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Applying developmental threshold models to evolutionary ecology

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Process-based models of development predict developmental rates and phenology as a function of physiological responses to multiple dynamic environmental factors. These models can be adapted to analyze diverse processes in evolutionary ecology. By linking models across life stages, they can predict life cycles and generation times. By incorporating fitness, they can identify environmental and physiological factors that limit species distributions. By incorporating population variance, they can investigate mechanisms of intraspecific variation or synchronization. By incorporating genetics, they can predict genotype-specific phenology under diverse climatic scenarios and examine causes and consequences of pleiotropy across life stages. With further development, they have the potential to predict genotype-specific ranges and identify key genes involved in determining phenology and fitness in variable and changing environments.

Modeling phenology to understand evolutionary ecology

Changes in phenology (the timing of developmental events; see Glossary) in response to changing climate are widely observed and can have critical consequences for organismal fitness and population performance [1–5]. Phenology determines which life stages are exposed to which seasonal conditions and thus can strongly affect life-history expression, generation time, and population dynamics. Predicting phenological responses to different climatic environments is therefore important for understanding how organisms, populations, and species will respond to future climate change.

Process-based developmental models are powerful tools for predicting phenology under complex natural conditions (e.g., [6–17]). Such models use dynamic environmental inputs to predict developmental rates and the timing of phenological transitions. Historically they have been employed primarily in agronomic applications or ecological projections of important events such as bud break or insect emergence dates. However, such models also have potential

to provide insight into diverse ecological and evolutionary processes, including species range limits, phenotypic plasticity in response to complex dynamic environments, and causes of phenotypic and genetic variation within and among populations.

Here we discuss some potential applications of these models to evolutionary ecology. First, we describe how

Glossary

Canalization: the process of reducing variation; for example, among individuals in a population with respect to phenotypes that they express. For phenological traits, this can manifest as synchronization in developmental times.

Developmental threshold: the accumulated amount of 'developmental time' required for a given developmental stage to allow a transition to the next developmental stage. The time required is in developmental units (e.g., thermal time, degree days) rather than in calendar time units. Once a threshold level of developmental time has accumulated, the developmental transition occurs.

Developmental threshold model: a model used to predict the timing of a developmental transition. The timing of developmental transitions from one state to the next is modeled as a function of dynamic environmental factors that influence the accumulation of developmental time (see developmental threshold). Once a threshold level of developmental time has accumulated, the developmental transition occurs.

Habitat selection: the ability of an organism to determine (select or choose) the environment that it is exposed to.

Heritability: the proportion of total phenotypic variance that is genetic variance (i.e., caused by genetically based differences in phenotypes); total phenotypic variance includes both genetic and environmental variance. Higher heritability enables larger responses to selection, for any given strength of selection.

Maternal effects: also termed 'maternal environmental effects'. The influence of the environment experienced by maternal parents on the phenotype of their offspring.

Phenology: the timing of biological events such as germination, flowering, and bud break in plants or hatching, metamorphosis, and reproduction in animals.

Population-based threshold models (PBTMs): developmental threshold models that incorporate variation among individuals in a population with respect to developmental responses to environmental (or other) inputs.

Pleiotropy: the phenomenon in which one gene regulates more than one trait.

Process-based model: a model describing how a physiological process responds to environmental factors that is often used to predict developmental outcomes.

Quantal: a quantal response or trait is discontinuous and transitions from one discrete state to another; for example, from non-germinated to germinated or vegetative to reproductive. The phenotypes of quantal traits are frequently expressed as the percentage or proportion of individuals completing the developmental transition.

Reaction norm: the function that describes how a single genotype alters its phenotype in response to the environment.

Sensitivity threshold: the lower limit of a regulatory signal (environmental, hormonal, biochemical) that elicits a phenotypic response in an organism. When the signal level exceeds the threshold sensitivity, developmental time can accumulate. Sensitivity thresholds are physiologically determined and can be increased or decreased in response to environmental signals or developmental transitions and can vary among individuals.

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process-based developmental models, and developmental threshold models in particular, predict the timing of developmental transitions in complex environments and discuss how linking models of multiple life stages across the life cycle captures important dynamics in life cycle expression. Next, we discuss how further development of these models makes them applicable to addressing important issues in evolutionary ecology, specifically by incorporating fitness, population variance, and genetic differences among individuals.

Developmental threshold models: predicting phenology and life cycles in complex environments

Developmental threshold models predict the rate of development from one life stage to another, given a sequence of environmental conditions (Box 1). 'Developmental units' accrue over time according to relationships that describe developmental rate as a function of sensitivities to environmental factors. The effects of multiple environmental factors can be combined to define the rate of accumulation of developmental units. Once a threshold number of developmental units is attained, the developmental transition occurs; for example, the transition from seed to germinant or from egg to larva. This is an extremely flexible framework for predicting phenology in dynamic, complex environments. These and other models of phenology and developmental rates (e.g., [1,18,19]) have been successful in predicting the timing of phenological transitions, developmental rates, and growth rates more generally.

Individual developmental threshold models predict the timing of a single developmental transition. Linking multiple models of developmental transitions throughout the life cycle allows predictions of overall life cycle expression and the total amount of time required to complete a life cycle, or the generation time. Generation time is demographically important because it determines the number of generations that can be completed within a growing season and therefore influences population growth rate.

Linking individual developmental threshold models across the life cycle also incorporates an important dynamic that occurs in organisms developing in the wild: the timing of prior life-stage transitions determines the environmental conditions experienced by subsequent life stages, both within and across generations [20]. Environmentally cued phenology thereby acts as a form of habitat selection (Figure 1A), leading to important effects of one life stage on the following stages because the environment determined by one life stage affects the phenotypes expressed subsequently.

Linked developmental models incorporate these dynamics directly. They have been applied to predict bud break and fruit-maturation timing in trees [21], reproductive timing in crops [22,23], overall life cycle expression in annual plants [24], and the number of insect generations completed per season [25]. These models illustrate why accurate predictions of phenology and total generation time can be made only by incorporating the effects of the phenology of prior life stages on the environmental conditions that are experienced by subsequent ones. For instance, an empirically validated photothermal model [26] showed that flowering time and the expression of summer annual, winter annual, or autumn-flowering life histories depends critically on the seasonal timing of germination because germination time determined the amount of time before winter temperatures became prohibitive for further development.

The opportunity also exists to model cross-generational influences of maternal environmental effects by linking life stages across generations. The timing of reproduction determines the environmental conditions experienced during embryo development as well as the conditions that progeny are born or dispersed into. Maternal effects are known empirically to influence the expression of plant life histories [27,28], insect egg size and thereby growth rates [29], and even the demography of pest outbreaks ([30]; reviewed in [31]). They can be incorporated into developmental threshold models by allowing the progeny's developmental parameters to be defined as a function of maternal environmental factors.

Linked developmental threshold models can be used to predict overall life cycle expression across a geographical range or in novel climatic conditions. For example, Burghardt *et al.* [24] linked models of the timing of germination, flowering, and dispersal of *Arabidopsis thaliana* to show how the dynamics of all three processes contribute to the generation time and life-history variation that has been observed across its native range (Figure 1B,C) [24]. Wilczek *et al.* [32] predicted seasonal shifts in the flowering phenology of *A. thaliana* as a function of germination time across the species range under future climatic conditions.

Sensitivity analysis of these models can identify key physiological parameters that have the largest effect on phenology and life cycles (Box 2). For example, Burghardt *et al.* [24] found that changes in the seed dormancy of *A. thaliana* had larger projected effects on generation time than did changes in parameters affecting flowering time, based on a range of parameters known to occur in that species. Sensitivity analyses can also identify key environmental factors with the largest effect for any given set of physiological parameters (individual or genotype). For instance, Andreini *et al.* [33] found that early-flowering cultivars of fruit trees are most impacted by daily minimum temperatures because of their chilling requirement for bud dormancy release, while later-flowering cultivars are influenced primarily by daily mean temperatures.

In summary, developmental threshold models can be linked across the life cycle and across generations to predict integrated life cycle expression in complex environments, capture the important dynamics of habitat selection via developmental cuing and of maternal environmental effects, and project the expression of life cycles and generation times across present ranges and future climatic scenarios. When combined with sensitivity analysis, the models provide testable predictions about which physiological processes or environmental factors are most influential on life-history expression.

Incorporating fitness to predict species ranges

A crucial step toward adapting developmental and phenological models to applications in evolutionary ecology is to incorporate fitness consequences of developmental timing. Models that predict the seasonal timing of each life stage

Box 1. Developmental threshold models

Modeling rates of development as a function of variable environments

Developmental threshold models predict the timing of a developmental transition; for example, from seed to seedling or from egg to larva. The timing of that event is determined by stage-specific developmental rates, which are modeled as a function of temporally variable environmental inputs (Figure IA) (see Figure 1 in main text for further explanation of environmental factors depicted in the lower panel) and physiological responses to those inputs (Figure IB).

These models have an explicit temporal component. Developmental progress is calculated for small time intervals (e.g., hours or days), based on environmental conditions experienced during that time interval. Cumulative developmental progress is then summed over the time intervals.

The models estimate developmental progress of different life stages separately (e.g., seeds compared with vegetative seedlings). Each life stage can exhibit its own physiological responses to environmental conditions that regulate its rate of development toward the next life stage. This rate of development is a function of multiple dynamic environmental factors, or input signals. Typically, input signals are environmental, such as time at a chilling temperature, water availability, or ambient temperature. However, they can also be physiological, as in the level of a hormone required to cause a developmental transition. Most developmental models have factors that promote developmental progress as well as repressive components that reduce progress despite those promotive signals.

Developmental thresholds determine the timing of developmental transitions

A threshold level of developmental progress (developmental threshold), once attained, triggers the developmental transition (Figure IA; in this case from seed to seedling). This event occurs at a specific time, which determines the timing of that developmental event. The timing of this event therefore depends on what the environmental inputs were over the course of development and how that life stage responds to those inputs.

Physiological mechanisms of developmental responses to environmental factors

Physiological mechanisms underlying environmental responses are diverse and depend on the organism and the life stage being considered. For example, the rate of development from seed to germinant depends on soil water potential, Ψ (Figure IB, left), such that if the soil is too dry (below Ψ_b) no development will occur, but as ambient Ψ approaches that of pure water development occurs increasingly faster. Likewise, developmental rate can depend on temperature (Figure IB, center), such that developmental rate increases with increasing temperature, up to the optimal temperature; above the optimal temperature, the developmental rate declines with increased temperature. Photoperiod (Figure IB, right) regulates the timing of flowering in many plants. For long-day plants, little progress toward flowering is made when the photoperiod is less than a critical length, photoperiods longer than the minimum result in developmental time accumulation toward the flowering transition, and further increases in photoperiod do not increase developmental rate.
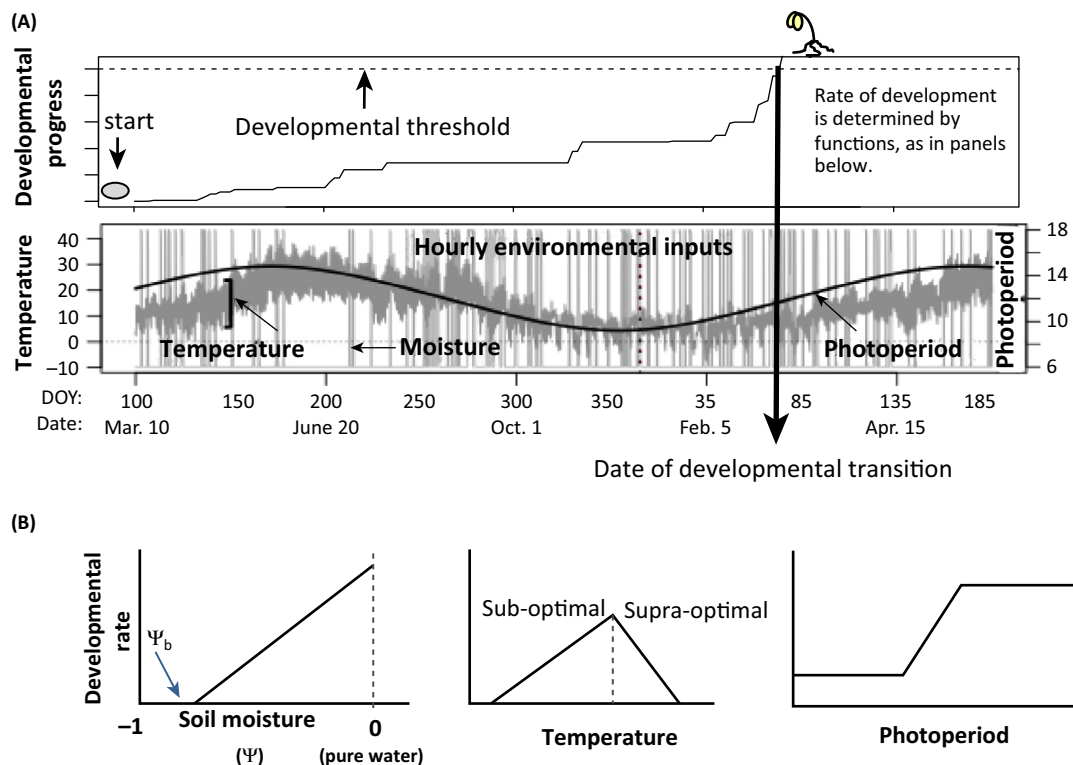

Figure I. (A) Schematic of a developmental threshold model. Bottom panel shows environmental factors that vary over a season (see Figure 1 for more details) and that influence the rate of development. Upper panel depicts the accumulation of developmental progress over time, for the developmental transition of seed to seedling. (B) Functions of how developmental rates respond to three environmental factors. From left to right: soil moisture, temperature, and photoperiod.

and thereby the environmental conditions experienced at each life stage, combined with knowledge of stage-specific environmental vulnerabilities and productivities, can be used to predict stage-specific survival and reproduction [34]. Such models have been used to predict the probability that organisms can complete their life cycles and reproduce successfully under particular environmental conditions (see Figure IA,B in Box 2).
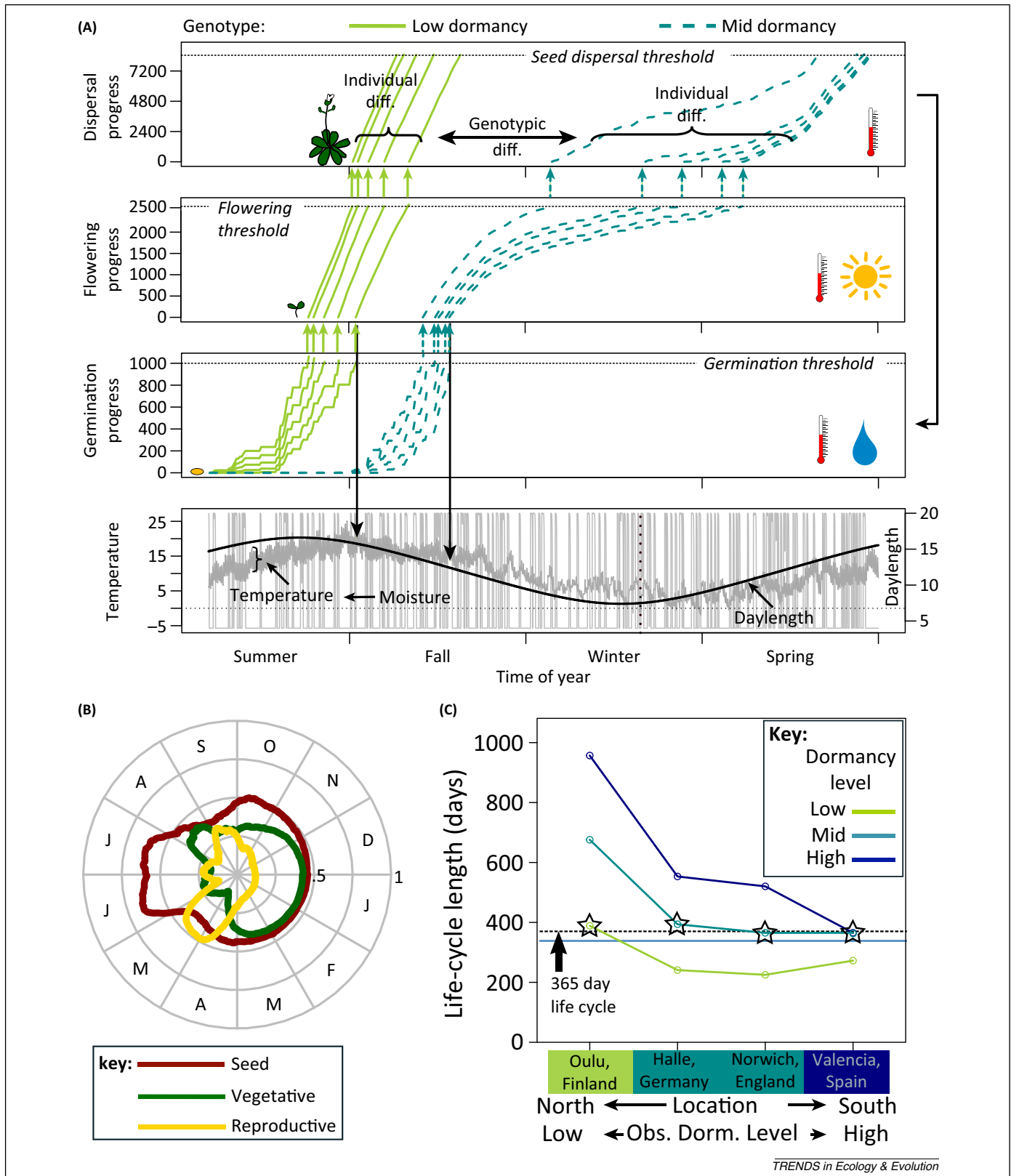
Figure 1. An integrated life cycle model to predict genotype-specific phenology and generation time across a species range. **(A)** General structure of an integrated model that links three developmental threshold models across life stages, based on the annual plant *Arabidopsis thaliana*. Environmental inputs over the course of a year (bottom panel) influence developmental rates of three life stages. The bottom panel shows environmental inputs over the course of a single year: photoperiod (smooth black line); precipitation events (vertical gray lines); and temperature (continuously varying gray lines). Beginning with the seed stage (second panel from bottom), progress toward germination proceeds in response to the environmental inputs of water availability and temperature. Green versus blue lines indicate different 'genotypes' with different parameter values for dormancy that reflect natural allelic variants known to occur in *A. thaliana*: low dormancy (green); and intermediate dormancy (blue). The multiple lines for each genotype represent random variation among individuals within a genotype in their rate of progress toward germination. Once the developmental threshold has been attained (transition to the next panel), seeds germinate and become vegetative rosettes. These rosettes experience environmental conditions determined by the time of germination (black arrows) and different individuals experience different environments because they germinated at different times. Rosettes progress toward the

(Figure legend continued on the bottom of the next page.)

Process-based developmental modeling approaches have been proposed to predict environment-dependent survival of animals as a function of the maintenance of energy and mass balances determined by specific developmental processes in specific environmental conditions [35]. These models have been applied to predict environment-dependent survival of amphibians [36], insects [37], and other organisms (reviewed in [35]). In plants, biochemical and developmental pathways have informed process-based models of stage-specific growth rates [19,38].

Process-based models of phenology have been combined with models of environment-dependent survival and reproductive success to predict species distributions ([39]) (see Figure IC in Box 2). Considering stage-specific environmental tolerances offers much greater resolution than standard environmental niche modeling approaches to predicting whether a species can occur in a specific location or climate. In novel climatic conditions or geographical locations, knowing what conditions would be experienced by different life stages, given phenological responses to the altered climate, would be useful for predicting overall performance and probability of persistence and could be used to identify vulnerable life stages.

Sensitivity analysis of models that integrate phenology and fitness can be used to identify developmental processes and environmental factors that are predicted to have the strongest influence on species distributions across extant or past ranges [40] or under future climatic scenarios (Box 2). Such analyses could be useful for predicting range changes of problematic or threatened species and which life stages are most influential. For example, one study of the dengue mosquito predicted the consequences of evolution of desiccation resistance at the egg stage for the persistence of the dengue mosquito across its present range and for establishment in novel locations [18].

The parameterization of process-based models is labor intensive and species-specific, whereas correlational approaches to predicting species distributions (such as environmental niche modeling) are much faster and broadly applicable. It has been argued, however, that process-based models have improved accuracy of prediction under environmental extremes and under nonequilibrium conditions such as environmental change and species range expansions [41]. Recently, there has been much exploration of how to combine these approaches and to use diverse information, including current distributional data, to parameterize process-based models ('inverse modeling'). For example, physiological information has been used as priors in Bayesian estimates of parameters [42] and those were then used to predict species distributions in nonequilibrium conditions [43,44].

Incorporating variance to investigate mechanisms of canalization or asynchrony

Many process-based models predict the mean behavior of populations without consideration of the variation around the mean [45]. Within populations, however, individuals often vary widely in their responses to environmental signals. This variation determines the strength of natural selection and the potential for evolutionary responses to it. To apply developmental and phenological models to issues of evolutionary ecology, environmental and genetic variation among individuals must be considered.

Population-based threshold models (PBTMs) (Box 3) can be used to model population variation in developmental responses to environmental inputs. Such models specifically incorporate variation among individuals in a population as an explanatory parameter to predict a given developmental event. In these models, the developmental event is fundamentally a quantal response in which an individual either has or has not passed through the event. Virtually any developmental transition where the phenotypic data are in the form of percentages or probabilities is quantal data at the individual level and many responses that are considered to be continuous or quantitative are actually quantal at a lower level of biological hierarchy. For example, seed germination is quantal in that an individual seed germinates or not, but the probability of germination or the percentage of a seed population that germinates is a continuous trait. Likewise, continuous quantitative developmental processes at the whole-organism level might be the outcome of quantal responses of individual cells (reviewed in [46]).

In these models, individuals in the population vary in the values of their developmental thresholds required for phase transition or in their sensitivity to the environmental signals that drive the accumulation of developmental time (Box 3). In the former case (see Figure IA in Box 3), the rate of accumulation of developmental time is the same among individuals in the same environment, but their cumulative requirements for the developmental transition vary. Alternatively, when individuals vary in their sensitivity to the

transition to flowering in response to temperature, photoperiod, and winter chilling. Once the threshold is reached (transition to next panel), seeds are matured at a rate that depends on temperature. Seeds are dispersed (final threshold in diagram) and the cycle begins again. Note how the phenotypic differences among individuals within and between genotypes change over time. The green genotype exhibits variation in germination time that results in a fairly constant level of variation in phenology throughout the life cycle. The blue genotype, which germinated on average later than the green, exhibits comparatively little variation in germination time but increasing variation in flowering time imposed by differences in the environmental conditions experienced at that time of year. However, during seed maturation individuals of the blue genotype resynchronize by the time of seed dispersal. Differences between the green and blue genotypes increase over the course of the life cycle. **(B)** The life cycle predicted for a single genotype in a single geographical location. The circle indicates a full year from January through December (indicated by letters in the circle). Lines represent the proportion of the simulated population, from zero (center) to one (outside perimeter), that is in each of three life stages: dark red, seed stage; green, vegetative stage; and yellow, reproductive stage. The simulation was conducted using climatic data from Norwich, UK and was run using data for 60 years; the model output is the mean of these model runs after a 15-year burn-in period, after which model results stabilized. Multiple bouts of flowering are observed, in late April, late June (a small proportion), and early September. Most of the population is in the seed stage during June and July and again in October. Such mixed life histories are observed in the field in this location. **(C)** The predicted generation time (life cycle length, *y*-axis) in four geographical locations (*x*-axis) for 'genotypes' with low, intermediate, and high seed dormancy. Simulations were based on climatic data from these four locations across the native latitudinal range of *A. thaliana*. Simulations used data for 40 years and the model output is the mean of these model runs after a 15-year burn-in period. Note that the differences among genotypes are much more pronounced in northern latitudes than in southern latitudes. A cline in dormancy alleles is known to exist, with more dormant alleles in southern latitudes and less dormant alleles in northern latitudes (panel below *x*-axis). Stars indicate the genotype that is known to exist in each location. The broken line that connects these stars shows that a generation time of close to 365 days is predicted to be expressed in each location. Therefore, genetic variation in dormancy appears to be able to canalize an annual life cycle across the geographical range of *A. thaliana*. B,C adapted from [24].

Box 2. Predicting phenology and species' distributions: examples with forest trees

Process-based models of phenology have been combined with models of environment-dependent fitness to predict species distributions. Much of this effort has been applied to predict the distributions of tree species.

Predicting phenology

Tree phenology has been modeled using process-based models of development that depend on temperature, photoperiod, and chilling effects on bud dormancy and subsequent growth [1,17] (Figure IA). Such models have been used to identify specific environmental factors and developmental processes that most strongly influence phenology throughout a species range.

From phenology to fitness

Phenology is an important determinant of fitness [1,70] because it determines the exposure of specific life stages to season-specific environmental stressors or environmental requirements for development and because it determines the time available to complete important processes such as fruit maturation (Figure IA). Phenology models have been linked to models of environment-dependent survival and reproduction to predict the probability that organisms can successfully reproduce under particular environmental conditions. PHENOFIT [1] is a process-based model that predicts tree phenology, survival, and reproductive success under different environmental scenarios; the probability of survival depends on tolerance to drought and frost and the probability of successful fruit maturation depends on the probability of frost damage to flowers, developing fruits, and leaves and the temperature-dependent rate of fruit maturation.
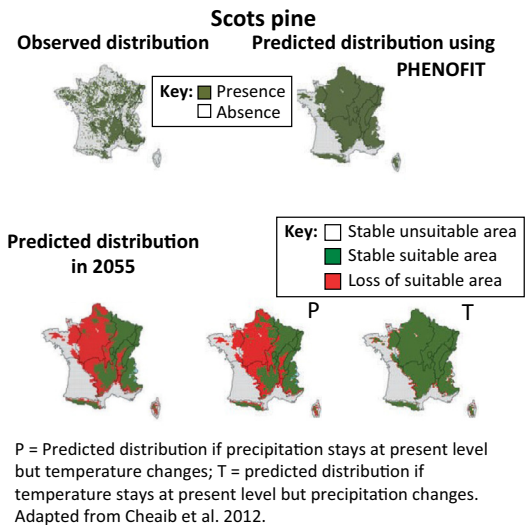
Predicting species distributions

Organismal distributions are defined by the conditions that permit the organism to survive and reproduce. Phenological models that are combined with models of environment-dependent survival and reproduction can predict the conditions under which organisms with specific developmental attributes are able to persist and thereby predict range limits of genotypes, ecotypes, or species. Such analyses can use future climate scenarios to project future species distributions and can evaluate the effect of specific environmental factors on distributions. For example, Scots pine in France is predicted to lose much suitable habitat in the future, caused primarily by changes in temperature rather than changes in precipitation [71]. Such analyses can also identify key developmental responses that limit distributions. In temperate tree species, Morin *et al.* [54] found that failure to mature fruits before frost set the northern and high-altitude range limit of some tree species in North America and an inability to break flower bud dormancy set the southern range limit (Figure IC).
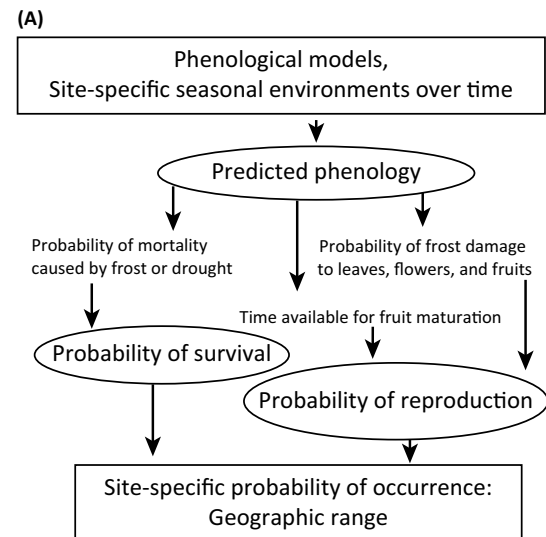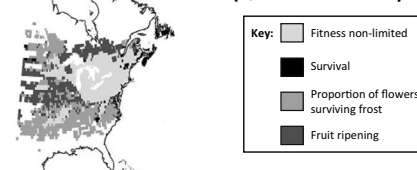
Adapted from Chuine and Beaubien 2001; Chuine 2010.

(B)   Identifying key environmental parameters that limit distributions

Scots pine

Observed distribution   Predicted distribution using PHENOFIT

Key: ■ Presence ☐ Absence

Predicted distribution in 2055

Key: ☐ Stable unsuitable area ■ Stable suitable area ■ Loss of suitable area

P   T

P = Predicted distribution if precipitation stays at present level but temperature changes; T = predicted distribution if temperature stays at present level but precipitation changes. Adapted from Cheaib et al. 2012.

(C)   Identifying key biological processes that limit distribution (*Quercus macrocarpa*)

Key: ☐ Fitness non-limited ■ Survival ☐ Proportion of flowers surviving frost ■ Fruit ripening

Adapted from Morin et al. 2007.

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Figure I. (A) Summary of the structure of PHENOFIT, a process-based model that predicts geographic ranges as a function of phenological responses to temporally variable climatic environments. (B) Results comparing the observed distribution of Scots pine to the distribution predicted by PHENOFIT in present climatic conditions (upper) and in future conditions (lower). (C) Summary of results that identify key biological processes (indicated in key) that limit the geographic distribution of *Quercus macrocarpa*.

Box 3. Population-based threshold models

Population-based threshold models (PBTMs) are illustrated here using a simple hydraulic analogy. A tank of water represents the input of environmental signals (X; such as temperature, water potential, day length). The levels of outlets from the tank represent the sensitivity thresholds of individuals in the population (X_b) to the signal. The rate of developmental progress is proportional to the amount by which the signal exceeds the sensitivity threshold ($X - X_b$). The cups represent the amount of developmental time accumulation required for the transition (θ_X); when the cups are full (time t_i), the transition occurs for that individual.

Shared sensitivity thresholds

The simplest PBTM is commonly used for thermal time or heat unit analyses (Figure IA), where X is the temperature, X_b is the base temperature below which developmental progress is not made (assumed to be the same for all individuals), and $\theta_X(i)$ is the accumulated thermal time required by individual i for the developmental transition that occurs at calendar time t_i. A normal distribution of $\theta_X(i)$ values will result in a sigmoid developmental progression through the population over time.

Different sensitivity thresholds

A common situation occurs when the developmental time requirements (θ_X) are the same among individuals but their sensitivity thresholds vary [$X_b(i)$] (Figure IB). The rate of developmental progression of each individual is proportional to the difference between its own threshold and the signal (or dose) level. In this case, a normal distribution of thresholds in the population results in a right-skewed time course of developmental transitions, which describes many population-based biological phenomena, such as seed germination.

Change in environmental signal

If the environmental signal decreases, the model automatically increases the time to the developmental transition for each individual in the population (t_i) according to their sensitivity thresholds (Figure IC). If the signal level is below the threshold for a fraction of the population, that fraction never achieves the transition (i.e., the time course reaches a plateau below 100%) and the developmental rates of the remaining members of the population are reduced in proportion to the amount by which the signal still exceeds their own thresholds [$X - X_b(i)$].

Change in sensitivity threshold in response to a change in the environmental signal

The sensitivity of organisms to environmental signals is generally under physiological control and can be adjusted in response to conditions, as illustrated by changing the positions of the outlets on the tank (Figure ID). If the sensitivity thresholds are shifted to a lower level (often accompanied by a reduction in variance), such as by after-ripening or vernalization, rapid and synchronous developmental rates can be restored even at a reduced environmental signal level.
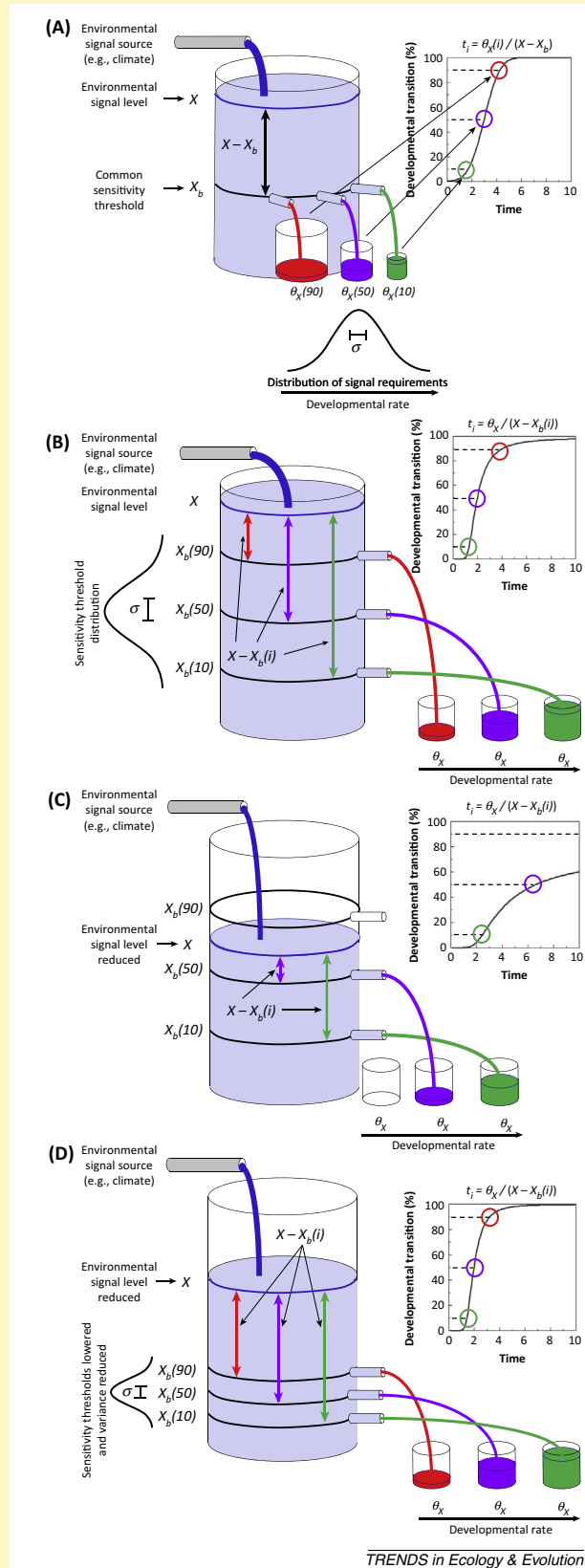

Figure I. Schematic of population-based threshold models. See text in Box 3 for further explanation of each panel.

environmental signal, their developmental time accumulation will progress at different rates even in an identical environment (see Figure IB–D in Box 3). Thus, PBTMs can model not only the mean time of a given transition, but the degree of population synchrony or temporal dispersion. PBTMs can model a wide range of phenomena by varying the population distributions of the developmental time requirements or of the sensitivity thresholds for perception of the environmental signal [47–49], including the probability of a developmental event under a given environmental scenario, the percentage of the population undergoing a developmental event at any given time, and the distribution of that event over time.

Populations, moreover, can comprise multiple subpopulations having different response parameters (e.g., [50]) and organisms perceive and respond to multiple environmental signals. The effects of both multiple subpopulations and multiple simultaneous signals can be modeled by combining the contributions of each toward reaching an overall developmental threshold [51,52].

When integrated across life cycles, developmental models of populations can investigate causes of synchronization or expression of variance in phenology (Figure 1A). For example, the model of Wilczek *et al.* [26] suggests that individual variation in germination timing in late summer might inflate variation in flowering time, whereas individuals germinating over several months in autumn might flower in relative synchrony – a hypothesis that could be tested with a PBTM. With such analyses, mechanisms of population synchronization, variance generation, and resynchronization across a life cycle can be explored, as well as the generation of phenotypic variance underlying bet-hedging.

Incorporating genetics to predict reaction norms, environment-dependent genetic expression, and genotype-specific phenology

Quantitative-genetic variation in physiological parameters [18,53] or population-genetic differences in anonymous alleles regulating a physiological process have been integrated with developmental models to predict survival under specific environmental regimes. Genetic variation can be incorporated into developmental threshold models by assigning a specific set of parameter values to different genotypes; the developmental phenotypes of each genotype can then be compared in different environmental scenarios. This approach has been applied to predict responses of different species [54] or ecotypes in models of species-wide ranges [1,33,40].

When the developmental phenotypes (e.g., timing of germination, flowering) of genotypes with different parameter values are simulated in different environmental scenarios, reaction norms can be predicted (e.g., [26]). This approach can further predict the environmental scenarios that elicit the least or greatest phenological differences among genotypes: that is, it offers a method to predict environment-dependent genetic variance in complex environments. For example, Burghardt *et al.* [24] found that phenotypic differences in generation time among genotypes are predicted to be greater in northern than in southern latitudes (Figure 1C). Wilczek *et al.* [26] found

that phenotypic effects of specific flowering-time alleles are most apparent when germination occurs during a 2-week window in early autumn, but were barely detectable when germination occurs at other times of the year. Therefore, these models can predict phenotypic differences among genotypes under different environmental scenarios or different genetic backgrounds. When combined with analysis of variance within genotypes, as discussed above, predictions of environment-dependent heritabilities may be possible. Environment-dependent genetic variances and heritabilities have been documented for decades; some environments mask genetic differences while others enhance them [55]. The ability to predict such environment-dependent genetic differences would be valuable for assessing environmental conditions that are likely to promote evolution by natural selection and those that would not.

When information on the function of specific genes is available, models can compare how allelic changes in specific loci would alter individual developmental processes or entire life cycles (Box 4) (e.g., [23]). For example, Wilczek *et al.* [26] modeled effects on flowering phenology of mutant alleles in environmental signaling pathways that caused plants to be unable to perceive specific seasonal cues. This analysis assessed how disruption of specific pathways would affect phenology and was then used to predict genotype-specific responses to climate change across a species range [32].

There is increasing potential to incorporate information on molecular-genetic pathways of environmental regulation of development into developmental threshold models. Studies of environment-dependent gene expression can identify the genes most sensitive to specific environmental inputs (e.g., for germination [56]). In some cases, the relationship between expression levels of particular genes and key developmental processes is known. For example, expression levels of the gene *FLOWERING LOCUS C* (*FLC*), which change in response to winter chilling, determine the degree of floral repression in *Arabidopsis* [57–59], which has been used as a parameter in developmental threshold models of flowering time. Such information on environment-dependent gene expression combined with knowledge of the relationship between expression level and key developmental transitions enables the merging of genetic pathways models with developmental threshold models of specific life stages and of entire life cycles (Box 4). For example, Satake *et al.* [60] modeled seasonal expression of *FLC* and the flowering promoter *FLOWERING LOCUS T* (*FT*) to describe accurately the seasonal timing of flowering and vegetative reversion in field populations of the perennial *Arabidopsis halleri* and used this model to predict that a warming climate will cause significant decreases in the length of the reproductive period.

It remains to be determined how changes at the gene or cell level are transduced into developmental transitions at the tissue or organ level. Individual cells can switch abruptly between developmental states based on the complement of transcription factors present in each cell, but developmental threshold models that posit gradual accumulation of developmental progress can accurately describe both mean trends and variation in developmental

Box 4. Building genetic pathways into developmental threshold models

Developmental threshold models derive much of their power from their simplicity: they represent complex developmental dynamics with small numbers of genotype-specific parameters. However, genetic technologies are identifying large numbers of genes involved in environmental responses across model and non-model species. As the number of candidate loci grows, linking allelic variation across loci to genotype-specific parameters (e.g., [72–74]) becomes more difficult. Gene network models describe how genes interact in pathways to transmit genetic signals and drive development. This information can be used to refine genetic parameters for developmental threshold models.

A gene network that controls vernalization requirements for flowering

As an example, many genes are known to play a role in the response of *Arabidopsis thaliana* flowering to winter chilling, or vernalization [75]. Wilczek *et al.* [26] modeled the effect of variation at four vernalization-related genes – *FLC*, *FRI*, *FVE*, and *VIN3* – based on the topology of the underlying gene network (Figure IA) [32]. *FLC* is a central hub of this network. High expression of *FLC* delays flowering and winter chilling (vernalization) represses *FLC* expression and activity. *FLC* is positivity regulated by the gene *FRI*, among others, and repressed by genes of autonomous pathways including *FVE*. Vernalization by several weeks of cold temperatures leads to epigenetic silencing of *FLC* by a pathway involving the gene *VIN3*. Gene network-guided parameterization of developmental threshold models

Wilczek *et al.* [26] used a vernalization submodel with seven parameters. They applied rules based on the gene network model to determine specific parameter modifications for each allele of the four genes (Figure IB). First, alleles of each gene directly affect only one parameter in the model. Second, genes in the same linear pathway have epistatic effects on pathway activity. Therefore, before winter chilling, functional alleles at *FRI* and nonfunctional alleles at *FVE* increase *FLC* activity when *FLC* is functional (manifested as slow-filling cups for these genotypes, because high *FLC* expression decreases progress toward flowering; see Box 3 for an explanation of the cups). Nonfunctional alleles at *VIN3* prevent repression of *FLC* by winter vernalization only if *FLC* is functional and highly expressed (manifested as a slow-filling cup for *vin3* after winter but rapidly filling cups for the other genotypes that have low *FLC* expression). Predictions of genotype-specific flowering time

These two rules allow environment-dependent predictions of flowering times of genotypes with any combination of functional and nonfunctional alleles at these four genes (Figure IC).
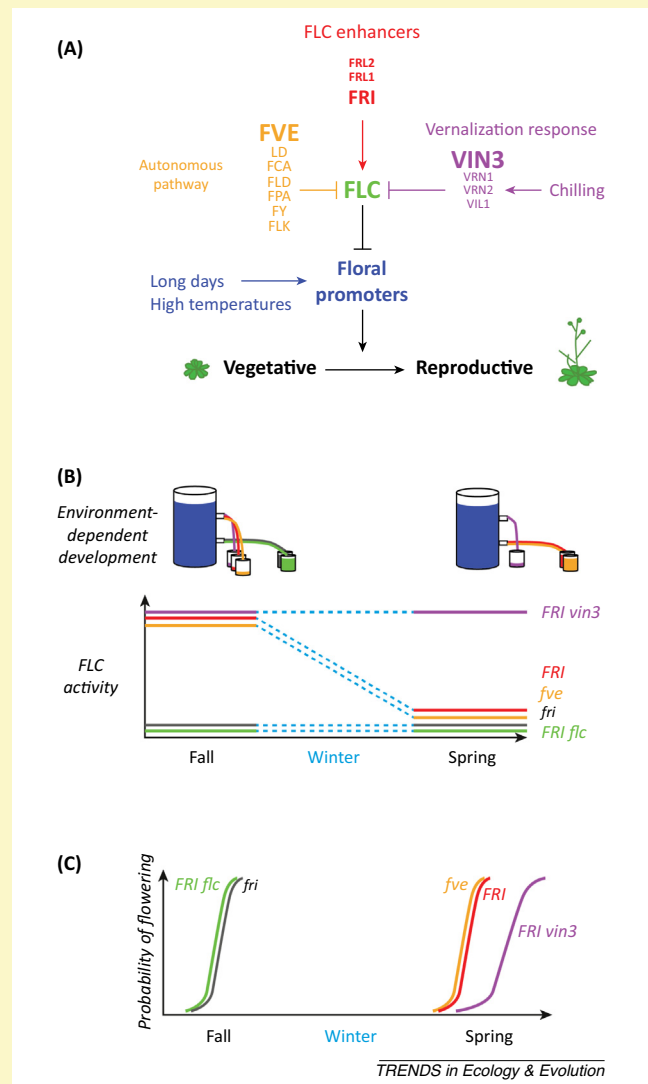

Figure I. Integrating genetic information into developmental threshold models. (A) The genetic pathway of flowering-time regulation in *Arabidopsis thaliana*. (B) Gene expression of *FLC* in different seasons (lower), as a function of the level of sensitivity of different genotypes (indicated by color) to the environmental signal of cold vernalization. Schematic in upper panel depicts genes with different environmental sensitivities. See Box 3 for more details on this schematic. (C) The probability of flowering in different seasons for different genotypes, as determined by the level of seasonal *FLC* expression of each genotype (depicted in B).

events within populations of cells. Developmental events in single cells can be triggered stochastically within a population of cells in response to internal or external factors and, in aggregate, eventually produce enough total signal to trigger an organ-level developmental event [47], as has been described for the gradual lifting of repression of flowering by vernalization in *A. thaliana* [61,62]. Whether this molecular mechanism applies to other developmental state changes is unknown [63], but mounting evidence suggests that epigenetic mechanisms such as those just discussed are important for triggering and maintaining many developmental transitions in plants [64] and these can function essentially as quantal phenomena at the genetic level.

When developmental threshold models of developmental transitions are linked across the life cycle, important consequences of pleiotropy can be investigated. Single genes can regulate multiple developmental transitions in response to environmental conditions. For example, several genes in flowering-time pathways have also been implicated in the regulation of germination (e.g., [65–68]). Models that compare similar versus independent environmental regulation of different life stages can evaluate potential outcomes of such genetic pleiotropy.

In addition, such models can investigate environmentally induced pleiotropy: a gene that alters the timing of one developmental transition also alters the seasonal environment next experienced (a form of habitat selection),

which influences the phenotypic expression of traits that exhibit plasticity to that environment. For example, a study of the seed dormancy gene *DELAY OF GERMINA-TION-1* (*DOG1*) in *A. thaliana* showed that *DOG1* influenced not only germination timing but also flowering phenology, and that it did so through its effects on germination [69]. *DOG1* altered not only phenotypic expression of post-germination traits but also the expression of allelic differences in other genes. Such dynamics thereby can influence fundamental patterns of genetic correlations among traits. Developmental threshold models support such empirical studies and have shown that variation in parameters regulating prior developmental transitions, such as dormancy, influence later life stages, such as flowering and generation time [24] (Figure 1). These models can therefore make predictions about phenotypic and genetic correlations under diverse environments.

Concluding remarks: integration across the life cycle while incorporating fitness, variance, and genetics

To our knowledge, no process-based model has incorporated all of the components discussed above, but such integration is possible and would be a powerful approach for studying ecological and evolutionary outcomes in variable or changing environments (Box 5).

Models that have combined linked life stages, a population-level approach to incorporate variance, and genetic information have been able to evaluate how allelic changes in genes regulating specific life stages influence phenotypic expression across the life cycle and how the geographical distribution of alleles influences the geographical distribution of life histories. In the case of *A. thaliana* (Figure 1),

seed dormancy influenced generation time expressed across the native range and the known geographical cline in the distribution of dormancy alleles was predicted to canalize an annual life cycle across the range of this species.

Models that have linked life stages within a generation and incorporated fitness have predicted species distributions in the past, present, and future (Box 2). They have also identified key developmental processes and environmental factors that limit species distributions and those that are likely to do so under scenarios of future climate change.

The developmental models that integrate life stages across generations (Figure 1) so far have not incorporated fitness. The models integrating phenology, fitness, and species distributions (Box 2) have not linked life stages across generations nor incorporated specific genetic information concerning the regulation of specific pathways. Neither has fully incorporated intrapopulation variation throughout the life cycle. Incorporating fitness into genetically informed models that link life stages within and across generations would allow predictions of genotype-specific ranges in present and future climatic scenarios and would allow estimates of the relative fitness of specific alleles. Sensitivity analyses of these models have the potential to identify specific genes and alleles that most strongly affect population performance and range limits under different climatic scenarios. Combining the fitness outputs of developmental threshold models with explicitly demographic models would allow predictions of genotypic growth rates and facilitate the analysis of effects of stochasticity, dispersal, and density-dependence that are already incorporated into demographic models. With such a synthesis, there is the potential to predict evolutionary responses to selection of specific developmental processes and the genetic pathways that regulate them. Incorporation of such genetic specificity into projections of the effects of climate change could enhance management decisions for both wild and cultivated systems.

Box 5. Future goals

Characterize the sources and consequences of within-population variation in developmental events

This requires studying developmental processes of individuals that comprise populations and assessing the contributions of environmental variance, stochasticity of gene expression, and genetic variance. Doing so could permit analysis of environment-dependent genetic variation and heritability, which is necessary for predicting responses to selection.

Incorporate environment-dependent fitness into genetically informed models that link life stages within and across generations

This would enable predictions of genotype-specific ranges in present and future climatic scenarios. It also has the potential to enable estimates of relative fitness of different genotypes in different locations and thereby generate evolutionary hypotheses concerning local adaptation.

Integrate the fitness outputs of developmental threshold models with demographic models

This would allow explorations of the effects of stochasticity, dispersal, and density dependence.

Conduct sensitivity analyses of fully integrated models

This could identify key physiological processes and environmental factors that limit species distributions.

Integrate molecular-genetic information, including genetic pathway structure, into developmental threshold models

This has the potential to identify key genes and alleles that contribute to local adaptation and limit geographic distributions.

Apply developmental threshold models to molecular-genetic processes

Evaluating how apparently quantitative or continuous traits can result from state shifts of quantal traits among populations of cells could clarify the mechanistic basis of developmental thresholds.

References

1 Chuine, I. and Beaubien, E.G. (2001) Phenology is a major determinant of tree species range. *Ecol. Lett.* 4, 500–510
2 Walther, G.R. *et al.* (2002) Ecological responses to recent climate change. *Nature* 416, 389–395
3 Menzel, A. *et al.* (2006) Altered geographic and temporal variability in phenology in response to climate change. *Glob. Ecol. Biogeogr.* 15, 498–504
4 Parmesan, C. (2006) Ecological and evolutionary response to recent climate change. *Annu. Rev. Ecol. Syst.* 37, 637–669
5 Bradshaw, W.E. and Holzapfel, C.M. (2008) Genetic response to rapid climate change: it's seasonal timing that matters. *Mol. Ecol.* 17, 157–166
6 Allen, P.S. *et al.* (2000) Hydrothermal time as a tool in comparative germination studies. In *Seed Biology: Advances and Applications* (Black, M. *et al.*, eds), pp. 401–410, CABI Publishing

7 Alvarado, V. and Bradford, K. (2002) A hydrothermal time model explains the cardinal temperatures for seed germination. *Plant Cell Environ.* 25, 1061–1069

8 Bradford, K.J. (2002) Applications of hydrothermal time to quantifying and modeling seed germination and dormancy. *Weed Sci.* 50, 248–260

9 Bradford, K.J. (2005) Threshold models applied to seed germination ecology. *New Phytol.* 165, 338–341

10 Allen, P.S. (2003) When and how many? Hydrothermal models and the prediction of seed germination. *New Phytol.* 158, 1–3

11 Welch, S.M. *et al.* (2003) A genetic neural network model of flowering time control in *Arabidopsis thaliana*. *Agron. J.* 95, 71–81

12 De Melo-Abreu, J.P. *et al.* (2004) Modelling olive flowering date using chilling for dormancy release and thermal time. *Agric. Forest Meteorol.* 125, 117–127

13 Cockram, J. *et al.* (2007) Control of flowering time in temperate cereals: genes, domestication and sustainable productivity. *J. Exp. Bot.* 58, 1231–1244

14 Hänninen, H. and Kramer, K. (2007) A framework for modelling the annual cycle of trees in boreal and temperate regions. *Silva Fenn.* 41, 167–205

15 McMaster, G.S. *et al.* (2008) Simulating the influence of vernalization, photoperiod and optimum temperature on wheat developmental rates. *Ann. Bot. (Lond.)* 102, 561–569

16 Meyer, S.E. and Allen, P.S. (2009) Predicting seed dormancy loss and germination timing for *Bromus tectorum* in a semi-arid environment using hydrothermal time models. *Seed Sci. Res.* 19, 225–239

17 Chuine, I. *et al.* (2013) Plant development models. In *Phenology: An Integrative Environmental Science* (Schwarz, M.D., ed.), pp. 275–293, Springer

18 Kearney, M. *et al.* (2009) Integrating biophysical models and evolutionary theory to predict climatic impacts on species' ranges: the dengue mosquito *Aedes aegypti* in Australia. *Funct. Ecol.* 23, 528–538

19 Weinig, C. (2014) Ecological genomics and process modeling of local adaptation to climate. *Curr. Opin. Plant Biol.* 18, 66–72

20 Donohue, K. (2014) Why ontogeny matters during adaptation: developmental niche construction and pleiotropy across the life cycle in *Arabidopsis thaliana*. *Evolution* 68, 32–47

21 Morin, X. (2008) Tree species range shifts at a continental scale: new predictive insights from a process-based model. *J. Ecol.* 96, 784–794

22 Hoogenboom, G. *et al.* (1994) BEANGRO: a process-oriented dry bean model with a versatile user interface. *Agron. J.* 86, 182–190

23 White, J.W. and Hoogenboom, G. (1996) Simulating effects of genes for physiological traits in a process-oriented crop model. *Agron. J.* 88, 416–422

24 Bughardt, L. *et al.* (2015) Modeling the influence of genetic and environmental variation on plant life cycles across landscapes. *Am. Nat.* (in press)

25 Stoeckli, S. *et al.* (2012) Impact of climate change on voltinism and prospective diapause induction of a global pest insect – *Cydia pomonella* (L.). *PLoS ONE* 7, e35723

26 Wilczek, A.M. *et al.* (2009) Effects of genetic perturbation on seasonal life history plasticity. *Science* 323, 930–934

27 Donohue, K. (2009) Completing the cycle: maternal effects as the missing link in plant life cycles. *Philos. Trans. R. Soc. Lond. B: Biol. Sci.* 364, 1059–1074

28 Galloway, L.F. and Etterson, J.R. (2007) Transgenerational plasticity is adaptive in the wild. *Science* 318, 1134–1136

29 Fox, C.W. and Czesak, M.E. (2009) Adaptive maternal effects: a case study of egg size plasticity in a seed-feeding beetle. In *Phenotypic Plasticity of Insects: Mechanisms and Consequences* (Whitman, D.W. and Ananthakrishnan, T.N., eds), pp. 781–815, Science Publishers

30 Rossiter, M.C. (1994) Maternal effects hypothesis of herbivore outbreak. *Bioscience* 44, 752–763

31 Mousseau, T.A. and Fox, C.W., eds (1998) *Maternal Effects As Adaptations*, Oxford University Press

32 Wilczek, A.M. *et al.* (2010) Genetic and physiological bases for phenological responses to current and predicted climates. *Philos. Trans. R. Soc. Lond. B: Biol. Sci.* 365, 3129–3147

33 Andreini, L. *et al.* (2014) Understanding dormancy release in apricot flower buds (*Prunus armeniaca* L.) using several process-based phenological models. *Agric. Forest Meteorol.* 184, 210–219

34 Rezende, E.L. (2014) Tolerance landscapes in thermal ecology. *Funct. Ecol.* 28, 799–809

35 Kearney, M. *et al.* (2010) Modelling the ecological niche from functional traits. *Philos. Trans. R. Soc. Lond. B: Biol. Sci.* 365, 3469–3483

36 Kearney, M. *et al.* (2008) Modelling species distributions without using species distributions: the cane toad in Australia under current and future climates. *Ecography* 31, 423–434

37 Crespo-Pérez, V. *et al.* (2013) Modeling temperature-dependent survival with small datasets: insights from tropical mountain agricultural pests. *Bull. Entomol. Res.* 103, 336–343

38 Chew, Y.H. *et al.* (2014) Multiscale digital *Arabidopsis* predicts individual organ and whole-organism growth. *Proc. Natl. Acad. Sci. U.S.A.* 111, E4127–E4136

39 Bykova, O. *et al.* (2012) Temperature dependence of the reproduction niche and its relevance for plant species distributions. *J. Biogeogr.* 39, 2191–2200

40 Saltré, F. *et al.* (2013) Climate or migration: what limited European beech post-glacial colonization? *Glob. Ecol. Biogeogr.* 22, 1217–1227

41 Dormann, C.F. *et al.* (2012) Correlation and process in species distribution models: bridging a dichotomy. *J. Biogeogr.* 39, 2119–2131

42 Hartig, F. *et al.* (2012) Connecting dynamic vegetation models to data – an inverse perspective. *J. Biogeogr.* 39, 2240–2252

43 Higgins, S.I. *et al.* (2012) A physiological analogy of the niche for projecting the potential distribution of plants. *J. Biogeogr.* 39, 2132–2145

44 Gritti, E.S. *et al.* (2013) Estimating consensus and associated uncertainty between inherently different species distribution models. *Methods Ecol. Evol.* 4, 442–452

45 Violle, C. *et al.* (2012) The return of the variance: intraspecific variability in community ecology. *Trends Ecol. Evol.* 27, 244–252

46 Trewavas, A.J. (2012) Information, noise and communication: thresholds as controlling elements in development. In *Biocommunication of Plants. Signaling and Communication in Plants* (Witzany, G. and Baluska, F., eds), pp. 11–35, Springer-Verlag

47 Bradford, K.J. and Trewavas, A.J. (1994) Sensitivity thresholds and variable time scales in plant hormone action. *Plant Physiol.* 105, 1029–1036

48 Bradford, K.J. (1995) Water relations in seed germination. In *Seed Development and Germination* (Kigel, J. and Galili, G., eds), pp. 351–396, Marcel Dekker

49 Allen, P.S. *et al.* (2007) Modeling of seed dormancy. In *Seed Development, Dormancy and Germination* (Bradford, K.J. and Nonogaki, H., eds), pp. 72–112, Blackwell

50 Mesgaran, M.B. *et al.* (2013) Importance of distribution function selection for hydrothermal time models of seed germination. *Weed Res.* 53, 89–101

51 Ni, B.R. and Bradford, K.J. (1993) Germination and dormancy of abscisic acid-deficient and gibberellin-deficient mutant tomato seeds. Sensitivity of germination to abscisic acid, gibberellin, and water potential. *Plant Physiol.* 101, 607–617

52 Alvarado, V. and Bradford, K.J. (2005) Hydrothermal time analysis of seed dormancy in true (botanical) potato seeds. *Seed Sci. Res.* 15, 77–88

53 Oddou-Muratorio, S. and Davi, H. (2014) Simulating local adaptation to climate of forest trees with a Physio-Demo-Genetics model. *Evol. Appl.* 7, 453–467

54 Morin, X. (2007) Process-based modeling of species' distributions: what limits temperate species range boundaries? *Ecology* 88, 2280–2291

55 Via, S. and Lande, R. (1987) Evolution of genetic variability in a spatially heterogeneous environment: effects of genotype–environment interaction. *Genet. Res.* 49, 147–156

56 Footitt, S. *et al.* (2014) Environment sensing in spring-dispersed seeds of a winter annual *Arabidopsis* influences the regulation of dormancy to align germination potential with seasonal changes. *New Phytol.* 202, 929–939

57 Sheldon, C.C. *et al.* (2000) The molecular basis of vernalization: the central role of *FLOWERING LOCUS C (FLC)*. *Proc. Natl. Acad. Sci. U.S.A.* 97, 3753–3758

58 Michaels, S.D. *et al.* (2003) Attenuation of *FLOWERING LOCUS C* activity as a mechanism for the evolution of summer-annual flowering behavior in *Arabidopsis*. *Proc. Natl. Acad. Sci. U.S.A.* 100, 10102–10107

59 Jarillo, J.A. and Piñeiro, M. (2011) Timing is everything in plant development. The central role of floral repressors. *Plant Sci.* 181, 364–378

60 Satake, A. *et al.* (2013) Forecasting flowering phenology under climate warming by modelling the regulatory dynamics of flowering-time genes. *Nat. Commun.* 4, 2303–2311

61 Satake, A. and Iwasa, Y. (2012) A stochastic model of chromatin modification: cell population coding of winter memory in plants. *J. Theor. Biol.* 302, 6–17

62 Angel, A. *et al.* (2011) A Polycomb-based switch underlying quantitative epigenetic memory. *Nature* 476, 105–108

63 Adrian, J. (2009) From decision to commitment: the molecular memory of flowering. *Mol. Plant* 2, 628–642

64 Kaufmann, K. (2010) Regulation of transcription in plants: mechanisms controlling developmental switches. *Nat. Rev. Genet.* 11, 830–842

65 Chiang, G.C.K. *et al.* (2009) A major flowering-time gene, *FLOWERING LOCUS C*, controls temperature-dependent germination in *Arabidopsis thaliana*. *Proc. Natl. Acad. Sci. U.S.A.* 106, 11661–11666

66 Penfield, S. and Hall, A. (2009) A role for multiple circadian clock genes in the response to signals that break seed dormancy in *Arabidopsis*. *Plant Cell* 21, 1722–1732

67 Bassel, G.W. *et al.* (2011) Genome-wide network model capturing seed germination reveals coordinated regulation of plant cellular phase transitions. *Proc. Natl. Acad. Sci. U.S.A.* 108, 9709–9714

68 Huang, D. *et al.* (2013) MicroRNAs and their putative targets in *Brassica napus* seed maturation. *BMC Genomics* 14, 130

69 Chiang, G.C.K. *et al.* (2013) Pleiotropy in the wild: the dormancy gene *DOG1* exerts cascading control on life cycles. *Evolution* 67, 883–893

70 Chuine, I. (2010) Why does phenology drive species distribution? *Philos. Trans. R. Soc. Lond. B: Biol. Sci.* 365, 149–3160

71 Cheaib, A. *et al.* (2012) Climate change impacts on tree ranges: model intercomparison facilitates understanding and quantification of uncertainty. *Ecol. Lett.* 15, 533–544

72 Hoogenboom, G. and White, J.W. (2003) Improving physiological assumptions of simulation models by using gene-based approaches. *Agron. J.* 95, 82–89

73 White, J.W. *et al.* (2008) Simulation-based analysis of effects of loci on flowering in wheat. *Crop Sci.* 48, 678

74 Brown, H.E. *et al.* (2013) Integration of molecular and physiological models to explain time of anthesis in wheat. *Ann. Bot. (Lond.)* 112, 1683–1703

75 Song, J. (2013) Remembering the prolonged cold of winter. *Curr. Biol.* 23, R807–R811