REVIEW PAPER

Formal description of plant morphogenesis

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Abstract

Plant morphogenesis may be characterized by complex feedback mechanisms between signals specifying growth and by the growth of the plant body itself. Comprehension of such feedback mechanisms is an ongoing research task and can be aided with formal descriptions of morphogenesis. In this review, we present a number of established mathematical paradigms that are useful to the formal representation of plant shape, and of biomechanical and biochemical signaling. Specifically, we discuss work from a range of research areas including plant biology, material sciences, fluid dynamics, and computer graphics. Treating plants as organized systems of information processing allows us to compare these different mathematical methods in terms of their expressive power of biological hypotheses. This is an attempt to bring together a large number of computational modeling concepts and make them accessible to the analytical as well as empirical student of plant morphogenesis.

Keywords: Computational modeling, geometry, mechanics, morphogenesis, plant growth, signaling.

Introduction

Humans have created a tremendous number of languages to communicate ideas. They constitute fundamental tools to describe our sensory experiences and rational thoughts. Traditionally, explanations on the nature of the universe were conducted with theological arguments. In the book *Timaeus*, for instance, Plato arrived at the conclusion of the existence of a universal architect who provides plants as kindred spirits for the reinforcement of humans. Gradually, this theological course of argumentation has been to a large extent superseded by a constructivist viewpoint, where model constructs are the main elements of explanation. D'Arcy Thompson (1942) in his treatise *On Growth and Form* provided a compelling case for a model of biological growth based on physical laws. He stated that,

> 'We begin by describing the shape of an object in the simple words of common speech: we end by defining it in the precise language of mathematics; and the one method tends to follow the other in strict scientific order and historical continuity.'

According to his reasoning, at the most fundamental scale of abstraction mechanisms of growth must all be physical. Hence, mathematics as the language of physical laws should naturally be the language of choice to describe biological growth. D'Arcy Thompson realized early that mathematics as a formal language has distinctive advantages over natural languages for describing and analysing morphogenesis. His specific proposition was the introduction of mathematical transformations of 2D diagram geometries of various biological patterns. This description of shape in geometric terms and representation of growth as a geometrical transformation allowed a quantitative comparison of different organisms. A recent extension and application of his ideas has been presented by Mitchison (2016).

In this review, we aim to present a survey of mathematical instruments that are helpful in the description of plant growth. Adopting D'Arcy Thompson's viewpoint, we consider plant growth as the result of physical signals that specify changes of plant form over time. Abstractly, a physical signal is simply a means to encode information, which can be processed in time as well as in space as a result of physical interactions with other signals. A large body of research in plant morphogenesis suggests that these signals can be biochemical (e.g. Leyser, 2018) or biomechanical (e.g. Kierzkowski and Routier-Kierzkowska, 2019) in nature, and form large signaling networks. Importantly, these signals are embedded in the plant structure itself, and therefore translate with the structure as it grows, affecting in turn the dynamics of signaling networks (Green, 1999). Plant growth can thus be controlled by complex feedback mechanisms whose dynamics are not easily predicted by the human mind. Advances in theoretical biology indicate that the evaluation of such complex hypotheses can be accomplished alternatively by computational models (Prusinkiewicz and Runions, 2012). Therefore, to provide a meaningful, formal description of plant morphogenesis, it seems expedient to express plant shape, signaling, and their respective changes over time computationally.

Specifically, plant shape alone can be conveniently described in geometric terms. There exists, however, an obstacle to expressing geometry on modern computer architecture. Computers process instructions in a strictly sequential order, and only a few instructions at a time. The description of plant morphogenesis in terms of spatial and temporal notions requires parallel processing of instructions and, therefore, cannot be naturally represented by computers. To overcome this limitation, new computational representations of shape and signaling have been developed in a variety of research areas such as mathematics, material sciences, computer graphics, and computational biology. The persisting trend towards placing computing power on the graphics card enables parallelized computing, which has the future potential to overcome the limitation of strictly sequential instruction processing.

In the first section of this paper, we review and compare different computational methods of representing geometry. We then introduce methods to formally represent signaling and consider their applications in the study of plant morphogenesis. These methods are numerous and come from a range of research fields. Often, they have been applied to express either biochemical or biomechanical signals, whereas modern hypotheses of morphogenesis demand the joint simulation of all the different kinds of signals involved in plant growth. The separate development of these methods in different research areas and their usually limited scope of use hinders their evaluation for this task. In summary, dynamic plant shapes can be described by both representations of geometry and representations of signaling.

Thus, the goal of this review is to present in a comparative way a large selection of different methods applicable to the description of morphogenesis. A mathematically rigorous comparison between different formalisms is, in the majority of the cases, impossible. This makes evaluating the use of different methods of computer modeling within plant biology inherently difficult. We can, however, compare these methods in their expressive power of morphogenetic hypotheses rather than the formalisms themselves. To accomplish such a comparison, we will abstractly treat signaling as an information-processing network (Nurse, 2008). The key feature of this network is its property of having temporal as well as spatial dimensions. Specifically, we refer to the spatial routes of information transfer as 'signal topology'. Analogously, plant shape can be described not only in geometric terms (e.g. size, orientation, spatial localization), but also by the connectivity between geometric objects, which we refer to as 'shape topology'. Hence, we aim at comparing different computational modeling paradigms in terms of shape and signal topology. Furthermore, we also discuss the accuracy and performance of the various methods. This is an attempt to bring together a large diversity of methods describing geometry as well as signaling, and to provide a high-level overview of the subject. Further reading relevant to the more technical aspects of the various methods are referenced throughout the text. To make these methods more accessible to the analytical as well as the empirical researcher, we give examples of biological applications.

Representation of geometry

> 'And, for geometry, till of very late times it had no place at all (at universities), as being subservient to nothing but rigid truth. And if any man by the ingenuity of his own nature had attained to any degree of perfection therein, he was commonly thought of a magician and his art diabolical.'
>
> Thomas Hobbes (1588–1679)

To describe plant shapes in accordance with the modeling paradigms postulated above, we need to understand how geometry is represented computationally. Perhaps surprisingly, only relatively few computational representations of geometry have emerged to date. The main motivation behind these studies is performance and accuracy, or in other words computation-time/memory demands and approximation of shape, respectively. We refer to representations with high computation-time demands as complex and with high memory demands as verbose. More verbose representations usually allow for faster computation times than less-verbose ones. This is what is called the time/space or complexity/verbosity trade-off, which provides us with a first, meaningful way to distinguish the various approaches of shape representation (Fig. 1).

The simplest and most verbose representation of geometry is the representation of discrete space by a lattice (Fig. 1). Discrete space can mathematically be represented as an *n*-dimensional lattice (grid) consisting of uniform elements with no overlaps and no gaps (regular tiling) (Fig. 2A). In a 2D lattice the elements are usually represented by pixels, in 3D they are called voxels; other geometries of lattice elements are possible (e.g. triangles, tetrahedra). The coordinate at each element is given by a pair (2D) or triplet (3D) of natural numbers referred to as an index. Computationally, lattices are trivial to represent as multi-dimensional arrays that define the connectivity between individual elements, i.e. the topology of shape. Rectangular

lattices with square cells have been used to represent plant tissues and to simulate polar auxin transport (Rolland–Lagan and Prusinkiewicz, 2005; Bayer *et al.*, 2009). Lattices have also used to represent Arabidopsis roots (Grieneisen *et al.*, 2007; Mironova *et al.*, 2012). While being mathematically and computationally simple, a uniform lattice-based representation is not very intuitive. Humans prefer hierarchical representations of objects, for example in terms of curvature or surfaces.

A hierarchical representation of shapes can be achieved by parametric piecewise-defined functions, i.e. given by a set of functions defined at specific positions in space. Generally, they take the form of:

$$F(x) \;=\; \sum_i a_i \, f_i(x)$$

where a_i is the parameter(s) of the representation and $f_i(x)$ are locally defined basis functions. The piecewise functions are used to define coordinates of geometric objects. In the simplest case they are linear functions. These can be used to define vertices
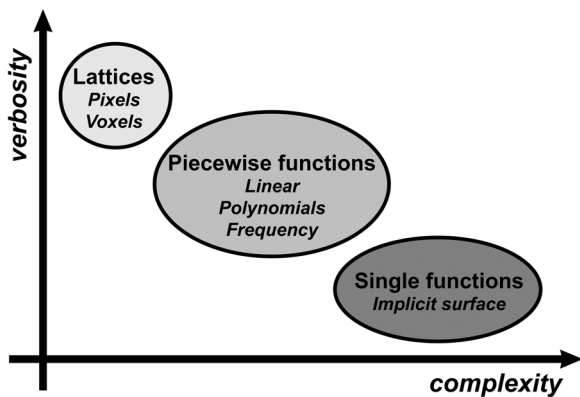

Fig. 1. Three categories of representations of geometry distinguished in terms of verbosity and complexity. Darker shades of grey indicate more accurate approximations of shape.

(points) of a mesh consisting of lines and polygons (Fig. 2B). Importantly, the objects need not be of the same dimension. The hierarchical relations between these geometric objects can be given by an incidence graph (Fig. 2C). For example, to model the geometry of a cell monolayer we can represent biological cells by t3D volumetric elements that can be bounded by 2D polygonal faces (cell walls), 1D edges, and 0D vertices (cell junctions) (Fig. 2D). This means that we can traverse both the incidence graph as well as the local neighborhood of geometric objects of the same dimension (topology of shape (Fig. 2C, D). For example, cell topology has been represented with 2D and 3D graphs for Arabidopsis roots, hypocotyls, and leaves (Montenegro-Johnson *et al.*, 2015; Carter *et al.*, 2017; Jackson *et al.*, 2017). Representations based on polygons and triangle meshes have been used to model a wide variety of different plant organs. For example, Runions *et al.* (2017) modeled leaves of different shapes (simple, lobed, or compound) as 2D structures consisting of polygons that represented the leaf margin, line segments that represented the veins, and triangle meshes that represented the leaf blade.

More advanced methods of compositing these elements in a unified way are given by quad-edge structures (Guibas and Stolfi, 1985), vertex–vertex systems (Smith, 2006), and cell complexes (Edelsbrunner *et al.*, 1995; Mjolsness and Cunha, 2012; Prusinkiewicz and Lane, 2013). The use of cell complexes and their advantages in modeling 3D cell division has been shown by Yoshida *et al.* (2014) (Fig. 3A), who described 3D models of the growing Arabidopsis embryo with cell walls represented by a triangular mesh. A similar approach has also been used to model the development of Arabidopsis hypocotyls (Bassel *et al.*, 2014).

The piecewise functions that approximate a given shape need not necessarily be linear and thus limited to geometries such as lines, triangles, or other polygons. Instead, low-degree polynomial functions can be used to define smooth curves or surfaces. This is a slightly less verbose way of representing
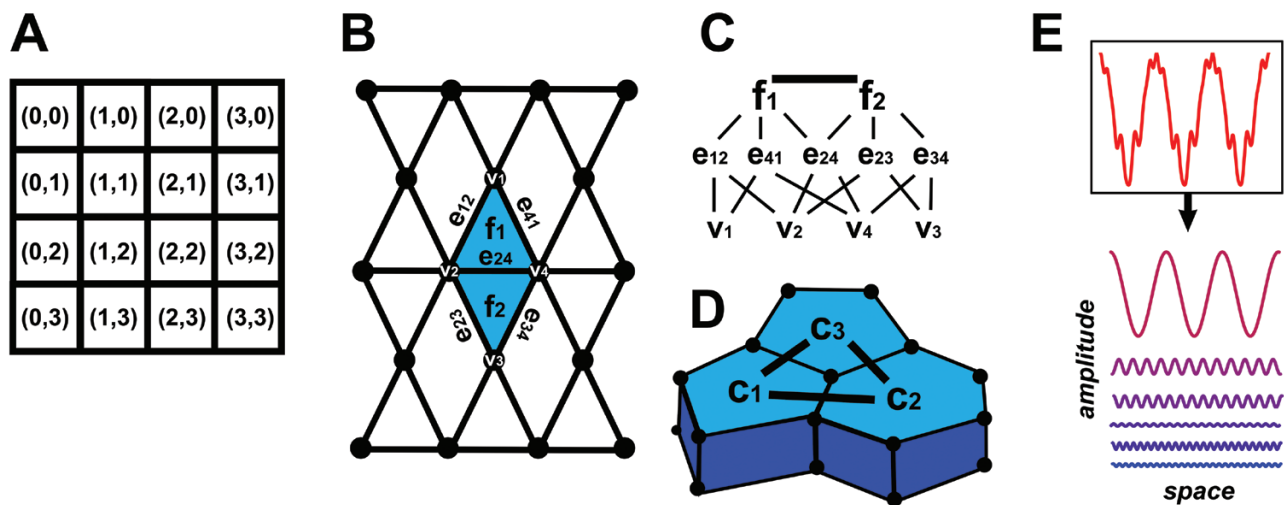

Fig. 2. Illustrative diagrams of different methods of computational representation of geometry. (A) Two-dimensional grid with indexed elements shown in brackets. (B) Triangle mesh composed of different geometric objects: vertices (v), edges (e), and faces (f). (C) Incidence graph describing the connectivity of the geometric objects shown in (B), indicated by thin lines; the neighborhood is indicated by the thick line.; (D) Graph (thick lines) indicating the topology of geometric objects for the 3D case, where C_1–C_3 are volumetric cells. (E) Fourier series decomposition of a periodic function of space (framed and indicated in red) expressing spatial frequency into sines and cosines (indicated in blue and purple). (B, C) Adapted from Lane (2015).
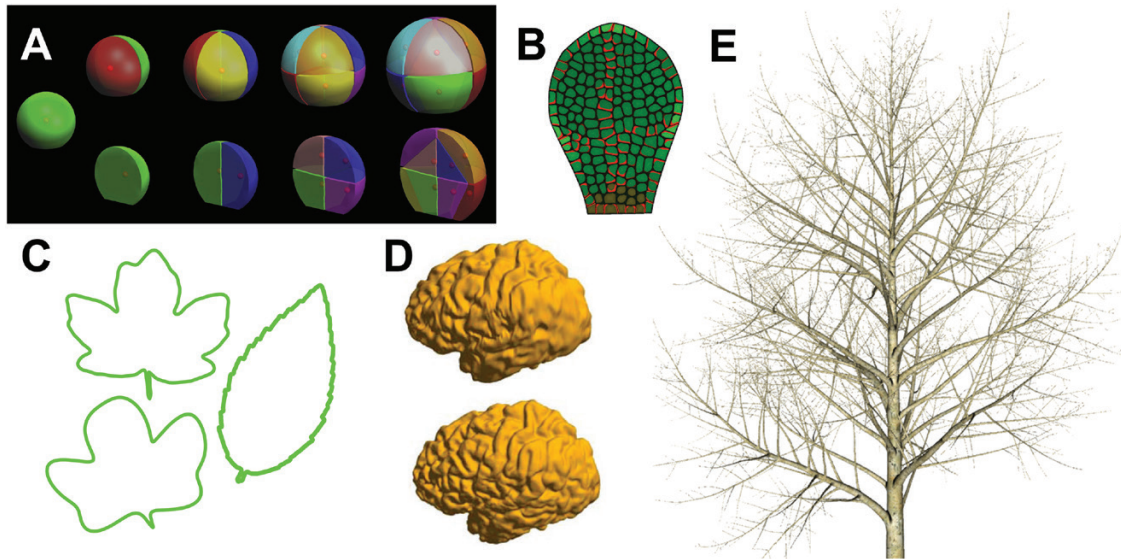
Fig. 3. Examples of results generated with different methods of shape representations. (A) Cell complexes used to express a cell division sequence in an Arabidopsis embryo (reprinted from Yoshida *et al.*, 2014). (B) Bezier surface representing the shape of an Arabidopsis leaf (reprinted from Smith and Bayer, 2009). (C) Different leaf shapes modeled with Fourier descriptors (method described in Klein and Svoboda, 2017). (D) Wavelet representation of the human brain with varying numbers of coefficients (1000, top; 5000, bottom) (reprinted from Dong *et al.*, 2009). (E) Implicit surface model of a tree (reprinted from Galbraith *et al.*, 2004).

geometry, since less information is needed to approximate shapes. Methods based on polynomial functions, for example Bezier or spline functions, have been used to model realistic geometries of plant organs such as leaves (e.g. Federl and Prusinkiewicz, 1999; Runions *et al.*, 2005; Smith and Bayer, 2009) (Fig. 3B). These polynomial representations are better suited to describing plant structures than linear representations, since strictly straight geometries are seldom encountered in nature. However, polynomial-function representations will typically change the global shape as a result of local modifications. Thus, they do not allow an easy refinement of shape approximations.

Interestingly, geometry can also be represented in a non-spatial way, for example as frequencies (Fig. 2E). In particular, methods based on the Fourier transform are a useful tool to represent spatial data (Staib and Duncan, 1992). The decomposition of spatial information into a series of sine and cosine waves allows its interpretation in terms of wavelength and amplitude, also known as spatial frequency. Representing data as frequencies results in an even less verbose representation of shapes and lends itself well to shape analysis (Fig. 3C) (Klein and Svoboda, 2017). The transformation of shape into the frequency domain also allows a hierarchical representation. Areas of low variation in spatial data are encoded in low frequencies whilst high variation is encoded as high frequencies (Fig. 2E). One problem with Fourier transforms in the context of 3D modeling is that shape features are usually aperiodic and local, whereas trigonometric functions are periodic and global. This limitation is addressed by wavelets that are defined at different positions in space (Schröder and Sweldens, 2000). The addition of positional information means that wavelets represent a mixed spatial and frequency approach, where they can be simultaneously localized in both space/time and the frequency domain. Wavelets have not been widely applied to represent

plant structures, but have been used to represent a diversity of polysaccharide layer patterns in pollen cell walls (Radja *et al.*, 2019). Away from plant biology, other shapes have been modeled as well, such as the human brain (Dong *et al.*, 2009) (Fig. 3D). Apparent advantages of wavelets are dynamic resolutions of geometry and even smaller memory requirements compared to other parametric methods.

The most complex methods of geometric representation considered in this review are given by single-value functions. This concept has been developed in solid modeling (Rvachev, 1963) and computer graphics (Ricci, 1973), where it is also referred to as 'implicit surface' modeling. The main idea is to use a single continuous function to define an object geometry in 3D Euclidean space as $f(x,y,z) \geq 0$, where the object surface (called the implicit surface) is the zero set $f(x,y,z)=0$. Hence, points in space can be evaluated by a single, real-valued function to determine whether they belong to the surface or object volume. Implicit surface methods have been used to represent plant structures, such as trees (Galbraith *et al.*, 2004) (Fig. 3E), or cell shapes in the leaf epidermis (Sapala *et al.*, 2018).

In summary, of the representations that we have discussed, the lattice-based methods are the most verbose, followed by piecewise functions, and single functions (Fig. 1). With respect to complexity, the sequence of methods of geometric representations is reversed. Generally, the more complex a method, the better is the resulting approximation of shape (Fig. 4). Theoretically, implicit surface methods seem to provide the best accuracy of approximation but, in practice, finding single, global functions is costly. Therefore, the best trade-off between performance and accuracy is provided by parametric piecewise functions, which are currently the most common representation of plant geometry.

Apart from the performance and accuracy trade-off, it is also useful to consider how flexible various representations
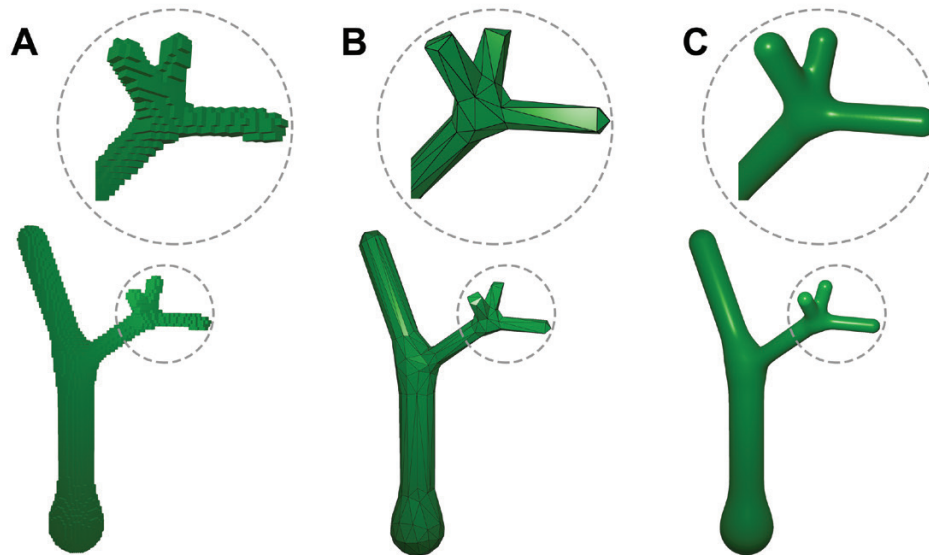
Fig. 4. Comparison of different methods of shape representation resulting in varying approximations of a simple branching structure. (A) Voxel representation, (B) linear piecewise functions, and (C) implicit surfaces (method described in Turk and O'Brien, 2005).

are in regard to changes of geometry and topology. This is important because the description of morphogenesis requires not only the representation of static plant shapes, but also their changes over time, i.e. development. Lattices by definition enforce a fixed geometry, which readily expresses growth by accretion (Coen *et al.*, 2017). However, such a fixed geometry cannot account for changes in shape arising due to symplastic plant growth, where contacts between neighboring cells are preserved (i.e. no cell sliding). In contrast, piecewise-defined function representations allow a more efficient expression of symplastic growth by adjusting the positions of geometric objects. For example, growth can be simulated by increasing the length of existing line segments, or by addition of new line segments. The latter method can also be used to simulate cell division (Barbier de Reuille *et al.*, 2006; Besson and Dumais, 2011). However, recalculations are required if topological conflicts are introduced, for example as a result of the addition or removal of geometric objects, or by large deformations. Due to their continuous character, single-function representations have a major advantage over other representations of geometry, since they never require a recalculation of topology. In summary, plant modelers have the choice between a fixed topology presented by lattice-based methods, the hierarchical topology provided by piecewise-defined function representations, and the flexible topology given by single-function representations.

Representation of signaling

'Cell and tissue, shell and bone, leaf and flower, are so many portions of matter, and it is in obedience to the laws of physics that their particles have been moved, moulded and conformed. They are no exceptions to the rule that God always geometrizes. Their problems of form are in the first instance mathematical problems, their problems of growth are essentially physical problems, and the morphologist is, ipso facto, a student of physical science.'

D'Arcy Thompson (1860–1948)

As implied earlier, a geometric representation of plant shape alone is not sufficient to formally express hypotheses of plant morphogenesis. In this review, we consider growth as the outcome of signaling that specifies changes of form over time. Independently of their nature, signals, such as transcription factors, hormones, enzymes, and mechanical signals, can be treated identically with regard to their mathematical description. Furthermore, we describe signaling abstractly as a process of information transfer in space. Since information can be transferred between different locations, such as molecules, cells, tissues, and organs, it is crucial to accurately describe the routes of information transfer. We refer to the formal description of these routes as signal topology.

Theoretically, at this point two differing perspectives of mathematical signal description can be assumed. Either the signal is described as a continuous variable and becomes a property of space or shape (Fig. 5A) or the signal is viewed discretely as an independent object located in space (Fig. 5B). For example, the diffusion of molecules can be represented as a continuous concentration distribution over a tissue representation (Turing, 1952; Meinhardt and Gierer, 1974). Similarly, other models of mass molecule movement such as polar transport have been expressed with such a continuous approach (Mitchison, 1981). Likewise, we can express the diffusion of molecules with a set of discrete elements that possess positions and move across a model tissue (Garnett, 2010). Essentially, these two descriptions only differ in scale of abstraction, i.e. microscopic versus macroscopic view. The discrete approach models information transfer at the scale of the signal representations themselves, whereas the continuous approach models it at larger scales of structural organization of plant form (e.g. representations of cells, tissues, and organs) where the collective action of signals is treated in an averaged way. Furthermore,
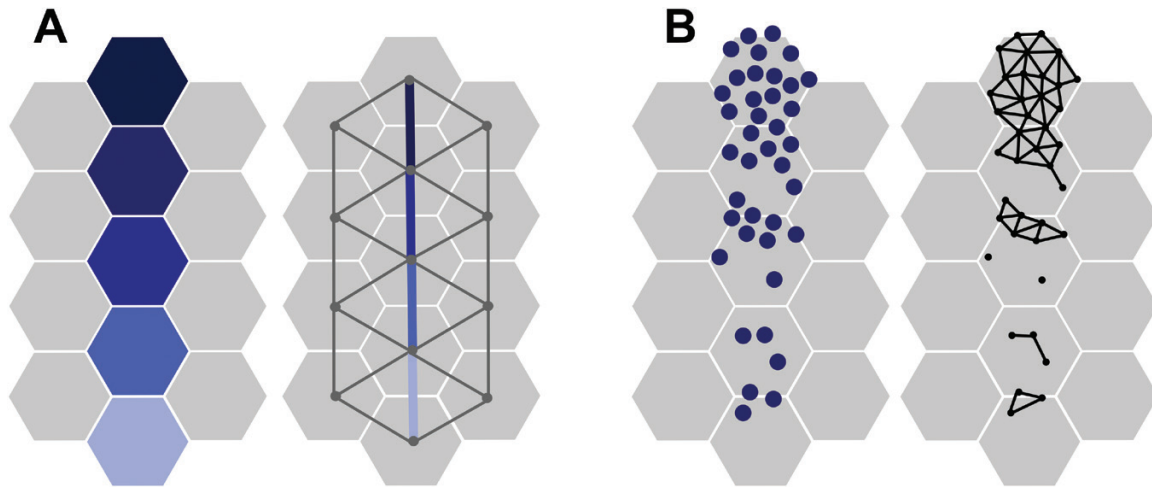
Fig. 5. Illustration of representations of signals associated with an idealized plant tissue (grey hexagons) at different scales of abstraction. (A) Continuous approach. The signal concentration is indicated by a blue color scale (left) and the signal topology is indicated by the graph (right). (B) Discrete approach. The blue disks indicate the positions of signal representations (left) and the signal topology is indicated by the graph (right).

the continuous approach allows signals to be described with mathematical functions, for example scalar value functions of the form $F(\vec{x},t)=s$, where $\vec{x}$ is a position in space, t is a measure of time, and s is a measure of the amount of a specific signal. However, in most cases, expressing relations between variables directly in the form of global functions is not possible. In this situation, the modeler can resort to approximations with, for example, differential equations and their numerical solutions such as finite difference methods.

Methods allowing the formal description of plant signaling have been developed in various research areas. By analogy to the representations of form introduced previously, we discuss these methods of signaling representation in three distinct groups, distinguished here in terms of verbosity, complexity, and flexibility (Fig. 6). The first group is again referred to as lattice-based methods, the second as off-lattice methods, and the third as continuous space methods.

Lattice-based methods

Historically, the first attempts at modeling spatial information transfer date back to Stanislaw Ulam (1962) and John Von Neumann (1966), although, similar approaches at the time had been used to describe the growth of bacterial colonies (Eden, 1961). Ulam and von Neumann introduced the notion of 'cellular automata', which has become nearly synonymous with lattice-based methods. Originally developed to model fluid dynamics and self-replication, it was quickly applied to modeling morphogenesis, such as growing branching structures. Signal topology is given by 2D or 3D lattices, consisting of indexed cells (Fig. 7). Each cell can be in a number of different states that are defined by natural or real numbers. A cell state can either represent a discrete or continuous signal. Individual cells may interact locally with their neighboring cells, which can change their states. The local interactions are determined by transition functions dependent on the current state of the cell and its neighbors (Fig. 7A). The transition function usually takes the form of relatively simple update rules of the kind 'if neighbor
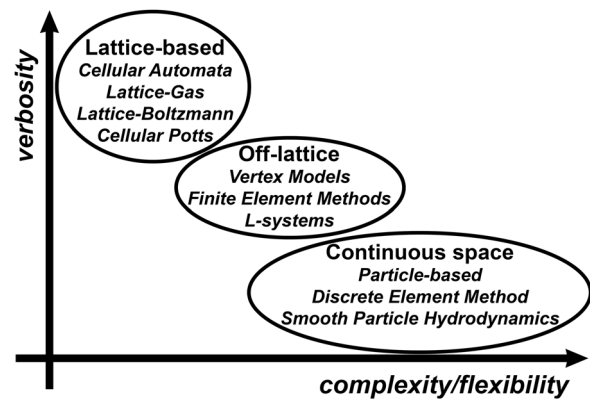

Fig. 6. Three categories of signaling representations distinguished by verbosity, complexity, and flexibility.

x state is y then change state to z'. All cells change their states synchronously throughout the simulation, and hence express the concept of spatial information transfer. Cellular automata have been applied to a broad range of physical, chemical, and biological systems (Hwang *et al.*, 2009).

In cases where the update rules are chosen due to probabilistic distributions, a cellular automaton is called stochastic; examples are Lattice-Gas and Lattice-Boltzmann models (Fig. 7B, C). These formalisms have been used to study signal interactions and transport in biological systems, such as tumor growth (Hatzikirou *et al.*, 2010) and brain aneurysms (Chopard *et al.*, 2010). However, no applications to plant biology have emerged to date. The Lattice-Gas models are designed to better express discrete signals compared to regular cellular automata. They allow more than one state to be stored in a cell, thus representing multiple discrete signal representations at one location and provide separate update rules to express signal propagation throughout the lattice (Fig. 7B). In contrast, Lattice-Boltzmann models better express the continuous representation of signals. Each lattice cell is associated with local, continuous distribution functions that are used to express an averaged, collective motion of signals (Fig. 7C). They have also been applied to express reaction–diffusion systems
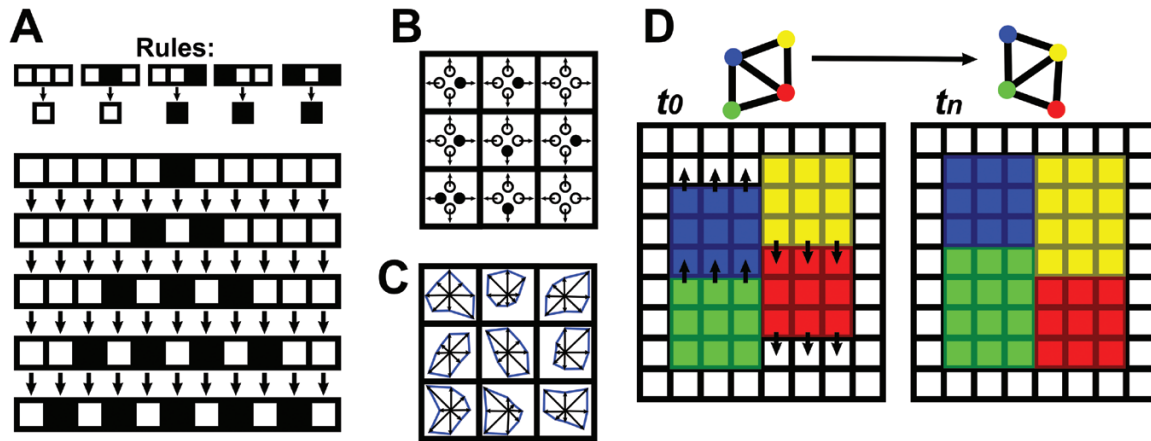
Fig. 7. Illustrations of Lattice-based methods for signaling representation. (A) Four simulation steps of a cellular automaton using a 1D grid. A state (white or black) is defined for each grid cell. One of five different transition rules is selected in each step. (B) Lattice-Gas method using a 2D grid, where a maximum of four discrete signal representations (agents) can be contained per grid cell. Black dots indicate cell locations occupied by an agent, white dots indicate empty locations. (C) Lattice-Boltzmann method using a 2D grid. Cell states are defined by continuous distribution functions (blue lines) that describe the bulk motion of signals. (D) Two time-steps (t_0, t_n) of a Cellular Potts method using a 2D grid. The cells shaded by the four colors form regions (t_0); region areas can increase or remain the same (t_n). The graphs at the top indicate the change of region topology.

(Ponce Dawson *et al.*, 1993). In the context of plant biology, both Lattice-Gas and Lattice-Boltzmann methods could be used to model the long-distance transport of biochemical signals, for example via the vascular system.

Another extension of cellular automata is provided by Cellular Potts models (Graner and Glazier, 1992; Merks and Glazier, 2005). Lattice cells are labeled and, together with other cells of the same label, define regions that can be used to represent biological cells, for example (Fig. 7D). Dynamics of regions are defined by a number of conditions, such as preferred perimeter or tension, which are encapsulated by global functions, i.e. Hamiltonian energy functions. A new state of individual cells in each simulation step is selected from a number of random states and indicated by the global function. We thus have local interactions among individual cells as well as regional interactions determining the shape of regions (Marée *et al.*, 2007). Consequently, the neighborhood of regions may change over time, meaning that signal topology can be considered to be dynamic at the scale of regions but fixed at the scale of cells (Fig. 7D). Cellular Potts models have been used in 2D representations of growing Arabidopsis roots, where cell growth and divisions are driven by turgor pressure and auxin (Grieneisen *et al.*, 2007). Specifically, the root cells are modeled as regions on a lattice that describes both the cell walls and the cell interiors. Root cell growth is a consequence of the movement of lattice cells driven by the difference of cell area and target area (interpreted as turgor pressure), which in turn is regulated by auxin concentration. The main disadvantage of current Cellular-Potts models in the context of plant morphogenesis is that cells can slide relative to each other, making the simulation of symplastic cell growth challenging.

Off-lattice methods

Signal topologies can be expressed with formal grammars, which are constituted by an alphabet of symbols, a set of rewriting rules, and an axiom (initial string of symbols). In biological modeling, formal grammars have been mainly used in the form of L-Systems. They were introduced by Aristid Lindenmayer (1968) to capture the growth of simple non-branching filaments of cyano-bacteria. They have subsequently been extended and adapted to branching structures such as neurons, human lungs, and plant shoots (Prusinkiewicz and Lindenmayer, 1990). L-systems extend the notion of strings of symbols to more complex data structures that have a state (modules) given by numerical parameters representing, for example, hormone concentrations. They employ synchronous replacement of modules according to replacement rules called production rules (Fig. 8A). In their most basic form, L-systems allow for communication via a lineage, meaning that rules are selected considering only the current state of a module (context-free L-systems). These L-systems can be useful when information is transferred via a cell lineage, for example, in case of genetic information (Prusinkiewicz *et al.*, 1988). However, the state of a module may also depend on the interactions with neighboring modules (context-sensitive L-systems) that represent, for example, morphogen diffusion between cells. Growth simulations based on L-systems have been applied to study patterns of shoot branching in relation to polar auxin transport in Arabidopsis and in *Physcomitrella* (Prusinkiewicz *et al.*, 2009; Coudert *et al.*, 2015). In these models, modules of L-Systems have usually only a left and right neighbor, meaning that signal topology is one-dimensional. An extension of the concept of L-Systems to express signal topologies of higher than one dimension has been proposed in the form of Map L-systems (Lindenmayer and Rozenberg, 1978) or MGS (Giavitto and Michel, 2001). Although L-systems represent module topology not geometry, the modules can be interpreted geometrically and visualized using computer graphics techniques. L-Systems have been used for the simulation of development of whole plants (Allen *et al.*, 2005; Mündermann *et al.*, 2005; Palubicki *et al.*, 2009) and plant organs, such as shoots (Prusinkiewicz *et al.*, 2007). In the latter case, different shoot architectures were obtained by the implementation of growth that was dependent on environmental
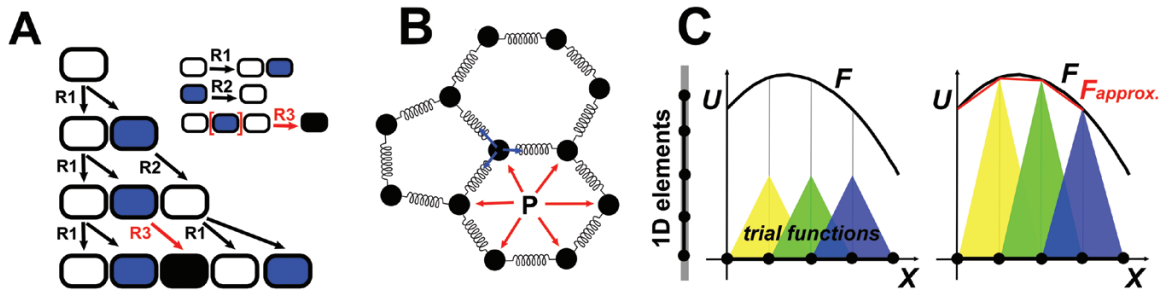
Fig. 8. Illustrations of Off-lattice methods for signaling representation. (A) L-Systems shown for three simulation steps. Different rules (R1–R3) are applied to an initial module, and the module states are indicated by the different colors. R1, R2 indicate context-free rules, whilst R3 a context-sensitive rule. (B) Mass–Spring model of a plant tissue with turgor pressure (P) and tensile stress (arrows). (C) Approximation process in the Finite Element method. A global non-linear function *F* (black line) defined over a 1D geometric domain is approximated by piecewise linear functions (red line, *F*approx.) with trial functions (triangles).

and exogenous factors. In the case of shoot branching in *Physcomitrella* (Coudert *et al.*, 2015), L-System modules were used to represent metamers and meristems of leafy shoots while also storing information about local auxin concentrations. Here, auxin was modeled as a continuous signal. The modules of the L-System were replaced by production rules that were selected based on their auxin concentrations, thus leading to the development of plausible shoot architectures. Signal topology is in this case identical to shape topology (connectivity between metamers and meristems), showing that L-Systems can be applied to model both signaling and shoot growth.

In contrast to L-Systems, Vertex models use explicit geometry, often defined by piecewise functions, to represent signaling. Vertex models have been used for a range of morphogenetic patterns, in particular for modeling the growth of epithelial cells (Fletcher *et al.*, 2014). In biomechanics and computer graphics they are also known as mass–spring models, Gaussian network models, or cell-systems, and among other things have been applied to represent the growth of plant tissues as a result of mechanical interactions of cells, turgor pressure, and mechanical properties of cell walls (de Boer *et al.*, 1992; Hamant *et al.*, 2008; Corson *et al.*, 2009; Merks *et al.*, 2011). Biomechanics of tissue can be modeled by elastic or viscoelastic springs that connect individual vertices and form polygons that represent cells (Dupuy *et al.*, 2008). The turgor pressure of cells generates forces that are exerted on the vertices and that impose a tensile stress on the springs (Fig. 8B). Growth can be implemented locally or globally by increasing spring lengths or by adding new springs. The change of spring length can be controlled chemically (e.g. by hormones, enzymes) or mechanically (by Young's modulus, Poisson ratio). Vertex models are commonly used for growth representations of the shoot apex (e.g. Hamant *et al.*, 2008; Uyttewaal *et al.*, 2012). For example, anisotropic growth is expressed by geometrically projecting cell wall directions onto a vector representing averaged microtubule orientations (Hamant *et al.*, 2008). The more parallel the cell wall directions are to the average microtubule orientation, the stiffer the spring constant values are set during growth simulation. This results in a differentiated distribution of spring constant values for cell walls, leading to the emergence of anisotropic cell growth.

Mass–spring models represent biomechanics discretely via a number of virtual springs. Alternatively, continuous approaches

of modeling mechanics using piecewise function representations of geometry also exist. When the plant structure is geometrically relatively simple, finite difference methods can be used to approximate differential equations. For example, the signaling dynamics of morphogens on idealized geometries of plant form have been expressed in this way (Smith *et al.*, 2006; Wabnik *et al.*, 2010; Abley *et al.*, 2013). However, when we assume plant shape to be complex, finite difference methods cease to easily approximate the continuous differential equations. For these more complex cases, Finite Element Methods (FEMs) can be used (Courant, 1994). These methods have seen success in material sciences as a means to analyse mechanical properties of structures. In plant biology, they were first applied to development in algae (Niklas, 1977) and to pollen tube growth Bolduc *et al.*, 2006. FEMs have subsequently been employed to describe the biomechanics of plant cells and tissues (Routier-Kierzkowska *et al.*, 2012; Fozard *et al.*, 2013; Bassel *et al.*, 2014; Majda *et al.*, 2017; Mosca *et al.*, 2017; Sapala *et al.*, 2018). Tissue is usually represented as a viscoelastic material where lower-scale information, such as cells, is treated homogenously and averaged out. The main idea behind the FEM is to numerically approximate differential equations with piecewise linear (trial) functions defined in space (Fig. 8C). More precisely, FEMs are a way to approximate global functions with systems of linear equations that can be solved numerically in efficient ways. The trial functions are defined on the vertices of geometric elements (called finite elements) that represent the shape, and are usually triangular for 2D and tetrahedral for 3D representations (see Fig. 8C for an illustration of a 1D element). However, many other element definitions are possible, including higher-order polynomial ones. The minimization of the error of the global function approximation depends on the geometry of the elements. Generally, smaller element sizes will result in more accurate approximations. This can be taken into account when constructing geometric representations of dynamic plant shape.

Growth as the result of biological mechanisms can be represented mathematically with growth tensors (Hejnowicz and Romberger, 1984; Coen *et al.*, 2004; Nakielski, 2008). Approaches have been proposed that express mechanical constraints based on FEMs in 3D together with growth tensors that result from spatially represented morphogen action. For example, such models have been applied to simulate various

patterns of phyllotaxy in Arabidopsis, the development of snapdragon flowers (Kennaway *et al.*, 2011), and growth in Arabidopsis leaves (Kuchen *et al.*, 2012). Furthermore, FEMs have been used to simulate cell growth during morphogenesis of the shoot apex and flower meristem (Boudon *et al.*, 2015). In this model, growth is expressed in terms of geometric transformation matrices. Specifically, the model divides growth into an elastic and a plastic deformation expressed as strain and growth tensors. This continuous model of cell growth is discretized using FEMs in the following way. At each cell–wall junction, nodes are placed that define triangular finite elements. The geometric transformations are performed on the finite elements, thus leading to symplastic growth. Anisotropy is introduced when the elastic strain tensor is constructed with differing values of Young's modulus. Mechanical properties of cell walls are expressed by a rigidity tensor. In this way, both the effects of biochemical and biomechanical signaling can be taken into account in a single transformation matrix.

Continuous space methods

In the least-verbose case of representing signal topology we would not store any topological information in data structures at all, but instead retrieve it in continuous space on demand. This is especially desirable when representing signals in a discrete way. Such an approach is used in a variety of methods, namely Agent- or Particle-based, Discrete Element, or Smoothed Particle Hydrodynamics.

Particles are defined by at least a position in space, but often also have a velocity and other attributes such as mass or geometry (Fig. 9A, B). Different distance metrics are defined to determine the local neighborhood of a particle (e.g. L2-norm, or Manhattan distance). Interactions between particles take the form of simple probabilistic or deterministic rules. These local interactions at particle scale can generate complex patterns at higher scales of organization (Macal and North, 2017). Particle-based methods were explored very early on in computational biology to study the growth of branching structures (Cohen, 1967). In plant biology, they have been used to describe microtubule patterns (Deinum *et al.*, 2017; Chakrabortty *et al.*, 2018; Mirabet *et al.*, 2018) and auxin transport (Garnett, 2010). Mirabet *et al.* (2018) represented microtubules as sets of

line segments in 3D space. In their model, microtubules can grow or shrink due to the addition or removal of line segments, interact with each other or with the cell surface, and respond to external signals. Particle methods have also been used to represent cells (Jönsson *et al.*, 2006), as well as branch segments (Pirk *et al.*, 2017), and architectural units of trees (Makowski *et al.*, 2019). They are currently used in a wide range of applications (Holcombe *et al.*, 2012) but seem to be less common in plant growth modeling.

Discrete Element Methods (DEMs) are a special case of the Particle-based method and emerged from material sciences to represent layers of different materials that can undergo significant deformations in time (Guo and Curtis, 2015). Such dynamic cases are often computationally too costly to represent with other approaches, for example with finite element methods. The main concept of DEMs is to represent particles as simple geometric objects such as spheres (elements) in space on which a number of idealized forces can act. In many cases this involves repulsion, spring, adhesion and dampening forces (Fig. 9C) (Van Liedekerke *et al.*, 2015). Positions and possibly orientations of elements are adjusted by mathematically integrating the resultant external forces. In practice, DEMs are known for having problems in representing the mechanics of very stiff materials due to the non-rigid connectivity specified by spring forces between elements. In the case of representing cells with particles, this can lead to unrealistic cell rearrangements that do not occur during symplastic plant growth. Despite these problems, they have been successfully employed in computational biology in recent years to represent the mechanics of tissues at the cellular and subcellular scale (Gardiner *et al.*, 2015; Diels *et al.*, 2016). Simple DEM models have been used to simulate growing shoot apices, where individual cells are represented by spheres constrained by hemi-spherical surfaces and the mechanical interactions occur based on repulsive forces between cell centers (Jönsson *et al.*, 2006). Gruel *et al.* (2016) extended this method by including the continuous diffusion of gene products or hormones. The dynamics of these molecules were defined for individual cells represented by geometric spheres.

A slightly more complex method compared to other particle-based ones is Smoothed Particle Hydrodynamics (SPH), which is a representation for fluid motion that is used, for example, in computer graphics and fluid dynamics. As is the case for
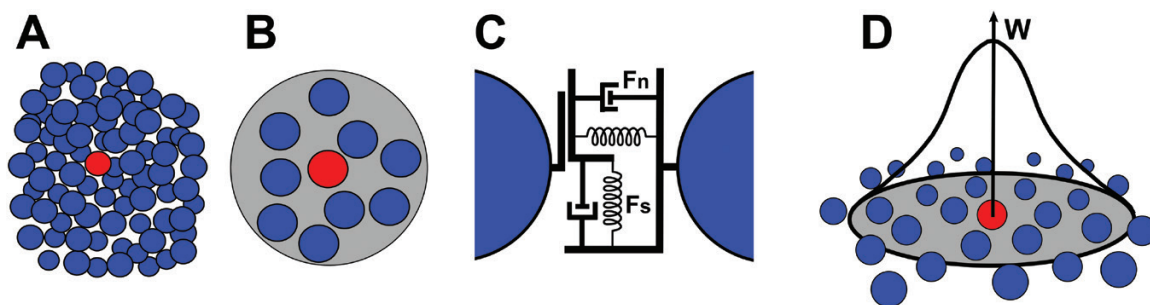

Fig. 9. Illustrations of continuous space methods for signaling representation. (A) Particle-based method, with blue and red circles representing signals. (B) Signal topology is calculated locally for individual particles (red) using distance metrics (grey disk). (C) Discrete element method, with mechanical forces between particles: spring and damping forces account for the viscoelastic behavior. F_n, normal forces; F_s, shear forces. (D) Smooth particle hydrodynamics. A local neighborhood of a particle (red) is defined by a distance metric (grey disk) over which interaction properties are smoothed by a kernel function (W).

other particle-based methods, the SPH method represents signals discretely with particles. The main distinction of SPH compared to other methods operating in continuous space is that particle interactions are expressed with local interpolation or kernel functions, such as Gaussian functions. These kernel functions allow particle interactions to be formulated relative to their distances from each other (Fig. 9D). Far-away particles, for example, can interact more weakly with each other than closer ones, resulting in a phenomenon called 'smoothing length'. To efficiently utilize SPH methods, the size of the radii of kernel functions is usually varied in space and time so that the resolution of the simulation can adapt itself to the local density of particles. This strikes a good balance between accuracy and performance. Examples where such methods have been employed in computational biology include simulations of the mechanics of plant and animal cells (Van Liedekerke *et al.*, 2010).

In summary, analogously to the shape representations described earlier, we can distinguish characteristics of signal representations in terms of their verbosity and complexity (Fig. 6). Thus, Lattice-based methods are the most verbose but least complex representations, followed by Off-Lattice methods where the connectivity between signal representations is explicit but not fixed in space. On the other hand, methods that rely on continuous space seem to be the most complex, because in this case topology is determined on demand. Theoretically, determining the local signal topology for one particle has to take into consideration all the other particles, which results in a quadratic time complexity. This constitutes a demand in calculation time that prevents most simulations from being computable in real time. Therefore, the computational implementation of continuous space methods is usually coupled with spatial partitioning (e.g. lattices) to exclude evaluations of distant particles, which improves performance significantly but makes the representation more verbose.

Another relevant aspect for modeling morphogenesis is the flexibility of the representations in accommodating topological changes. This may be less of an issue when modeling phenomena without significant changes in signal topology, but can be important in other cases. For example, the simulation of wound healing in response to grafting or tearing of tissue requires dynamic changes of topology to generate adequate approximations. In this regard, to accommodate such topological changes the three categories of methods can be treated similarly to their geometric counterparts: lattice-based methods are the least flexible description as they are defined by an explicit, temporally fixed topology; off-lattice methods represent signal topology explicitly, but the topology needs not be fixed in time; and continuous space methods are the most flexible, as signal topology is defined implicitly by providing local distance functions for this purpose.

Discussion

We shall refrain from exhaustively analysing all these methods and conclude this review by pointing out that the signal and shape representations discussed here are by no means exclusive.

They can be readily used in conjunction with each other to jointly describe biological growth. Fr example, Mkrtchyan *et al.* (2014) proposed a description of the epithelium that combines both a particle-based and vertex model. In this description, cell membranes were represented as mass–spring systems whilst advection of entire cells was described using a particle-based method. In plant biology, the simulation of large deformations in tissues has been accomplished by a mass–spring model representing individual cells whilst macroscopic tissue properties are represented by a finite element method (Ghysels *et al.*, 2009). Generally, a multi-scale model such as this allows specific signal representations to be expressed with different topologies and therefore may reflect underlying biological hypotheses more efficiently. Formalisms specifically prepared for such multi-scale descriptions of plant morphogenesis have been developed in recent years (Boudon *et al.*, 2015; Refahi *et al.*, 2016). It seems to us that determining appropriate scales of abstraction to express shape and signal topologies should generally precede quantitative descriptions of signal action when formulating models of morphogenesis.

Finding adequate scales of abstraction for a particular description of plant growth may not be immediately obvious. Generally, the discrete approach is arguably the more intuitive one, as humans tend to describe the world in rather discrete terms. Specifically, the use of simple rules that characterize signal action in the discrete approach is often a distinct advantage. Over a given time period, it usually allows a greater number of different biological hypotheses to be expressed compared to the continuous approach, which operates at a higher level of abstraction. For example, the difference between a model where two signals either inhibit or promote each other can usually be expressed by only changing a single interaction rule in the discrete approach. This can often be accomplished even during the simulation time, enabling immediate evaluation by the modeler. This advantage lends itself very well to studying patterns characterized by a high degree of self-organization (Deinum *et al.*, 2017). The mathematical description of a large number of discrete elements, however, can become complex. Furthermore, higher-scale patterns arising due to local interactions between elements can be difficult to comprehend due to the lack of efficient analytical tools.

On the other hand, the continuous approach allows signaling with functions to be described. Thus, relations between variables are expressed in a very parsimonious way. Continuous representations of patterning processes also lend themselves well to mathematical analysis. Examples of succinct biological relations elucidated by formal analysis can be found in the description of pollen tube growth, where cell radius is described as a function of turgor pressure and the secretion rate of the cell wall material (Campàs and Mahadevan, 2009), or in branch curvature in plants in terms of graviceptive and proprioceptive sensitivities (Bastien *et al.*, 2013). While the representation of biological pattern formation with continuous functions can lead to insightful biological laws, their formulation is by no means a trivial task. Theoretical biology seems to be less successful in this regard compared to other areas of research, for example physics where very accurate laws of nature have been formulated.

Reflecting on the relative merits and drawbacks of the discrete and continuous methods of representation of signaling leads us to conclude this review with a bold prediction. In light of the lack of simple, abstract laws of morphogenesis that unify biomechanical and biochemical signal action, we believe that the advantage provided by the discrete signal representation method of being able to quickly evaluate different biological hypotheses will see a gradual shift towards this approach. Consequently, we predict that particle-based methods, currently used to a lesser degree compared to other methods within the theoretical plant research community, will see an increase in popularity in the future.

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