set up a new pipeline to reconstruct trajectories of individual nuclei with auxin signal and response information. Using this quantitative information we are currently investigating which form of temporal integration is being performed by the cells, and what parameters may explain the delays observed between genes that respond to auxin at diffent stages of organ development.

This work is part of a collaboration with Hugo Caumon, Ph.D. student, along with Carlos Galvan-Ampudia and Teva Vernoux from the Signal team of the RDP.

Integrating models of auxin transport and response in the SAM

The interplay between the plant hormone auxin and its polarized efflux carrier PIN1 is key to create the accumulations that lead to the creation of new organs in the Shoot Apical Meristem. Along with the PIN1-mediated transport of auxin, an important mechanism that has been widely leveraged by computational models to reproduce phyllotactic patterns is the positive feedback of auxin concentration on the PIN1 transporters. However, the recent spatiotemporal quantifications of auxin and PIN1 polarity dynamics [5] revealed hitherto unobserved behaviours that challenge the established understanding of the auxin-PIN1 feedback mechanism and of the onset of transcriptional responses to auxin that trigger organogenesis.

One of those observations is the appearance of fronts of auxin accumulation travelling in the opposite direction to auxin fluxes, and we tested whether existing models of polar auxin transport including feedback on PIN1 had the ability to generate such travelling fronts. These models were implemented using a simulation library developed in the team, on idealised 1D and 2D tissue templates. In addition, we used a novel, physics-inspired framework to study the global organisation of PIN1 polarity in the SAM. We also started integrating mathematical models of the auxin temporal integration mechanism, hypothesised to play a central role in the transcriptional response to auxin in [5].

This work is realized within the internship and subsequent Ph.D. thesis of John Thampi, supervised by Christophe Godin in collaboration with Teva Vernoux from the Signal team of the RDP lab. The work on polar auxin transport will be gathered in a review article in the course of 2025.

Gibberelin signaling and internode specification in the Shoot Apical Meristem

We study the role of other signaling molecules in the patterning of the meristem, notably an active form of gibberelic acid (GA). Using time-lapse imaging of living SAM tissues expressing a fluorescent GA biosensor and stained with a cell wall marker, we developed a method quantify GA levels for every cell of the epidermal layer from confocal images.

Through a quantitative analysis of the spatial distribution of GA levels and of cell growth and division features computed from manually determined cell lineages, we evidenced a role for gibberelins in the patterning of the meristem. The high values of GA signaling coincide with low-growth cells located between organ primordia regions, which are actually precursors of internodes. Furthermore, the cell division plane orientation is shown to be regulated by GAs to establish typical cell file patterns, highlighting the contribution of GA to internode specification in the SAM.

This work was part of an ongoing collaboration with the Signal team of the RDP and has been published in Nature Communications this year [17].

Transport of auxin and branching patterns in mosses

Branching patterns are key determinants of plant morphology, and similar lateral branching modes have evolved separately in the leafy shoots of two major groups of land plants, the vascular plants (among which flowering plants) and the bryophytes (among which mosses), driving their independent architectural diversification. In both lineages, the inhibition of lateral branches by auxin is a shared key mechanism, and long-range polar auxin transport is known to play a central role in branching control in vascular plants. Yet in bryophytes, like the model moss species *Physcomitrium patens*, evidence suggests that auxin might only rely on diffusion through plasmodesmata (microscopic channels that link neighboring cells) to regulate branch distribution. However, whether this "symplasmic" auxin diffusion is a realistic biophysical mechanism, sufficient to explain the observed branch distribution patterns, still had to be assessed.

In collaboration with Yoan Coudert (RDP lab), we address this fundamental problem by developing a physics-based, 3D computational model of symplasmic auxin diffusion in the moss shoot, integrating molecular, cell and tissue scales. Each step of model design is guided by geometry measurements and biological experiments. Our integrative approach has demonstrated that branching control based solely on symplasmic diffusion for intercellular auxin movement can account for the observed branching patterns at the whole-shoot level. It also provides mechanistic interpretations of the changes in branch distribution caused by genetic perturbations affecting callose-dependent symplasmic permeability, as well as the unexpected increase in branch spacing robustness during shoot development. Altogether, our findings reveal that branching patterns arising from an auxin diffusion-based regulatory mechanism exhibit a specific developmental signature, not reported in vascular plants, but well exemplified in the moss *Physcomitrium*.

This work is carried out in the context of the Ph.D. thesis of Jeanne Abitbol-Spangaro (year 3 in 2024) co-supervised by Christophe Godin, and a publication has been submitted in early 2025.

7.6 Regulation of branching mechanisms in plants

Participants: Romain Azaïs, Christophe Godin, François Parcy *(External Collaborator)*, Corentin Bisot, Henri Péchoux.

- 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 [2] [24].

As a follow-up of this work, Mariana Juste, an undergraduate strudent from the University of Mexico supervised by Pr. Eugenio Azpeitia, came to France for a 3.5 months internship in the Mosaic team to work on extensions of the above inflorescence gene regulation network. In particular, she studies the role of transcriptions factors that transmit environmental signals to the plant.

Gene essentiality and topological analysis of regulatory networks

This year, as part of a project with Bayer Crop Science, we addressed the problem of identifying gene essentiality based on the topological properties of gene regulatory networks. To this end, we first developed a benchmark method for predicting essentiality using transcriptomic data. We then explored various pattern recognition techniques, similar to those studied in our team in the context of trees [1, 8, 13]. Additionally, through detailed topological analyses of the networks, we demonstrated that in certain organisms, the essentiality of a significant number of genes can not be predicted solely from topological properties.

Branching structure development in mycorrhizal fungi

Mycorrhizal fungi build networks to exchange nutrients with plant roots. Relying on host carbon, they face trade-offs between construction costs, coverage, and long-distance nutrient transport. How they manage these challenges is unclear. A custom robot for time-lapse imaging conctructed in AMOLF Lab, made it possible to track over 500,000 fungal nodes and measured 100,000 cytoplasmic flow paths. We discovered fungi use 'self-regulating' waves: growing tips expand nutrient-absorbing mycelium, controlled by fusion. This strategy minimizes carbon costs while expanding beyond depleted zones to find new plants and nutrients. Networks maintain steady transport efficiency while adding loops for faster connections. Fungi also widen tubes and accelerate flows along main routes. These findings reveal how fungi optimize their networks for efficient nutrient trade, shaped by millions of years of evolution. This work, resulting from a collaboration with the AMOLF Lab, has been accepted as a publication in Nature in November 2024.

7.7 Integration of processes for morphogenesis

Participants: Alexis de Angeli *(External Collaborator)*, Christophe Godin, Guillaume Metsdgah.

Electro-chemico-mechanical model of stoma opening

Few models integrate at the various chemico-physical mechanisms that regulate cell shape change. In collaboration with the team of Alexis de Angeli in Montpellier, specialized in the biology of stomata, our main objective is to develop a multi-membrane, multiphysics model for the regulation of plant

cell volume control and to illustrate this model on the process of opening and closing stomata cells. More precisely, we seek to integrate electro-chemical and hydro-mechanical processes in an explicit and mechanistic way, while keeping the model easy to interpret. For this, we unify the various physical processes by gathering their contributions into a common global energy function. This energy function naturally brings modularity to the model, as its components can be added or removed without impact on the other components of the system. In addition, it keeps generic features (e.g. implementation of the main physical processes) well separated from specific ones (e.g. choice of specific transporters, etc.). We exploit this approach to simulate ion transfer between the subcellular compartments of a guard cell during stoma opening. This results are being reported in a paper in preparation.

Spatial dynamics of the Arbuscular Mycorrhizal Fungal network

The outcomes of arbuscular mycorrhizal (AM) symbiosis vary widely, influenced by plant and fungal species as well as soil conditions, making predictions difficult. During this symbiosis, plants provide photosynthetically fixed carbon to fungi, which use it to grow nutrient-absorbing networks in the soil. The nutrients fungi deliver to plants affect the plants' future carbon investments in the fungi, influencing nutrient acquisition. Building on previous work, in collaboration with AMOLF lab in the Netherlands, we measured plant carbon investment in fungal networks and phosphorus uptake over time. We found a consistent proportional relationship between the plant's carbon allocation to fungi and the phosphorus fungi transfer back, regardless of fungal strain differences. Incorporating this proportionality into a model reveals how fungal traits, plant control, and soil conditions interact to shape symbiosis outcomes. This insight helps reinterpret past data and develop testable hypotheses about AM symbiosis dynamics.

7.8 New computational approaches for morphogenesis

Participants: Olivier Ali, Frédéric Boudon *(External Collaborator)*, Romain Azaïs, Solune Denis, Christophe Godin, Henri Péchoux, Nino Salomon.

- Research Axes: RA1 (Representations of forms in silico) & RA2 (Data-driven models)
- Key Modelling Challenges: KMC2 (Efficient computational mechanical models of growing tissues) & KMC3 (Realistic integrated digital models)

Theoretical and numerical investigations around Markov models

The cellular Potts model can be used to describe tissues and cellular complexes. It emerged in bioinformatics as a derivation of statistical physics models (in particular, Ising model and Potts model). The cellular complexes σ described by this model are distributed according to the Gibbs measure $\mu(\sigma) \propto \exp(-\beta H(\sigma))$ where H denotes the energy function of the system.

To simulate this probability distribution, MCMC-type techniques are used, which tend to minimize the energy H. These techniques are difficult to analyze from both theoretical and numerical points of view. In particular, their convergence rate is complicated to obtain, and we know that the algorithm can be trapped in low-energy valleys that are not the global minimum.

As part of the ALAMO project, we are seeking to propose alternative algorithms to MCMC methods, and to better characterize existing methods so as to be able to precisely quantify the accuracy of the results obtained.

This year, as part of the start-up phase of the project, we have been working in three main areas: on small state spaces for which exact solutions are achievable by enumeration, we have carried out numerical analyses of several MCMC algorithms, enabling us to construct first numerical indicators of convergence. On the other hand, we have made significant progress on the proof of convergence of a cell division algorithm inspired by the Potts model. Finally, we have begun to explore new simulation techniques inspired by contour models.

We also took a slight detour to investigate the estimation of the division rate in growth-fragmentation models. Specifically, we conducted a rigorous theoretical and numerical comparison of state-of-the-art

nonparametric methods. This analysis revealed that none of the currently available methods uniformly outperforms the others, even within the same model. Achieving this result required detailed studies of the convergence properties of Markov chains and vector-valued martingales. These findings underscore the importance of exploring the aggregation of state-of-the-art methods to enhance estimation performance. A paper will be submitted early next year.

Developing a python DEC-library for plant morphodynamics

Modeling morphogenesis of living organisms requires to numerically solve systems of ODEs and PDEs on cellularized domains. Currently, state-of-the-art approaches rely on classic *Finite Element Methods (FEM)* and require a precise triangulation[3] of the domains at stake [27]. This is a tedious task, for the natural cellularization of these domains must be preserved, even when cells are expanding and dividing.

To alleviate this difficulty, we got inspired by recent advances in the field of computer graphics, where a new method to solve differential systems has been developed: *Discrete Exterior Calculus (DEC)* [29].

Over the past years, in the context of the *Action Exploratoire Discotik* 9.3, we have been developing a `python` library, named *dxtr* (6.1.3), to adapt the tools of *DEC* within the context of plant morphodynamics.

Our objective with this library is to provide the community with efficient tools (data structures and algorithms) to estimate differential systems on simplicial complexes, inspired by developmental biology. After two years and a half of development, a first version is currently being finalized, along with an extensive documentation, the manuscript is written and its submission will be done in the coming days.

Riemannian L-systems.

We are used to think of the development of forms in biology as a process that takes place in our 3-dimensional Euclidean space. However, various forms, patterns or processes in biology take naturally place in a non-euclidean space. The vein networks of leaves for instance grow within the leaf blade, which is in general a growing curved (non-euclidean) surface. Likewise, molecular signals are transported actively or passively within tissue layers (eptihelia) that are in general curved 2-D or 3-D domains. Modeling the growth or dynamics of these systems thus requires that we account for the curved nature of the underlying medium and involves the use of advanced geometric concepts (geodesics, curvature, parallel transport, etc.) coming from differential geometry and connected mathematical fields such as differential topology, algebraic topology ...

To address this issue, we developed over the last years a new major extension of L-systems, called Riemannian L-systems, that makes it possible to simulate the growth of patterns or the movement of molecules within curved 2-D domains. The framework provides a declarative language (as an extension of the L-Py language for modeling L-systems) high level primitives to develop models and simulations within curved spaces. In these models, growing structures follow in general geodesics. Deviation from these geodesic lines can be used or interpreted as resulting from extra forces due to various physical or chemical origins. A paper describing this new paradigm and its associated language has been submitted in April 2024 [20] and is currently under revision.

Simulating vein patterns in leaf blades.

We started to use Riemannian L-systems to simulate venation patterns in leaf blades. Considering leaf blade as Riemannian medium with non null curvature, geodesics in the blades naturally take the forms of curves. We wondered what should be the metric of the blade so that veins, considered as geodesics, can reproduce main leaf venation patterns observed in nature. This work was carried out in the context of the internship of Nino Salomon, L3 ENS de Lyon, 2 months.

7.9 Miscellaneous

Participants: Christophe Godin.

[3] or tetrahedrization in 3D

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

Neuronal stem cells produce a limited number of neurons with distinct shapes and functions, which must be carefully regulated for proper brain development. In our study on the Drosophila Lin A/15 neuroblast lineage, we found that it generates motoneurons (MNs) and glia, but 40% of the MNs are eliminated through apoptosis. Two RNA-binding proteins, Imp and Syp, regulate this process: Imp promotes MN survival, while Syp triggers apoptosis.

Late-born MNs are eliminated because they lack the transcription factor (TF) code needed for proper morphology, unlike early-born MNs. By altering Imp and Syp expression, we shifted the late MNs' TF code to match early MNs, enabling their survival. Similarly, introducing early MN TFs into late MNs also prevented apoptosis.

These findings link Imp and Syp to controlling both the number and identity of MNs via TF regulation. Since Imp and Syp are conserved in vertebrates, this research provides insights into broader neurogenesis mechanisms and highlights the Drosophila model as a powerful tool for studying these processes. This paper has been published this year in eLife [15]

8 Bilateral contracts and grants with industry

Project with Bayer Crop Science (2024)

Participants: Romain Azaïs, Henri Péchoux.

Genes are segments of DNA containing instructions for protein production, which are critical for cellular functions. Gene expression is tightly regulated by complex interactions within gene regulatory networks. Among the thousands of genes in an organism, some are essential for cellular survival and development. These essential genes, when inactivated or removed, result in cell death or the inability of the organism to grow normally. Identifying essential genes is important for fundamental biology, medicine, and agriculture, as they can serve as key therapeutic or agricultural targets, such as in developing drugs to inhibit cancer-specific essential genes or targeting pathogenic fungi for novel treatments.

The identification of essential genes in fungi, particularly pathogenic ones, is challenging due to technical complexities in genetic manipulation and the polynucleated nature of fungal spores. These challenges, coupled with the need for cost-effective and high-throughput methods, make experimental approaches labor-intensive. To address this, Bayer's Disease Control branch has shifted towards computational methods, focusing on RNA-seq data analysis to predict gene essentiality. This strategy aims to streamline the identification of potential fungicide targets, moving away from traditional, broad-spectrum chemical production.

In 2024, a collaborative project between Bayer Crop Science in Lyon and our Inria project-team, leveraging expertise in machine learning, network analysis, and fungal genetics, led to the supervision of a joint internship. This initiative aimed to develop interpretable machine learning methods to predict essential genes in some pathogenic fungi, as well as validate these methods using the model organism *Neurospora crassa*, whose essential genes are already experimentally characterized.

9 Partnerships and cooperations

9.1 International initiatives

9.1.1 Participation in other International Programs

The CNRS and its French partner institutions, created created in 2020 the International Research Laboratory "Computing Plant Morphogenesis (CompuMorph)" involving scientists from : - the Reproduction et Développement des Plantes Lab - Supervising bodies : CNRS, INRA, Université Claude Bernard Lyon 1 and Ecole normale supérieure de Lyon - Director since 2024: Christophe Godin, - and the Sainsbury Laboratory Cambridge University, Director sinec 2022: Henrik Jönsson.

The support to this project takes the form of dedicated financing aiming at covering part of the international extra cost arising from the conduct of the research programme, which complements funds directly contributed by the participating laboratories and research teams.

This year, the IRP organized an international workshop on Plant Computational Biology Workshop at ENS de Lyon, 4th-8th Nov.

9.2 International research visitors

9.2.1 Visits of international scientists

- Mariana Yuste, Master student from the University of Mexico (Prof. Eugenio Azpeitia). Mariana visited the team from October 2023 to January 2024. She worked on the development of genetic models of inflorescence growth.
- Feng Zhao from the School of Ecology and Environment, Northwestern Polytechnical University, Xi'an Shaanxi, China paid a 3 months visit (September-November 2024) to the team to collaborate on his Anther atlas project and learn how to use the Gnomon and Morphogenetics platform.

9.2.2 Visits to international teams

- Corentin Bisot made several visits to its co-superviser's Lab (Tom Shimizu, AMOLF) in Amsterdam, The Netherlands.

9.3 National initiatives

Inria ADT - Gnomon / Naviscope (2021-2024)

Participants: Olivier Ali, Romain Azaïs, Guillaume Cerutti, Emmanuel Faure *(External Collaborator)*, , Christophe Godin, Jonathan Legrand, Arthur Luciani, Grégoire Malandain *(External Collaborator)*, , Karamoko Samassa, Teva Vernoux *(External Collaborator)*.

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 developments carried out in this ADT project aim to set up a complete ecosystem for the study of dynamical biological systems. Through Gnomon, users will have the possibility to carry out their own numerical experimentation project, relying on available plugins or developing new ones for their applications, programming models to simulate developing forms, and dynamically visualizing the generated structures. The Gnomon application stands as a central tool to conceive intuitively both analysis and modelling pipelines, but it will interact with other software issuing from the Inria Défi Naviscope (2019-2023): BioImage-IT for batch-processing datasets with distributed computations, and MorphoNet for interacting with the computation results through a web-based 3D+t browser. 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 ADT - Mechaverse (2024-2026)

Participants: Olivier Ali, Julien Derr, Manuel Petit, Gonzalo Rivella.

The BVPy library 6.1.4 is a python library aimed at implementing Boundary Value Problems *(BVP)* and Initial Boundary Value Problems *(IBVP)* in the Finite Element Method paradigm. Such problems are ubiquitous in the study of morphogenesis and the BVPy library provides tools to address them, not only to the researchers and engineers of the team but also to external collaborators. Since its first release [31], the users of the library have raised a number of limitations (*e.g.* impossibility to consider dynamical meshes, abscence of tools to design 3D cellularized domain, compatibility of the library with the newest versions of its main dependence - FEniCS-X). Solving these limitations have become critical for two PhD students of the team are relying on the library to develop their scientific projects.

The goal of the project is to address these limitations. To that end, Gonzalo Rivella has been recruited in October 2024 to develop the needed new features and to roll-out an updated version of BVPy.

Inria 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” Finte 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.

Inria AEx ALAMO (2023 - 2027)

Participants: Romain Azaïs, Henri Péchoux.

Stochastic lattice models are of constant interest to the scientific community, both for their fundamental properties and the wide variety of applications they offer, notably in statistical physics, computational biology and population ecology. Their numerical simulation often requires the use of MCMC (Markov chain Monte Carlo) techniques. The ALAMO project aims at proposing alternative algorithms for the simulation of these models by studying and estimating the law of the contours formed by the nodes of the lattice having common characteristics. By controlling the error to the target distribution, these new simulation techniques will allow to fine-tune the MCMC algorithms or even to overcome some of their limitations and could therefore offer a credible alternative.

Partners:

- Benoît Henry, Institut Mines Télécom Nord Europe à Lille.
- Philippe Andrey, INRAE Versailles.

ANR Cell Whisper (2020 - 2024)

Participants: Christophe Godin, Patrick Lemaire *(External Collaborator)*, , Grégoire Malandain *(External Collaborator)*.

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

ANR Netflux (2022 - 2025)

Participants: Christophe Godin, Ibrahim Cheddadi, Guillaume Cerutti.

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, (Teva Vernoux)
- Ecole Polytechnique, Saclay (Arezki Boudaoud)
- University of Singapour (Yuchen Long)
- University of Helsinky (Juan Alonso-Serra)

ANR Fractals (2024 - 2028)

Understanding the different strategies of how organisms adapt to external changes, such as temperature increase, is of critical importance. Robustness to environmental variation is often related to phenotypic plasticity. Strikingly, some organisms are even able to adapt by drastically modifying their shape (plants or filamentous structures such as slime molds). In the latter case, the organism adapts by modifying its complex fractal structure, deeply redefining its growth and transport processes. The project aims to understand this adaptive fractal remodeling process. Slime-molds display two levels of fractality (intracellular cytoskeleton and plasma membrane). Temperature is one of the main factors affecting motion. To date, no work has been focused on network morphogenesis and topology, nor on the evolution of the membrane to explain motion response to temperature change. We will develop and test the idea

that plasticity and resilience toward temperature change could be connected with the ability of the organism to dispatch its fractality between either level.

On the mathematical and computational side, based on recent work of partners, we will model these living forms with the aim of obtaining specific (discrete) differential operators on fractal structures, in order to express the evolution equations associated with the morpho-biological phenomena. To date, the exploration of the likely interactions between the mathematical theory and the biological phenomena which occur in fractal-shaped living forms remain an unexplored field.

The project FRACTALS aims at developing and applying a new mathematical framework to model the dynamics of a fractal cytoskeleton network, along with its fractal membrane, in response to external stresses, in particular, heat stresses, its adaptation and its resilience.

Partners:

- Sorbonne Université, Paris (Claire David, coordinator)
- Université Paul Sabatier, Toulouse (Audrey Dussutour)
- University of California, Riverside (Michel Lapidus)

10 Dissemination

10.1 Promoting scientific activities

10.1.1 Scientific events: organisation

- Olivier Ali
  - Co-organizer of the 8th Plant Computational Biology Workshop, pcbw2024. A 5-day yearly international scientific conference held at ENS Lyon in November 2024.
- Romain Azaïs
  - Co-organization of a session on “Distances between Measures” at the Journées de Statistique in Bordeaux (May 2024).
  - Co-organization of a workshop on “Conformal Inference” at the Institut Henri Poincaré in Paris (January 2024).
- Christophe Godin
  - Chair of the 8th Plant Computational Biology Workshop, pcbw2024, 4-8 Nov. 2024, ENS Lyon. (60 participants)
  - Chair of the Hydrofield international workshop,10-12 Apr. 2024, ENS Lyon (50 participants)

10.1.2 Scientific events: selection

Reviewer for conference papers

- Olivier Ali: SIGGRAPH 2024.
- Romain Azaïs: International Conference on Learning Representations 2024

10.1.3 Journal

Member of editorial boards

- Christophe Godin
  - Academic Editor in PLoS Computational Biology
  - Member of the Editorial Advisory Board of Plant in Silico
  - Associate Editor Frontiers in Plant Sciences, section Plant Biophysics and Modeling
  - Recommender of the Journal Peer Community In (PCI) Mathematical and Computational Modeling

Reviewer - reviewing activities

- Olivier Ali: Scientific Reports
- Romain Azaïs: Advances in Data Analysis and Classification; Journal of Open Source Software; IEEE Transactions on Neural Networks and Learning Systems
- Julien Derr: New Phytologist, The plant journal
- Christophe Godin: American Journal of Botany, Springer Book on Phyllotaxis.

10.1.4 Invited talks

- Olivier Ali
  - Rencontres du GDR Imabio (Grenoble, september 2024, link).
- Romain Azaïs
  - Séminaire de l'équipe Probabilités et Statistique de l'Institut Montpelliérain Alexander Grothendieck
  - École Jeunes Chercheuses et Jeunes Chercheurs en Informatique Mathématique (Université de Nantes); a chapter of collaborative book was written based on this course [23]
  - Séminaire de l'équipe Statistique et Optimisation de l'Institut Mathématique de Toulouse
  - Séminaire de l'équipe BioSP du centre INRAE d'Avignon
  - Séminaire de l'équipe Probabilités et Statistique du Laboratoire de Mathématiques et de leurs Applications de Pau (online)
- Guillaume Cerutti
  - Gnomon Computational Platform - Reproducible digital experimentation for the study of morphogenesis (Plant Computational Biology Workshop, 11/2024, Lyon, France)
- Christophe Godin
  - Using computational models to understand plant development. Indo-French Plant biology workshop (ENS and IISER), May 30th 2024.
  - Analyzing auxin transport fields at the shoot apical meristem. First workshop on Finite Elements for cell and tissue morphogenesis, 9-13 Sep 2024, Frejus France.
  - Virtual Plants and Genetic regulation. Rencontres ENS de Lyon - Limagrain, Oct 9th 2024.
  - Plant Computational Biology Workshop. Growing forms in Curved Spaces. 4-8 Nov 2024, Lyon, France.
  - Riemannian L-systems. Wageningen working group on Functional Structural Plant modeling, invited online presentation, 22nd November 2024, See Video

10.1.5 Leadership within the scientific community

- Olivier Ali
  - Elected member (since 2023) of the Inria Commission d'Évaluation.
- Romain Azaïs: elected member (since 2022) and president (since Summer 2024) of the Mathematical Statistics group of the French Statistical Society
- Christophe Godin
  - Group leader of the Inria Mosaic project-team
  - Coordinator of the ANR project Hydrofield (2021-2024)

  - Scientific coordinator of the Gnomon computational platform project

- Guillaume Cerutti
  - Technical coordinator of the Gnomon computational platform project

10.1.6 Scientific expertise

- Olivier Ali
  - Scientific expert for the HCERES evaluation of Institute Jean-Pierre Bourgin (Inrae/AgroParisTech).
  - Member of the assessment committees for two new Inria teams (Texel & Genscale) in 2024. (CE activity)
  - Member of the IFSP assessment committee of Inria for 2024. (CE activity)
  - Member of the national Ripec C3 committee of Inria for 2024. (CE activity)
  - Member of the national "détachement" committe of Inria for 2024. (CE activity)
- Christophe Godin
  - Member of the Scientific Committee of the National Explorae Program coordinated by INRAe
  - Member of the Inria Scientific Orientation Committee (COS) of the Inria Center of Lyon University.
  - Working group coordinator of the instruction of a Inria project-team creation in the Lyon center

10.1.7 Research administration

- Olivier Ali
  - Webmaster for the Inria CE.
  - Coordinator for three Inria Team Evaluations (Petrus, Aromath & Sycomore). (CE activity)
  - Member of the organizing committee of the prospective seminar on the Inria Theme 2.3 (Algorithm, Formal methods and Cryptology). (CE activity)
- Romain Azaïs: elected member of the Comité de Centre du centre Inria de Lyon
- Christophe Godin
  - Member of the Inria Project-Team committee of the Inria Center of Lyon University.
  - Member of the management committee of the RDP lab, Lyon.
  - Correspondent for information and scientific editing (IES) at the Lyon Inria center

10.2 Teaching - Supervision - Juries

10.2.1 Teaching

- Olivier Ali
  - Practicals (TD) on dynamical systems, Master 1 Biosciences, ENS Lyon (8h).
- Romain Azaïs
  - Supervised classification at level Master 2 in Applied Mathematics (Univ. Lyon 1 and ENS Lyon)
  - Fourier analysis at level Master 1 in Biology (ENS Lyon)
- Guillaume Cerutti

  - Practicals (TD) on Fourier analysis, Master 1 Biosciences, ENS Lyon (8h)

- Elsa Gascon
  - TD introduction aux fondamentaux de biologie cellulaire, Licence de biologie, ENS Lyon (4h)
  - TP de neurophysiologie et de physiologie végétale, Licence de biologie, ENS Lyon (22h)
  - TD modélisation des systèmes biologiques, L3 biologie, ENS Lyon (16h)
  - TP de physique et chimie des systèmes biologiques (2), Licence de chimie, ENS Lyon (11h)
  - Cours Cellules et tissus biologiques, Master de chimie, ENS Lyon (6h)
  - TD de biologie moléculaire et génétique, Master de chimie, ENS Lyon (5h)
- Annamaria Kiss
  - Lectures for the "Modelling in biology" L3 level course at the ENS de Lyon, Department of Biology (4h).
- 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 : Olivier Ali (8h tutorials), Guillaume Cerutti (8h, tutorials), and Romain Azaïs (8h lecture).
  - 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 (12h).
  - In charge of the "Modelling in biology" L3 level course at the ENS de Lyon, Department of Biology (lecture, tutorials, exam, 11h).
  - Mentoring for L3 and M2 students (19h)
  - Creation and responsability of a new teaching unit for CPES students (new interdisciplinary undergraduate program at ENS): Physics of life. (14h)
- Christophe Godin
  - Class on Osmosis for CPES students, L3 ENS de Lyon, November 2024 (2h)
  - Class for non-specialists: Les plantes dans tous les états: Phyllotaxis, Mar. 2024, (2h)
- Manuel Petit
  - Python programming practicals for L3 students, ENS de Lyon, January 2024 (18h)

10.2.2 Supervision

- Olivier Ali
  - PhD supervisor of Elsa Gascon
  - Co-supervisor of ADT engineer Gonzalo Revilla Mut
  - member of the thesis comitees of Rawen Ben-Malek (Université Paris-Saclay, IJPB) & Özer Erguvan (Swedish University of Agricultural Sciences, UPSC, Sweden)

- Romain Azaïs
  - PhD supervisor of Henri Pechoux
  - Internship supervisor of Solune Denis and Henri Pechoux
- Julien Derr
  - PhD supervisor of Lucie Poupardin
  - Co-supervisor of ADT engineer Gonzalo Revilla.
  - member of the thesis comitees of Steve De Rose (Unistra) & Marianne Lang (Univ Clermont)
- Christophe Godin
  - PhD supervisor of Landry Duguet (co-supervision Teva Vernoux, RDP, Lyon)
  - PhD co-supervisor of Jeanne Abitbol-Spangaro (co-supervision Yoan Coudert, RDP Lyon)
  - PhD co-supervisor of Corentin Bisot (co-supervision Tom Shimizu, AMOLF lab, Netherlands)
  - PhD supervisor of John Thampi (co-supervision Teva Vernoux, RDP Lab)
  - Internship supervisor of Nino Salomon (L3 Ens de Lyon)
  - Internship co-supervisor of Samara Gher (with Stefanie Wuhrer, Inria Grenoble)
  - Internship supervisor of Mariana Yuste (3.5 months from Mexico University)
  - member of the Comité de Suivi de Thèse (CST) of Melanie de Oliveira e Silva, University of Paris-Saclay, May 2024.
  - member of the Comité de Suivi de Thèse (CST) Schayma Ben Marzougui, University of Lyon.

10.2.3 Juries

- Olivier Ali
  - Member of the INRIA Jury CRHC/CRHC-8 2024 (CE activity)
  - Member of the INRIA Jury CRCN/IFSP Lyon 2024
- Christophe Godin
  - Jury member of Landry Duguet's PhD defense, December 2024.
  - HDR director and jury member of Jessica Bertheloot's Habilitation, University of Angers, Sept. 2024.
  - Jury member of Yann Boursiac's Habilitation in Biology (HDR), University of Montpellier, May 2024.
  - Jury member of Emmanuel Faure's Habilitation (HDR) in Computer Science, University of Montpellier, Fev. 2024.

10.3 Popularization

10.3.1 Specific official responsibilities in science outreach structures

- Christophe Godin
  - Coordination with Jeanne Abitbol-Spangaro of the series of Chalk Talks entitled *Back To Basics* in the RDP lab, which aims at promoting interdisciplinarity and spreading new ways of viewing old scientific topics in the Lab.

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10.3.2 Productions (articles, videos, podcasts, serious games, ...)

- Christophe Godin
  - Interview for the journal Epsiloon on Phyllotaxis and fractals
  - Interview for the journal La Recherche on the forms of the living world
  - Interview for the Times of India
  - Interview for Inria internal communication: Video

10.3.3 Participation in Live events

- Guillaume Cerutti, Arthur Luciani, Manuel Petit, Karamoko Samassa:
  - Presentation of the Gnomon platform to the DevTech day of the Inria Sophia-Antipolis Center.
- Christophe Godin
  - Presentation to high school students (2nde) of researcher's job (organised by Inria at ENS de Lyon, June 2024).

11 Scientific production

11.1 Major publications

[1] R. Azaïs and F. Ingels. 'The Weight Function in the Subtree Kernel is Decisive'. In: *Journal of Machine Learning Research* 21 (Apr. 2020), pp. 1–36. URL: https://hal.archives-ouvertes.fr/hal-02097593 (cit. on pp. 13, 22).

[2] E. Azpeitia, G. Tichtinsky, M. Le Masson, A. Serrano-Mislata, J. Lucas, V. Gregis, C. Gimenez, N. Prunet, E. Farcot, M. Kater, D. Bradley, F. Madueño, C. Godin and F. Parcy. 'Cauliflower fractal forms arise from perturbations of floral gene networks'. In: *Science* 373.6551 (2021), pp. 192–197. DOI: 10.1126/science.abg5999. URL: https://hal.archives-ouvertes.fr/hal-03291136 (cit. on p. 22).

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[5] C. Galvan-Ampudia, G. Cerutti, J. Legrand, G. Brunoud, R. Martin Arevalillo, R. Azaïs, V. Bayle, S. Moussu, C. Wenzl, Y. Jaillais, J. U. Lohmann, C. Godin and T. Vernoux. 'Temporal integration of auxin information for the regulation of patterning'. In: *eLife* 9 (7th May 2020). DOI: 10.7554/eLife.55832. URL: https://hal.archives-ouvertes.fr/hal-02368529 (cit. on pp. 19, 20).

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[7] L. Guignard, U.-M. Fiuza, B. Leggio, J. Laussu, E. Faure, G. Michelin, K. Biasuz, L. Hufnagel, G. Malandain, C. Godin and P. Lemaire. 'Contact area-dependent cell communication and the morphological invariance of ascidian embryogenesis'. In: *Science* (10th July 2020). DOI: 10.1126/science.aar5663. URL: https://hal.inria.fr/hal-02903409.

[8] F. Ingels and R. Azaïs. 'Enumeration of Irredundant Forests'. In: *Theoretical Computer Science* 922 (27th Apr. 2022), pp. 312–334. DOI: 10.1016/j.tcs.2022.04.033. URL: https://hal.science/hal-02511901 (cit. on pp. 13, 22).

[9] B. Leggio, J. Laussu, A. Carlier, C. Godin, P. Lemaire and E. Faure. 'MorphoNet: an interactive online morphological browser to explore complex multi-scale data'. In: *Nature Communications* 10.2812 (2019), pp. 1–8. DOI: 10.1038/s41467-019-10668-1. URL: https://hal.archives-ouvertes.fr/hal-01938153 (cit. on p. 10).

[10] Y. Refahi, A. Zardilis, G. Michelin, R. Wightman, B. Leggio, J. Legrand, E. Faure, L. Vachez, A. Armezzani, A.-E. Risson, F. Zhao, P. Das, N. Prunet, E. Meyerowitz, C. Godin, G. Malandain, H. Jönsson and J. Traas. 'A multiscale analysis of early flower development in Arabidopsis provides an integrated view of molecular regulation and growth control'. In: *Developmental Cell* 56.4 (Feb. 2021), 540–556.e8. DOI: 10.1016/j.devcel.2021.01.019. URL: https://hal.inrae.fr/hal-03299500 (cit. on p. 10).

[11] F. Zhao, F. Du, H. Oliveri, L. Zhou, O. Ali, W. Chen, S. Feng, Q. Wang, S. Lü, M. Long, R. Schneider, A. Sampathkumar, C. Godin, J. Traas and Y. Jiao. 'Microtubule-Mediated Wall Anisotropy Contributes to Leaf Blade Flattening'. In: *Current Biology - CB* 30.20 (2020), p. 3972. DOI: 10.1016/j.cub.2020.07.076. URL: https://hal.archives-ouvertes.fr/hal-02370615.

11.2 Publications of the year

International journals

[12] J. Alonso-Serra, I. Cheddadi, A. Kiss, G. Cerutti, M. Lang, S. Dieudonné, C. Lionnet, C. Godin and O. Hamant. 'Water fluxes pattern growth and identity in shoot meristems'. In: *Nature Communications* 15.1 (2024), p. 6944. DOI: 10.1038/s41467-024-51099-x. URL: https://cnrs.hal.science/hal-04680262 (cit. on pp. 6, 9, 16).

[13] R. Azaïs and F. Ingels. 'Detection of common subtrees with identical label distribution'. In: *Theoretical Computer Science* 988 (12th Mar. 2024). DOI: 10.1016/j.tcs.2023.114366. URL: https://hal.science/hal-04171279 (cit. on pp. 6, 13, 22).

[14] A. Bauer, O. Ali, C. Bied, S. Boeuf, S. Bovio, A. Delattre, G. Ingram, J. F. Golz and B. Landrein. 'Spatiotemporally distinct responses to mechanical forces shape the developing seed of Arabidopsis'. In: *EMBO Journal* 43.13 (3rd June 2024), pp. 2733–2758. DOI: 10.1038/s44318-024-00138-w. URL: https://hal.science/hal-04262711 (cit. on p. 15).

[15] W. Guan, Z. Nie, A. Laurençon, M. Bouchet, C. Godin, K. Chérif, A. Darnas and J. Enriquez. 'The role of Imp and Syp RBPs in precise neuronal elimination by apoptosis through the regulation of TFs'. In: *eLife* 12.RP91634 (14th Aug. 2024). DOI: 10.7554/eLife.91634.2. URL: https://cnrs.hal.science/hal-04246082 (cit. on p. 25).

[16] V. Hernández-Hernández, O. C. Marchand, A. Kiss and A. Boudaoud. 'A mechanohydraulic model supports a role for plasmodesmata in cotton fiber elongation'. In: *PNAS Nexus* 3.7 (12th July 2024), pgae256. DOI: 10.1093/pnasnexus/pgae256. URL: https://hal.science/hal-04681218 (cit. on p. 17).

[17] B. Shi, A. Felipo Benavent, G. Cerutti, C. Galvan-Ampudia, L. Jilli, G. Brunoud, J. Mutterer, E. Vallet, L. Sakvarelidze-Achard, J.-M. Davière, A. Navarro-Galiano, A. Walia, S. Lazary, J. Legrand, R. Weinstain, A. M. Jones, S. Prat, P. Achard and T. Vernoux. 'A quantitative gibberellin signaling biosensor reveals a role for gibberellins in internode specification at the shoot apical meristem'. In: *Nature Communications* 15.1 (17th Apr. 2024), p. 3895. DOI: 10.1038/s41467-024-48116-4. URL: https://hal.science/hal-04574130 (cit. on p. 21).

Reports & preprints

[18] R. Azaïs and B. Henry. *Maximum likelihood estimation for spinal-structured trees*. July 2024. URL: https://hal.science/hal-03109867 (cit. on p. 14).

[19] É. Dilly, S. Neukirch, J. Derr and D. Zanchi. *Critical phenomena in helical rods with perversion*. 14th Dec. 2024. URL: https://hal.science/hal-04838602 (cit. on p. 18).

[20] C. Godin and F. Boudon. *Riemannian L-systems: Modeling growing forms in curved spaces*. 4th Apr. 2024. URL: https://inria.hal.science/hal-04535182 (cit. on p. 24).

[21] H. Oliveri and I. Cheddadi. *Hydromechanical field theory of plant morphogenesis*. 2024. DOI: 10.48550/arXiv.2409.02775. URL: https://inria.hal.science/hal-04867942 (cit. on p. 16).

[22] L. Riglet, C. Quilliet, C. Godin, K. John and I. Fobis-Loisy. *Geometry and cell wall mechanics guide early pollen tube growth in Arabidopsis thaliana*. 5th Feb. 2024. DOI: 10.1101/2024.02.05.578915. URL: https://hal.science/hal-04470407 (cit. on p. 11).

Educational activities

[23] R. Azaïs. 'Construction d'estimateurs pour les processus markoviens déterministes par morceaux'. Doctoral. France, June 2024. URL: https://hal.science/hal-04567166 (cit. on p. 31).

11.3 Cited publications

[24] E. Azpeitia, F. Parcy and C. Godin. 'Cauliflowers or how the perseverance of a plant to make flowers produces an amazing fractal structure'. In: *Comptes Rendus. Biologies* 346.G1 (2023), pp. 75–83. DOI: 10.5802/crbiol.120. URL: https://inria.hal.science/hal-04242307 (cit. on p. 22).

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[27] G. Cerutti, O. Ali and C. Godin. 'DRACO-STEM: An Automatic Tool to Generate High-Quality 3D Meshes of Shoot Apical Meristem Tissue at Cell Resolution'. English. In: *Frontiers in Plant Science* 8 (Mar. 2017), pp. 13–15. DOI: 10.3389/fpls.2017.00353. URL: http://journal.frontiersin.org/article/10.3389/fpls.2017.00353/full?%5C&utm%5C_source=Email%5C_to%5C_authors%5C_%5C&utm%5C_medium=Email%5C&utm%5C_content=T1%5C_11.5e1%5C_author%5C&utm%5C_campaign=Email%5C_publication%5C&field=%5C&journalName=Frontiers%5C_in%5C_Plant%5C_Science%5C&id=233281 (cit. on p. 24).

[28] J. Derr, R. Bastien, É. Couturier and S. Douady. 'Fluttering of growing leaves as a way to reach flatness: experimental evidence on Persea americana'. In: *Journal of the Royal society interface* 15.138 (2018), p. 20170595 (cit. on p. 12).

[29] M. Desbrun, A. H. 4. I. International and 2003. 'Discrete exterior calculus for variational problems in computer vision and graphics'. In: *ieeexplore.ieee.org* () (cit. on p. 24).

[30] É. Dilly, S. Neukirch, J. Derr and D. Zanchi. 'Travelling Perversion as Constant Torque Actuator'. In: *Physical Review Letters* 131.17 (Oct. 2023), p. 177201. DOI: 10.1103/PhysRevLett.131.177201. URL: https://hal.science/hal-04067727 (cit. on p. 18).

[31] F. Gacon, C. Godin and O. Ali. 'BVPy: A FEniCS-based Python package to ease the expression and study of boundary value problems in Biology.' In: *Journal of Open Source Software* 6.59 (Mar. 2021), pp. 1–6. DOI: 10.21105/joss.02831. URL: https://hal.inria.fr/hal-03175968 (cit. on p. 27).

[32] C. Godin and F. Besnard. 'Hierarchical Developmental Timeline Warping: a generic method to design realistic plant architecture models'. In: *10th conference on Structural-Functional Plant Models*. Berlin, Germany, Mar. 2023 (cit. on p. 14).

[33] O. Hamant, M. G. Heisler, H. Jonsson, P. Krupinski, M. Uyttewaal, P. Bokov, F. Corson, P. Sahlin, A. Boudaoud, E. M. Meyerowitz, Y. Couder and J. Traas. 'Developmental Patterning by Mechanical Signals in Arabidopsis'. English. In: *Science* 322.5908 (Dec. 2008), pp. 1650–1655. DOI: 10.1126/science.1165594. URL: http://adsabs.harvard.edu/cgi-bin/nph-data%5C_query?bibcode=2008Sci...322.1650H%5C&link%5C_type=ABSTRACT (cit. on p. 15).

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