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A model of the evolution of larval feeding rate in *Drosophila* driven by conflicting energy demands

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Abstract Energy allocation is believed to drive trade-offs in life history evolution. We develop a physiological and genetic model of energy allocation that drives evolution of feeding rate in a well-studied model system. In a variety of stressful environments *Drosophila* larvae adapt by altering their rate of feeding. *Drosophila* larvae adapted to high levels of ammonia, urea, and the presence of parasitoids evolve lower feeding rates. Larvae adapted to crowded conditions evolve higher feeding rates. Feeding rates should affect gross food intake, metabolic rates, and efficiency of food utilization. We develop a model of larval net energy intake as a function of feeding rates. We show that when there are toxic compounds in the larval food that require energy for detoxification, larvae can maximize their energy intake by slowing their feeding rates. While the reduction in feeding rates may increase development time and decrease competitive ability, we show that genotypes with lower feeding rates can be favored by natural selection if they have a sufficiently elevated viability in the toxic environment. This work shows how a simple phenotype, larval feeding rates, may be of central importance in adaptation to a wide variety of stressful environments via its role in energy allocation.

Keywords Trade-offs · Experimental evolution · Age-structure · *Drosophila melanogaster*

Introduction

A fundamental component of the modern theory of life-history evolution has been the concept of trade-offs (Roff and Fairbairn 2007a; van Noordwijk and de Jong 1986; Zera and Harshman 2001, 2011). This idea was perhaps most concretely made by Cody (1966) in his development of a theory of clutch size. Cody's idea, and that of more recent adherents, has been that energy is a fundamental limiting resource and that allocation of energy to different life-history related traits therefore involves trade-offs (Flatt and Heyland 2011; van Noordwijk and de Jong 1986).

Trade-offs between reproduction and some other fitness components are often the target of research on life history trade-offs. Important research has come from both studies of natural and lab adapted populations—each presents their own strengths and weaknesses. For example, wing polymorphism in the cricket *Gryllus firmus* has been shown to be due to an energetic trade-off between wing production and fecundity (Roff and Fairbairn 2007b; Zera 2009; Zera and Harshman 2001, 2009). However, we lack the detailed knowledge of the evolution of this polymorphism which we would typically have available for laboratory evolved populations.

In laboratory evolved populations of *Drosophila*, one phenotype that responds to stressful larval environments is larval feeding rate, measured as the number of sclerite retractions per minute while feeding (Burnet et al. 1977; Joshi and Mueller 1988). Feeding rates may increase in response to crowding (Joshi and Mueller 1988) or they may decrease in response to toxins in the food (Borash et al. 2000) or exposure to parasites (Fellowes et al. 1999). One study also documented a decrease in competitive ability and, thus, presumably in larval feeding rates in response to the evolution of adult learning behaviors (Mery and

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Kawecki 2003). Feeding rates are known to affect competitive ability for food (Burnet et al. 1977; Joshi and Mueller 1988) but are also expected to affect energy acquisition and growth rates (Mueller et al. 2005).

Thus, we have very strong empirical evidence that adaptation in *Drosophila* to a variety of stressful environments involves a common physiological trait. We develop a physiological model that unifies these apparent disparate observations through the simple concept of energy allocation. Consequently although motivated by specific observations in *Drosophila* we suggest one of the unifying themes in life-history evolution, energy allocation, is driving *Drosophila* larval evolution (Stearns 1992; Roff 1992). Although the physiological model suggests feeding rates may maximize energy intake we do not simply assume evolution maximizes energy intake. Rather we develop a specific population genetic model that suggests the fine tuning of energy intake is due to a fitness component trade-off e.g. increased viability for increased development time.

A model of energy acquisition and feeding rates

Toxic food environments

The goal of our physiological model is to take into account the various energy acquiring and expending activities that are a function of feeding rates. We first take an optimization approach and ask what feeding rate maximizes the energy intake, per unit time. Evolution may not maximize energy uptake. However, we can explore the relationship between feeding rates and energy uptake as a way of suggesting possible empirical research that might help determine if this has indeed occurred.

Following our earlier work (Mueller et al. 2005), we model feeding efficiency, metabolic rate and food consumption. As a crude approximation we will use linear models for each of these, which may be valid in the vicinity of an equilibrium feeding-rate even if there is a non-linear relationship over the entire range of feeding rates. We use the term feeding efficiency to mean the fraction of ingested food that is digested by larvae. Feeding efficiency is a decreasing function of feeding rate. Empirical support for this claim come from a comparison of two different sets of crowding-adapted (fast feeding) and control (slow feeding) *Drosophila* populations (Joshi and Mueller 1996; Mueller et al. 1991). These studies showed that fast feeding larvae required more food to reach the same critical minimum size as control larvae. We can use the probability of surviving on 4.5 mg of food as a surrogate measure of feeding efficiency. The higher this probability is the more

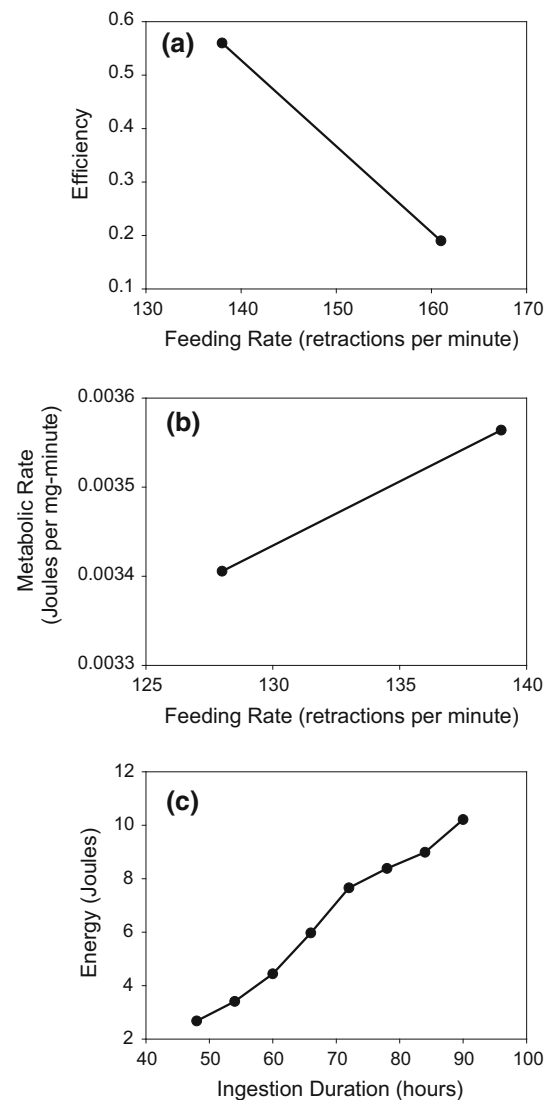


Fig. 1 **a** The relationship between feeding rates and efficiency. The data come from two populations of *Drosophila melanogaster*, called *r*-selected (slow feeding) and *K*-selected (faster feeding). The feeding rate data are from Joshi and Mueller (1988) and the efficiency data is from Mueller (1990). Using the data from Table 2 of Mueller (1990) a linear regression was used to estimate the probability of surviving on 4.5 mg of yeast. A more efficient genotype would have a higher chance of surviving on a fixed level of food and hence our use of the word “efficiency” for the y-axis label. **b** The metabolic rates of *Drosophila melanogaster* populations that differ in their feeding rates. The slower feeding data point is from populations adapted to high levels of ammonia while the higher feeding rate data point is from control populations. The feeding rate measurements come from (Borash et al. 2000) and the metabolic rate measurements come from Mueller et al. (2005). **c** The amount of energy fixed as biomass in *Drosophila* larvae given varying periods of time to feed. The data come from the UU female population described in Santos et al. (1997). The adult dry weight of flies was converted to Joules using the conversion of 27.8 J/mg as described in Djawdan et al. (1996)

efficient the genotype. The study of Mueller (1990) shows a negative correlation between feeding efficiency and feeding rate (Fig. 1a).

Here we assume that relationship in Fig. 1a is due to the fact that energy extracted from consumed food is greater the longer the food sits in the digestive system (with some limits) and that the time the food resides in the digestive system is inversely proportional to the feeding rate (Burnet et al. 1977).

Let f_r be the larval feeding rate, $E(f_r)$, be the fraction of food digested by larvae feeding at a rate f_r (in all the notation that follows a subscript “r” denotes a rate, Table 1). We use the linear model,

$$E(f_r) = a_1 + a_2f_r, \tag{1}$$

where we assume that $a_2 < 0$ (see Fig. 1a).

Since feeding involves movement of both the head and entire body we assume that metabolic rate (M_r) increases as a function of feeding rate. The few results that exist are consistent with this assumption (Fig. 1b). Thus,

$$M_r(f_r) = b_1 + b_2f_r, \tag{2}$$

and we assume $b_2 > 0$.

We presume that larvae consume more food per unit time as their feeding rate increases although we know of no direct measurements of food consumption to support this assumption. It has been shown that fast feeding larvae synthesize more lipid than slow feeding larvae (Foley and Luckinbill 2001) When *Drosophila* larvae are given a fixed period of time to feed the amount of energy they fix as biomass increases in proportion to the time they feed (Fig. 1c, Santos et al. 1997). Here we assume that if the time to feed is fixed those larvae that feed faster will consume more food. Clearly when $f_r = 0$ then the consumption rate, C_r , should also be zero. However, since the consumption rate may be non-linear over its entire range we will allow for a non-zero y-intercept when we model consumption in the vicinity of a feeding rate equilibrium. Then the linear consumption rate function is,

$$C_r(f_r) = c_1 + c_2f_r, \tag{3}$$

and we assume $c_2 > 0$.

For larvae feeding in normal food we set the net rate of energy intake, Δ_r , to the difference between energy intake and energy expenditure or $C_r(f_r)E(f_r)d_1 - M_r(f_r)$, where d_1 is a constant representing how much energy is extracted from digested food. Replacing these functions with their linear relationships we get,

$$\Delta_r = (a_1c_1d_1 - b_1) + [d_1(a_2c_1 + a_1c_2) - b_2]f_r + a_2c_2d_1f_r^2. \tag{4}$$

This quadratic equation in f_r will have a single maxima which can be found by differentiating Eq. (4) and setting the resulting equation to 0 and solving for the feeding rate that gives the maximum energy yield, f_r^* as

$$f_r^* = \frac{b_2 - d_1(a_2c_1 + a_1c_2)}{2a_2c_2d_1}. \tag{5}$$

Next we are interested in the feeding rate that maximizes food intake when the larvae are in an environment with either ammonia or urea. We assume that larvae consuming a toxic compound will need to detoxify it thereby incurring an energy cost of, say e_1 units of energy per unit of food consumed. The cost per unit time of consuming toxic food is then just the consumption rate times this cost or $(c_1 + c_2f_r)e_1$. This means that the net energy intake rate in a toxic environment is, $\tilde{\Delta}_r = \Delta_r - (c_1 + c_2f_r)e_1$. From this equation it is clear that net energy intake in a toxic environment will be less than in the non-toxic environment, that is $\tilde{\Delta}_r < \Delta_r$ as long as $c_1 + c_2f_r > 0$ which is required by Eq. (3) to insure positive consumption rates. Following the same analysis that gave rise to Eq. (5) we get the maximum yielding feeding rate in the toxic environment as,

$$f_r^{**} = \frac{b_2 + c_2e_1 - d_1(a_2c_1 + a_1c_2)}{2a_2c_2d_1}. \tag{6}$$

For Eqs. (5) and (6) to be biological feasible feeding rates they must be greater than 0. However the denominators of Eqs. (5) and (6) are negative indicating the numerator must also be negative. Since b_2 and c_2e_1 must be positive then $d_1(a_2c_1 + a_1c_2)$ must also be positive and greater than the $b_2 + c_2e_1$. From this we conclude that $b_2 - d_1(a_2c_1 + a_1c_2) < b_2 + c_2e_1 - d_1(a_2c_1 + a_1c_2)$. After dividing the left and right side of this inequality by the negative denominator, $2a_2c_2d_1$, we have $f_r^* > f_r^{**}$. In other words in a toxic environment larvae will get a higher rate of energy return by feeding at a slower rate than they would feeding in a toxin free environment.

If we take the first partial derivative of f_r^{**} with respect to e_1 we get $[2a_2d_1]^{-1}$, which is always negative. Thus, any increase in e_1 , the cost of detoxifying food, will decrease the feeding rate that maximizes energy intake. This highlights the direct relationship between the cost of detoxification and feeding rates.

Nutrition has been studied extensively in adult *Drosophila*, for instance to examine its effects on longevity (Lee et al. 2008), but is much less studied in larvae. If we take the first partial derivative of f_r^* with respect to d_1 , the energy content of digested food, we get a term which is always positive. Thus, if the nutritional content of the food is decreased, e.g. d_1 is decreased, then the optimal feeding rate should decrease. Mathematically the energy intake function is a second order in f_r with a negative coefficient in front of the f_r^2 term. Thus, at high feeding rates the intake of energy will level off and eventually decrease. The energy consuming term is a linear increasing function of

feeding rates and thus the optimal feeding rate will occur at the point the difference between these two functions is greatest. Changes in d_1 only affect the height of the energy consumption function. Thus, increasing d_1 will cause an increase in the optimum while a decrease will cause the maximum difference to occur at a lower feeding rate. In the discussion we will use this result to suggest some simple experiments to test this model.

Evolution of slower feeding rates

We are now interested in studying the evolution of feeding rates using the results described in the previous section. Suppose we have two alternative genotypes: a fast feeding, toxin sensitive genotype and a slow feeding toxin resistant genotype. We know that the net rate of energy intake of the fast feeding genotype is Δ_r . Prior research with *Drosophila* has shown that the larvae must reach a critical size, say m , measured in energy units, (Bakker 1961; Mueller 1988a) to successfully pupate. It will then take the fast feeding genotype m/Δ_r min to reach this critical minimum size. In a similar fashion we conclude that the slow feeding genotype will take $m/\tilde{\Delta}_r$ min to reach its critical minimum size and this time will be greater than m/Δ_r because $\Delta_r > \tilde{\Delta}_r$. Thus, the slow feeding genotype will take longer to develop but in a toxic environment it should have superior survival since it is using energy to detoxify the food. These set of facts are exactly what have been observed in populations of *Drosophila* which has evolved in crowded cultures (Borash et al. 1998). In these crowded environments high levels of ammonia build up in the cultures over time due to the deposition of ammonia waste by large numbers of larvae. There is a genetically distinct group of larvae in these crowded cultures that develop quickly, feed quickly but are more sensitive to ammonia than a second group which develops slowly, feeds slowly and is more resistant to ammonia (Borash et al. 1998).

In this model we will focus on the increased development time as the primary negative fitness impact of feeding slowly although slow feeding larvae also suffer reduced competitive ability. We assume that female fecundity is not affected by the resistance genotype although we relax this assumption later. The genetic model is a single locus with two alleles. Although we assume each genotype reproduces only once, different genotypes reproduce at different times as described in the previous paragraph. Accordingly, we break time into discrete intervals, $x = 1, 2, \dots, \delta$, where δ is the oldest age of reproduction among all genotypes.

The evolutionary scenario we will examine is a population of fast feeding, toxin sensitive individuals that are suddenly moved to a toxic environment. In this setting we derive the conditions that allow a slower developing, toxin

resistant genotype to become established in the population. Let genotype A_1A_1 be the resident, fast feeding, toxin sensitive genotype that has age-specific survival probabilities equal to $p(x) = 1$, for $x = 1, 2, \dots, t_{11} - 2$, w_{11} for $x = t_{11} - 1$, and 0 otherwise. Thus the probability if the A_1A_1 genotype surviving to age t_{11} (viability) is $p(1) \times p(2) \dots \times p(t_{11} - 1) = 1^{t_{11}-2}w_{11} = w_{11}$. Of course the viability effects are probably manifest during the entire larval stage not just the last age-class prior to reproduction. However, as we will see below only the product of those survival probabilities matter so setting up the model in this fashion does not affect our final conclusions.

For the heterozygote, $p(x) = 1$, for $x = 1, 2, \dots, t_{12} - 2$, w_{12} for $x = t_{12} - 1$, and 0 otherwise. Finally for the toxin resistant homozygote, A_2A_2 , $p(x) = 1$, for $x = 1, 2, \dots, t_{22} - 2$, w_{22} for $x = t_{22} - 1$, with $t_{22} \geq t_{12} > t_{11}$. The genotypes A_1A_1 , A_1A_2 , and A_2A_2 produce F offspring at ages t_{11} , t_{12} , and t_{22} respectively. If we let $B(t)$ be the total number of zygotes produced at time t and $p_i(t)$ be the frequency of allele A_i at time t among these zygotes, then we can use the difference equations developed by Charlesworth (1994, equation 3.14a-b) to describe allele frequency change over time as,

$$B(t)p_i(t) = g_i(t) + \sum_{x=1}^t B(t-x) \sum_j p_i(t-x)p_j(t-x) \times l_{ij}(x,t)m_{ij}(x,t)$$

$$B(t) = \sum_i g_i(t) + \sum_{x=1}^t B(t-x) \sum_{ij} p_i(t-x)p_j(t-x) \times l_{ij}(x,t)m_{ij}(x,t)$$

where $l_{ij}(x,t)$ is the chance of genotype A_iA_j surviving to age- x at time t , $m_{ij}(x,t)$ is the fertility of genotype aged- x at time t , and $g_i(t) = \frac{1}{2} \sum_{x=t+1}^{t_{22}} \sum_j [N_{ij}(x-t,0) + N_{ji}(x-t,0)]l_{ij}(x,t)m_{ij}(x,t)$, with $N_{ij}(x,0)$ being the number of A_iA_j individuals alive at time 0.

Using the simple life-histories of the three genotypes described above the Charlesworth equations can be greatly simplified to,

$$B(t)p_2(t) = g_2(t) + B(t-t_{22})p_2^2(t-t_{22})w_{22}F + B(t-t_{12}) \times p_1(t-t_{12})p_2(t-t_{12})w_{12}F, \tag{7a}$$

$$B(t) = g_1(t) + g_2(t) + B(t-t_{11})p_1^2(t-t_{11})w_{11}F + 2B(t-t_{12})p_1(t-t_{12})p_2(t-t_{12})w_{12}F + B(t-t_{22})p_2^2(t-t_{22})w_{22}F, \tag{7b}$$

where $g_1(t) = N_{11}(t_{11}-t,0)w_{11}F + N_{12}(t_{12}-t,0)w_{12}F$, $g_2(t) = N_{22}(t_{22}-t,0)w_{22}F + N_{12}(t_{12}-t,0)w_{12}F$, and $N_{ij}(k,0)$ are the number of individuals of genotype A_iA_j , aged- k that were present at time 0. We note that with these types of genetic models there is no simple characterization

Table 1 A summary of parameters used in the models

Parameter	Description	Dimension
f_r	Feeding rate	Retractions per minute
$E(f_r)$	Fraction of ingested food that is digested	None
a_1	y-intercept of $E(f_r)$	None
a_2	Slope of $E(f_r)$	(Retractions per minute) ⁻¹
$M_r(f_r)$	Metabolic rate	Joules per minute
b_1	y-intercept of $M_r(f_r)$	Joules per minute
b_2	Slope of $M_r(f_r)$	Joules per minute/retractions per minute
$C_r(f_r)$	Consumption rate	Joules per minute
c_1	y-intercept of $C_r(f_r)$	Joules per minute
c_2	Slope of $C_r(f_r)$	Joules per minute/retractions per minute
Δ_r	Net energy intake with no detoxification	Joules per minute
d_1	Fraction of digested food that is converted to metabolic energy	dimensionless
e_1	Detoxification cost as a fraction of food intake	Dimensionless
$\tilde{\Delta}_r$	Net energy intake with detoxification	Joules per minute
t_{11}, t_{12}, t_{22}	Age of reproduction for the A_1A_1 , A_1A_2 , and A_2A_2 genotypes respectively	Time units
w_{11}, w_{12}, w_{22}	Probability of surviving to the age of reproduction for the A_1A_1 , A_1A_2 , and A_2A_2 genotypes respectively	Dimensionless
F_{11}, F_{12}, F_{22}	Fertility for the A_1A_1 , A_1A_2 , and A_2A_2 genotypes respectively	Offspring produced per individual

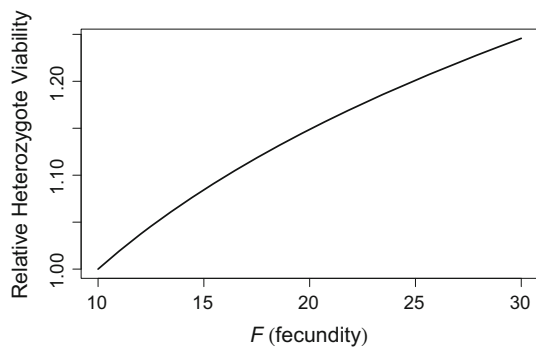


Fig. 2 Initial increase conditions as a function of fecundity. The heterozygote viability needed to permit the A_2 allele to increase when rare is expressed as its value relative to the homozygote viability, e.g. w_{12}/w_{11} and is equal to $(w_{11}F)^{(t_{12} - t_{11})/t_{11}}$. The parameter values were $t_{12} = 12$, $t_{11} = 10$, $w_{11} = 0.1$

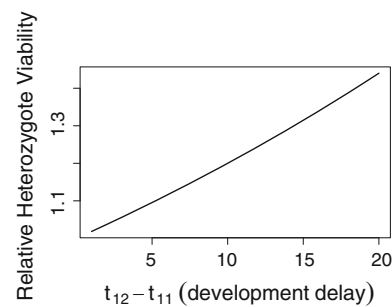


Fig. 3 Initial increase conditions as a function of difference in the development time of the heterozygote and resident homozygote, e.g. $t_{12} - t_{11}$. The heterozygote viability needed to permit the A_2 allele to increase when rare is expressed as its value relative to the homozygote viability, e.g. w_{12}/w_{11} . Fecundity was constant at 12, $t_{11} = 10$, $w_{11} = 0.1$, and t_{12} varied from 11 to 30

of fitness since it depends on fecundity, survival and the timing of reproduction in a complicated manner. It is only under some special conditions that we can assume that the rate of exponential growth derived from the Lotka–Euler equation is equivalent to fitness (e.g. see chapter 3, Charlesworth 1994).

We first study the conditions that permit the initial increase of small numbers of A_2 alleles in the vicinity of an equilibrium with A_1 fixed. Under these conditions, all the A_2 bearing genotypes are assumed to be heterozygotes and $t \geq t_{11}$. In the vicinity of this equilibrium,

$B(t) \cong B(t - t_{11})w_{11}F$. This is an t_{11} -th order difference equation with an asymptotic solution, $B(t) = \hat{\lambda}^{t_{11}}$, where, $\hat{\lambda} = \sqrt[t_{11}]{w_{11}F}$. We next derive the time dependent dynamics of a small perturbation, ε_2 , to the A_2 allele frequency and determine if it will increase within the generation of the A_1A_1 homozygotes, e.g. t_{11} time units. The approximate linear dynamics are given by, $\hat{\lambda}^t \varepsilon_2(t) = \hat{\lambda}^{t-t_{12}} \varepsilon_2(t - t_{12})w_{12}F$, or

$$\varepsilon_2(t) = w_{12}F \hat{\lambda}^{-t_{12}} \varepsilon_2(t - t_{12}) \tag{8}$$

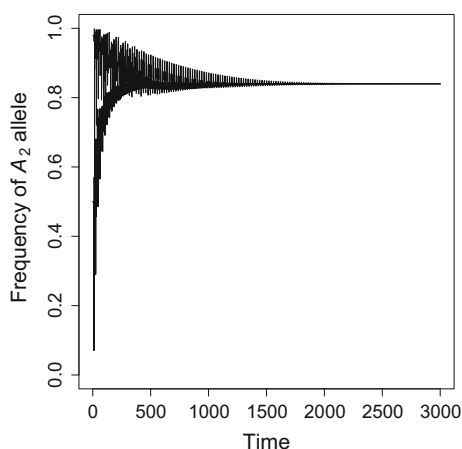


Fig. 4 Frequency of the A_2 allele among zygotes over time. The viability values were, w_{11} , w_{12} , and w_{22} were 0.1, 0.5 and 0.7 respectively. The ages of reproduction, t_{11} , t_{12} , and t_{22} were 12, 16, and 20 time units respectively. All genotypes were assigned a fecundity of 15. These parameters satisfy the conditions of Eq. (10) for a protected polymorphism. Equation (7a, b) were used to generate the allele frequency trajectories above

Equation 8 is a t_{12} th order difference equation with an asymptotic solution, $\varepsilon_2(t) = \hat{\lambda}^t$, where $\hat{\lambda} = \sqrt[t_{12}]{w_{12}F\hat{\lambda}^{-t_{12}}}$. If $\hat{\lambda}^{t_{11}} > 1$, then the A_2 allele should increase relative to the A_1 allele and become established in the population. To determine whether the A_2 allele will become fixed, go to an equilibrium or perhaps enter a cycle would require additional analysis. After some algebra we find that the condition that will permit the A_2 allele to increase when rare is,

$$(w_{12}F)^{1/t_{12}} > (w_{11}F)^{1/t_{11}}. \tag{9}$$

It is interesting that even though all genotypes have the same fecundity the parameter F is part of the condition for initial increase. This is because the advantage to earlier development is a function of fecundity: with increasing F , the fitness advantage of earlier reproduction increases due to the exponential increase in progeny over time. Of course if these genotypes reproduced at exactly the same time, e.g. $t_{12} = t_{11}$, then the initial increase condition would reduce to $w_{12} > w_{11}$ and evolution would no longer depend on the value of F . If we look at the relative viability of the heterozygote (w_{12}/w_{11}), we see that the viability advantage that is needed for the A_2 allele to increase-when-rare increases as F increases (Fig. 2). As the developmental delay of the heterozygote increases, the relative viability advantage needed for the A_2 allele to increase-when-rare increases (Fig. 3).

A protected polymorphism requires that both the $\hat{p}_1 = 1$ and the $\hat{p}_2 = 1$ equilibria be unstable which will be the case when,

$$(w_{12}F)^{1/t_{12}} > (w_{11}F)^{1/t_{11}} \text{ and } (w_{22}F)^{1/t_{22}} > (w_{11}F)^{1/t_{11}}. \tag{10}$$

Although we know if the protected polymorphism conditions are satisfied neither allele will be fixed we can't say anything specific about the polymorphism. There may be stable points, multiple locally stable points or stable cycles. We next study these protected polymorphisms with some specific examples. We show an example of a protected polymorphism (Fig. 4). The approach to this equilibrium is oscillatory since the leading eigenvalue is a complex number. The structure of this model produces multiple eigenvalues with the same modulus. The initial conditions will determine which of these dominates and thus the details of this oscillatory behavior. This example produces a polymorphism even though there is no overdominance in any single fitness component. The heterozygote viability is sufficiently larger than the A_1A_1 homozygote viability that it has superior fitness despite the 4 days developmental delay. However the A_2A_2 homozygote's viability while greater than the A_1A_1 homozygote is not sufficient to insure the fixation of the A_2 allele. Although allele frequencies get very close 1.0 we do not expect allele fixation. This model assumes an infinite population size so the conditions for a protected polymorphism (Eq. 10) guarantee that natural selection will prevent allele frequency fixation. However, in a finite population it may certainly be the case that fluctuations this extreme could push the A_2 allele to fixation due to random loss of all A_1 carrying genotypes.

The model can be generalized to allow fecundity to vary among genotypes. Let the fecundity of A_1A_1 , A_1A_2 , and A_2A_2 be F_{11} , F_{12} , and F_{22} respectively. Then the equivalent of the initial increase condition, Eq. (9), is,

$$(w_{12}F_{12})^{1/t_{12}} > (w_{11}F_{11})^{1/t_{11}}. \tag{11}$$

Discussion

It is well established that larval feeding rates are highly correlated with competitive ability (Burnet et al. 1977; Joshi and Mueller 1988). Given this fact why would there be extensive additive genetic variation for larval feeding rates? One explanation is that selection on feeding rates varies over time and space. While competitive ability is important in certain types of crowded environments (Bo-rash et al. 1998) it may also decrease the efficiency of energy intake which may have a deleterious fitness impact in other environments (Joshi and Mueller 1996; Mueller 1990). In this paper we argue that certain kinds of toxic larval environments may in fact favor the evolution of reduced feeding rates as a consequence of the improved energy intake of slower feeding larvae.

Laboratory evolution experiments have shown that *Drosophila* larvae adapted to high levels of urea may have

nearly the same viability in high urea as control populations have in standard food (Shiotsugu et al. 1997) however, their development time is demonstrably increased. Adaptation to toxic environments containing high levels of urea and ammonia are accompanied by the evolution of lower larval feeding rates (Borash et al. 2000) consistent with the theory developed in this paper.

Our genetic model assumes a penalty for slow feeding in the form of delayed development and thus reproduction. In the laboratory this penalty can be removed by forcing all flies, even those that develop quickly to reproduce at the same time. This of course would be expected to make the evolution of slower feeding and resistance to toxins easier than suggested in the more general model we develop in this paper. In a natural environment flies could reproduce multiple times which was not included in our models. However, the faster development time and single time of reproduction modelled here would still be a major contributor to the outcome of evolution in natural populations.

Other stressful environments

Drosophila populations also respond evolutionarily to parasitoid stress by lowering feeding rates (Fellowes et al. 1999). Even though it appears that the response of larvae to parasitoid stress involves an immune response that is energetically costly it is not directly proportional to food consumption. Thus the previous model would not seem to cover this type of evolution. It may not be unreasonable to assume that the metabolic rate might increase due to this more or less constant background energy requiring immune response. In the previous model that would affect the y-intercept of the metabolic model, e.g. b_1 . However the value of f_r^* is not affected by b_1 . But, if this adaptive immune response increases b_2 , then that will lead to a reduction in f_r^* , since the numerator of Eq. (5) is negative.

Crowding

Previous theoretical and experimental work have suggested that natural selection in crowded *Drosophila* cultures would favor the evolution of higher feeding rates due to the increased competitive ability of fast feeding larvae (Joshi and Mueller 1988; Mueller 1988a, b). However, under this theory (Mueller 1988a) there was no penalty to feeding fast. It was assumed that the larvae consumed food until it was gone and the faster feeding larvae, who consumed more food, would be larger and thus more likely to have achieved the minimum size needed for successful pupation. Under the model developed in the previous section larvae that fed faster than the optimum rate would in fact have a reduced net energy intake and thus would be smaller when

all the food was gone relative to slower feeding larvae that were at the optimum.

Crowded environments are likely to be heterogeneous. In fact in these cultures you can at times see hundreds of larvae crowded around one small section of food and a nearby patch be almost unoccupied. Fast feeding is also associated with roving behavior (Mueller et al. 2005; Sokolowski et al. 1997). The advantage of feeding fast in these environments may be in the ability of the faster feeding larvae to find high quality patches of food before slow feeding larvae do. Fast feeding is also not unconditionally favored in crowded environments. In one experimental system it was demonstrated that there is a polymorphism for both fast and slow feeding larvae possibly as a result of temporal heterogeneity that arises in crowded lab populations (Borash et al. 1998).

Testing the theory

Several avenues exist for testing aspects of the theory developed in this paper. For instance we saw that decreasing the energy content of food, d_1 , should lower feeding rates. If larvae are able to sense the nutritional values of food and plastically change their feeding rate to conform to the optimal rate then we should be able to experimentally demonstrate this by measuring feeding rates in yeast solutions diluted to different levels. Flies allowed to evolve on low nutrition food evolve faster development times and thus possibly faster feeding rates on this food although they are also smaller as adults (Kolss et al. 2009). It is unclear if these observations are contrary to the theory outlined here or not. One recent experiment found no change in larval consumption rates as they adapted to poor quality food (Vijendravarma et al. 2012).

The theory is also premised on the assumption that slower feeding larvae will extract more energy from the food they consume. This could be tested with larvae that feed at different rates under the same conditions, such as a comparison of urea or ammonia adapted populations and their ancestral controls. Likewise gross food consumption should differ between larvae with different feeding rates under the same conditions.

The adaptation to toxic environments is premised on the need to use energy to detoxify these compounds that are ingested along with the food. The presence of increased activity among relevant biochemical pathways to detoxify either ammonia or urea could be empirically studied in *Drosophila* with standard RNA expression arrays.

Drosophila encounter toxins in their natural environments and the evolutionary scenario outlined here may have been relevant. For instance, *Drosophila recens*, *putrida*, and *tripunctata* breed and develop in mushrooms with high levels of *a*-amanitin. This compound will kill many organisms including naïve species of *Drosophila* like

Drosophila melanogaster but is well tolerated by these mycophagous species (Jaenike et al. 1983). Likewise, *Drosophila schellia* develops in fresh *Morinda* fruit that has high levels of octonoic acid that is normally toxic to *sechellia*'s close relatives like *Drosophila simulans* (R'kha et al. 1991). Finally, *Drosophila pachea* cannot grow without the presence of sterols found in the cactus *Lophocereus schottii* which are in turn toxic to many other species of *Drosophila* (Heed and Kircher 1965).

On a larger scale the model developed here also suggests a mechanism for delayed maturity. Most explanations of age at maturity revolve around the benefits to adults of being larger—typically due to their increased fecundity or mating success (Stearns 1992, chpt 6). The mechanisms developed here suggest that increasing pre-adult survival could be the important driver of postponed maturity.

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