

FOCUSED REVIEW

A space for time. Exploring temporal regulation of plant development across spatial scales

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SUMMARY

Plants continuously undergo change during their life cycle, experiencing dramatic phase transitions altering plant form, and regulating the assignment and progression of cell fates. The relative timing of developmental events is tightly controlled and involves integration of environmental, spatial, and relative age-related signals and actors. While plant phase transitions have been studied extensively and many of their regulators have been described, less is known about temporal regulation on a smaller, cell-level scale. Here, using examples from both plant and animal systems, we outline time-dependent changes. Looking at systemic scale changes, we discuss the timing of germination, juvenile-to-adult transition, flowering, and senescence, together with regeneration timing. Switching to temporal regulation on a cellular level, we discuss several instances from the animal field in which temporal control has been examined extensively at this scale. Then, we switch back to plants and summarize examples where plant cell-level changes are temporally regulated. As time cannot easily be separated from signaling derived from the environment and tissue context, we next discuss factors that have been implicated in controlling the timing of developmental events, reviewing temperature, photoperiod, nutrient availability, as well as tissue context and mechanical cues on the cellular scale. Afterwards, we provide an overview of mechanisms that have been shown or implicated in the temporal control of development, considering metabolism, division control, mobile signals, epigenetic regulation, and the action of transcription factors. Lastly, we look at remaining questions for the future study of developmental timing in plants and how recent technical advancement can enable these efforts.

Keywords: cell identity regulation, development, Phase transition, temporal regulation, timing.

INTRODUCTION

Time is generally associated with change, as Aristotle stated “if nothing changes, there is no time.” This review focuses on how timing is regulated in plant development. While not exhaustive, we aim to provide an overview of currently known examples and mechanisms involved in the temporal control of plant development at various spatial scales. Several excellent recent reviews have previously focused on developmental timing in plants (Coen & Prusinkiewicz, 2024; Swift et al., 2022). In this review, we look mainly at examples and mechanisms of temporal regulation of development in *Arabidopsis thaliana*. We examine questions such as: when are mechanisms in play that slow down or speed up developmental transitions and how do these mechanisms regulate developmental timing?

A first major challenge is defining temporal regulation in the context of development. Temporal control can be imagined as a clock, measuring regular oscillations, or an hourglass, measuring a change in a level until a threshold is reached (Johnson & Day, 2000). Here we mostly focus on the hourglass view, looking less at absolute time and circadian rhythms and instead focusing on the relative timing of developmental events. In plant development, temporal information is often intermingled with spatial and environmental signals; as a result, questions of developmental timing are tightly linked to these factors.

A second challenge is capturing the different scales at which temporal regulation exists. Temporal and environmental signals come together to regulate major phase transitions such as germination and flowering at a systemic

level. In addition, recent findings have found that temporal regulation also exists on the scale of a single-cell type or cell identity. In this review, we will look at mechanisms that act not only on a systemic level, including plant phase transitions, but also at a local, cell environment level.

When we consider the cell and the local scale, we encounter our third challenge: How is a cell's identity defined? When discussing cell identity and fate, we will use terminology similar to that used in Rusnak et al. (2024), where *cell fate* is defined by the ultimate end point of the cell's lineage and *cell identity* changes on the way there. A cell's fate or identity is classically determined by looking at its morphology, location, and function. However, plant cell fate can be flexible and local changes can change their trajectory (Rusnak et al., 2024; Ryu et al., 2021). For example, if leaf epidermal cells undergo abnormal periclinal divisions, inner cells can gain mesophyll fate; furthermore, genetic ablation of root endodermal cells can trigger neighboring pericycle cells to re-enter the cell cycle to contribute to the loss of ablated cells (Gehrke et al., 2023; Marhavý et al., 2016). In addition to morphology, location, and function, marker lines and transcriptome analyses can help define cell identity. Technological advances such as single-cell or nucleus approaches and multiplexed *in situ* hybridization help increase the fidelity with which specific cell identities can be defined (Adema et al., 2024; Nobori et al., 2023; Oliva & Lister, 2023). These advances also highlight the identity heterogeneity within a cell type and the challenges in capturing all aspects of a cell's "identity." In addition, these new features can help to identify transition points between different cell identity stages and confirm the existence of mixed cell identities (Shahan et al., 2022). Here we consider the regulation of cell identity and how identity changes or progression are controlled in time.

In this review, we start by outlining *when* the timing of developmental transitions is regulated. We start with the systemic or global level: describing transitions that involve whole organs or plants. Next, we look at examples of local temporal regulation in animal development, where these processes have been studied more extensively. Then we switch back to plant development to discuss similar local level temporal regulation. Next, instances of *what* factors influence timing are considered, including different systemic and local environmental factors in plants that weigh into determining when transitions take place. Afterwards, we outline *how* temporal control is enacted, considering diverse mechanisms. Finally, we summarize some remaining questions surrounding timing in plant development events and highlight recent technological advances that can contribute to answering these questions. Since our review spans and connects several complex fields, we lack the space to provide extensive background for each field or topic. We therefore refer to excellent in-depth

reviews in the respective field of study indicated with an asterisk (*).

WHEN: EXAMPLES OF TEMPORAL REGULATION

During the plant's life, its requirements and functionalities change, and it generates dedicated organs and cell types to match these, undergoing large phase transitions as well as more subtle regulatory changes. Historically, temporal control of plant development has primarily been studied at a systemic level. Here, we start by outlining some examples of this systemic level temporal control before discussing examples of temporal control at a local level in both animal and plant systems.

Plant phase transitions: temporal regulation on a systemic level

Phase transitions mark crucial changes in the plant's body plan, drastically changing its growth and development; as a result, their timing is tightly regulated (Figure 1).

Following seed maturation, seeds initially are dormant until germination is triggered. After ripening, stratification, light, and nitrate all promote germination, with the exact timing of germination depending on the relative strengths of dormancy promoting and breaking factors (Bentsink & Koornneef, 2008; Buijs, 2020; Finkelstein et al., 2008*). The protein DELAY OF GERMINATION (DOG1) and the hormone Absciscic Acid (ABA) accumulate during seed maturation, and help establish dormancy, with dormancy levels varying across Arabidopsis genotypes and correlating with DOG1 and ABA levels (Figure 1) (Bentsink & Koornneef, 2008; Née et al., 2017; Soppe & Bentsink, 2020). In addition, LAFL (LEAFY COTYLEDON1, LEC1, ABSCISIC ACID INSENSITIVE3, ABI3, FUSCA3, FUS3, and LEC2) Transcription factors (TFs) are major regulators of embryogenesis, seed maturation, and dormancy, with LAFL mutants having various dormancy defects, such as *abi3* seeds being viviparous and *fus3* seeds showing reduced dormancy and viability (Gazzarrini et al., 2004; Suzuki et al., 2003). Recent work has expanded on LAFLs preventing precocious germination, identifying interactions between SEED DORMANCY FOUR-LIKE 1 (SFL1) and its paralogues with LAFLs to influence the timing of dormancy breaking, potentially by affecting chromatin remodeling (Gazzarrini & Song, 2024; Zheng et al., 2022). Other studies further expanded on a role of epigenetic modifications in dormancy, finding that RELATIVE OF EARLY FLOWERING 6 (REF6)-mediated H3K27 demethylation is necessary for robust germination and that KRYPTONITE (KYP)/SU(VAR)3-9 HOMOLOG (SUVH4), a histone methyltransferase, decreases seed dormancy (Pan et al., 2023; Sajeev et al., 2024; Zheng et al., 2012).

Plants next undergo the juvenile-to-adult transition, also called the vegetative phase change, after which leaf morphology changes with adult leaves having a larger length/width ratio and a more complex, serrated shape

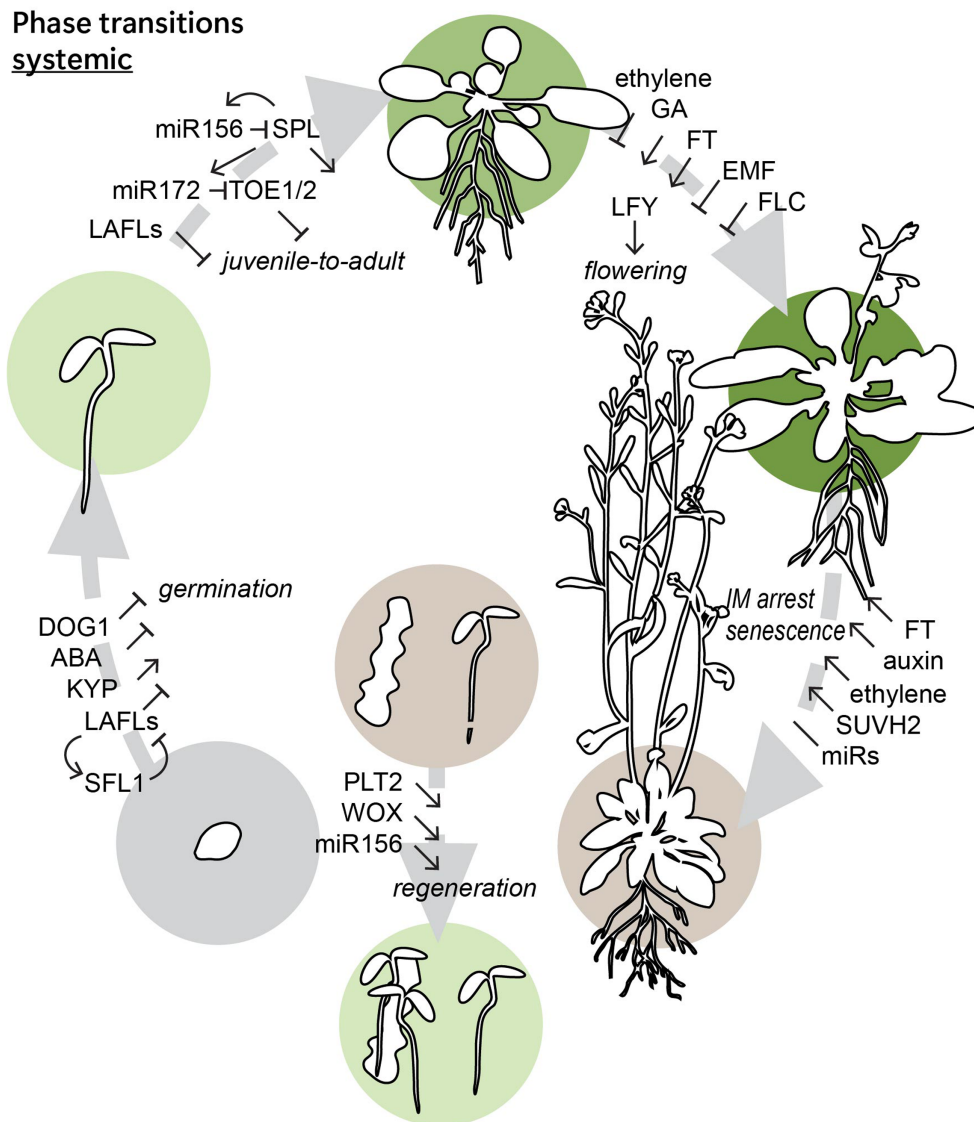


Figure 1. Major plant phase transitions and their regulators.

During plant development, the timing of systemic phase transitions (germination, the transition from juvenile to adult, flowering time, and senescence) is regulated by various factors. While not classically included in the phase transitions, upon induction or wounding, regeneration is a similar major reprogramming event which depends on temporal regulation. ABA, abscisic acid; DOG1, delay of germination; EMF, embryonic flower; FLC, flowering locus C; FT, flowering time; FUS3, FUSCA3; IM, inflorescence meristem; KYP, kryptonite; LAFLs, leafy cotyledon1 (LEC1), abscisic acid insensitive3 (ABI3), FUSCA3 (FUS3), and LEC2; LFY, leafy; PLT, plethora; REF, relative of early flowering; SFL, seed dormancy four-like; SPL, squamosa-promoter binding protein-like; SUVH, SU(VAR)3-9 homolog; TOE, target of early activation tagged; WOX, Wuschel-related homeobox.

(Poethig & Fouracre, 2024*). In *Arabidopsis* under long-day conditions, this transition occurs after it has produced about six leaves (Doody et al., 2022). On a cellular level, adult leaves have smaller cells and produce trichomes on both surfaces (Manuela & Xu, 2020). The timing of the vegetative phase change is regulated by the miR156/157-SPL pathway (SQUAMOSA-PROMOTER BINDING PROTEIN-LIKE) with miR156/157 levels decreasing over time and SPL protein levels increasing (Figure 1) (Manuela & Xu, 2020; Wu et al., 2009; Zheng et al., 2019). The expression level of

miR156/157 forms a threshold and is influenced by environmental signals, epigenetic regulators, and LAFL expression (Gao et al., 2022; He et al., 2018; Wang & Perry, 2013). In addition, LEC2 or FUS3 affects the vegetative phase change, and the loss of either results in a shorter vegetative phase as a result of either increased H3K27me3 or reduced ethylene signaling, respectively (Gao et al., 2022; Gazzarrini & Song, 2024; Lumba et al., 2012).

Next, in the transition to flowering, the morphology and function of the shoot apical meristem are changed to

form the inflorescence meristem (Freytes et al., 2021*). Under long-day conditions, this transition takes place in *Arabidopsis* after producing 9.5 leaves (Suh et al., 2003). The switch to flowering is preceded by a rapid increase in LEAFY (LFY), a pioneer TF considered the master regulator of flowering (Figure 1) (Jin et al., 2021; Weigel et al., 1992; Weigel & Nilsson, 1995). In short-day conditions, the floral transition is delayed by several weeks, with LFY expression increasing gradually over time (Blázquez et al., 1997). The timing of the floral transition and LFY expression is regulated by phytohormone (gibberellic acid, ethylene) accumulation and changes in photoperiod signaling which affect histone marks, DNA methylation, TF activity, and FLOWERING LOCUS T (FT) expression (Freytes et al., 2021; Lee et al., 2020; Weigel et al., 1992; Yamaguchi, 2021; Zhu, Chen, et al., 2020). It is crucial that flowering is not induced prematurely and several epigenetic regulators prevent early flowering. EMBRYONIC FLOWER 1 (EMF1) and EMF2 are a transcriptional repressor and a Polycomb group protein that both prevent premature flowering and *emf* mutants flower directly at germination, completely bypassing vegetative shoot growth (Sánchez et al., 2009; Yoshida et al., 2001). Continued expression of flowering repressor FLOWERING LOCUS C (FLC) ensures delayed flowering until after a cold period in winter-annual *Arabidopsis* varieties. The FLC expression is controlled by several programs including the activity of FRIGIDA (FRI), epigenetic silencing through VERNALIZATION (VRN) activity, and production of the FLC antisense RNA COOLAIR (Bastow et al., 2004; Maple et al., 2024; Swiezewski et al., 2009).

Finally, at the end of an annual plant's life cycle, it undergoes senescence (Figure 1). Various regulatory TFs, receptors, kinases/phosphatases, phytohormones, epigenetic regulators, and regulatory RNAs act together to set the timing for senescence, including termination of flowering and initiation of leaf senescence (Kim, Kim, et al., 2018). Termination of flowering is highly synchronized, and the inflorescence is arrested through the activity of FLOWERING LOCUS T (FT) at the end of a predetermined though flexible time (González-Suárez et al., 2020, 2024; Miryeganeh et al., 2018). The timing of floral termination additionally depends on auxin production in recently produced fruits (Ware et al., 2020). The exact timing of leaf senescence is controlled by the integration of ethylene signaling, which promotes senescence (Grbić & Bleeker, 1995); levels of microRNAs miR156, miR164, miR172, and miR840 (Zhang et al., 2021); expression levels of members of the NAC, WRKY, and MYB TF families (Kim, Park, et al., 2018; Woo et al., 2013); and chromatin state affected by SUVH2 levels (Ay et al., 2009). In addition, light affects the timing of senescence, with the ratio of red versus far-red light (R:FR) affecting senescence through the photoreceptor Phytochrome B (PhyB) and far-red light via Phytochrome A and the TF FAR-RED ELONGATED HYPOCOTYL3

(FHY3) (Lee et al., 2021; Sakuraba, 2021; Sakuraba et al., 2014; Tian et al., 2020).

Wounding response, regeneration, and stress-induced formation of new organs are major reprogramming events that are part of many plants' life cycle (Ikeuchi et al., 2019*; Kareem et al., 2016). The regenerative ability of the plants can be enhanced *in vitro* using different approaches. Several TFs (PLETHORA [PLT], CUP-SHAPED COTYLEDON, WUSCHEL-RELATED HOMEODOMAIN family members), epigenetic modifications, environmental signals, energy status, and mechanical signals have all been shown to modulate regeneration (Figure 1) (Chen et al., 2024; Kim, Yang, et al., 2018; Larriba et al., 2021; Lee et al., 2024; Pan et al., 2019; Serivichyaswat et al., 2022; Shanmukhan et al., 2021). Several of these factors have been shown to affect the temporal dynamics of regeneration. In the root, PLT2/BABYBOOM expression both reflects and influences the different developmental zones, and during root regeneration, it acts in a dose-dependent manner with increased levels of PLT2 slowing down the root tip re-establishment (Durgaprasad et al., 2019; Galinha et al., 2007). Shoot regenerative rate and competence from callus are correlated with the level of miR156 (Zhang et al., 2015). Finally, callus of mutants with altered chromatin accessibility develop new shoots faster (increased accessibility) or slower (decreased accessibility) when placed on shoot induction media (Li et al., 2011; Li, Zhang, et al., 2024; Liu, Zhang, et al., 2018; Shemer et al., 2015).

Altogether, the timing of plant phase transitions depends on the integration of many components, with several key players (miR156-SPL, LAFLs, FT) playing roles in multiple transitions.

Lessons from animal systems: cell identity

While the timing of plants' major phase transitions has been studied in some detail, our understanding of temporal regulation at a cell identity level is more limited. By contrast, the field of animal development has a more extensive history studying developmental timing at a cellular level. Comparing timing differences between species, investigating temporal morphogen dynamics, and the finding that the specification of certain cell identities depends on developmental timing have all resulted in a robust body of work in temporal regulation in animal development (El-Danaf et al., 2023; Patil & van Zon, 2024; Wang et al., 2021). Here we look at four examples and use these to think about scales and mechanisms through which the timing of cell development is affected.

During Axolotl (*Ambystoma mexicanum*) limb or tail regeneration, the timely remodeling of chromatin prevents premature activation of regeneration and developmental-related genes (Figure 2a). Single-cell transcriptomic studies found that differentiated fibroblast cells dedifferentiate and reactivate the embryonic program for limb development

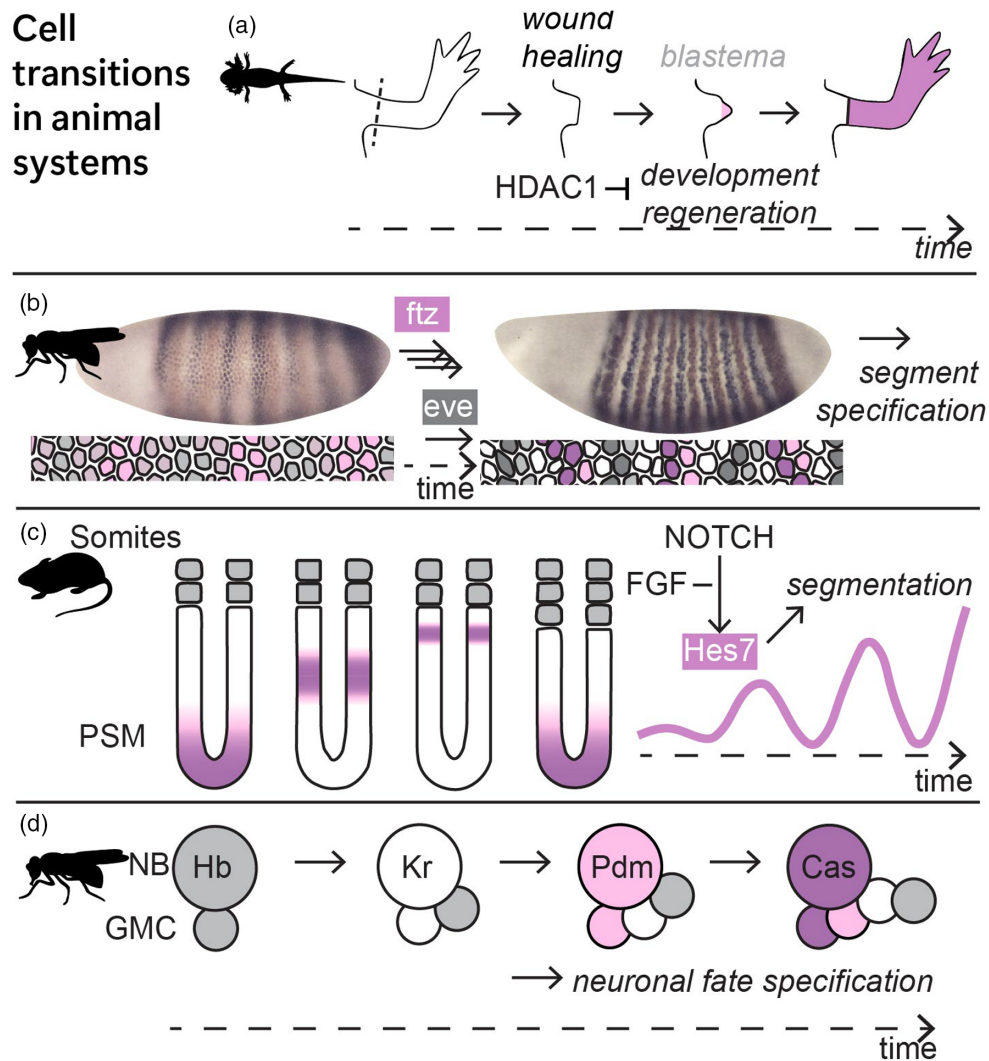


Figure 2. Cell fate transitions in animal systems and their temporal regulators.

(a) Axolotl limb regeneration.

(b) *Drosophila* larval patterning.

(c) Vertebrate presomitic mesoderm segmentation.

(d) *Drosophila* neuronal fate specification.

Cas, Castor; eve, even-skipped; FGF, fibroblast growth factor; ftz, fushi tarazu; Hb, Hunchback; HDAC, histone deacetylase; GMC, ganglion mother cell; HES7, Hes family BHLH transcription factor 7; Kr, Kruppel; lin, abnormal cell lineage protein; NB, neuroblast; Pdm1/2, POU domain protein 1 and 2; PSM, presomitic mesoderm.

(Gerber et al., 2018). Overall, cellular heterogeneity first decreases during blastema formation but increases again as the cells begin to differentiate (Gerber et al., 2018). HISTONE DEACETYLASE (HDAC) inhibiting drugs were found to prevent successful tail regeneration, and HDAC1 expression in nerve cells was shown to be crucial to the regeneration process (Voss et al., 2019; Wang et al., 2019). By unraveling transcriptomic changes during regeneration, researchers have now shown that HDAC1 activity prevents premature upregulation of developmental genes in the wound healing stage (Wang et al., 2021). Thus, here regulation of chromatin accessibility mediates temporal control over cell identity development.

During *Drosophila melanogaster* embryogenesis, the pair-rule genes *fushi tarazu* (*ftz*) and *even-skipped* (*eve*) undergo dynamic shifts in their expression before defining the edges of individual segments (Figure 2b) (Lim et al., 2018). Live imaging revealed that *ftz* stripes move faster than *eve* stripes (Lim et al., 2018). Transcription changes from short, dim bursts to longer, brighter bursts over time and depends on the activities of two enhancer elements (Birnie et al., 2023). Next, patterning of the anteroposterior axis is controlled by sequential expression of three timer genes: *caudal*, *dichaete*, and *odd-paired* (Clark et al., 2022). In the tail region, their expression is delayed, and this region segments later, after blastocyst

segmentation (Clark et al., 2022). In short, the speed and relative timing of patterning factors help with correct and timely fate assigning.

Temporal oscillations of pair-rule genes generate repetitive epithelial blocks during somitogenesis in arthropods and vertebrates (Figure 2c) (Clark et al., 2019). The timing of segmentation-related oscillations differs between species and can have dramatic effects on the final body plan: faster segmentation in corn snake embryos results in the formation of many more, smaller somites as compared to zebrafish, mouse, and chicken embryos that share conserved gradient systems (Gomez et al., 2008). When comparing mouse and human systems (2–3 versus 5–6 h oscillations), the speed of biochemical reactions including protein production and degradation was found to contribute to the difference in developmental rate in the embryos (Diaz-Cuadros et al., 2023; Matsuda et al., 2020). In addition, the number of introns in the mouse *Hes Family BHLH Transcription Factor 7* (*Hes7*) gene contributes to segmentation timing: when two *Hes7* introns are removed, its oscillation and somite segmentation are sped up by about 9% (Harima et al., 2013). Finally, in cultured zebrafish presomitic mesoderm (PSM) cells, exogenous signals such as FIBROBLAST GROWTH FACTOR are not required to generate a wave pattern, but they can slow down this internal timer *in vitro* (Rohde et al., 2024). Thus, differences in segmentation timing are essential, and they are mediated by basic properties of the factors involved.

Finally, during drosophila neuroblast (NB) development, spatial information initially determines neuroblast identity, but the subsequent specification of ganglion mother cell (GMC) fates takes place without further spatial information (Figure 2d). Instead, NBs undergo several rounds of asymmetric divisions, each time producing a large NB and a small GMC that inherits the expression of the current fate-regulating temporal TF (Doe, 2017; Pollington et al., 2023). NBs and the formed GMCs subsequently express Hunchback (Hb), Kruppel (Kr), POU domain protein 1 and 2 (Pdm1/2), and Castor (Cas) to regulate unique neuronal fates (Grosskortenhaus et al., 2005; Homem & Knoblich, 2012). In models, general activation with feedback repression appears sufficient to generate the temporal TF cascade, with the first transition (Hb to Kr) depending on cell division (Doe, 2017; Grosskortenhaus et al., 2005). This is an example of cell identity specification depending on the timing of its specification through division.

In animal development, the regulation of cell identity and pattern formation at a local level is known to involve temporal in addition to spatial mechanisms. Drawing inspiration from this field, we are interested in exploring similar mechanisms in plant development (Meyerowitz, 2002). To study the temporal regulation of local development in plants, the identification of transitions whose timing is precisely regulated remains the main challenge.

Cell identity over time: temporal regulation on a local level

A cell's identity is tightly regulated and generally progresses toward its final cell fate along a set trajectory. Many studies have sought to elucidate regulators of cell fate and identity, but few have identified temporal regulators of identity progression. In this section, we explore examples of local regulation of developmental timing, considering single cell and organ level control.

In the root, space and time are aligned along the root's length (Motte et al., 2019*). This makes it relatively straightforward to track development but challenging to separate spatial from temporal regulation. In general, the sizes of different root zones correlate with the time spent in each zone and mutants affected in their root zonation often also have “faster” or “slower” cell identity development when measured spatially (Verbelen et al., 2006). Factors such as the PLTs, which affect root zone sizes, appear to have very general roles that include both spatial and temporal effects (Aida et al., 2004). However, general regulators of development and differentiation such as MINIYO (IYO) and RPAP2 IYO Mate (RIMA) were shown to speed up or delay differentiation events across root cell types (Figure 3a) (Muñoz et al., 2017; Sanmartín et al., 2011). Root cell identities strongly influence each other, and ablation experiments have shown a strong influence of a cell's position on its fate (Gehrke et al., 2023; van den Berg et al., 1995). However, development of some root cell identities appears controlled in a temporal manner: PLT2 misexpression can delay phloem differentiation while the PAX–BRX–PIP5K1 module (PROTEIN KINASE ASSOCIATED WITH BRX, BREVIS RADIX and PHOSPHATIDYLINOSITOL-4-PHOSPHATE-5-KINASE) mediated auxin canalization speeds up differentiation (Aliaga Fandino et al., 2024; Roszak et al., 2021). In rice, higher order OsRSL (RHD SIX-LIKE) mutants have delayed root hair emergence while misexpression of OsRSLs results specifically in premature root hair differentiation (Kim et al., 2017).

During leaf development (Lv et al., 2023*), a proliferative phase is followed by differentiation progressing from tip to base. In juvenile leaves, a proliferative burst takes place, correlating with SPL9 levels (Figure 3b) (Li, Jenke, et al., 2024). In addition, ANGUSTIFOLIA 3/GRF-INTERACTING FACTOR 3 (AN3), a positive regulator of cell proliferation, was shown to prevent precocious differentiation during leaf development (Ezaki et al., 2024).

In the stomatal lineage, identity transitions are mediated by master regulator bHLH TFs (Bergmann & Sack, 2007*; Kim et al., 2022; Liu, Mair, et al., 2024; Smit & Bergmann, 2023). While these regulators are generally considered necessary and sufficient, recent discoveries suggest that this is not always the case. SPEECHLESS (SPCH) plays a dominant role in promoting Asymmetric Cell Divisions (ACDs) and lineage entry but does not and can not induce

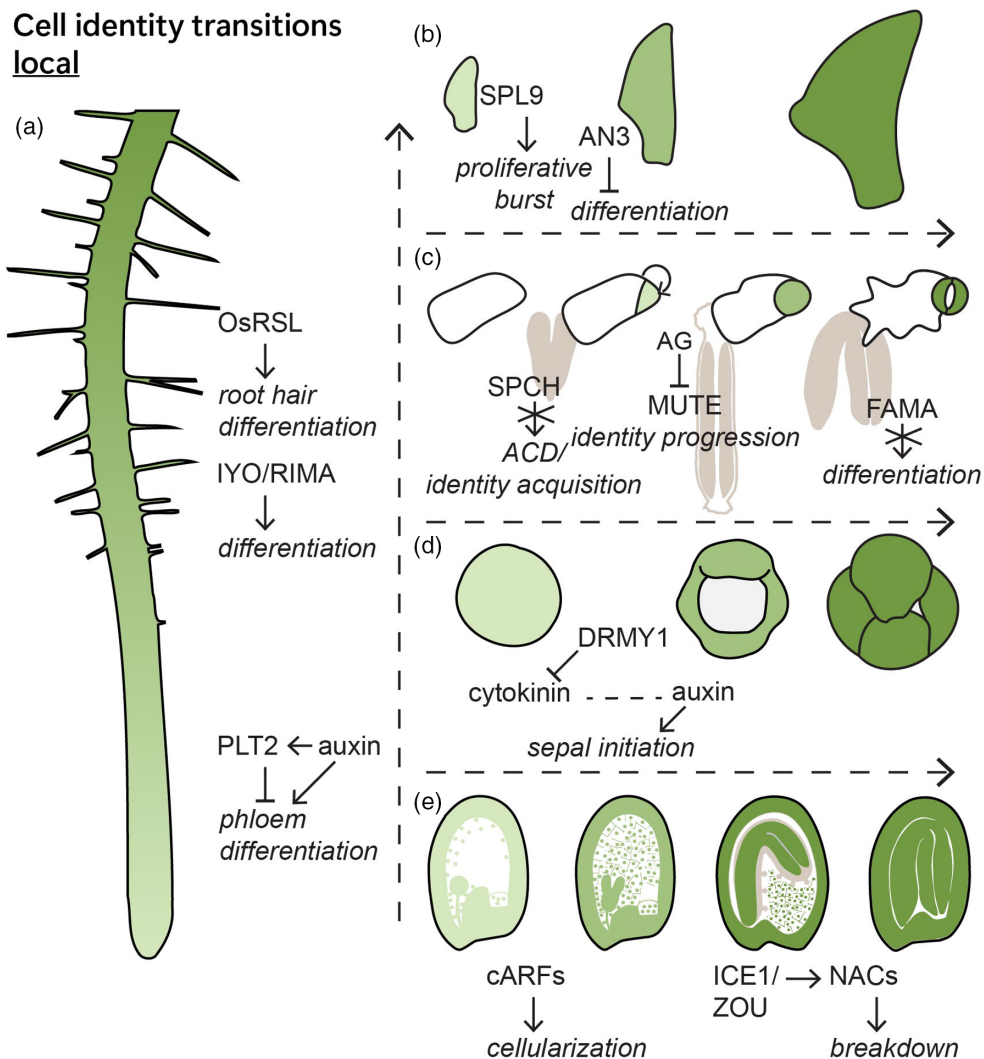


Figure 3. Plant cell identity transitions regulators.

- (a) Cell differentiation in root development.
 (b) Leaf cell proliferation and expansion.
 (c) Stomatal lineage progression during embryogenesis and gynoecial valve development.
 (d) Endosperm cellularization and breakdown.
 (e) Sepal initiation robustness and uniformity.

ACD, asymmetric cell divisions; AG, *agamous*; AN, *angustifolia 3/GRF-interacting factor*; cARF, clustered auxin response factor; DRMY, development-related MYB-like; ICE, inducer of CBP expression; IYO, *miniyo*; NAC, NAM ATAF CUC; *OsRSL*, RHD six-like; *PLT*, *plethora*; *SPCH*, *speechless*; *SPL*, *squamosa-promoter binding protein-like*.

this change during the heart to torpedo stages of embryogenesis (Figure 3c) (MacAlister et al., 2007; Smit et al., 2023). After lineage initiation, the timing of *MUTE* expression and Guard Mother Cell (GMC) identity are influenced by a cell size threshold, and this change is in turn accompanied by lengthening of the cell cycle as the cell proceeds to divide symmetrically (Gong et al., 2023; Han et al., 2022; Pillitteri et al., 2007). This transition is delayed in stomatal cells located on the gynoecial valves, where stomatal cells are arrested as meristemoids through the action of the floral regulator *AGAMOUS* (AG) (Brazel et al., 2023). AG represses *MUTE* transcription, which ensures that stomatal

maturation coincides with fertilization (Brazel et al., 2023). Finally, *FAMA*'s role driving guard cell differentiation is hampered during embryogenesis, a time when stomatal cells do not but apparently also can not differentiate (Ohashi-Ito & Bergmann, 2006; Smit et al., 2023). This temporal block can be circumvented by removing embryos from the ovule, suggesting a role for extraembryonic factors (Zuch et al., 2023).

Robust timing of sepal initiation is needed for proper flower bud closure (Roeder, 2021*) (Figure 3d). Mutants with altered sepal initiation timing have varying sepal sizes resulting in incomplete flower bud closure (Zhu, Klasfeld,

et al., 2020). Flower bud closure is influenced by DEVELOPMENT RELATED MYB-LIKE1 (DRMY1) which regulated TARGET OF RAPAMYCIN (TOR) activity, ribosomal content, and translation, eventually controlling the timing and position of sepal initiation inhibition (Kong, Zhu, Pan, et al., 2024; Kong, Zhu, Scarpin, et al., 2024).

Finally, the timing of endosperm cellularization and subsequent elimination is tightly controlled and affects seed size and viability (Figure 3e) (Bente & Köhler, 2024; Doll & Ingram, 2022*; Hehenberger et al., 2012). The timing of cellularization is controlled through the expression of clustered AUXIN RESPONSE FACTOR (cARF) with levels of cARF depending on parental contributions: later expression results in a delay and earlier expression in premature cellularization (Butel et al., 2024). As the embryo expands, the endosperm needs to be eliminated to make space. Programmed cell death (PCD) of endosperm cells needs to happen slowly enough to keep supporting the embryo but quickly enough to prevent restriction of embryo growth. ZHOUP1 and INDUCER OF CBP EXPRESSION 1 (ICE1) are two TFs that are required for this endosperm breakdown through their control of downstream NACs that promote Programmed Cell Death (Denay et al., 2014; Doll et al., 2023).

Overall, while developmental timing has not been a major focus in studies of cell identity and patterning, above examples indicate that temporal control is also present on a local level, often in specific organ contexts.

WHAT: FACTORS THAT INFLUENCE TEMPORAL REGULATION

Plants need to adapt their body plan to the environment, responding to changes in factors such as temperature, light conditions, salinity, and nutrient availability. In addition to the environmental conditions sensed by the plant, each cell also responds to its direct environment. Here we describe several environmental factors that were described to affect the timing of developmental events.

Systemic environment

Temperature affects plant form either directly through temperature-dependent action of regulatory factors or indirectly by affecting metabolism and water homeostasis (Li et al., 2022*). Here we focus on how temperature directly influences the regulation of major transitions, the main example being seasonal temperature regulating the timing of flowering. To prevent premature flowering, the cold-activated bHLH TF ICE1 induces expression of *FLC*, resulting in SUPPRESSOR OF OVEREXPRESSION OF CO 1 (SOC1) repression and delayed flowering (Lee et al., 2015). By contrast, at optimal temperatures, SOC1 reduces ICE1 binding to the *FLC* locus (Lee et al., 2015). This results in a feedback loop integrating cold with other floral signals to ensure optimal timing. By contrast, high temperatures

speed up the transition to flowering. Both PHYTOCHROME INTERACTING FACTOR 4 (PIF4) and the alternative splicing of FLOWERING LOCUS M (FLM) are temperature-responsive and act upstream of FLOWERING LOCUS T (FT) to speed up flowering under warmer temperatures (Balasubramanian et al., 2006; Jin & Ahn, 2021). Winter cold is a required signal for the flowering of winter-annual varieties of Arabidopsis. Vernalization activates the expression of VRN genes (VRN1, VIN3, and VIN5) that contribute to the silencing of the floral repressor FLC, thereby inducing flowering (Maple et al., 2024). Separately, FRIGIDA (FRI) forms nuclear condensates under cold temperatures, taking it away from the *FLC* locus where it promotes H3 trimethylation at K4 and K36 and transcriptional activation under warm conditions (Zhang et al., 2023). The antisense RNA *COOLAIR* can physically associate with the *FLC* locus and accelerates its shutdown in the cold by promoting FRI condensates (Csorba et al., 2014; Zhu et al., 2021). Temperature also affects the timing of germination. Germination at low temperatures is slowed down by the cold-induced accumulation of DOG1. By contrast, seed dormancy can be released via stratification, where cold temperature and dark result in changes in the expression of ABA and GA-related genes (Yan & Chen, 2020).

Other major environmental factors regulating plant phase transitions include light and photoperiod (Li et al., 2022*). Phytochromes, cryptochromes, and phototropins sense light and control, among others, the timing of senescence and flowering (Lymperopoulos et al., 2018). For instance, the ratio of red versus far-red light (R:FR) affects the timing of leaf senescence via PhyB and FHY3 (Lee et al., 2021; Sakuraba, 2021; Sakuraba et al., 2014; Tian et al., 2020). FHY3 competes with PIF4 (PHYTOCHROME INTERACTING FACTOR) to repress NON YELLOWING1 and STAY GREEN1 (NYE1 and SGR1), two key regulators of leaf senescence, leading to delayed senescence (Wang et al., 2023). The B BOX (BBX) family of TFs contributes to light-regulated developmental processes including flowering (Song et al., 2020). BBX13 acts as a negative regulator by delaying flowering under long-day conditions by affecting CO binding on the *FT* promoter (Rahul et al., 2024).

Salinity and nutrient availability were found to affect the speed of germination and the floral transition. For example, under fluctuating salinity conditions and during high osmotic stress levels, ERECTA (ER) modulates seed germination, and reduced ER signaling under these conditions lowers and slows down germination (Nanda et al., 2019). ABA is likely a mediator of this process as ABA-related genes are upregulated under salinity stress, and ER triple mutants showed increased ABA sensitivity (Nanda et al., 2019). Flowering time partially depends on nutrient availability: Under low N conditions, the phosphorylation of FLOWERING BHLH 4 (FBH4) is reduced,

resulting in nuclear localization of FBH4 and activating CO/FT pathways promoting early flowering (Sanagi et al., 2021). Under low P conditions, *Arabidopsis* flowering is delayed through the reduction of FT, LFY, and APETALA1 transcripts (Cho et al., 2017). Conversely, increased P did not speed up flowering, indicating that the nutrients themselves might not supply specific signals, but instead, limiting conditions slow down development.

Local environment

Each cell experiences its own micro-environment with local cues influencing cell growth and identity. A cell can adopt a new identity depending on its neighbors as shown in cell ablation experiments (Gehrke et al., 2023; van den Berg et al., 1995). Mobile signals such as hormones, peptides, and microRNAs (miRNAs) inform a cell of its environment and guide identity changes over time (see the How section). For example, CLE33 and CLE45, as well as auxin levels, both control the timing of protophloem sieve element differentiation (Aliaga Fandino et al., 2024; Carbonnel et al., 2023).

In addition to mobile signals, a cell's exposure to mechanical cues can influence its development. In response to wounding, cell ablation, or stretching experiments, mechanical signals influence cell division orientation and gene expression, indirectly or directly affecting cell identity (Hamant et al., 2008; Majda et al., 2022; Roszak et al., 2021; Zhang et al., 2022). In addition, mechanical conflicts can be created through alterations in cell wall properties, resulting in local heterogeneity or overall changed properties, eventually altering cell polarity and/or identity (Varappambath et al., 2022; Wolf, 2022). However, there are currently no examples known of mechanical cues and cell wall properties regulating development timing for.

HOW: MECHANISMS OF TEMPORAL REGULATION

After exploring examples of the regulation of development timing, here we discuss mechanisms employed to regulate developmental timing. In addition, often the outputs of several mechanisms are integrated, increasing complexity and robustness.

Metabolic rates and protein turnover

Metabolic rate and protein turnover set the pace for rates of growth and development. In animals, metabolic rate scales with body size and is shown to influence cell fate (Diaz-Cuadros et al., 2023; Kleiber, 1947). In animal systems, NAD(H) redox balance and mitochondrial activity, respectively, can partially explain species differences in the speed of the segmentation clock and in the rate of neuronal maturation (Figure 4a) (Diaz-Cuadros et al., 2023; Iwata et al., 2023; Rayon, 2023). In plants, metabolism can affect development through glucose signaling, with glucose-activated TOR kinase influencing genome-wide

H3K27me3 through the phosphorylation of FERTILIZATION-INDEPENDENT ENDOSPERM (FIE), a component of the Polycomb Repressive Complex 2 (PRC2) complex (Ye et al., 2022). Inhibiting TOR kinase activity results in a decrease in overall H3K27me3 levels and a delay in the transition to flowering (Ye et al., 2022).

RNA and protein metabolism have been implicated in controlling the timing of developmental transitions and differentiation. The rate of transcriptional elongation is correlated with the ability to differentiate in both animal and plant systems (Figure 4a) (Li et al., 2021; Sanmartín et al., 2012). In *Arabidopsis*, IYO, an interactor of RNA polymerase II, together with its interactor RIMA influences the timing of differentiation, and misexpression of either results in premature differentiation across cell types (Muñoz et al., 2017; Sanmartín et al., 2011). In addition, an imbalance in ribosome components affects translation of developmental regulators, and abnormal translation dynamics result in the production of ectopic non-hair cells in the root, slower tissue regeneration, and slower seed germination (Horiguchi et al., 2012; Wang et al., 2020). Finally, protein degradation rates affect the speed of the segmentation clock in human and mouse systems: altered Hes7 protein stability results in altered cell cycle length and segmentation (Matsuda et al., 2020; Rayon et al., 2020).

Cell division and cell cycle-dependent regulation

Temporal regulation of cell identity changes often involves coordination of cell cycle length and division dynamics. Cell cycle length varies across organisms, cell types, and developmental stages, with various mechanisms responsible for its regulation (Jones et al., 2019; Loeffler, 2023; Soufi & Dalton, 2016). Sizer-based mechanisms have been described to control division timing in plant SAM and stomatal cells. In the SAM, cell cycle progression depends on KIP-related protein 4 (KRP4) levels, and KRP4 gets diluted by cell growth to time the G1/S transition (Figure 4b) (D'Ario et al., 2021). In stomatal development, meristemoids undergoing ACDs change to GMC fate when a birth size threshold is reached (Gong et al., 2023). Upon transition to GMC fate, MUTE then induces the expression of SIAMESE-RELATED (SMR) proteins including SMR4, lengthening G1, resulting in a slower Symmetric Cell Division (SCD) (Han et al., 2022). Thus, in this case cell cycle length and timing, both seem to reflect and affect cell identity. In general, in leaf, relative organ age affects division rate and cell cycle length: leaf number and cell position along the leaf's proximodistal axis affect SPL9 levels, which promote division by activating CYCLIN D3 family genes (Li, Zhang, et al., 2024). As a result, younger leaves undergo a proliferative burst with faster cell cycles and a delay in differentiation and maturation (Li, Jenke, et al., 2024). In the root, cells

instead speed up their cell cycle as they age. This change in division rate is affected by reactive oxygen species (ROS), and recent findings show that the antioxidant glutathione enables fast divisions during regeneration by causing a truncated G1 phase in cells that reprogram their fate first (Lee et al., 2025; Rahni & Birnbaum, 2019; Tsukagoshi et al., 2010).

Mobile signals

Mobile signals are crucial for coordinating development by integrating local positional information, but developmental timing is also influenced by them. Here we discuss how hormones, peptides, and microRNAs contribute to the regulation of developmental transitions.

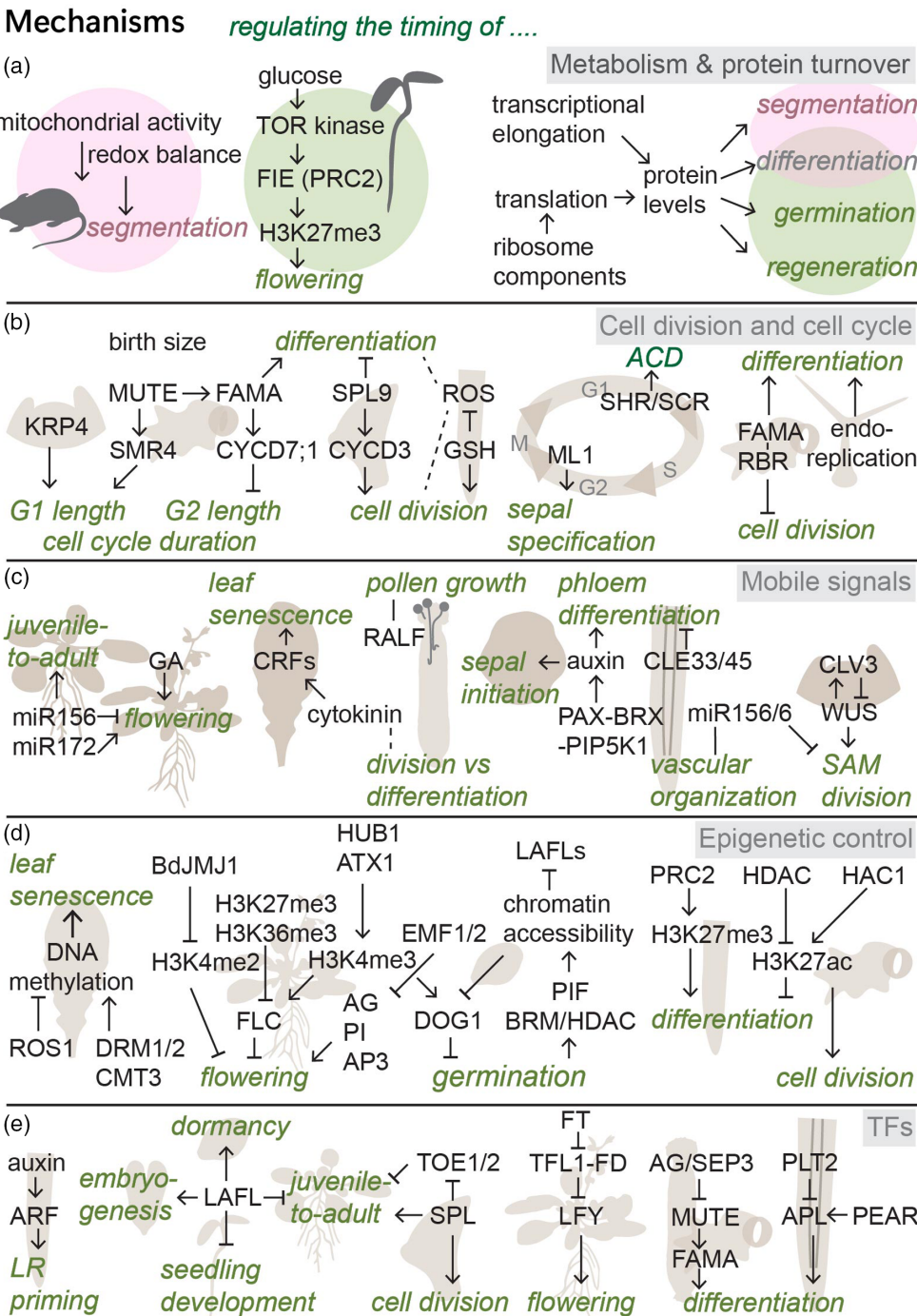


Figure 4. Examples of mechanisms regulating the timing of plant developmental events.

- (a) Metabolism and turnover affecting animal and plant development.
 (b) Regulation of cell division, cell cycle duration, and progression.
 (c) Mobile signals: hormones, peptides, and miRNAs.
 (d) Epigenetic modifications and chromatin accessibility.
 (e) TFs.

ACD, asymmetric cell divisions; AG, agamous; AN, angustifolia 3/GRF-interacting factor; AP, apetala; APL, altered phloem development; ARF, auxin response factor; ATX, *Arabidopsis trithorax*; BdJMJ, jumonji; BRM, brahma; CLE33, clavata3/embryo surrounding region-related33; CMT, chromomethylase; CRF, cytokinin response factor; CUC, cup shaped cotyledon; CYCD, cyclin D; DOG1, delay of germination; DRM, dormancy-associated protein; EMF, embryonic flower; FIE, fertilization-independent endosperm; FLC, flowering locus C; FD, flowering locus D; FT, flowering time; GA, gibberellic acid; GSH, glutathione; HAC, histone acetyltransferase; HDAC, histone deacetylase; HUB, histone monoubiquitination; KRP, KIP-related protein; KYP, kryptonite; LAFLs, leafy cotyledon1 (LEC1), abscisic acid insensitive3 (ABI3), FUSCA3 (FUS3), and LEC2; LFY, LEAFY; ML, meristem layer; PAX-BRX-PIP5K1, protein kinase associated with BRX, brevis radix, and phosphatidylinositol-4-phosphate-5-kinase; PEAR, phloem early DNA-binding-with-one-finger; PI, pistillata; PIF, phytochrome interacting factor; PLT, plethora; PRC, polycomb repressive complex; RALF, rapid alkalization factor; RBR, retinoblastoma-related; REF, relative of early flowering; ROS, reactive oxygen species; SCR, scarecrow; SEP, sepalata; SFL, seed dormancy four-like; SHR, shortroot; SMR, siamese-related; SPL, squamosa-promoter binding protein-like; TFL, terminal flower; TOE, target of early activation tagged; TOR, target of rapamycin; WOX, Wuschel-related homeobox.

Hormone levels and signaling define thresholds for several phase transitions (Figure 4c). For example, GA levels control the timing of flowering, and reduced GA levels delay flowering (Lee et al., 2020). Cytokinins influence the leaf senescence timing through the activity of cytokinin-induced CYTOKININ RESPONSE FACTOR (CRF) TFs (Wu et al., 2021). As a result, *crf1,3,5,6* mutants have delayed leaf senescence, while CRF1/3/5-overexpressing leaves undergo senescence earlier (Raines et al., 2016). Hormone dynamics also influence local developmental events. Cytokinins speed up cell division, delay the onset of differentiation, and extend the period of cell proliferation in leaves (Skalák et al., 2019; Wu et al., 2021; Zhang et al., 2005). During gynoecium development, cytokinin levels similarly control the balance between division and differentiation in internal tissues and outgrowths (Cerbantez-Bueno et al., 2024). Here, cytokinin signaling and levels of D3-type cyclins determining cell cycle timing are connected by the TF SPATULA (SPT) (Cerbantez-Bueno et al., 2024). Auxin affects the timing of protophloem sieve element differentiation (Aliaga Fandino & Hardtke, 2022). Phloem sieve element cells differentiate before other cell types in the root; the timing of this differentiation is regulated by the polarly localized PAX-BRX-PIP5K1 module, which controls local auxin canalization, speeding up differentiation (Aliaga Fandino et al., 2024). When instead this module is assembled ectopically in developing xylem vessels, it promotes faster differentiation of xylem vessels (Aliaga Fandino et al., 2024). Looking at combined hormone effects, auxin-cytokinin dynamics also regulate spatiotemporal sepal patterning, and disrupting either affects the relative timing of sepal initiation, and as a result the number and size of sepals (Kong, Zhu, Pan, et al., 2024; Kong, Zhu, Scarpin, et al., 2024).

Plants produce and respond to signaling peptides and small proteins to guide development; here, we use FT, CLAVATA3/EMBRYO SURROUNDING REGION-RELATED (CLE), and Rapid ALKalinization Factor (RALF) peptides as examples in temporal regulation at systemic and local levels. FT encodes a small mobile protein whose

transcription in the phloem depends on environmental factors. After production in the leaf phloem, the protein acts in the SAM together with FLOWERING LOCUS D (FD) to control the timing of the transition to floral fate (Corbesier et al., 2007; Freytes et al., 2021). CLE peptide signaling regulates proliferation and differentiation rates in both apical and vascular meristems (Berckmans et al., 2020; Etchells & Turner, 2010; Willoughby & Nimchuk, 2021). The most studied, CLAVATA3 (CLV3), forms part of a feedback loop with WUSCHEL (WUS) controlling SAM size (Figure 4c) (Han et al., 2020). During embryogenesis, removing CLV3 results in delayed downregulation of WUS, continued division, and an eventually larger WUS domain (Schoof et al., 2000). In the vasculature, CLE33 and 45 prevent neighboring cells from acquiring protophloem identity and prevent young protophloem cells from differentiating prematurely (Carbonnel et al., 2023). Several RALF family members were shown to control and be controlled during pollen-pistil interactions involving spatial and temporal regulation by the two parents (Abarca et al., 2021). These RALFs control when pollen tube rupture takes place and whether, later, a second pollen tube can exit the septum if fertilization fails (Somoza et al., 2021; Zhong et al., 2022).

Finally, mobile miRNAs regulate spatial and temporal development in the vegetative phase transition, flowering, and vascular patterning among others (D'Ario et al., 2017; Liu, Yu, et al., 2018). miR156 and miR172 play pivotal roles in the juvenile-to-adult transition by regulating SPL and AP2-like transcripts (Figure 4c) (He et al., 2018; Poethig & Fouracre, 2024). Overexpression of miR156 prolongs the vegetative phase and delays flowering while overexpression of miR172 accelerates flowering; however, the exact mechanisms and factors controlling miR156 and miR172 levels and the timing of the transition remain unresolved (Poethig & Fouracre, 2024; Wu et al., 2009). miR399 and miR169 both induce flowering in response to environmental signals: miR399 is temperature-responsive and targets the phosphate homeostasis gene PHOSPHATE 2 (PHO2), and miR169 is upregulated under abiotic stress to target AtNF-YA2 transcripts (Liu, Yu, et al., 2018). Finally, miR165

and miR166 target PHABULOSA and REVOLUTA and play central roles in vascular development and during embryogenesis; their timely sequestration by ARGONAUTE 10 is required for SAM development and maintenance (Miyashima et al., 2011; Zhou et al., 2015).

Epigenetic control

Epigenetic modifications and resulting changes in chromatin accessibility often correlate with cell identity changes (Birnbaum & Roudier, 2017; Huang & Sun, 2022; Ma et al., 2019; She et al., 2013). Here, we discuss the roles of epigenetic mechanisms such as DNA methylation and histone tail modifications in controlling the timing of developmental transitions.

DNA methylation of promoter regions is influenced by and influences development through gene repression (Hemenway & Gehring, 2023). DNA methylation declines during senescence and influences the timing of the onset of leaf senescence, with hypermethylated REPRESSOR OF SILENCING1 (*ros1*) and hypomethylated triple DORMANCY-ASSOCIATED PROTEIN 1/2, CHROMOMETHYLASE 3 (*drm1/2 cmt3, ddc*) mutants displaying a fast or slower onset of leaf senescence, respectively (Figure 4d) (Ogneva et al., 2016; Vatov et al., 2022). However, both types of mutants show a faster progression after the first symptoms, and the underlying mechanisms remain unknown (Vatov et al., 2022). The timing of flowering is also influenced by DNA methylation, which eventually affects the FLC expression. The quadruple *drdd* (DEMETER (DME) family of 5-methylcytosine DNA glycosylases) mutants show early flowering due to hypermethylation and reduced FLC expression at the seedling stage (Vatov et al., 2022; Williams et al., 2022). On the local scale, DNA methylation-free plants have severe developmental defects (He et al., 2022).

Modification of histone tails alters chromatin accessibility and influences gene expression levels. Flowering time is one of the developmental transitions heavily regulated by histone 3 modifications. In winter-annual Arabidopsis varieties, FLC transcription is upregulated by H3K4me3 deposition promoted by HISTONE MONOUBIQUITINATION1 (HUB1) and ARABIDOPSIS TRITHORAX1 (ATX1) (Figure 4d) (Lu et al., 2024). In addition, vernalization promotes silencing of the floral repressor FLC by replacing active H3K36me3 with repressive H3K27 trimethylation (Huang et al., 2021). In *Brachypodium distachyon*, the timing of flowering is influenced by the histone demethylase JUMONJ1, which is required for H3K4me2 demethylation at the loci of flowering time regulations VRN1 and INDETERMINATE1 (Liu, Li, et al., 2024). During seed maturation, H3K4 methyltransferases (ATXs), along with HUB genes and the proteasome alpha subunit F1 (PAF1) complex, promote DOG1 transcription to induce dormancy and regulate germination timing (Xiao

et al., 2017). Upon germination, large changes in chromatin accessibility result in the repression of LAFLs and DOG1 and an increased GA/ABA ratio, necessary for the transition to postembryonic growth (Xiao et al., 2017). This chromatin reorganization is in part facilitated by PHYTOCHROME INTERACTING FACTORS (PIFs) upon exposure to light, together with chromatin regulators BRAHMA (BRM) and HDACs, resulting in large transcriptional changes upon germination (Bouyer et al., 2017; Kawakatsu et al., 2017; Liew et al., 2024; Xiao et al., 2017).

EMF1 and EMF2 contribute to the regulation of histone tail methylation and ubiquitination to regulate flowering, and removing either results in precocious flowering upon germination (Yoshida et al., 2001). EMF1 is a member of the PRC1 complex, and EMF2 is part of the EMF-PRC2 complex, and they act to repress the flower homeotic genes *AGAMOUS* (*AG*), *PISTILLATA*, and *APETALA3* (Kim et al., 2010; Yang et al., 2017).

On a more local level, in root development, HDAC activity promotes differentiation and the PRC2 complex contributes to maintaining the cell's differentiated status (Ikeuchi, Iwase, Rymen, et al., 2015; Ikeuchi, Iwase, & Sugimoto, 2015). Advances in single cell/nucleus ATACseq approaches are now allowing more in-depth investigations of how changes in chromatin accessibility correlate with and potentially result in changes in cell identity (Dorrity et al., 2021; Shahan et al., 2021). For example, in the stomatal lineage, reprogramming of accessibility occurs at the transition to differentiation, and the SWI/SNF complex and HISTONE ACETYLTRANSFERASE1 (HAC1) are required to maintain the differentiated, non-dividing state of mature Guard Cells (Kim et al., 2022; Liu, Mair, et al., 2024). Thus, epigenetic changes can control the timing of phase transitions and are correlated with cell identity changes.

Transcription factors and gene regulatory networks

During plant development, cell identity and fate are regulated by complex gene regulatory networks involving various Transcription Factors (TFs). The structures of these allow for the integration of various signals and generation of temporal variation in target gene expression, resulting in expression pulses or delays (Alvarez et al., 2021; Coen & Prusinkiewicz, 2024; Van Den Broeck et al., 2020). Together with space- and time-specific expression of regulators, these structures ensure that cell fate and identity changes are robustly controlled. Here we discuss examples of TFs contributing to the timing of developmental events.

ARF transcription factors regulate lateral root priming in the Quiescent Centre. Temporal auxin oscillations are converted into pulsating gene activation signals by the modulation of ARF activity (Figure 4d) (Bellows et al., 2023). Auxin signaling and thus Aux/IAA degradation dynamics are integrated with shoot-derived light signals to mark the positions of future lateral roots by discrete gene

expression peaks (Kircher & Schopfer, 2018; Reyes-Hernández & Maizel, 2023). Thus, dynamic signals come together to create discrete temporal outputs.

LAFL TFs play key roles in several developmental transitions, and their ability to induce specific reprogramming events means their expression needs to be temporally restricted (Figure 4d) (Gazzarrini & Song, 2024). LEC1, FUS3, and LEC2 are expressed during the early stages of embryogenesis, where they increase chromatin accessibility to promote embryonic programs (Gazzarrini & Song, 2024; Tao et al., 2017). During embryo maturation, LAFLs then promote seed dormancy, and several LAFL mutants display reduced seed viability (Raz et al., 2001; Wang & Perry, 2013). The LAFLs co-regulate the timing of the vegetative phase transition, as LEC2 induces embryonic miR156 expression, and FUS3 modulates ethylene response, influencing vegetative growth (Gazzarrini & Song, 2024). Upon vegetative growth, most LAFLs are repressed, and ectopic vegetative expression results in the induction of somatic embryogenesis or production of cotyledon-like leaves (Gazzarrini et al., 2004; Gazzarrini & Song, 2024; Lotan et al., 1998).

SPL TFs are the master regulators of vegetative phase change, and their protein levels are controlled by miR156 levels (Wu & Poethig, 2006). In turn, SPLs, including SPL9, induce the expression of miR156, thus forming a negative feedback loop (Wu et al., 2009). In juvenile leaves, SPL9 is responsible for inducing a leaf age-dependent proliferative burst (Li, Jenke, et al., 2024). During the induction of the vegetative phase change, SPL levels are influenced by additional factors such as sugar affecting transcription and ABA signaling, which affects SPL phosphorylation (Dong et al., 2021; Meng et al., 2021). Threshold levels of SPLs then induce the vegetative phase transition in part through the expression of miR172, a miRNA that limits levels of TARGET OF EARLY ACTIVATION TAGGED (EAT) (TOE) 1/2, a TF that represses adult leaf features (Fornara & Coupland, 2009; Poethig & Fouracre, 2024).

LEAFY (LFY) is a pioneer TF that initiates flowering. It can trigger cellular reprogramming and alter gene expression to initiate floral transition even in root explant cells (Jin et al., 2021; Lai et al., 2021). Precocious LFY expression causes premature flowering, and thus, LFY expression timing is carefully regulated through the activities of various flowering factors (Weigel et al., 1992; Weigel & Nilsson, 1995). LFY transcription is repressed by the TERMINAL FLOWER 1 (TFL1) – FD complex and promoted when FT competes with TFL1 to prevent binding to and repression of LFY (Yamaguchi, 2021; Zhu, Klasfeld, et al., 2020). LFY itself then induces chromatin opening, allowing other TFs to bind and promote floral meristem identity genes (Freytes et al., 2021).

Stomatal differentiation on gynoecial valves is controlled in part by the floral organ regulators AGAMOUS

(AG) and SEPALLATA3 (SEP3), with stomatal differentiation timed to coincide with fertilization (Figure 4d) (Brazel et al., 2023). AG and SEP3 suppress MUTE transcription, preventing stomatal lineage progression early on in fruit development; over time, decreasing levels of AG and SEP3 allow for MUTE transcription and stomatal differentiation upon fertilization (Brazel et al., 2023). AG was previously shown to suppress leaf traits in gynoecial valves, and these findings indicate that stomatal fate progression, but not stomatal fate initiation, is one of those traits (Ó'Maoiléidigh et al., 2018).

The PLT TFs orchestrate the timing of protophloem development in the root meristem by forming a gradient that inhibits PHLOEM EARLY DNA-BINDING-WITH-ONE-FINGER (PEAR)-induced phloem differentiation. PLTs prevent early PEAR activity by inhibiting the expression of its target gene ALTERED PHLOEM DEVELOPMENT (APL) (Roszak et al., 2021). As PLT levels decrease, PEAR TFs can induce the expression of APL and promote differentiation; in this process, PLT2 is necessary and sufficient, as ectopic PLT2 expression can delay phloem differentiation (Roszak et al., 2021).

While the TFs mentioned above are pivotal, they do not act in isolation and instead are part of broader, interconnected gene regulatory networks that act together with other signaling pathways and TFs. This ensures precise spatiotemporal coordination of plant development.

CONCLUSION AND PERSPECTIVES

Plant body plans develop robustly under the control of a myriad of developmental regulators. Thus far, the timing of plant development has mainly been studied in the context of phase transitions, but recent insights indicate that temporal regulation also exists on a local scale and controls or limits cell identity and patterning in specific situations. One of the challenges in identifying temporal control on the local scale is that this control seems often not to be present in all instances or contexts: a trend in the current examples is that temporal control is limited to specific tissue types or developmental stages. We anticipate that studying cell identity across more contexts will reveal additional examples of temporal regulation.

Temporal regulation of plant development can further be unraveled using new technical advancements. Single cell or single nucleus omics technologies enable a more detailed look into cell identity and allow better tracking of identity changes (Adema et al., 2024; Nolan & Shahan, 2023; Ryu et al., 2021; Swift et al., 2022). These approaches can also help elucidate complex cell identities such as mixed identities or cell identity variation between tissues (Kim et al., 2021; Lee et al., 2023; Petersen et al., 2024; Shahan et al., 2022). Answering questions on the temporal regulation of phase or identity transitions requires studying these changes in their natural context as

Box 1. Bullet point summary

- Temporal regulation in plants has been examined in the systemic context of phase transitions, and their regulators have been studied extensively.
- Control of developmental timing at a local scale, limiting local organ or cell identity transitions, has gained attention in recent years, but separating temporal from spatial control remains challenging.
- Environmental signals and tissue context play large roles in controlling the developmental timing of plant phase transitions and cell identity regulation.
- Molecular mechanisms controlling the timing of developmental events are varied and complex, and often act through the integration of multiple factors.

Box 2. Open questions

- 1 How are the effects of the multiple factors that control each plant phase transition weighted and integrated?
- 2 At what stages and in which cell types and organs are cell identity and patterning temporally regulated during plant development?
- 3 How common is temporal regulation independently from spatial, tissue, and environmental factors?
- 4 What molecular mechanisms are employed in the temporal regulation of cell identity? How do they determine the correct timing of developmental events?
- 5 Are there common mechanisms that control the local timing of development across tissues or developmental stages?

much as possible. Spatial omics and multiplexed FISH approaches now allow for visualization of many transcripts, while advances in time course and time lapse imaging enable tracking cells in their native context over time (Adema et al., 2024; Harline & Roeder, 2023; Nobori et al., 2023; Nolan & Shahan, 2023). Finally, novel CRISPR technologies allow for lineage tracing and spatiotemporally specific knockout of fate regulators (Decaestecker et al., 2019; Donà et al., 2023; Gehrke et al., 2023). Now that we are touching upon the temporal restriction and regulation of cell identity more and more, these technologies can help better define, identify, and track cell identities as well as manipulate them in a more targeted way to separate temporal from other, spatial, effects.

In conclusion, the timing of developmental events has been studied at both systemic and local scales. Systemic changes, phase transitions, that affect the whole plant have been studied in some detail and more mechanisms are being unraveled. By contrast, local regulation, where timing is controlled at a cell or tissue level, is now being investigated more and more. It will be exciting to see when, where, and how local developmental timing is being regulated (Boxes 1 and 2).

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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