Journal of Biology

BioMed Central

Minireview

# The proximate determinants of insect size

Joseph Parker and Laura A Johnston

Address: Department of Genetics and Development, College of Physicians and Surgeons, Columbia University, 701 West 168th Street, New York, NY 10032, USA.

Correspondence: Joseph Parker. Email: jp2488@columbia.edu; Laura A Johnston. Email: lj180@columbia.edu

Published: 2 August 2006

*Journal of Biology* 2006, **5:**15

The electronic version of this article is the complete one and can be found online at http://jbiol.com/content/5/5/15



## Abstract

One of the least understood aspects of animal development - the determination of body size - is currently the subject of intense scrutiny. A new study employs a modeling approach to expose the factors that matter in the control of insect size.

When we think of a specific animal species, most often we picture a creature of a particular size: giraffes are of a certain stature - larger than geckos, and larger again than grasshoppers. But if we were to measure some adult giraffes, we would see they tended to differ in size. This is because genetic differences between individuals contribute to disparities in body size, and also because size is a particularly phenotypically plastic attribute - that is, a trait subject to non-heritable, environmentally induced variation. As a consequence, we should really think of a species as displaying a characteristic size range or distribution, rather than a characteristic size *per se*. Why then does an animal species exhibit a distinct size range?

This question has two answers, the first of which is evolutionary and invokes the selective forces that shaped the species' body-size distribution. These are many, including physiological factors, biomechanical constraints, sexual selection, fecundity and multiple aspects of ecology. Body size is a significant correlate of fitness, and there is a wealth of literature on this subject for a variety of species (see [1,2] and references therein). Furthermore, plasticity of body size is itself adaptive, enabling growing animals to survive in environments prone to fluctuations in the quantity and quality of food.

The second answer provides a proximate explanation and refers to the developmental processes that determine size in individuals. Understanding these should augment the power of evolutionary explanations of body size; after all, developmental mechanisms cause the variation in size on which selection operates. So what factors decide exactly where in the possible size range a given individual will find herself when fully developed? This question lacks a cohesive answer, because the mechanisms controlling animal growth remain largely mysterious. A working description of a system that determines body size is, however, being approached through studies on insects. In this issue of *Journal of Biology*, Frederick Nijhout, Goggy Davidowitz and Derek Roff [3] illuminate yet more of this uncharted territory by demonstrating how genetic and environmental variables interact to determine adult body size in a species of hawkmoth, the tobacco hornworm *Manduca sexta*.

A *Manduca* caterpillar is a genetically programmed feeding machine. As it feeds, nutrients are converted into new

tissue, and the body grows. Body expansion is restricted by the caterpillar's chitinous exoskeleton, in particular the inflexible head capsule, so postembryonic development is punctuated by a serious of molts, in which the cuticle is shed and the underlying epidermis is allowed to grow. Periods between molts are termed instars, of which *Manduca* has five, and during all but the last instar, the young insect increases in size by a constant proportion (the value of which is termed the 'growth ratio'). The size of the adult moth depends on the mechanism that causes feeding and growth to cease towards the end of larval life, at which point the caterpillar reaches its peak weight. In *Manduca*, like all insect species studied so far, cessation of growth hinges on a large pulse of the steroid hormone ecdysone. On reaching a specific weight in the final instar (the 'critical weight'), secretion of the sesquiterpenoid hormone juvenile hormone (JH) from a gland in the brain stops, and the circulating hormone is degraded in the caterpillar's blood by a boost in levels of the enzyme juvenile hormone esterase. JH clearance then permits another hormone, prothoracicotropic hormone (PTTH), to induce the ecdysone pulse, but only during an 8-hour time window that recurs on a circadian cycle; if JH clearance precedes this window, PTTH secretion is delayed until the window arrives. Once secreted, the increased levels of ecdysone cause the larva to empty its gut, begin searching for a place to pupate, and ultimately to metamorphose into the adult moth.

Somewhere hidden in this sequence of events are the parameters that together fix the peak weight of the larva. What are they, and how does one go about finding them? Larval growth, and its termination, is complex, so that simultaneously studying several of its functioning parts in conventional experiments is difficult. In such a case, a modeling approach can prove useful, in which one simulates the system *in silico*, achieving biological realism by parameterizing the model with real-world data. Model validity is gauged by examining whether simulations can mimic the observed behavior of the real-world system, and one can also probe the behavior of the system, by changing one or more parameters at a time.

## Modeling body-size determination

Nijhout *et al.* [3] quantified the growth trajectory of larval *Manduca* and found that instar to instar, mass increases exponentially until the critical weight is attained (Figure 1). After this point the growth rate slows, until growth is finally terminated by ecdysone secretion. They also deduced that the critical weight is related to the growth ratio: it occurs when, in the final instar, the caterpillar has grown by the same proportion it grew in each previous instar. With these pieces of information, they constructed a model designed to predict peak larval weight based on three parameters: the growth rate (before and after critical weight is attained); the critical weight itself; and the time between realization of critical weight and secretion of PTTH and ecdysone. Values for these parameters can be readily extrapolated from a simple set of measurements.

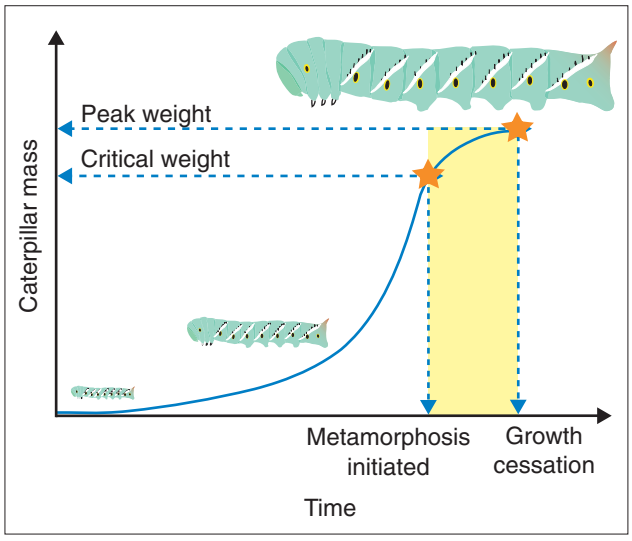


**Figure 1**
Factors that determine body size in *Manduca sexta*. In *Manduca*, peak larval weight depends on three parameters: the growth rate (the slope of the curve), the weight at which metamorphosis is initiated (the critical weight), and the length of time between attainment of critical weight and the large ecdysone pulse that terminates feeding and growth (shaded yellow).

Using larvae from four independent genetic strains (two of which differ grossly in size compared with the wild-type strain), they tested the model by comparing the real peak weights the larvae attained to the peak weights predicted by measuring the requisite parameters and running the model. The two sets of values matched each other almost perfectly, confirming the validity of the model and indicating that the chosen parameters are likely to be the principal determinants of size. Peak size thus seems to be purely the result of how fast the caterpillar grows, the weight at which it commits to metamorphosis, and the length of time it takes from this point until it stops feeding. These three variables combined appear to be the link between growth of the larval tissues and the final body size of the larva. The relationship is complicated, however, as varying one parameter can have knock-on consequences for the others: for example, the onset of critical weight affects the timing of the ecdysone pulse, and the growth rate affects the time at which critical weight is attained. This interdependence of the three size determinants forces us to concede that body

size is not the product of a single process, but of a nonlinear system of interactions.

Of all environmental factors, animal size is particularly dependent on temperature and food quality, with lower temperatures [4] and better diets generally producing larger adults. In *Manduca* these two variables share specific relationships with the three size determinants: the critical weight and growth rate both depend on food quality, but the time interval between critical weight attainment and ecdysone secretion does not. On the other hand, both this latter parameter and the growth rate are related to temperature, but the critical weight is not [5,6]. By providing evidence for a causal connection between the three parameters and body size, the model accounts for how differences in temperature and food quality lead to differences in size; hence, we have a working model for phenotypic plasticity of *Manduca* body size. In addition, all three parameters can vary genetically between different strains [7,8], so the model provides a framework for understanding how both genetic and environmental variables act together to determine body size.

## Where next?

Now that they have been exposed, these three fundamental parameters should become the focus of research into body size that will ground the observation of body-size plasticity - and the existence of body-size distributions - in specific processes understood at the molecular, cellular and physiological levels. Although we are some way off this goal, it is worth thinking about how these parameters might be controlled. Condensed into the growth rate parameter is a process of great complexity. Growth in insects (and in vertebrates for that matter) relies on insulin-like ligands that relay the nutritional status of the animal to individual cells. Cells then respond by altering their metabolism accordingly, resulting in cell growth (increased cell size) and cell division (reviewed in [9]). Expansion of the entire organism is tightly controlled, a point made evident by the close scaling of body proportions with size during larval life. So how does the growth rate of individual cells relate to the growth rate of the whole body? The relationship could be quite simple: the exponential growth of the larval body during instars could be the product of a linear rate of cell growth (set by the rate of protein translation, itself dependent on nutritional intake), and the rate of increase in cell numbers (which is exponential for most structures). The contribution of each process to size plasticity might vary depending on the environment - for example in the fruit fly *Drosophila melanogaster*, changes in cell growth account for the inverse relationship between body size and temperature [10,11], whereas changes in cell number are thought to underlie the response of body size to diet [10].

The mechanisms by which critical weight is internally assessed by the *Manduca* larva, and how the attainment of critical weight leads to JH clearance, are also far from clear. The allusive relationship between critical weight and the growth ratio noted above leads Nijhout *et al*. [3] to propose that critical weight perhaps triggers events similar to those that initiate molting at the end of previous instars. A triggering mechanism involving cuticle stretch reception, as occurs in heteropteran bugs (so-called 'true' bugs) [12,13], or a system similar to that proposed for *Drosophila*, in which the prothoracic gland (the source of ecdysone secretion) is used to assess size [14], are suggested as possibilities. In *Drosophila* larvae, the developing imaginal discs - the progenitor tissues of the adult ectoderm - also seem to influence events in the last larval instar. Damaged discs delay the onset of pupariation until they repair themselves [15], but here again, precisely how they do it is surrounded by uncertainty. One hypothesis is that growing discs might secrete an inhibitor of pupariation or metamorphosis until they reach a threshold size or level of developmental complexity, after which point secretion would stop. Such a mechanism could provide the larva with a checkpoint to synchronize the development of these unconnected structures, operating in parallel with the body-size-determining mechanisms to control body proportionality.

Clearly, much is still to be learned about the control of body size, and the model proposed by Nijhout *et al*. [3] is an abstraction of a far more complex system of interactions. Nevertheless, it explains size determination at a necessary and comprehensible level of complexity, and demonstrates very well the utility of modeling in testing the completeness of our knowledge at this level. Because of the model's accuracy, the authors used it as a predictive tool to explore how body size might evolve. Evolution of any of the three determinants of size is expected to cause body-size evolution, and in fact this has been shown empirically for a large-bodied laboratory strain of *Manduca*, in which evolution of all three parameters fully accounts for its larger than normal size [8].

Nijhout *et al*. [3] explore this idea further, and show how iterations of the model, in which the three parameters are varied, define a three-dimensional 'volume of evolvability'. This is a field of parameter space corresponding to the potential body-size range that quantitative evolution of the size-determining system could produce. Insects vary massively in size, from the microscopic (the 139-mm male of the parasitoid wasp *Dicopomorpha echmepterygis*), to the gargantuan (the 18-cm long longhorn beetle *Titanus giganteus*). How much of the spectrum of insect size can the model account for? It is likely that the model has extremely broad applicability. For example, it might account for size variation in many Lepidoptera (butterflies and moths) and in

other insects in which a size-regulation system similar to that of *Manduca* is conserved. Similar research in taxonomically diverse species is needed before we can say with some certainty that the same three parameters control size across the Insecta, and variants of the model will be needed to explain phenotypic plasticity of body size in taxa that differ in their response to environmental variables. Whatever the case, the model for *Manduca* provides a valuable starting point for exploring the proximate basis of size diversity in the largest class of organisms on Earth, shedding light on the question of why species occupy the size ranges they do.

## References


1. Roff DA: *The Evolution of Life Histories. Theory and Analysis.* New York: Chapman and Hall; 1992.
2. Stearns SC: *The Evolution of Life Histories.* Oxford: Oxford University Press; 1992.
3. Nijhout HF, Davidowitz G, Roff DA: **A quantitative analysis of the mechanism that controls body size in *Manduca sexta*.** *J Biol* 2006, **5:**16.
4. Atkinson D: **Temperature and organism size - a biological law for ectotherms?** *Adv Ecol Res* 1994, **25:**1-58.
5. Davidowitz G, D'Amico LJ, Nijhout HF: **Critical weight in the development of insect body size.** *Evol Dev* 2003, **5:**188-197.
6. Davidowitz G, D'Amico LJ, Nijhout HF: **The effects of environmental variation on a mechanism that controls insect body size.** *Evol Ecol Res* 2004, **6:**49-62.
7. Davidowitz G, Roff DA, Nijhout HF: **A physiological perspective on the response of body size and development time to simultaneous directional selection**. *Integr Comp Biol* 2005, **45:**525-531.
8. D'Amico LJ, Davidowitz G, Nijhout HF: **The developmental and physiological basis of body size evolution in an insect.** *Proc Biol Sci* 2001, **268:**1589-1593.
9. Oldham S, Hafen E: **Insulin/IGF and target of rapamycin signaling: a TOR de force in growth control.** *Trends Cell Biol* 2003, **13:**79-85.
10. Robertson FW: **Studies in quantitative inheritance. XIII. Interrelations between genetic behavior and development in the cellular constitution of the *Drosophila* wing.** *Genetics* 1959, **44:**1113-1130.
11. Azevedo RB, French V, Partridge L: **Temperature modulates epidermal cell size in *Drosophila melanogaster*.** *J Insect Physiol* 2002, **48:**231-237.
12. Nijhout HF: **Stretch-induced molting in *Oncopeltus fasciatus*.** *J Insect Physiol* 1979, **25:**277-282.
13. Nijhout HF: **Abdominal stretch reception in *Dipetalogaster maximus* (Hemiptera: Reduviidae).** *J Insect Physiol* 1984, **30:**629-633.
14. Mirth C, Truman JW, Riddiford LM: **The role of the prothoracic gland in determining critical weight for metamorphosis in *Drosophila melanogaster*.** *Curr Biol* 2005, **15:**1796-1807.
15. Simpson P, Berreur P, Berreur-Bonnenfant J: **The initiation of pupariation in *Drosophila*: dependence on growth of the imaginal discs.** *J Embryol Exp Morphol* 1980, **57:**155-165.