MINISYMPOSIUM

CROSS-TALK BETWEEN CELLS AND EXTRACELLULAR MATRIX IN PLANT AND ANIMAL DEVELOPMENT

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Minisymposium Keywords: Extracellular matrix, Cytoskeleton, Plant & animal development, Spatial models

At first glance, plant and animal development are very different: where the former is a life-long process, intrinsically connected with adult growth, the latter is mostly focused at the beginning of life. Animal cells migrate, whereas plant cells are tightly connected to one another. These differences in developmental modes enable very different life styles: the one facilitates highly versatile adaptation to given local circumstances, whereas the other allows for optimizing the local circumstances through mobility and behaviour. Ultimately, these differences derive from the cell walls that immobilize plant cells.

The extracellular matrix (ECM), of which the plant cell wall and animal proteins like collagen or fibronectin are examples, offers a unifying perspective on plant and animal development. The ECM serves as a medium for chemical and mechanical intercellular communication. Cells create, modify and respond to the ECM, while at the same time differential growth can deform the ECM, hence integrating mechanical and morphological cues across scales.

In both plants and animals, the cytoskeleton plays an important role in sensing and manipulating the ECM. In plants, the highly anisotropic structure of the lignocellulosic cell wall is organized by the microtubule cytoskeleton. These microtubules, in turn, can orient themselves along wall stresses, thus influencing the future cell wall properties and resulting stress patterns. In animals, the actomyosin cytoskeleton generates contractile forces which locally remodel the matrix. Plant and animal cells may thus be seen as agents with similar capabilities, but operating under different circumstances – and, therefore, collectively developing into very different organisms.

This minisymposium will bring together mathematical modellers working on plants and animals. We are convinced that the various modelling approaches used in both "worlds" to capture the interaction between cells and their ECMs will lead to cross-kingdom inspiration.

Minisymposium: Cross-talk between cells and extracellular matrix in plant and animal development

ON GROWTH AND FORM IN PLANTS AND ANIMALS: CROSSTALK BETWEEN CYTOSKELETON AND EXTRACELLULAR MATRIX

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Keywords: Cytoskeleton, Extracellular matrix, Focal adhesions, Plant cortical microtubules.

Development has two major aspects: the geometrical aspect of morphogenesis and the regulatory aspect of coordinated cell fate specification. These processes require extensive communication, between neighboring cells as well as over larger distances.

A major role in this communication is played by the extracellular matrix (ECM). The ECM both constrains and enables (complex) growth (patterns). It provides a scaffolding for cells and tissues, and a medium for longer range mechanical communication. All these help coordinate cell fate decisions. Moreover, the ECM can also be a functional aim in itself, for example as the structural component of bones, cartilage and wood.

In this talk we outline the intricate interplay between cells and ECM by contrasting two examples from animals and plants. First, shape and cell fate of animal cells strongly depend on substrate stiffness. The cytoskeleton senses these mechanical properties through focal adhesions, which in turn exert pulling forces on the ECM and thus modify its properties. Second, plant cortical microtubules guide the anisotropic deposition of cell wall material and can, at the same time, respond to wall mechanical stresses by adjusting their collective organization. A central question is how such collective behaviour arises from the dynamic properties of individual microtubules.

These examples together illustrate how plant and animal cells develop in different parameter regimes by common principles, and that methodological advances from both fields can inspire across kingdoms.

Minisymposium: Cross-talk between cells and extracellular matrix in plant and animal development

A THEORY THAT PREDICTS BEHAVIORS OF DISORDERED CYTOSKELETAL NETWORKS

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Keywords: Actomyosin networks, Contractility, Unifying theory.

Networks made of cytoskeletal filaments drive many morphological changes of cells, and the contractile actomyosin meshwork at the cell cortex in particular determines the shapes and arrangements of animal cells. Although the network components and their properties are known, and networks can be reconstituted in vitro, the requirements for contractility are still poorly understood. Many mechanisms for contraction have been proposed, but they are limited in scope and not predictive. Here, we describe a theory that predicts whether an isotropic network will contract, expand, or conserve its dimensions, depending on the activities of the elements that connect the filaments. The theory correctly predicts the behavior of in vitro networks consisting of actin filaments with varying combinations of motors and crosslinkers, and explains why contractility requires both crosslinkers and motors. For any combination of crosslinking elements, contraction is the dominant behavior of networks constituted of flexible filaments. By contrast, networks of rigid filaments can be either contractile or extensile. Our results suggest that pulsatility is an intrinsic behavior of contractile networks if the filaments are not stable but turn over. The theory offers a unifying framework to think about mechanisms of contractions or expansion, and provides the foundation for studying a broad range of processes involving cytoskeletal networks and a basis for designing synthetic networks.

Minisymposium: Cross-talk between cells and extracellular matrix in plant and animal development

WHY PLANTS MAKE PUZZLE-SHAPED CELLS

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Keywords: Morphogenesis, Leaf pavement cells, Mechanical stress, Cell shape.

The shape and function of plant cells are thought to be closely related. The puzzle-shaped epidermal cells that appear in the epidermis of many plants are a striking example of a complex cell shape, however their functional benefit has remained elusive. We propose that these intricate forms provide an effective strategy to reduce mechanical stress in the cell wall. When tissue-level growth is isotropic, we hypothesize that lobes emerge at the cellular level to prevent formation of large isodiametric cells that would bulge under the stress produced by turgor pressure. Data from various plant organs and species support the relationship between lobes and growth isotropy, which we test directly with mutants where growth direction is perturbed. Using simulation models we show that a mechanism actively regulating cellular stress plausibly reproduces the development of epidermal cell shape. Together, our results suggest that mechanical stress is a key driver of cell-shape.

Minisymposium: Cross-talk between cells and extracellular matrix in plant and animal development

MECHANICAL MODEL TO STUDY PLANT DEVELOPMENT

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Keywords: Mechanical cell wall model, Root bending, Lateral root emergence.

We present a discrete mechanical modeling framework to study the development of plant tissues and organs. The model enables the simulation of processes typical for plant development, anisotropic growth in elongated organs such as the root and hypocotyl, or the emergence of lateral roots. The two-dimensional method is built up by mass points, springs and hinges mimicking the cell wall's microstructure. To solve the dynamic equations of motion of mass points we assume elastostatics and use Verlet integration. We formulate a stiffness tensor for the springs and hinges as a function of the linear elasticity tensor and the geometry of the mesh. This allows us to: i) formulate the material's properties for small deformations in terms of linear elasticity, ii) conserve material properties during growth, and iii) implement anisotropic material properties based on experimental data. We characterize the material properties of the model in numerical simulations for finite elastic and plastic deformations.

Plant growth involves expansion of fibrils of the cell wall and addition of new material. To model growth we adjust the resting configuration of the spring lattice. When due to turgor-driven expansion, springs exceed a certain length we add new mass points, springs and hinges. In plant development the rupture of cell walls happens, for instance during penetration of upper cell layers by emerging lateral roots. We model this process by the removal of springs, nodes and hinges.

Finally, we demonstrate the value of the method in simulations of asymmetric growth resulting in organ bending as well as cell wall rupture in plant root development. The method can be used as a building block in multilevel models, e.g. by coupling it to models for cytoskeletal, hormonal and gene regulatory processes.

Acknowledgements: This work was supported by the Netherlands Scientific Organization (Nederlandse Organisatie voor Wetenschappelijk Onderzoek) [864.14.003 to L.D.W. and K.H.W.J.t.T.]

Minisymposium: Cross-talk between cells and extracellular matrix in plant and animal development

DISCRETE ELEMENT MODEL OF THE CELL TO EXPLORE HOW HUVECS RESPOND TO MECHANICAL PROPERTIES OF THE SUBSTRATE

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Keywords: Discrete Element Modeling, Traction Force Microscopy, Angiogenesis.

Cells and their environment interplay through chemical and mechanical interactions. Knowledge of this interplay helps us understand how cells migrate and interact with one another; this is fundamental to developmental processes. In addition to sensing the mechanical properties of its environment, the cell also imparts forces. We present a computational model of the cell that integrates the mechanisms of force exertion: discrete focal adhesions coupled to actin stress fibers. With it we seek to explain our findings on the behavior of Human Umbilical Vein Endothelial Cells (HUVEC). This can provide valuable information on angiogenesis, the process of blood vessels formation from existing vasculature.

We use discrete element method (DEM) to model a cell, such that we can locally tune mechanical properties of the cell. The cell consists of a number of particles connected via an elastic and a resistive element to capture viscoelasticity of the cell; the nodes are connected such that they form a triangular mesh representing the cell surface. We use a Maugis-Dugdale model to model contact between the resulting triangular elements of the cell and a substrate plane. Along with bending rigidity and volume and area conservation, the model captures cortical mechanics and recreates cell spreading behavior.

We also present our most recent advances in analysis of cellular tractions in 2.5 D in HUVECs. Tractions are acquired via measurement of embedded bead displacements in polyacrylamide gels and calculated via Traction Force Microscopy (TFM).

HUVECs are cultured on gels of different stiffness (1.4, 2.7, and 4.5kPa) and functionalized with fibronectin or collagen, thus varying both mechanical properties of the substrate and the ligand sensed by the cells. Our spatiotemporal analysis of traction field evolution at a subcellular scale reveal the effect of varying substrate stiffness at the sites of traction exertion. We find that on collagen, total force exerted increases continuously with stiffness; while on fibronectin, total force plateaus at the intermediate stiffness. Normalized values show that relative increase in force on fibronectin with increasing stiffness is larger than on collagen. Interestingly, the regions over which force is exerted are smaller but more abundant in fibronectin, particularly as stiffness increases, accounting for the sharp increase but saturation of force exerted by cells on fibronectin.

The computational model shows great potential in exploring this local regulation of force exertion and capturing spatiotemporal dynamics of this mechanism while modeling the deformation of an entire endothelial cell. Insight into local force exertion and regulation in endothelial cells can be used to further our understanding of developmental processes, including sprouting angiogenesis, as well as pathological processes (e.g. cancer biology), and can be used for tissue engineering applications.

Acknowledgements: FWO and EU's Horizon 2020 research and innovation programme (Marie Skłodowska-Curie Grant Agreement n665501)