

A Stochastic Model for Predicting Age and Mass at Maturity of Insects

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Submitted August 29, 2019; Accepted February 25, 2020; Electronically published June 15, 2020

Online enhancements: appendix. Dryad data: <https://doi.org/10.5061/dryad.g4f4qrfmm>.

ABSTRACT: Variation in age and mass at maturity is commonly observed in populations, even among individuals with the same genetic and environmental backgrounds. Accounting for such individual variation with a stochastic model is important for estimating optimal evolutionary strategies and for understanding potential trade-offs among life-history traits. However, most studies employ stochastic models that are either phenomenological or account for variation in only one life-history trait. We propose a model based on the developmental biology of the moth *Manduca sexta* that accounts for stochasticity in two key life-history traits, age and mass at maturity. The model is mechanistic, describing feeding behavior and common insect developmental processes, including the degradation of juvenile hormone prior to molting. We derive a joint probability density function for the model and explore how the distribution of age and mass at maturity is affected by different parameter values. We find that the joint distribution is generally nonnormal and highly sensitive to parameter values. In addition, our model predicts previously observed effects of temperature change and nutritional quality on the expected values of insect age and mass. Our results highlight the importance of integrating multiple sources of stochasticity into life-history models.

Keywords: maturation, growth, life history, stochastic.

Introduction

Age and mass (i.e., size) at maturity are covarying life-history traits strongly associated with lifetime fitness (Cole 1954; Stearns 1992; Roff 2002). As a result, there has been substantial interest in understanding how they covary and evolve in response to factors such as temperature (Atkinson 1994; Davidowitz et al. 2005), predation

(Abrams and Rowe 1996; Sharpe and Hendry 2009), sexual selection (Wiklund and Fagerström 1977; del Castillo and Núñez-Farfán 1999), and diet (Teder et al. 2014). The vast majority of these studies assume that growth and maturation are deterministic (Gadgil and Bossert 1970; Charlesworth 1980; Stearns and Koella 1986; Marty et al. 2011; Kuarinen and Hutchings 2012), meaning there is only one outcome and it is fully determined by the parameter values and initial conditions. Effectively, this approach assumes that individuals with shared genetic and environmental backgrounds will exhibit identical patterns of growth and maturation. However, individual variation in age and mass at maturity that is not attributable to shared genetic or environmental factors has been observed in many organisms, including plants (Thompson et al. 1991), amphibians (Wilbur and Collins 1973), fish (Morita and Morita 2002), and invertebrates (Diamond and Kingsolver 2010).

When there is substantial individual variation in maturation or growth, the application of deterministic life-history models has been shown to bias inferences about genetic differences between populations and optimal life history (Grimm and Uchmański 2002; Heino et al. 2002; Vindenes and Øystein 2015). An alternative approach that avoids this bias requires treating growth or maturation as stochastic, that is, allowing the same parameter values and initial conditions to produce a range of outcomes. Such variation might arise from multiple unmeasured or unknown processes, including plastic responses to microenvironments (Dieckmann and Heino 2007) and developmental noise (Scheiner et al. 1991; Woods 2014). Heino et al. (2002) was among the first studies to directly incorporate stochasticity into models of age and mass at maturity, describing what are known as probabilistic maturation reaction norms (PMRNs). The PMRN approach assumes that similar individuals have the same deterministic growth function but mature probabilistically, such that they stop growing (and become adults) with probability (<1) equal

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Am. Nat. 2020. Vol. 196, pp. 227–240. © 2020 by The University of Chicago. 0003-0147/2020/19602-59449\$15.00. All rights reserved.
DOI: 10.1086/709503

to a function of current age and/or mass. Thus, some individuals in a population mature early, some keep growing and mature late, and the end result is a population with a distribution of ages and masses at maturity. PMRNs were an important step forward in that they provided a simple way of accounting for stochastic variation in life-history traits. As a result, they have become a standard tool in fisheries research for distinguishing between genetic and non-genetic differences between populations (Olsen et al. 2004; Morita and Fukuwaka 2006; Uusi-Heikkilä et al. 2011; Plaistow et al. 2015).

Despite this utility, for several reasons PMRNs fall short of providing a general method of accounting for stochastic variation in age and mass at maturity. First, PMRNs are largely phenomenological in the sense that both the structure of the maturation function and the distribution of process error (i.e., stochastic variation) are generally based on fits to empirical data rather than on knowledge of underlying developmental processes. Thus, while a fitted PMRN might provide an accurate description of the trade-offs (i.e., dependencies) between age and mass at maturity for a particular population at one time and place, it would not necessarily be correct to use that PMRN to predict trade-offs for different temporal, environmental, or genetic contexts (Dieckmann and Heino 2007). Second, studies using PMRNs typically estimate the parameters of the maturation function by optimizing linear or generalized linear models (Harney et al. 2012). An important limitation of this approach is that it assumes that stochastic variation can be accurately described by a standard distribution (e.g., normal, Poisson) and that such variation does not change over the life span of an individual. Consequently, PMRNs may not be accurate if (1) stochasticity arises from multiple undescribed sources, each with different error distributions (e.g., behavioral plus microenvironmental differences), and (2) different stages of development are affected by different processes. Both are likely common in natural populations.

Finally, while PMRNs account for stochastic variation in the timing of maturation, they do not explicitly account for stochastic variation in mass gain. Stochastic variation in mass gain has been observed under highly controlled conditions (e.g., Riska et al. 1984; Klingenberg 1996) and even among clones (Harney et al. 2012; Cressler et al. 2017), meaning that stochastic mass gain is likely present in many populations. Multiple approaches have been proposed for modeling stochastic mass gain, such as extensions to the von Bertalanffy growth function (von Bertalanffy 1957; Shelton and Mangel 2012), but to our knowledge none have been paired with stochastic models of maturation such as PMRNs. Therefore, evolutionary biologists are currently accounting for stochastic variation in either maturation or mass gain, but not both.

Integrating these two components in a general and useful way is problematic when maturation and growth functions are phenomenological. However, developing mechanistic models for age and size maturity is difficult because it requires knowledge of the underlying processes of growth and development, knowledge that is not available for most organisms (Bernardo 1993; Nijhout 2003). A notable exception is insects, where a long history of work on the developmental biology of *Manduca sexta* and *Drosophila melanogaster* has provided important insights into the processes affecting mass gain and the timing of maturation (Nijhout et al. 2014). For *M. sexta* especially, much is known about the physiological processes affecting both body mass and the timing of metamorphosis (Nijhout and Williams 1974; D'Amico et al. 2001; Davidowitz et al. 2003, 2004; Davidowitz and Nijhout 2004; Helm and Davidowitz 2015). This has led to the development of complex deterministic models that can accurately predict mean age of maturity and adult body mass for laboratory populations as well as the response of these traits to temperature and diet quality (Nijhout et al. 2006; Davidowitz et al. 2016). Nevertheless, we are aware of no studies that have used these insights to develop more sophisticated stochastic models of insect age and mass at maturity. Models incorporating variation in underlying insect developmental processes would avoid the need to rely on standard distributions for describing higher-level (i.e., composite) outcomes such as maturation. More broadly, mechanistic models could be used to develop an understanding of both cause and effect relationships during maturation and help to clarify the dependencies between life-history traits, such as age and mass at maturity. Finally, the methods used to derive a mechanistic model that combines stochastic maturation with stochastic mass gain in insects could be applied to other systems for which developmental processes are well characterized, such as *Daphnia* sp. (Ebert 1994) and zebra fish (Clelland and Peng 2009).

In this article, we develop a stochastic model that predicts the joint distribution of insect age and mass at maturity. To do so, we synthesize previous work on the feeding behavior and developmental endocrinology of *M. sexta*. We use random variables to describe the timing and outcome of well-characterized feeding and maturation processes, such as the secretion of prothoracicotropic hormone following the passing of the critical weight (Nijhout and Williams 1974). We then formally combine them to produce a joint probability density function for age and mass. This function allows us to predict the distribution of insect age and mass at maturity across a wide range of parameter values. In "Results," we explore the impact of varying model parameters on the joint distribution, generating hypotheses about how different conditions can affect the dependencies between insect age and mass.

Methods

Overview

A large body of work has focused on determining the factors that control insect mass and maturation time. Studies involving the model organisms *Drosophila melanogaster* and *Manduca sexta* in particular have informed deterministic models of insect development (Nijhout et al. 2006, 2014; Shingleton et al. 2008; Zuo et al. 2012). Many of these models focus on processes occurring during the final larval instar, as it is the period most closely linked to adult body mass. For instance, *M. sexta* larvae gain nearly 90% of their larval mass during the final (fifth) instar (Nijhout et al. 2006). Similarly, *D. melanogaster* gains more than 70% of its larval mass during its final (third) instar (Mirth et al. 2005). In developing our stochastic model, we therefore follow previous work and focus on modeling development of the final instar (herein, “caterpillar”) but note that it would be relatively straightforward to extend our model to include multiple life stages.

Below, we outline the assumptions of the stochastic model, which is based on *M. sexta* biology and may be conceptually divided into two components: (1) stochastic mass gain and (2) stochastic maturation. For both components, we incorporate known insect biology but do not attempt to provide an exhaustive accounting of all insect behaviors or developmental processes (e.g., Chapman and de Boer 1995). Rather, our goal is to describe key processes contributing to mass gain or maturation and in doing so produce a complex model that is capable of accounting for multiple sources of stochasticity. Based on the assumptions of the model, we then derive probability density functions for the joint distribution of mass gain and maturation time. Finally, we use these formulas to demonstrate the strong sensitivity of the joint distribution to different parameter values.

Justification and Description of the Stochastic Mass Gain Model

We begin by specifying a model that accounts for stochastic variation in mass gain over a life stage and that is grounded in the biology of insect feeding. To do so, we assume that caterpillar behavior can be usefully divided into two categories: feeding and nonfeeding. Feeding activities include biting and ingesting food, while nonfeeding activities include locomotion, grooming, digesting, and resting. Simplifying the time budget of a caterpillar in this way helps make our model tractable but can also be justified insofar as mass gain for insects—and, indeed, most any organism—is clearly associated with the total time spent feeding. Furthermore, validating more complex models of insect behavior would be exceptionally difficult with-

out highly replicated data from continuous (or nearly so) observations of developing insects, data that are unavailable for most species. Our simplification of caterpillar activity allows us to generate complex joint distributions for age and mass using only six parameters (see below), some of which are already known for species such as *M. sexta*. For other species, estimates could be obtained using straightforward experimental manipulations and using data covering relatively short time intervals.

Second, we assume that throughout development, caterpillars alternate between “bouts” of feeding and nonfeeding (fig. 1a). This assumption is reasonable given that many herbivorous insect larvae, including *M. sexta*, appear to feed in continuous bouts of variable duration interrupted by continuous bouts of nonfeeding, also with variable duration (Simpson 1982; Reynolds et al. 1986; Bowdan 1988). The start and stop times of bouts is generally consistent with a class of stochastic processes known as homogeneous Poisson processes (Wiepkema 1968; Slater 1974; Reynolds et al. 1986; Bowdan 1988; Timmins et al. 1988; Simpson et al. 1989; Bernays and Woods 2000). In particular, the time between the end of a feeding bout and the start of a new feeding bout for *M. sexta* is approximately exponentially distributed, in line with the distribution of waiting/interevent times of Poisson processes (Ross 2014). Therefore, in addition to assuming that caterpillars alternate between bouts of nonfeeding and feeding, we assume that the duration of these bouts is exponentially distributed. We assign λ_x as the mean rate at which caterpillars switch from feeding and λ_y as the rate at which they switch from nonfeeding. These rates correspond to the expected number of bouts per unit time, and thus larger values of λ_i are associated with shorter bout durations (i.e., caterpillars spend less time feeding or nonfeeding per bout). Last, we assume that these rates do not change over time (i.e., that they are homogeneous).

Note that λ_x is distinct from an ingestion rate insofar as it describes how long caterpillars feed rather than the rate at which they ingest food or accumulate mass. We assign a separate parameter, α , to describe the mass gained per unit time spent feeding. Mass gain could also be described as a function of the total time (i.e., $\alpha(t)$) or could itself be a random variable, but here we restrict our attention to the case where it is a constant.

Justification and Description of the Stochastic Maturation Model

The mass gain model outlined above describes how caterpillars gain mass when alternating between two states. However, it does not predict when caterpillars will reach maturity and stop switching between the states. For this we need a model of maturation that allows for stochastic variation

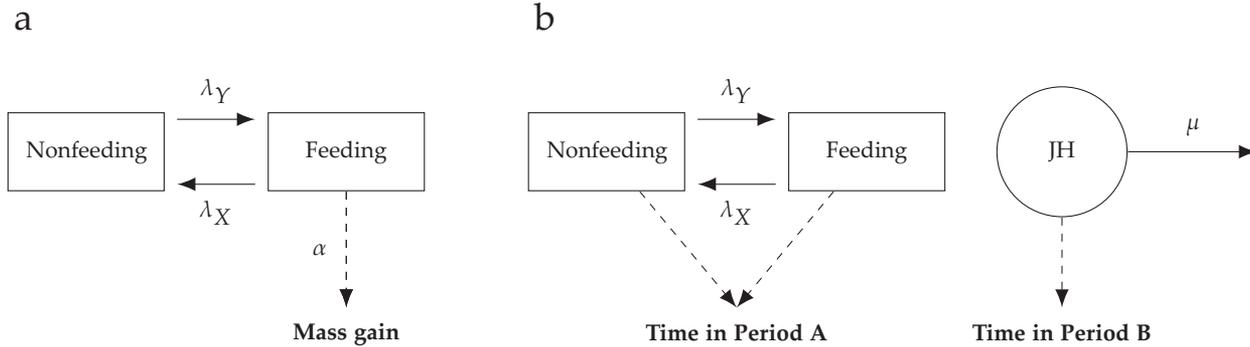


Figure 1: Conceptual diagram of the models of stochastic mass gain (*a*) and maturation (*b*) that make up the full development model. For mass gain, caterpillars are assumed to alternate between feeding and nonfeeding behaviors (i.e., feeding/nonfeeding “bouts”), switching back and forth at random according to rates λ_Y and λ_X . Caterpillars gain mass only during feeding bouts, and therefore mass at maturity is determined (dashed lines) by the time spent feeding multiplied by α , mass gain per unit time feeding. Maturation time is determined by how long caterpillars spend in both the critical weight period (period A) and the cessation of growth period (period B). The critical weight period ends when caterpillars reach the critical weight, w , but its duration is the total time spent both feeding and nonfeeding. The duration of period B is the time required to degrade j quantity of juvenile hormone (JH) at constant degradation rate μ . Simulations of the full model are shown in figure 2.

in maturation time (i.e., the total time spent in feeding and nonfeeding states). Previous work with *D. melanogaster* and *M. sexta* shows that the insect maturation from final larval instar to pupa can be divided into two distinct periods: (A) the period prior to the degradation of circulating juvenile hormone (JH), an important regulating hormone, and (B) the period in which JH degrades and is followed by pupation. Dividing development in this way is supported by the established role of JH as an inhibitor of insect metamorphosis (Nijhout 1994; Gilbert 2012; Nijhout et al. 2014). In particular, for all holometabolous insects, JH inhibits the neurosecretory hormone, prothoracicotropic hormone (PTTH), which in turn stimulates the prothoracic glands to release ecdysone, the steroid that induces ecdysis (molting). So long as JH circulates and inhibits PTTH, insect larvae will not molt into pupae, and thus JH acts as a primary control for the timing of insect maturation.

In *M. sexta*, JH degradation is triggered when caterpillars attain a “critical weight” (Nijhout and Williams 1974; Davidowitz et al. 2003), and the period prior to this event is known as the critical weight period. We follow this biology in our model, assuming that the duration of period A is determined by the time it takes caterpillars to attain a critical weight, w , given that they are continuously alternating between feeding and nonfeeding states (fig. 1*b*, left). For other insects, the degradation of JH and the release of PTTH may have different triggers. For example, in Hemiptera the cessation of growth appears to be driven by abdominal stretch receptors (Wigglesworth 1934), and in *D. melanogaster* it appears to be driven by factors related to nutrition (Colombani et al. 2003). Nevertheless, so long as the trigger for JH degradation is related to mass and

caterpillars alternate between feeding and nonfeeding, clearly the length of period A must be determined by the time spent in both states.

We assume that the duration of period B, known as the cessation of growth period, is governed by the kinetics of JH degradation. We assume that caterpillars begin this period continuing the feeding bout in which they obtained the critical weight. For simplicity, we also assume that all individuals begin with the same amount of JH. During period B, circulating JH is assumed to be sequestered by JH-binding proteins or broken down by JH esterases (Hammock 1985). Once all JH has been broken down, the cessation of growth period ends, and we assume that the caterpillar “matures.” We model this process using a stochastic compartment model, a common approach in pharmacokinetics for modeling the fate of metabolites in live organisms (Jacquez 1996). We assume an initial quantity of JH, j , is contained in a single compartment from which discrete quantities are removed at random according to a constant degradation rate μ (fig. 1*b*, right). Thus, JH removal is treated as a homogeneous Poisson process with rate μ . This is a simplified stochastic analog of the first-order deterministic model of JH degradation for *M. sexta* described in Nijhout and Reed (2008).

We incorporate the aforementioned developmental biology in our model by assuming that caterpillar maturation occurs as follows: Caterpillars begin the critical weight period (A) in a nonfeeding state, where they alternate between nonfeeding and feeding until they reach a critical weight w . Then, caterpillars enter the cessation of growth period (B) in the feeding state and continue to switch states

until the latent process of JH removal terminates and they begin molting.

Simulating Stochastic Mass Gain and Maturation

Given the stochastic mass gain and maturation models described above, it is straightforward to simulate the two models together to produce samples of the joint distribution of age and mass at maturity. However, prior to simulating the full model, it is helpful to first visualize how exponentially distributed feeding and nonfeeding times may combine to produce realizations of maturation time and mass gain. Suppose we ignore any latent developmental processes and assume that a caterpillar will experience exactly three full bouts of both feeding and nonfeeding in each of periods A and B. To simulate this, we generate six nonfeeding times (y_1, y_2, \dots, y_6) by sampling from an exponential distribution with rate λ_y and six feeding times (x_1, x_2, \dots, x_6) by sampling from an exponential distribution with rate λ_x . Then, we simply alternate them to produce a realization of this simplified scenario. Here, the length of the critical weight period is the sum of ($y_1, x_1, y_2, x_2, y_3, x_3$), the length of the cessation of growth period is the sum of ($x_4, y_4, x_5, y_5, x_6, y_6$), and total maturation time is simply the sum of all samples (fig. 2a, X-axis). To

simulate stochastic mass gain (fig. 2a, Y-axis), we simply take the samples of feeding times (x_1, x_2, \dots, x_6) and convert them to units of mass. Assuming that mass gain per unit time feeding is 1 ($\alpha = 1$), the result is caterpillars gaining mass in a stepped fashion until reaching their final mass at maturity, the sum ($x_1 + x_2 + \dots + x_6$).

Simulating the full model is only slightly more complicated: mass gain and time spent in period A can be simulated by alternating samples of feeding and nonfeeding times, converting the feeding times to mass gain, and stopping sampling once a caterpillar reaches the critical weight, w . Similarly, time spent in period B is simply how long it takes to randomly degrade j amount of JH, while mass gain can be simulated by alternating feeding and nonfeeding until this time has elapsed. In figure 2b, we illustrate 25 such simulations for each of three different parameter sets. Below we formally derive the joint probability density function for the full model.

Derivation of Joint Probability Density Function

Our main objective is to derive a probability density function (pdf) for mass gain and maturation time based on probability theory and the aforementioned feeding and developmental processes (e.g., clearance of JH). Such

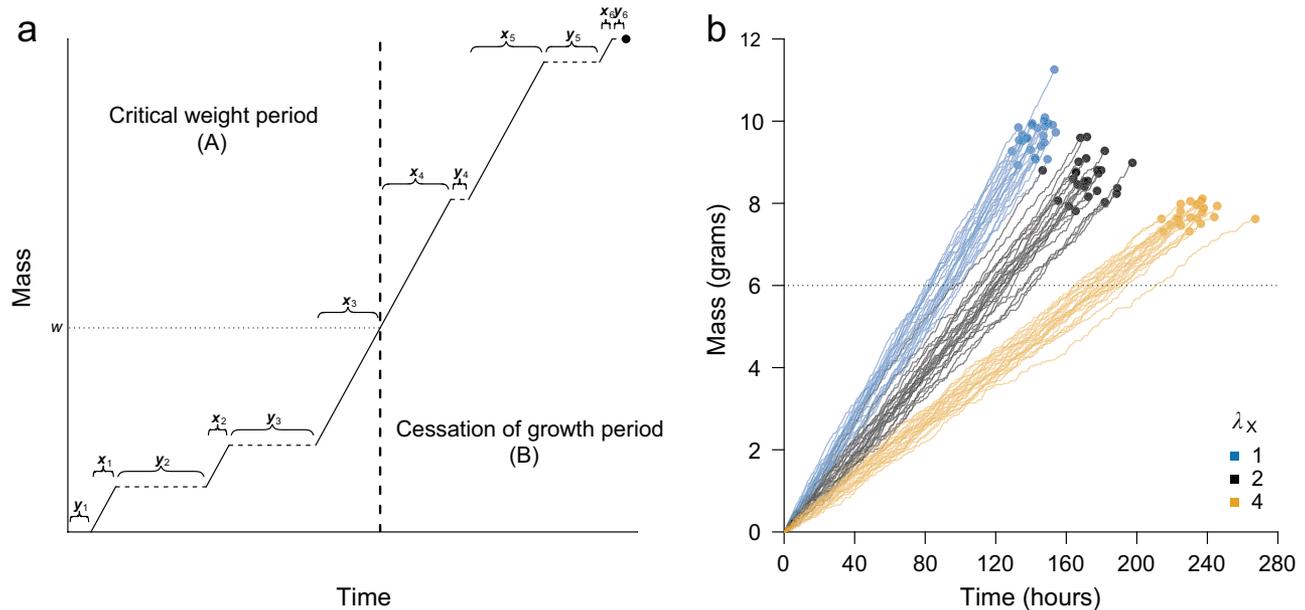


Figure 2: Simulations of stochastic mass gain and maturation. *a*, One realization of a simplified version of the model with fixed bout number. Segments labeled y_i and x_i represent the duration of the i th nonfeeding or feeding bout, respectively. Caterpillars gain mass only during feeding bouts, and for illustrative purposes we assume that mass gain per unit time feeding, α , is 1. Here we assume three bouts of each type per period (divided by dotted line). The (effective) critical weight, w , is shown on the Y-axis. *b*, Simulations of the full model with no fixed bout number for three different values of the feeding switch rate, λ_x . Lines represent ages and masses from the start of the final instar to maturation (points) and include many switches between feeding and nonfeeding. The dotted line indicates the critical weight, $w = 6$. Twenty-five simulations are shown for each parameter set (other parameters were $\lambda_y = 2$, $\alpha = 0.1$, $j = 100$, and $\mu = 2$).

functions are preferred over simulations for a number of reasons, including (1) they provide an exact description of the joint distribution of age and mass at maturity; (2) they can be used to derive formulas for expected value, variance, covariance, and correlation; (3) they can be inspected to determine links between parameter values and probabilities; and (4) they can be used in maximum likelihood estimation to optimize model parameters from data.

Let the random variables X and Y represent the total time spent feeding and nonfeeding, respectively. Assuming there are K feeding/nonfeeding bouts, they are the sums

$$X = X_1 + X_2 + \dots + X_K = \sum_{i=1}^K X_i, \quad (1)$$

$$Y = Y_1 + Y_2 + \dots + Y_K = \sum_{i=1}^K Y_i, \quad (2)$$

with $X_i \sim \text{Exponential}(\lambda_x)$ and $Y_i \sim \text{Exponential}(\lambda_y)$ based on the assumptions that caterpillar switch from feeding/nonfeeding according to exponential distributions (see above).

Let X_A and Y_A represent the total feeding and nonfeeding times for the critical weight period (A), and let X_B and Y_B represent the times for the cessation of growth period (B). Maturation time during period A is $Z_A = X_A + Y_A$, during period B is $Z_B = X_B + Y_B$, and over the full life stage is $Z = Z_A + Z_B$. Finally, let mass gain during periods A and B be M_A and M_B , with $M_i = \alpha X_i$, where α is a constant reflecting the mass gained per unit time spent feeding.

Probability Functions Associated with the Critical Weight Period. During the critical weight period, caterpillars are assumed to switch between nonfeeding and feeding until they reach a critical weight, a fixed trait we denote as the parameter w . Based on our assumption that caterpillars gain mass only during feeding bouts, they must attain this weight during a feeding bout. From these assumptions, it is straightforward to derive the distributions for both time and mass gain in period A, Z_A and M_A .

Given that caterpillars end the critical weight period the instant they attain the critical weight, clearly $M_A = w$. Furthermore, since α is the mass gained per unit time spent feeding, the moment a caterpillar attains w it will have spent exactly w/α time feeding, meaning $X_A = w/\alpha$.

Deriving the distribution for Z_A is more complicated. Since $Z_A = X_A + Y_A$, we must first obtain a distribution for the nonfeeding time in period A, Y_A . From equation (1), this requires describing K_A , the number of nonfeeding bouts during the critical weight period. In figure 2a, for illustrative purposes we assumed that K_A was fixed at 3, but we cannot make this assumption here because the full

model has caterpillars randomly alternating between feeding and nonfeeding until they reach critical weight w . Therefore, K_A must be a random variable that is in some way conditioned on w . What, then, is its distribution? The answer lies in recognizing two facts: (1) so long as caterpillars begin in the nonfeeding state and end in the feeding state, there must be an equal number of feeding and nonfeeding bouts during the critical weight period, and (2) the number of feeding bouts is the result of a renewal process (Cox 1962; Cox and Isham 1980) insofar as it is an integer that increases based on a sequence of continuously distributed waiting times (Ross 2014). Here, we are interested in the probability distribution of the stopping time of the renewal process, that is, the integer denoting the minimum number of elements in the sequence that are needed such that their sum meets or exceeds w/α . The probability mass function (pmf) of the stopping time (usually denoted as $N(t) + 1$, where t is the stopping threshold; in our case, $t = w/\alpha$) is given by (Cox 1962; Cox and Isham 1980)

$$\Pr\left(K_A = N\left(\frac{w}{\alpha}\right) + 1 = k\right) = G^{(k-1)}\left(\frac{w}{\alpha}\right) - G^{(k)}\left(\frac{w}{\alpha}\right), \quad (3)$$

where $G^{(k)}$ is the cumulative distribution function (cdf) of the k -fold convolution of the exponentially distributed (rate λ_x) waiting times (i.e., feeding times). Conveniently, the convolution of k independent and identically distributed (i.i.d.) exponential random variables each with rate λ_x is a gamma random variable with shape parameter k and scale parameter λ_x (Ross 2014). Thus, equation (3) can be expressed as

$$\Pr(K_A = k) = \left(1 - \sum_{n=0}^{k-2} \frac{\exp(-\lambda_x(w/\alpha))(\lambda_x(w/\alpha))^n}{n!}\right) - \left(1 - \sum_{n=0}^{k-1} \frac{\exp(-\lambda_x(w/\alpha))(\lambda_x(w/\alpha))^n}{n!}\right), \quad (4)$$

which reduces to the equation shown in table 1.

Since Y_A is the sum of K_A exponentially distributed random variables (see eq. [1]), the conditional probability density $f_{Y_A}(y|K_A = k)$ is simply the density of a gamma distribution with shape parameter k and scale parameter λ_y . Given w/α , λ_y , and λ_x , it is therefore straightforward to marginalize out K_A to obtain the formula for $f_{Y_A}(y)$, as shown in table 1. This formula can be evaluated numerically using partial sums. Finally, since $Z_A = w/\alpha + Y_A$ (see above), the pdf for Z_A may be written in terms of the pdf for Y_A , specifically

$$f_{Z_A}(z) = f_{Y_A}\left(z - \frac{w}{\alpha}\right). \quad (5)$$

The resulting equation for $f_{Z_A}(z)$ is shown in table 1.

Table 1: Probability mass/density functions (pmf/pdf) of the insect development model

Description	Value or pmf/pdf
Critical weight period:	
Feeding time	$X_A = w/\alpha$
Mass gain	$M_A = w$
No. bouts,	$\frac{(\lambda_X(w/\alpha))^{k-1} \exp(-\lambda_X(w/\alpha))}{(k-1)!}$
$\Pr(K_A = k), k \geq 1$	
Nonfeeding time,	
$f_{Y_A}(y)$	$\sum_k f_{\text{GAM}}(y; k, \lambda_Y) \frac{(\lambda_X(w/\alpha))^{k-1} \exp(-\lambda_X(w/\alpha))}{(k-1)!}$
Development time,	
$f_{Z_A}(z)$	$\sum_k f_{\text{GAM}}\left(z - \frac{w}{\alpha}; k, \lambda_Y\right) \frac{(\lambda_X(w/\alpha))^{k-1} \exp(-\lambda_X(w/\alpha))}{(k-1)!}$
Cessation of growth period:	
Development time,	$f_{\text{GAM}}(z; j, \mu)$
$f_{Z_B}(z)$	
Mass gain,	
$f_{M_B}(x Z_B = z)$	$\exp\left(-\frac{\lambda_X}{\alpha}x\right) \left(\left(\frac{I_1(2\sqrt{z\alpha - x\phi})}{\exp((\lambda_Y/\alpha)(z\alpha - x))\sqrt{z\alpha - x}} - \frac{\phi}{2} \right) \left(\frac{I_2(2\sqrt{h\phi}) + I_0(2\sqrt{h\phi})\sqrt{h}}{\exp((\lambda_Y/\alpha)h)\sqrt{h\phi}} dh \right) - \frac{(\lambda_Y/\alpha)(\lambda_X/\alpha) \int_0^{z\alpha-x} I_1(2\sqrt{h\phi})}{2\phi} dh \right)$
	$+ \frac{\lambda_Y}{\alpha} \exp\left(-\frac{\lambda_X}{\alpha}x\right) \left(1 + \phi \left(\int_0^{z\alpha-x} \frac{I_1(2\sqrt{h\phi})}{\exp((\lambda_Y/\alpha)h)\sqrt{h}} dh \right) \right), \quad \phi = \sqrt{\frac{\lambda_Y \lambda_X}{\alpha} x}$

Note: For both the critical weight period and the cessation of growth period, parameters λ_Y and λ_X are the rates of the exponentially distributed waiting times between nonfeeding and feeding bouts. Parameter w is the critical weight, α is mass gain per unit time feeding, μ is the degradation rate of juvenile hormone (JH), and j is the (discrete) amount of JH present at the beginning of the cessation of growth period. f_{GAM} is the pdf of the gamma distribution. The summation in the pdf of Y_A is across all possible values of k (number of feeding bouts) and can be evaluated numerically using partial sums. For the conditional distribution of M_B , I_n is the modified Bessel function of the first kind of order n . R scripts for all functions, including the joint pdf of the full model, are provided in the Dryad Digital Repository (<https://doi.org/10.5061/dryad.g4f4qrfmm>; Legault and Kingsolver 2020) and at https://github.com/legault/Stochastic_maturatoin_growth. Further details on the derivations of the formulas are discussed in the main text.

Probability Functions Associated with the Cessation of Growth Period. The length of the cessation of growth period, Z_B , is determined by how long it takes j quantity of JH to (randomly) degrade. Since JH degradation is a Poisson process, the pdf for the time to degrade one unit of JH is an exponential distribution with rate μ . Removals are assumed to be independent, and so the pdf of the time to degrade all JH is the convolution of j i.i.d. exponential random variables. This convolution is known to be a gamma distribution with shape parameter j and scale parameter μ , and so we use this distribution to represent Z_B in table 1.

The distribution of feeding time, X_B , and thereby mass gain, M_B , is conditioned on the timing of JH degradation. We are interested in the conditional probability density that a caterpillar spends x time feeding during an interval of length z , specifically, $f_{X_B}(x|Z_B = z)$. Even though caterpillars are assumed to begin this period by continuing their last feeding bout in period A, because of the memoryless property of the exponential distribution, we can treat this first bout like all other exponentially distributed feeding bouts. Therefore, the repeated switches between feeding and nonfeeding during this period can be characterized as an alternating renewal process with exponentially distributed waiting times, for which the exact cdf of the residence time in a state is known (Takács 1957; Barlow and Hunter 1961). While the original cdf in Takács (1957) applies to the residence time in what we call the nonfeeding state, it can be reformulated to apply to the feeding state. We took the derivative of this new formula to obtain the pdf. The conditional density $f_{M_B}(x|Z_B = z)$ (shown in table 1) follows easily from this, since f_{X_B} is part of the exponential family and is therefore closed under scaling.

Given the marginal pdf of Z_B and the density of M_B conditioned on Z_B , the joint density function of maturation time and mass gain during the cessation of growth period, $f_{Z_B, M_B}(z, x)$, is simply the product of the first and last formulas for period B in table 1.

Joint Probability Density of the Full Model

Having derived pdfs for (Z_A, M_A) and (Z_B, M_B) (see table 1), it is straightforward to obtain the joint distributions of maturation time ($Z = Z_A * Z_B$; $*$ is the convolution symbol) and mass ($M = M_A * M_B$). Since variables from periods A and B are independent, the joint density is the integral

$$f_{Z, M}(z, m) = \int_{v=w/\alpha}^{\infty} f_{Z_A}(z-v) f_{Z_B}(v) f_{M_B}(m-w) dv, \quad (6)$$

where f_{Z_A} , f_{Z_B} , and f_{M_B} are shown in table 1 (for the sake of space, we omit the full equation from the table).

In the appendix (available online), we validate the pdfs derived above by comparing them to independently simulated data: they align nearly exactly for all parameter values considered. Additionally, in the appendix we provide R functions for evaluating each of the formulas in table 1.

Analysis of the Full Model

The six parameters in our model are feeding switch rate (λ_x), nonfeeding switch rate (λ_y), critical weight (w), mass gain per unit time feeding (α), amount of JH at the beginning of the cessation of growth period (j), and the degradation rate of JH (μ). In "Results," we examine how variation in some of these parameters affects the joint distribution of age and mass at maturity. For the purposes of comparison to the biology of *M. sexta*, we make the following additional assumptions about the units of these parameters: rates λ_x , λ_y , and μ reflect switches or degradations per hour; w is in grams; and α is grams per hour feeding.

Where possible, we chose parameter values that reflected the known biology of *M. sexta*. For instance, the critical weight of *M. sexta* is 6–6.5 g (D'Amico et al. 2001) and is largely insensitive to environmental factors (Nijhout 2003). Thus, we assumed that the critical weight did not vary and set $w = 6$. Similarly, under laboratory conditions we have observed *M. sexta* feeding one to six times per hour, and so we set $\lambda_x = 1, 2$, and 4 and $\lambda_y = 1, 2$, and 4, representing averages of one to four switches per hour. For the remaining parameters, values were chosen such that final masses/ages were within previously observed ranges for the species (e.g., late-instar *M. sexta* caterpillars are rarely larger than 15 g). These values were $\alpha = 0.05, 0.1$, and 0.2; $j = 100$; and $\mu = 1, 2$, and 4.

The four parameters we varied were λ_x , λ_y , μ , and α . Variation in λ_x or λ_y could reflect differences in feeding behavior, vigilance, or digestion. Since μ is the degradation rate of a hormone, variation in this parameter could arise from temperature variation, since temperature is known to affect chemical kinetics. Finally, variation in α , mass gain per hour, could reflect differences in the nutritional quality of the food being consumed.

For all parameter sets considered, we evaluated (numerically) the joint pdf described above (eq. [6]) for a 150×150 grid of Z and M values. Numerical evaluation involved the first $50/\alpha$ terms of the partial sum in the pdf of Z_A , which we found to provide a reasonable balance between exactness and tractability. We created contour plots of the resulting probability densities to approximate the joint distribution of age and mass at maturity.

We also considered the sensitivity of the joint distribution to simultaneous changes in λ_x , λ_y , and μ , which

we report in the appendix. In addition, to compare the distributions generated by our model to analogous multivariate normal distributions, we evaluated the expected values (\mathbb{E}) of Z , M , Z^2 , M^2 , and ZM . These values were used to estimate the variance (Var), covariance (Cov), and Pearson correlation coefficient (Cor) of age and size at maturity. Using the package *mvtnorm* (Genz et al. 2019), we then generated multivariate normal distributions for Z and M setting the means, variances, and covariances equal to the aforementioned evaluations. We compare these multivariate normal distributions to those of our model in the appendix.

Results

Sensitivity of the Joint Distribution of Maturation Time and Mass Gain

In figure 3, we show the impact of varying individual model parameters on the joint distribution of maturation time (Z) and mass at maturity (M). As feeding switch rate (λ_x) increases and holding all other parameters constant (fig. 3a; $\lambda_y = \mu = 2$, $j = 100$, $w = 6$, $\alpha = 0.1$), the highest-density regions (i.e., darker contours) shift toward higher maturation time, Z (Y -axis), and lower mass at maturity, M (X -axis). With respect to maturation time, increasing the feeding switch rate affects the duration of the critical weight period by increasing the number of bouts that occur during this period. Since a feeding bout must always be followed by a nonfeeding bout, this increases the duration of nonfeeding and thereby increases maturation time. With respect to mass, a higher feeding switch rate means that caterpillars spend relatively less time feeding during the cessation of growth period and therefore gain less mass overall. In addition to causing shifts in the expected values of Z and M (contained in the innermost contour in fig. 3a), increasing λ_x alters the shape and orientation of the highest-density regions, shrinking the tails of the distribution on the mass axis and rotating it toward the maturation time axis.

As nonfeeding switch rate increases (fig. 3b; $\lambda_x = \mu = 2$, $j = 100$, $w = 6$, $\alpha = 0.1$), the highest-density regions shift toward higher mass at maturity and shorter maturation time. With respect to maturation time, higher λ_y means that each nonfeeding bout is shorter, and therefore the length of the critical weight period is also shorter. Mass increases as λ_y increases largely because faster switches out of the nonfeeding state means that caterpillars spend more of the cessation of growth period feeding. Again, the shape and orientation of the highest-density regions appear sensitive to changes in λ_y , with increases leading to smaller tails on the maturation time axis and rotating the distribution toward the mass axis.

Increasing the degradation rate of JH (fig. 3c; $\lambda_x = \lambda_y = 2$, $j = 100$, $w = 6$, $\alpha = 0.1$) shifts the highest-density regions to lower values of Z and M . Since μ is relevant only for the cessation of growth period, the reduction in Z can be explained by the fact that higher degradation rates shorten the cessation of growth period. With respect to mass, a shorter interval Z_b means that caterpillars spend less total time feeding. Here, increasing μ appears to affect only the shape of the distribution, shrinking the tails of the distribution on both axes.

The joint distribution of age and mass at maturity is highly sensitive to changes in parameter α , mass gain per hour feeding (fig. 3d; $\lambda_x = \lambda_y = \mu = 2$, $j = 100$, $w = 6$). As α increases, the highest-density regions shift from an area of long maturation time and low mass to an area with short maturation time and high mass. The effect on maturation time Z can be explained by the fact that higher values of α mean that caterpillars gain more mass per feeding bout and thus require fewer feeding bouts (and paired nonfeeding bouts) before reaching the critical weight. The increases to mass gain M is driven largely by increased feeding efficiency during feeding bouts in the cessation of growth period. Increasing α has a striking effect on both the shape and the orientation of the joint distribution, greatly expanding the tails on the mass axis and rotating the distribution toward the mass axis.

Discussion

Understanding variation in and trade-offs among life-history traits, such as age and size at maturity, is key for predicting how organisms will respond to environmental change. Mechanistic models of life-history traits (i.e., trade-off functions *sensu* Roff 2002) are available for only a small subset of organisms and are largely deterministic, meaning that they predict that all individuals with shared genetic backgrounds/environments will have the same age and mass at maturity. As a consequence, trade-offs between age and maturity are also treated as deterministic; for example, early-maturing individuals will always be small, and late-maturing individuals will always be large. However, empirical studies indicate that there is substantial individual variation in age and mass at maturity across populations, taxa, and environments. Thus, similar individuals experiencing the same environment do not exhibit the same life-history traits, and trade-offs between these traits are much more complex. Much of this individual variation is effectively stochastic, necessitating the development of stochastic life-history models.

Previous authors interested in modeling trade-offs between age and mass at maturity have proposed stochastic models of either maturation time (e.g., PMRNs; Heino et al. 2002) or mass gain (e.g., Shelton and Mange, 2012).

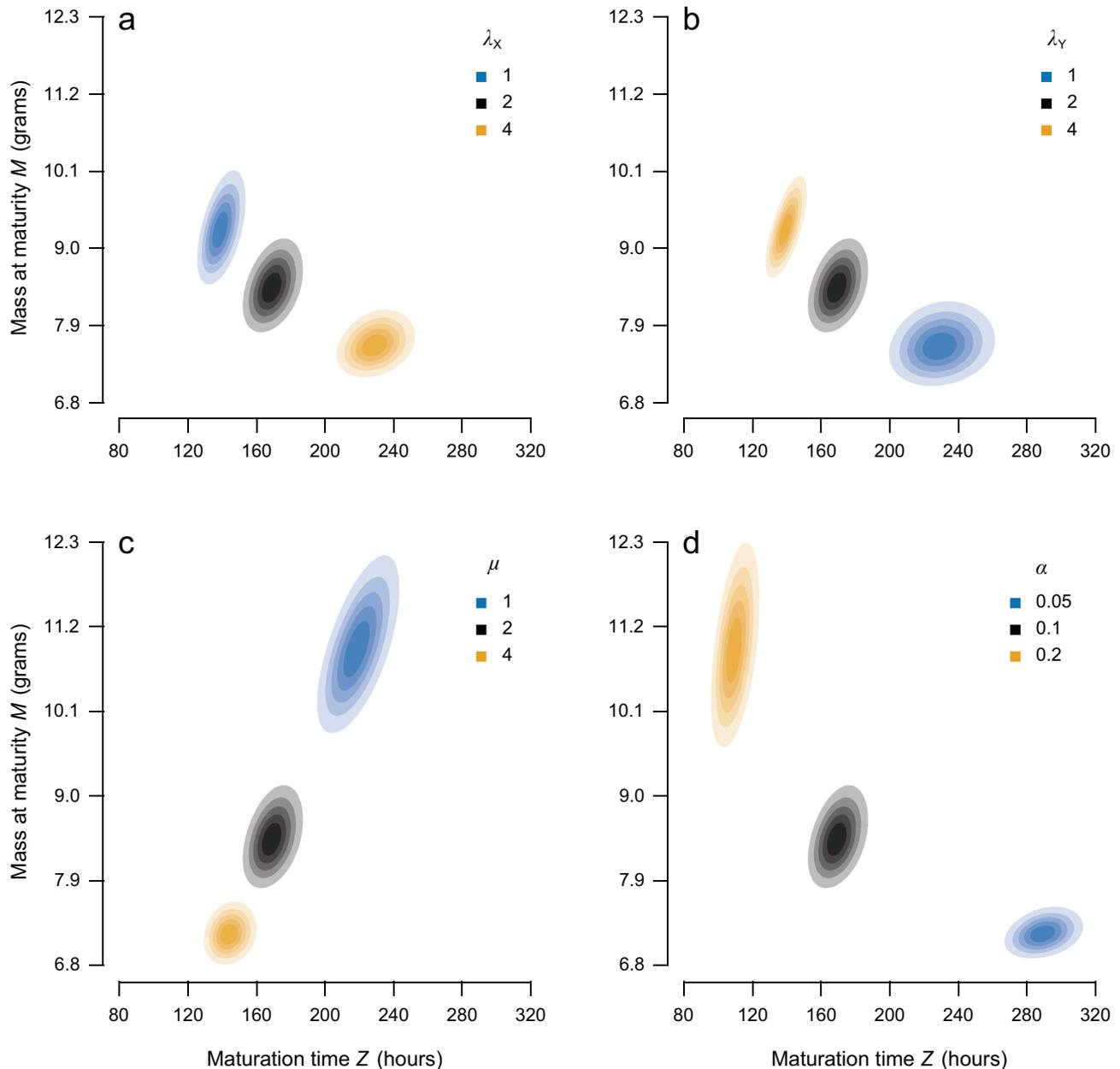


Figure 3: Contour plots of the joint distribution of age (Z) and mass (M) at maturity from the stochastic model. Different colors show how the joint density of Z and M is affected by varying parameter values (see key) for (a) feeding switch rate (λ_x), (b) nonfeeding switch rate (λ_y), (c) the degradation rate of juvenile hormone (μ), and (d) mass gain per unit time feeding (α). Darker shades of color represent more probable combinations of maturation time and mass (i.e., higher joint probability densities). The same 150×150 grid was used to generate all contours.

Commonly, standard distributions (e.g., normal, lognormal) are used to describe variation in these “macroscopic” life-history traits that result from multiple underlying processes (but see Shelton and Mangel 2012). We developed a model that accounts for stochasticity in both maturation time and mass gain and does not require that such traits follow a standard distribution. Rather, the model uses ran-

dom variables to describe underlying (“microscopic”) developmental and behavioral processes known to occur in holometabolous insects and combines them to generate a joint distribution of age and mass at maturity. We derived a joint probability density function for the model and then evaluated it numerically to explore the sensitivity of the distribution to different parameter values. We found that the

resulting, generally nonnormal distribution of age and mass and maturity was highly sensitive to parameter values in terms of changes to the expected values and variances (table A1, available online) as well as changes in the size, shape, and orientation of the highest-density regions (fig. 3).

The stochastic model, which has only six parameters, is based on the biology of *Manduca sexta*, for which the determinants of adult body size (i.e., adult mass) and maturation time are well understood (Nijhout et al. 2014). However, many of the underlying developmental processes, such as the initiation of molting following the degradation of JH, are thought to occur in most insects. Therefore, the model can, in present form or with minor modifications, be used to predict age and mass at maturity for insects generally. Applying the model to noninsect systems could be done with relatively few modifications, such as adding more periods of development, setting different triggers for the termination of development periods, or describing hormonal degradation using other kinds of compartment models. Even with such modifications, the basic structure of the model (fig. 1), its underlying probability functions (table 1), and how they are combined to create the full model (e.g., eq. [6]) would remain largely unchanged. This flexibility is particularly important given that the vast majority of evolutionary studies that account for stochastic variation during maturation (using PMRNs) involve fish rather than insects (Dieckmann and Heino 2007).

In addition to deriving a general model of age and mass at maturity, we examine how parameter values influence the resulting joint distribution. As shown in figure 3 and table A1, many characteristics of this distribution are highly sensitive to parameter values. For example, the variance of age at maturity (i.e., maturation time, Z) is significantly affected by changes in the nonfeeding switch rate, λ_V , while variance of mass at maturity (M) depends strongly on α , the mass gained per unit time feeding. Demonstrating such sensitivity is important for two reasons: (1) our results illustrate the wide range of age and mass distributions that can emerge in the absence of genetic and environmental variation, and (2) we show that measures of trait distributions will not necessarily be constant across different conditions. Point 2 is particularly relevant for cases where data on age and mass maturity in one context are used to predict their distribution in another (e.g., assuming constant variance in mass for two different environments). That is, such predictions may be flawed if development is affected by multiple sources of stochasticity.

Predicting the effects of environmental change on trait variation is particularly important, and at least two sets of results provide some insight into the effects of such change in our model. For instance, parameter α , mass gain per unit time feeding, can be thought of as analogous to

the nutritional quality of food. As we show, increasing α strongly increases variation in mass at maturity but decreases variation in age at maturity (fig. 3d). Similarly, the degradation of JH can be thought of as a chemical reaction, and so increases in μ are analogous to increases in temperatures. We show that increasing μ decreases variation in both age and mass at maturity (fig. 3c). These predictions illustrate how environmental change could alter patterns of stochastic variation and covariation between life-history traits, even in the absence of phenotypic or genetic variation.

The distributions shown in figure 3 differ substantially from analogous multivariate normal distributions (fig. A3; table A1; figs. A1–A3 are available online). These differences are important because multivariate trait distributions are commonly assumed to be normal or close to normal, yet for this model and range of parameter values, they are not. Furthermore, it suggests that measures such as the correlation and covariance may provide only limited information about dependencies between traits when they are the result of complex developmental processes.

In theory, it would be possible to apply the probability density functions provided in table 1 and fit the model to experimental or observational data on the growth and maturation of *M. sexta* or another insect. However, we lacked the data to do so. Nevertheless, we did use observational data to inform the range of parameter values considered in our analysis. Using these values, we also observed changes to the expected values of our joint distributions that were consistent with at least two well-known patterns in nature. For instance, the decreases in maturation time and mass at maturity as the degradation rate increases (fig. 3c) are consistent with what is known as the temperature-size rule (e.g., Atkinson 1994), a pattern found in most insects (including *M. sexta*) whereby higher temperatures lead to smaller body sizes (i.e., smaller masses) and faster maturation times. Similarly, increases in α (i.e., more efficient conversion of feeding time to mass gain) lead to a shift from low mass at maturity and long maturation time (fig. 3d, black contours) to high mass at maturity and short maturation time (fig. 3d, blue contours), the same pattern observed for *M. sexta* populations raised on low- versus high-quality diet (Diamond and Kingsolver 2010). Consistency with these patterns is an important step toward fully validating this model.

When multiple sources of stochastic variation are ignored, inferences about genetic differences between populations can be severely biased (Grimm and Uchmański 2002; Heino et al. 2002; Vindenes and Øystein 2015). Thus, by accounting for stochasticity in both mass gain and maturation time, our model reduces such bias. Furthermore, since the model describes known developmental processes, it overcomes a major criticism of PMRNs

(Marshall and McAdam 2007), the most commonly used class of stochastic life-history models. Our model also avoids many of the other issues associated with phenomenological models of age and mass at maturity, such as their lack of generality and the difficulty of understanding dependencies between age and mass when they are modeled separately.

Despite overcoming these issues, it is important to consider some of the limitations of our approach. First, we assume that parameter values (e.g., feeding switch rate) do not change over time. While this assumption is relatively well supported for both field and laboratory *M. sexta* (Reynolds et al. 1986; Bernays and Woods 2000), some insect species, such as *Schistocerca americana*, appear to exhibit diurnal or other time- or environment-dependent patterns in their feeding behavior (Chapman and Beerling 1990). One method to account for such effects would be to treat parameters not as fixed values but as functions of time/environment, effectively modeling feeding and other developmental processes as nonhomogeneous Poisson processes. Modeling development in this way would be more realistic but would be challenging since closed-form solutions for nonhomogeneous models are largely unavailable (for more information on simulating nonhomogeneous Poisson processes, see Legault and Melbourne 2019). Second, our model considers growth and development over only a single larval instar. As we note, extending the model to other instars would be possible, but it is likely that each instar would require different components of the model as well as different parameter values. For example, *M. sexta* head size differs significantly across instars, morphology that would likely affect how much they could ingest in a feeding bout (represented by parameter α). Finally, our model overlooks the role of ecdysone, the hormone released when JH is fully degraded, in the growth and maturation process. In *M. sexta*, this hormone is generally associated with a complex suite of “wandering” behaviors that include the cessation of feeding, locomotion, and voiding gut contents (Dominick and Truman 1985). Such behaviors would likely affect final mass and age at maturity distributions and could be important to include in extensions to the model.

We have derived a model that accounts for stochasticity in both maturation time and mass gain in the insect *M. sexta* and thus is capable of generating more accurate and unbiased predictions of age and body size for the species. The proposed model and its derivation are general to insects and could easily be extended to other organisms. Thus, our work provides a starting point for researchers interested in developing more comprehensive system-specific models of age and mass at maturity. Such models may be particularly informative when age and mass trade-offs in nature exhibit strong sensitivity to genetic and/or environmental variation.

Acknowledgments

We are grateful to H. F. Nijhout and H. A. Woods for their comments on the manuscript. We also thank two anonymous reviewers for their helpful comments, and especially Ben Nolting for providing detailed suggestions that substantially improved the manuscript. Funding was provided by a National Science Foundation grant to J.G.K. (NSF IOS-1555959).

Statement of Authorship

G.L. conceived an initial stochastic model that both G.L. and J.G.K. refined into the final model. G.L. derived the probability functions and coded them. G.L. and J.G.K. analyzed the model, developed the visualizations, and wrote the article.

Data and Code Availability

R scripts for simulating the model and evaluating the probability functions can be found in the Dryad Digital Repository (<https://doi.org/10.5061/dryad.g4f4qrfmm>; Legault and Kingsolver 2020) and at https://github.com/legault/Stochastic_maturation_growth.

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