Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Plant Biology

Heterogeneity and its multiscale integration in plant morphogenesis

Léo Serra, Nicolas Arnaud, Faïçal Selka, Catherine Rechenmann, Philippe Andrey and Patrick Laufs

Heterogeneity is observed at all levels in living organisms, but its role during the development of an individual is not well understood. Heterogeneity has either to be limited to ensure robust development or can be an actor of the biological processes leading to reproducible development. Here we review the sources of heterogeneity in plants, stress the interplay between noise in elementary processes and regulated biological mechanisms, and highlight how heterogeneity is integrated at multiple scales during plant morphogenesis.

Address
Institut Jean-Pierre Bourgin, INRA, AgroParisTech, CNRS, Université Paris-Saclay, 78000 Versailles, France

Corresponding author: Laufs, Patrick (patrick.laufs@inra.fr)

Current Opinion in Plant Biology 2018, **46**:18–24

This review comes from a themed issue on **Cell biology**

Edited by **Ram Dixit** and **Elizabeth Haswell**

https://doi.org/10.1016/j.pbi.2018.07.001

Introduction

Heterogeneity$^{\gamma}$ ($^{\gamma}$=see definition in glossary in Box 1) is an inherent feature of all living organisms. It is observed at all organization levels and contributes to the function of higher-level structures: diverse molecules interact to form specialized sub-cellular structures that together build cells which, in multicellular organisms, can acquire different identities and form complex organs. Recently, another type of heterogeneity within specific structures, which could at first sight appear homogeneous, has gained attention. For instance, at the organ level, seemingly identical lateral root primordia can be formed by heterogeneous contributions of founder cells [1•]; at the tissue level, Arabidopsis leaf epidermal pavement cells are heterogeneous in size and shape [2]; and at the cellular level cortical microtubules (CMT) and cellulose synthase trajectories vary between the different sides of epidermal cells of etiolated hypocotyls [3,4].

With the expansion of quantitative approaches, the number of processes that now appear as involving heterogeneity is rapidly increasing. This raises two major questions: how is heterogeneity generated, and what are its biological consequences? In this review, we discuss some recent insights gained from reports of heterogeneity at different scales and its integration$^{\gamma}$ between different functional levels within a plant.

Subcellular processes are sources of heterogeneity

Gene expression is by nature a highly stochastic$^{\gamma}$ process [5]. At the whole plant level, gene expression shows noise$^{\gamma}$ levels that are under genetic control, but the origin (intrinsic$^{\gamma}$ or extrinsic noise$^{\gamma}$) could not be identified [6]. At the individual cell level, gene expression fluctuates over time in leaf cells, mostly as a consequence of extrinsic noise [7•] (Figure 1), as reported for prokaryotes and other eukaryotes [[7•]]. At the system level, additional levels of noise may arise from the gene regulatory network (GRN) topology. For instance, the noise in the expression of a gene coding for a transcription factor affects the expression of its downstream targets and when TFs target TF genes, noise propagates within the GRN [9]. One way to reduce this propagation relies on redundant regulations by multiple TFs that provide robustness to the transcriptional output of a gene [10,11].

Noise in gene expression can be used to generate heterogeneity in plants. For instance, a link between noise and plasticity in gene expression has been observed in Arabidopsis [12]. Noisiness of gene expression is used to drive differentiation during sepal development [13••]. Expression of the ATML1 TF in epidermal sepal cells shows a high level of noise. When ATML1 level exceeds a threshold in receptive cells in the G2 phase, it triggers endoreduplication and hence giant cell formation. This generates a loose pattern within the epidermis where the average proportion of giant cells, but not their position, is determined. This resembles the formation of retinal mosaics in Drosophila [14] or the selection of odorant receptors in mammals [15]. Relying on noise in gene expression to control cell fate when a precise pattern is not absolutely required may be more cost efficient than complex deterministic networks.

Stochasticity can also drive heterogeneity in other cellular components such as the cell wall. At the molecular level,

Box 1 Glossary

Heterogeneity is a property of a system that refers to its composite nature or to the variability of the elements that compose this system.

Integration refers to the processes/mechanisms whereby the individual characteristics and behaviors of cells are summed, leading to global growth at the tissue or organ scale.

Noise refers to the random variations in a biological process. For instance, gene expression level can fluctuate over time in a single cell (*intrinsic noise*), or vary between genetically identical cells growing in a homogenous environment (*extrinsic noise*). Noise can be measured by the coefficient of variation, the dimensionless ratio of the standard deviation over the mean.

Intrinsic noise is directly related to the stochasticity of the molecular interactions driving a biological process and occurs without variations in the number of molecules. It differentially affects biological processes of the same kind within a given cell.

Extrinsic noise results from variations in the amount or activity of molecules that drive a biological process. Such variations can be observed between individual cells and affect similarly all the biological processes of the same kind occurring in a cell.

Robustness is an inherent property of a system that provides invariable output in response to input variations or heterogeneity.

Stochasticity refers to a random biological process that cannot be accurately predicted as it is governed by probabilistic laws. Stochasticity is observed in chemical reactions involving multiple partners present at low numbers leading to infrequent interactions.

while overall occurrence of the different monomers in lignin polymers is genetically and developmentally controlled, their precise polymerization pattern in the cell wall appears stochastic, leading to a high diversity of structures [16,17]. At a larger scale, cell walls are also heterogeneous, as a result of biologically regulated processes. In the epidermis of dark-grown Arabidopsis hypocotyls, specific loosening of the longitudinal anticlinal cell walls triggers anisotropic cell expansion. It is only in the latter step that CMT arrays and associated cellulose deposition switch to a preferentially transverse orientation to consolidate anisotropic growth [18]. The formation of lobes in Arabidopsis leaf epidermal pavement cells involves heterogeneity not only along but also across the cell wall [19••]. In both cases, spatial heterogeneity in the mechanical properties of the cell wall was attributed to heterogeneous distribution of pectins with different chemical properties, which suggests that pectins offer a more versatile way of tuning cell wall mechanical properties than other components such as cellulose microfibrils. These examples illustrate how chemical heterogeneity leads to mechanical heterogeneity, which in turn drives growth anisotropy.

Heterogeneity is also observed in the cell membrane system at multiple scales. Within the plasma membrane, the importance of polar distribution of proteins for patterning processes and physiology has been well demonstrated [20,21]. At the scale of the entire membrane system, rare phospholipids, the phosphatidylinositol-phosphates (PIPs), are heterogeneously distributed, with the amount of phosphatidylinositol 4-phosphate (PI4P) increasing from the Golgi apparatus to the endosomal compartments to reach a maximum at the plasma membrane [22–24]. The local accumulation of this anionic lipid in the inner layer of the plasma membrane provides negative membrane surface charges, which establish a specific electrostatic identity and direct the plasma membrane localization of proteins such as PINOID or BRI1 KINASE INHIBITOR1 involved in hormone signaling [23,25••]. In animal cells, interaction between cationic residues of membrane protein and PIPs promotes the formation of nanodomains within the membrane [26,27], a mechanism also occurring in plants as the localization of the REMORIN proteins into nanodomains requires PI4P [28••]. This example illustrates the interaction between stochastic physical mechanisms and regulation by biological processes in the generation of heterogeneity at the cellular level.

Cell growth and division are heterogeneous processes

Heterogeneity in cellular patterns progressively appears during the formation of most organs: for instance, in both the developing embryo or in the lateral root primordium, growth and division patterns are initially stereotypical but become later more variable while preserving a stereotypical organ shape and size [1•,29,30]. This suggests that fundamental cellular processes such as division and growth generate heterogeneity in the cellular patterns during development. In the shoot apical meristem (SAM), in which cell size is rather uniform, cell division timing and cell growth are coordinated at the individual cell level by a size-dependent accumulation of cyclin-dependent kinase activity that controls cell cycle progression [31,32••]. Cell division can be described according to a complex rule intermediate between critical size and critical size increment models [33••]. In addition, precision in the orientation of the division plane is controlled by a particular CMT structure, the preprophase band [34••]. Despite these regulatory systems, cell size just after division is variable due to unequal division [32••]. Cell division is an important source of heterogeneity, not only because daughter cells can have unequal sizes but also because of the unequal partitioning of molecules that may increase noise in biological processes such as gene expression [35]. Following an asymmetrical division, the smallest daughter cell grows at a faster rate than the largest one, thus partially compensating for the original difference in size [33••]. A similar observation was made at a larger scale in the sepal, in which smaller epidermal cell lineages grow faster to catch up with larger cell lineages resulting in a homogenization of cell size [36•]. However, at later stages, differences in clone sizes are further amplified by growth. This indicates that mechanisms that integrate cell growth and cell division are acting at the multicellular or organ levels and that they are subjected to developmental regulations. However,