Parasitic castration: a perspective from a model of dynamic energy budgets

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Synopsis Models of the evolution of virulence have typically focused on increased mortality, one of two negative effects that parasites can inflict on their host. Those that consider the other effect, fecundity reduction, can predict that parasites should completely sterilize their hosts. Although this prediction seems extreme, sterilization features prominently in a fascinating strategy, parasitic castration. Such castration can be accompanied by gigantism (unusually large growth of infected hosts), long infectious periods, and fecundity compensation (where, before heavy parasite burdens ensue, newly infected hosts reproduce earlier/more than they would if not infected). Using a model of dynamic energy budgets (DEB), we show how these results readily emerge, assuming that parasites consume energy reserves of the host. The simple, but mechanistic, DEB model follows energy flow though hosts and parasites, starting with ingestion, and continuing with storage of assimilated energy, and use of those reserves for growth and reproduction, as allocated by the host according to the ''κ-rule''. Using this model, we compare and contrast two strategies for parasites. ''Consumers'' only steal energy from their hosts, thereby indirectly altering allocation of energy to growth and reproduction, reducing fecundity, and enhancing mortality. ''Castrators'' steal energy but also directly modify the scheme by which hosts allocate reserve energy, shunting resources from reproduction to growth. Not surprisingly, the model predicts that this strategy should promote gigantism, but it also forecasts longer infectious periods and fecundity compensation. Thus, commonly observed characteristics of parasitic castration readily emerge from a mechanistic model of energy flow using a minimal number of assumptions. Finally, the DEB model for both ''consumers'' and ''castrators'' highlight that variation in resources supplied to hosts promotes variation in virulence in a given host-parasite system, holding all else equal. Such predictions highlight the potential importance of resource ecology for virulence in disease systems.

Introduction

Currently, theories of evolution of virulence often predict that host–parasite interactions should evolve towards intermediate levels of virulence and intermediate levels of transmission of the parasite. This finding emerges from many different models of host–parasite co-evolution whose foundation rests on three common assumptions: parasites exert virulent effects on survivorship of their hosts; virulence and transmission are positively related; and these negative effects on host lifespan are unavoidable consequences of exploitation of the host's resources by parasites (Anderson and May 1981, 1982; Bremermann and Pickering 1983; Bull 1994; Lenski and May 1994; Nowak and May 1994; Read 1994; Ebert and Herre 1996; Frank 1996; Lipsitch et al. 1996). Given these components, the models predict that intermediate virulence and transmission should arise as the net result of a balancing act by parasites between reaping benefits of their own reproduction and suffering the costs of harming their hosts. While these assumptions and predictions likely apply to many disease systems, they do not seem to embrace another prominent, virulent effect: parasites can dramatically reduce fecundity of their hosts.

In general, energy drawn from infection cannot be used for reproduction or growth. Therefore, if parasites—and immune defense against infection—both drain limited energy resources from their hosts, infection could virulently reduce fecundity. More debate surrounds whether parasite-mediated fecundity reduction reflects ''strategy'' by hosts or parasites. The host-strategy arguments typically rest on consideration of the energetic costs of immune defense or up-regulation. For instance, if a host mounts an active defense against disease, it must redirect energy resources (that otherwise could be allocated to current reproduction) to defeat infection and

From the symposium ''Ecology and Evolution of Disease Dynamics'' presented at the annual meeting of the Society for Integrative and Comparative Biology, January 3–7, 2007, at Phoenix, Arizona.
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Integrative and Comparative Biology, volume 47, number 2, pp. 295–309
doi:10.1093/icb/icm057
Advanced Access publication June 18, 2007

ensure future reproduction (van Baalen 1998; Hurd 2001; Day and Burns 2003). In contrast, the parasite-oriented perspective imagines fecundity reduction as purely the result of consumption of resources by parasites. From this viewpoint, parasites essentially steal resources from their hosts and convert them into new propagules that then infect new hosts; therefore, virulent effects on survival of hosts are incidental byproducts of depletion of host resources (Hurd 1990; Polak 1996; Bonds 2006).

Amidst this debate, models that formalize the evolution of virulent effects on fecundity can yield a startling conclusion: if reproduction of hosts and pathogens are negatively related, theory readily (but not always) predicts that parasites could evolve that completely shut down reproduction by the host (Ebert and Herre 1996; Jaenike 1996; Gandon et al. 2002; O'Keefe and Antonovics 2002; Bonds 2006). In fact, some authors suggest that incomplete sterilization suggests suboptimal performance by parasites (Jaenike 1996). This prediction of complete fecundity reduction seems remarkable given that sterilization of hosts is certainly not a ubiquitous feature of all host–parasite interactions. Nonetheless, ''parasitic castration'' has definitely received a great deal of attention as an interesting life-history strategy of parasites (Baudoin 1975; Ebert et al. 2004; Bonds 2006). Baudoin (1975, p 348) offered a helpful working definition of parasitic castration: ''a destruction or alteration of gonad tissue, reproductive behavior, hormonal balance, or other modification that results in reduction in host reproduction above and beyond that which results from nonselective use of host energy reserves by the parasite''. This definition emphasizes that castrators directly influence allocation of the host's resources away from reproduction, likely through hormonal control or by attacking the endrocrine glands of the host (Hurd 2001; Ebert et al. 2004). Thus, from this perspective, castration is usually viewed as a ''strategy'' of the parasite.

By actively shunting resources away from reproduction, parasitic castrators can catalyze two remarkable phenomena: ''gigantism'' and ''early-infection fecundity compensation''. Gigantism involves greatly enhanced growth of infected hosts, and it has puzzled parasitologists for some time (Ebert et al. 2004). This phenomenon occurs in diverse taxa of hosts and parasites (and microherbivores, which essentially act as parasites on their hosts) (Lafferty and Kuris 2002). A compilation presented here (Table 1) emphasizes that the castration–gigantism combination occurs most often (or perhaps, is most commonly noted) in crustacean–microparasite and snail-trematode systems but also appears in plant–ant, fish–worm, and beetle–fungus pairs. Frequently, castrator systems are thought to involve parasites that are rather large relative to their hosts (e.g., the many snail–trematode examples) (Table 1; Lafferty and Kuris 2002) but the crustacean-microparasite cases, especially those with the zooplanktonic *Daphnia* as host, broaden that host size-parasite size perspective. In fact, Ebert et al.'s (2004) study of the *Daphnia*–bacteria (*Pasteuria*) interactions provides one of the most thoroughly documented cases of parasitic castration. Their results ultimately motivated the present study (see Table 2 for predictions from their work).

The ''early-infection fecundity compensation'' phenomenon has provoked interest because it adds an intriguing twist—it might indicate strategic response of hosts to infection by castrators. Once infected, hosts can reproduce earlier and/or produce more offspring than they might have otherwise. Seen in the field and laboratory (Thornhill et al. 1986; Polak and Starmer 1998; Ebert et al. 2004; Chadwick and Little 2005) and predicted by theory (Bonds 2006), this response by the host could indicate enhanced investment in reproduction before maximal burden from castrators drops fecundity to zero. Such a response seems to make sense from a life history perspective, since age at first reproduction in particular has important implications for lifetime fitness of hosts (Forbes 1993; Bonds 2006). Two recent studies with parasites of *Daphnia* (Ebert et al. 2004; Chadwick and Little 2005) highlight this fecundity compensation and even show variation in this response among host genotypes. Such variation perhaps indicates that parasite-mediated natural selection could act on this strategy.

Given these extant predictions and observations, our goal here was to take a step back from questions about evolution of virulence and parasitic castration. Instead, we examine how hosts, their resources, and their parasites interact at the level of the individual host. In many ways, the core ideas studied here already seem familiar—parasites steal resources from their hosts and therefore virulently reduce survivorship and/or fecundity (Bonds 2006). However, we tackle these notions by explicitly modeling the dynamic energy budget (DEB) of the host. Using dynamic energy budgets, we can add more mechanistic muscle to this discussion. To do so, we borrow from DEB theory that has been already developed by Kooijman (1993) with *Daphnia* in mind. His powerful models are simple, mechanistically justifiable, and effectively capture the dynamics of reproduction and growth of a diverse array of organisms.

Table 1 Examples of systems in which parasitic castrators may stimulate growth of the host and cause gigantism

Parasitic castrator	Host	Study	References
Ant—*Allomerus cf. demerarae*	Plant—*Cordia nodosa*	S	Yu et al. 1998
Ant—*Allomerus octoarticulatus*	Plant—*Hirtella myrmecophila*	S	Izzo and Vasconcelos 2002
Ants	Plant—*Humboldtia brunonis*	S	Gaume et al. 2005
Ants—*Crematogaster nigriceps*	Plant—*Acacia drepanolobium*	S	Stanton et al. 1999
Bacteria—*Pasteuria ramosa*	Crustacean—*Daphnia magna*	E	Ebert et al. 2004; Jensen et al. 2006
Dinoflagellate—*Blastodinium contortum*	Crustacean—*Pseudocalanus sp.*		Baudoin 1975
Fungus—*Nosema whitei.*	Beetle—*Tribolium castaneum*	E	Blaser and Schmid-Hempel 2005
Fungus—*Pleistophora ovariae*	Fish—*Notemigonus chrisoleucas*	S	Summerfelt and Warner 1970
Fungus—*Polycaryum laeve*	Cladoceran—*Daphnia pulicaria*	S	Johnson et al. 2006
Tape worm—Ligula intestinalis	Fish—*Rutilis rutilus*	S	Loot et al. 2002
Tape worm—*Schistocephalus solidus*	Fish—Three–*spined stickleback*	E	Arnott et al. 2000
Trematode	Clam—*Macoma balthica*	S	Lim and Green 1991
Trematode—*Cercaria batillariace*	Snail—*Batillaria cumingi*	S	Miura et al. 2006
Trematode—*Diplostomum phoxini*	Snail—*Lymnea peregra*	E	Ballabeni 1995
Trematode—*Echinostoma revolutum*	Snail—*Lymnea elodes*	E/S	Sorensen and Minchella 1998
Trematode—*Halipegus occidualis*	Snail—*Heliosoma anceps*	E	Keas and Esch 1997
Trematode—*Microphallus piriformes*	Snail—*Littorina saxatilis*	S	Gorbushin and Levakin 1999
Trematode—*Microphallus piriformes*	Snail—*Littorina saxatilis*	S	McCarthy et al. 2004
Trematode—*Schistosoma manson*	Snail—*Biomphalaria alexandrina*	E	Ibrahim 2006
Trematode—*Schistosoma mansoni*	Snail—*Biomphalaria glabrata*	E	Gerard and Theron 1997
Trematodes	Snail—*Hydrobia ulvae*	E	Mouritsen and Jensen 1994
Trematodes–	Snails	R	Mouritsen and Poulin 2002
Worm—*Acanthocephalus sp.*	Isopod—*Asellus hilgendorfi*	S	Kakizaki et al. 2003

The column "Study" indicates if data were obtained from field surveys (S), from laboratory experiments (E), or a combination thereof (E/S). Review articles are denoted with R.

Table 2 Summary of empirical results and predictions from Ebert et al.'s (2004) study of a bacterial parasitic castrator (*Pasteuria ramosa*) that infects a zooplanktonic crustacean host (*Daphnia magna*)

Number	Parameter/variable of interest	Predictions for "castrators" versus "consumers" and/or uninfected hosts
1	Size at death: gigantism	Hosts parasitized by castrators should be larger than uninfected and consumer-infected hosts at a given age
2	Age at death	Hosts are older when they die from parasitism by a castrator than by a consumer parasite
3	Age at 1st reproduction	Parasitized animals reproduce at an earlier age than uninfected animals and those infected with consumers
4	Reproductive rate	Hosts parasitized by castrators should have a lower mean reproductive rate than those parasitized by consumers
5	Parasite production	Hosts parasitized by castrators should yield more parasite at death than do those parasitized by consumers
6	Initial dose of spores	Higher initial dose of spores should: (A) castrate the host more quickly (B) make hosts achieve larger size (C) yield higher production of spores

In this summary, we extend Ebert et al.'s (2004) predictions to contrast a castrating strategy with what we call a "consumer"—a parasite that steals resources from the host with similar traits as the castrator but does not directly influence allocation of energy into growth and reproduction (see text in the Model section for more description of the two strategies).

Furthermore, they have been applied to a variety of scenarios ranging from environments with variable food (Muller and Nisbet 2004) to population dynamics (Kooi and Kooijman 1994; Kooijman et al. 1999) and ecotoxicology (Kooijman and Bedaux 1996). The standard DEB model (Kooijman 1993; Nisbet et al. 2000) captures how hosts store energy assimilated from foraging and then allocate a fixed proportion of that reserve to growth (κ) and reproduction ($1-\kappa$), following the κ-rule. To this model, we add parasites that steal from the host's energy reserves to produce new parasites.

Indeed, here we develop a DEB model for hosts and their castrating parasites. Elsewhere, we have adapted the basic DEB to include a parasite that only consumes the energy reserves of its host to reproduce and maintain itself (Hall et al., unpublished manuscript). This DEB-parasite model confirms that, by stealing energy, parasites with this "consumer" strategy should reduce fecundity, growth, and survivorship of their hosts. It also readily captures resource-dependent virulent effects of a fungal parasite (*Metschikowia*) on survivorship and fecundity of a *Daphnia* host—but this virulence arises indirectly from resource competition from the parasite, not from direct manipulation of the host's allocation regime by parasites. Here, we contrast this "consumer" strategy with a "castrator" that we assume can directly alter this allocation scheme of the host. Specifically, the castrator causes the host to shunt energy towards growth at the expense of reproduction. In doing so, the model readily predicts gigantism; very high production of the parasite; prolonged life of the host; and earlier age at first reproduction. We also see that the extent of these virulent effects should definitely depend upon the food supply to hosts—in other words, virulence should depend upon the resource ecology of the host (Smith et al. 2005; Lively 2006). All of these patterns arose in the studies on *Daphnia–Pasteuria* (Ebert et al. 2004; Table 2) and highlights the explanatory power and empirical relevance of these DEB-parasite models.

Model

Common wisdom suggests that parasitic castrators steal energy from their hosts and directly and indirectly influence allocation of the host's energy to growth versus reproduction (Bonds 2006). To capture this biology, we first summarize the DEB used to track energy flow through the host, largely drawing on Kooijman's (1993) derivation (but presented here in simplified notation with fewer compound parameters) (Table 3, Fig. 1). For brevity's sake, we only consider the case of an ectothermic, heterotrophic host that does not change shape—a host essentially like the *Daphnia* that has motivated this work (Ebert et al. 2004). Given these initial assumptions, the core of the model considers how the "kappa (κ)-rule" governs how the animal utilizes reserve energy (E) for growth ($\mathrm{d}V/\mathrm{d}t$) and reproduction ($\mathrm{d}R/\mathrm{d}t$) (Table 1, Fig. 1; Hall et al., unpublished manuscript). After describing that core, we detail how the starving host changes and begins to flout the κ-rule. We develop a scheme for determining whether a parasite that steals reserve energy persists with the parasite or kills it, and compare and contrast the two key strategically kinds of parasites: "consumers" and "castrators" (Fig. 1).

The Kooijman DEB model

This model assumes that the rate at which energy is catabolized ($\mathrm{d}C/\mathrm{d}t$) by the host for growth, reproduction, and maintenance (C) (Fig. 1) equals the difference between the rate of assimilation of energy from food ($\mathrm{d}A/\mathrm{d}t$) and the rate of change in the volume of energy stored in the animal ($\mathrm{d}E/\mathrm{d}t$). Assimilation rate ($\mathrm{d}A/\mathrm{d}t$) depends upon a maximal rate, a, which scales with the surface area ($V^{2/3}$) of the animal (Fig. 1B), and a hyperbolically saturating function (i.e., the classic type-II functional response (Fig. 1B):

$$\frac{\mathrm{d}A}{\mathrm{d}t} = aV^{2/3}\left(\frac{F/c}{h+F/c}\right), \tag{1}$$

where F is food volume and c is the container volume (yielding density F/c), h is the half-saturation constant, and V is the structural volume of the animal. Rate of change of energy reserves (e.g., fat deposits, $\mathrm{d}E/\mathrm{d}t$):

$$\frac{\mathrm{d}E}{\mathrm{d}t} = \frac{\mathrm{d}(eV)}{\mathrm{d}t} = V\frac{\mathrm{d}e}{\mathrm{d}t} + e\frac{\mathrm{d}V}{\mathrm{d}t} \tag{2}$$

involves two components: change in reserve per unit existing structural volume ($\mathrm{d}e/\mathrm{d}t$, where e is energy "density"), and reserve content of new growth ($\mathrm{d}V/\mathrm{d}t$). Reserve energy (E), then, is the product of energy density (e) and structural volume (V, i.e., $E = eV$). We assume that change in energy density, $\mathrm{d}e/\mathrm{d}t$, is the difference between uptake of food resources and use of internal energy:

$$\frac{\mathrm{d}e}{\mathrm{d}t} = \frac{aV^{2/3}}{V}\left(\frac{F/c}{h+F/c} - \frac{e}{e_M}\right), \tag{3}$$

where e_M is the maximum density of energy (and $E_M \equiv e_M V$) and energy density is used according to first-order kinetics. If we combine equations (1–3),

Table 3 Variables and parameters of the dynamic-energy-budget model for parasitic castrators

Term	Units	Definition	Value or range
State variables			
A	mm^3	Assimilated energy	–
C	mm^3	Utilized energy	–
e	–	Energy density ($=E/V$)	–
E	mm^3	Energy volume ($=eV$)	–
F	mg C	Food (algae)	–
N	mm^3	Volume of the parasite	–
R	babies	Reproduction (babies)	–
t	day	time	–
V	mm^3	Structural volume of the host	–
Parameters			
a	mg C mm^{-2} day^{-1}	SA- specific maximal assimilation rate	3.3
a_N	day^{-1}	Maximal assimilation rate, parasite	1.2×0.7
c	l	Volume of food container	0.1
d	day^{-1}	Combined loss rate, parasite	0.05
E_0	mm^3	Investment of energy reserve per baby	$(0.85)^3$
e_M	–	Maximal energy density	1.0
F_0	mg C	Initial food, replenished at interval T	0.02–0.1
g	–	Volume-specific cost of growth	m/κ
h	mg C/l	Half-saturation constant, host	0.16
h_N	mm^3	Half-saturation constant, parasite	0.1
m	day^{-1}	Volume specific maintenance rate	0.2
N_0	mm^3	Initial spore volume consumed by animal	10^{-5}–10^{-3}
q	–	Metabolic cost of baby production	0.8
T	Days	Interval of food replenishment	1.0
V_P	mm^3	Volume at puberty	$(1.4)^3$
ε	–	Maximal conversion efficiency, host	0.7
ε_N	–	Maximal conversion efficiency, parasite	0.7
κ, κ_0	–	Fraction of energy spent on growth	0.2
ρ	–	Mechanical threshold of infected host	1.0

we can re-express utilization rate of reserve energy as:

$$\frac{dC}{dt} = e\left(\frac{aV^{2/3}}{e_M} - \frac{dV}{dt}\right) = E\left(\frac{aV^{2/3}}{E_M} - \frac{dV}{V dt}\right); \quad (4)$$

Remarkably, this equation does not directly depend upon assimilated energy (A), but instead depends upon energy reserves (e or E) and body volume (V).

When the host is not parasitized and food is relatively abundant, allocation of internal energy reserves by the host towards growth versus reproduction/maturity follows the kappa (κ)-rule (Fig. 1). That is, the animal allocates a fixed proportion (κ) of energy to growth, and the remaining proportion ($1-\kappa$) towards development (if body size is less than volume at puberty, $V < V_P$) or for reproduction (if $V \geq V_P$). This κ-rule representation, then, assumes a trade-off between growth and reproduction. Thus, the host devotes utilized energy to growth and maintenance at the rate:

$$\kappa\frac{dC}{dt} = g\left(\frac{dV}{dt}\right) + mV, \quad (5)$$

where the first term on the right-hand side denotes growth (dV/dt) and associated cost of synthesis of new biovolume (g), and the second term captures cost to maintain current volume (at rate m). Using equations (4 and 5), one can then derive the equation for rate of growth (dV/dt):

$$\frac{dV}{dt} = V\left[\frac{\kappa a V^{2/3}(E/E_M) - mV}{\kappa E + gV}\right], \quad (6)$$

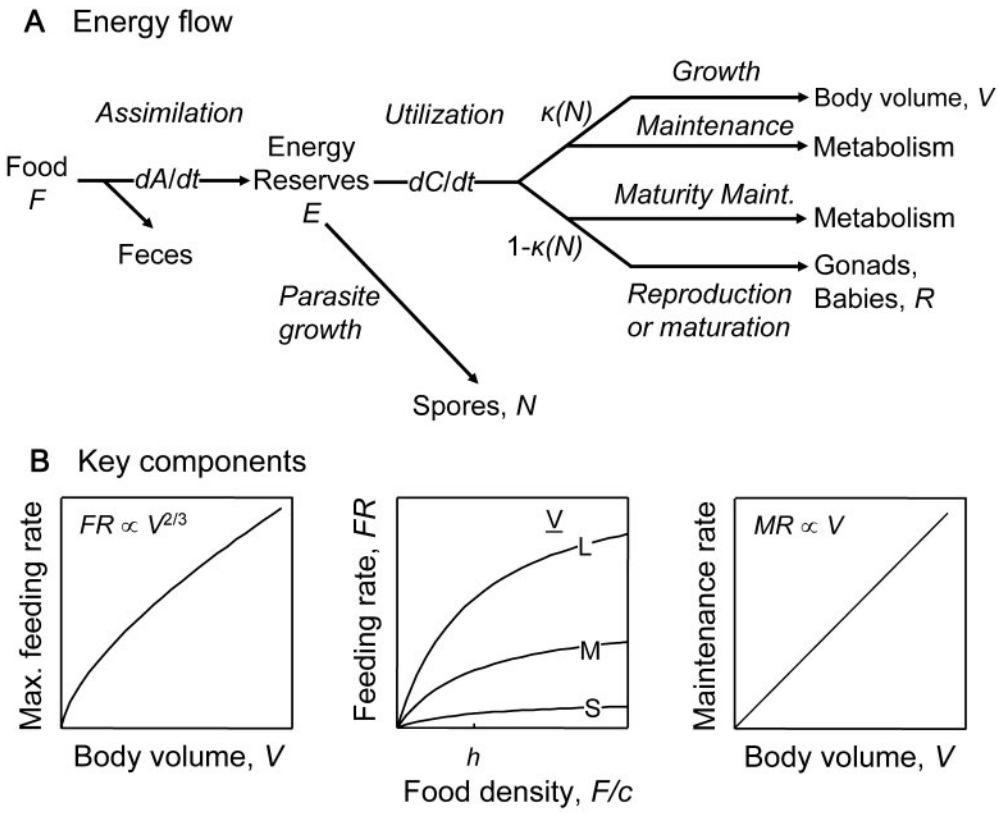

Fig. 1 Conceptual diagram of dynamic energy flow through the parasitized host animal. (**A**) According to Kooijman's (1993) model, energy from consumed food is assimilated (at rate d*A*/d*t*) and converted into internal energy reserves (*E*). This stored energy is then utilized (catabolized, at rate d*C*/d*t*) and a fixed proportion (κ) of it is shunted into growth of structural volume (*V*) and related maintenance, and the rest ($1-\kappa$) is shunted into reproduction and maturation (*R*) with related costs. Both types of parasites, the "consumer" and the "castrator", steal from the energy reserve of the host to produce new parasite. However, the castrator also alters the kappa (κ)-function (Fig. 2), shunting more catabolized energy into growth and less into reproduction. (**B**) Key aspects of the DEB for the host include (1) maximum feeding rate (*FR*) increases proportionately to surface area ($V^{2/3}$), (2) feeding rate also increases hyperbolically with food density (where *h* is the half-saturation constant of the classic type-II functional response), *F*/*c* (3) due to the relationship between surface area and maximal feeding rate, larger animals (L) eat at a higher rate than do medium-sized (M) or small-sized (S) animals at a given density of food; and (4) maintenance rate (MR) increases proportionately with body volume.

where we have converted energy densities (e, e_M) into energy reserves (E, E_M) for reasons that will become apparent once parasites are introduced. Here, growth in structural volume depends upon food supply only indirectly, through reserve energy (E).

Remaining reserves are utilized for development, reproduction, and associated costs. Rate of reproduction (dR/dt) then follows:

$$\frac{\mathrm{d}R}{\mathrm{d}t} = \left(\frac{q}{E_0}\right)\left[(1-\kappa)\frac{\mathrm{d}C}{\mathrm{d}t} - \frac{(1-\kappa)}{\kappa} m V_P\right], \qquad (7)$$

where q is the cost of converting energy reserve of the mother into the energy reserve of the offspring ($0<q<1$), E_0 is the energy volume required to produce an offspring, and ($1-\kappa$) denotes the fractional allocation for development and reproduction. This equation for reproduction also includes a second term (in the brackets) for "maturity maintenance" (see Kooijman 1993 for development and justification of this term). If the animal is a juvenile, it allocates energy for development at a rate equivalent to the entire term in brackets—after replacing V_P with V. Given these assumptions, the DEB model for the non-parasitized host (in energetic stage 1) then consists of equations (3, 6, and 7).

Starvation and food dynamics in the Kooijman model

Before adding parasites, we must consider the energy dynamics of starving hosts because parasites presumably draw energy reserves to very low levels. By doing so, such depletion of resources by parasites indirectly alters the allocation of resources by the host. In fact, when food becomes scarce and/or reserve energy becomes low, the host cannot follow the κ-rule but instead must change allocation

of energy to growth and reproduction. The host animal stops growing when $dV/dt = 0$. In this state of "moderate" starvation, this no-growth point occurs at (from eqn. 6):

$$\frac{aV^{2/3}}{E_M}E = \frac{mV}{\kappa}, \tag{8}$$

which arises when the rate of use of energy reserves (right-hand side) equals the rate of maintenance of existing body volume (left-hand side). For present purposes, we assume that the animal cannot shrink, which is approximately true of the focal *Daphnia* host that we have in mind (i.e., $dV/dt \geq 0$). Even though the host animal ceases to grow, it still follows normal dynamics of energy storage (eqn. 2) and must pay maintenance costs for current volume, mV, and maturity, $m(1-\kappa)\min(V,V_P)/\kappa$. Thus, a slightly different reproductive rate (dR/dt) emerges for moderately starved animals:

$$\frac{dR}{dt} = \left(\frac{q}{E_0}\right)\left(\frac{dC}{dt} - mV - m\left(\frac{1-\kappa}{\kappa}\right)V_P\right). \tag{9}$$

Here, utilization rate (dC/dt) still follows that presented earlier (eqn. 4), except now the animal does not grow ($dV/dt = 0$).

Of course, this representation of a compromised energetic state of the host assumes that requirements for maintaining maturity and somatic tissues are met. If conditions worsen still and maintenance requirements are not met, i.e., $dC/dt < mV + (1-\kappa)\min(V_P,V)/\kappa$, then allocation shifts yet again. In this "severe" state of starvation, the animal's utilization of energy (dC/dt) is set to exactly cover maintenance costs, the animal does not reproduce (i.e., $dR/dt = 0$), and reserve dynamics (dE/dt) become:

$$\frac{dE}{dt} = aV^{2/3}\left(\frac{F/c}{h + F/c}\right) - \left(mV + m\left(\frac{1-\kappa}{\kappa}\right)\min(V_P,V)\right), \tag{10}$$

which equals the assimilated energy (first term, right hand side) minus combined maintenance costs (second term). Death occurs when reserve energy is depleted ($E = 0$). When this occurs, food levels reach the grazer's minimal requirement for food abundance (which is analogous to R^* in more standard resource-competition theory). Any slight drop in reserve energy below this point will kill the host.

The DEB model in good and bad conditions does not completely capture experimental conditions like those in the study by Ebert et al. (2004) until it specifies food dynamics. Typically, the host-grazer depletes some amount of food each day (assuming no production of that food), but experimenters dutifully replenished that food to initial conditions (F_0) daily. Therefore, between replenishment intervals (T), food density declines at rate:

$$\frac{dF}{dt} = -\frac{aV^{2/3}}{\varepsilon}\left(\frac{F/c}{h + F/c}\right), \tag{11}$$

where ε is the maximum conversion efficiency. As the animal grows, it consumes an increasingly large proportion of its daily food allotment.

Adding the parasite: "consumers" and "castators"

Now that the DEB model has been fully specified to include the various states of energetic distress, we can finally (!) include parasitism (Fig. 1). We add a "consumer" parasite (N) by assuming that it feeds on energy sequestered in the host (E) according to its own saturating (type II) functional response. Thus, change in reserve energy through time becomes:

$$\frac{dE}{dt} = V\frac{de}{dt} + e\frac{dV}{dt} - \frac{a_N}{\varepsilon_N}\left(\frac{E}{h_N + E}\right)N, \tag{12}$$

where h_N is the half-saturation constant for the parasite, a_N is the maximal assimilation rate, and ε_N is the conversion efficiency with which the parasite turns host energy into new parasite. The parasite then grows according to a classic equation for a consumer of a resource (Grover 1997):

$$\frac{dN}{dt} = a_N\left(\frac{E_N}{h_N + E_N}\right)N - m_N N, \tag{13}$$

where m_N lumps various loss rates (e.g., maintenance, death) of the parasite into a single parameter. Readers should note that we use such an equation for parsimony: it greatly simplifies the dynamics of growth and reproduction by the parasite.

Our "consumer" strategy for the parasite assumes that the parasite only alters the allocation of energy indirectly, by depleting the internal energy reserves (E) of the host. Thus, the model predicts that the "consumer" parasite will grow until it has depleted the E of the parasite's minimal energy requirement. This requirement, E_N^*:

$$E_N^* = \frac{h_N m_N}{a_N - m_N} \tag{14}$$

arises from setting the *per capita* growth of the parasite, $dN/(N dt)$, equal to zero (eqn. 15), and it represents the minimal amount of energy reserve that the parasite needs to just offset its metabolic losses (again, similar to R^* in analogous resource-competition models; Grover 1997). Since this

energetic requirement is greater than zero, the model indicates that our focal parasite cannot directly kill its host *Daphnia* by starving it (since death occurs when $E=0$ and $E_N^* > 0$). Essentially, parasites should draw reserve energy for its minimal requirement, perhaps first shutting down growth then reproduction, but then persist with the host. The possibility of coexistence of the parasite with the host flouts the biology of the parasitic "obligate killers" of *Daphnia* that we consider here (Ebert 2005). Notwithstanding, another problem emerges: efficient parasites (i.e., those that have low E_N^*) that can deplete E to very low levels achieve unreasonably high volumes within the host (e.g., an order of magnitude greater than structural volume, V, of the host). This result seems rather unrealistic, since surely the host's body structure can only support a finite volume of parasite. As a first approximation, we assume that the parasite (N) indirectly kills the host shortly after a "mechanical" threshold:

$$N = \rho V \tag{15}$$

is crossed, where parameter ρ is a proportional mechanical limit of the host to support the parasite. At this $N=\rho V$ threshold, we assume that the animal can no longer feed. As food intake stops, E quickly or eventually drops to zero as the animal struggles to meet its metabolic demands and energy uptake by the thieving parasite. Once the energy reserve is depleted, the host dies and parasites can then be released to infect new hosts. Given this reasoning, within-host dynamics becomes a race between two key thresholds for the parasite; if the minimal resource requirement (eqn. 14) is reached before the mechanical threshold (eqn. 15), the host will live with persistent infection. Otherwise, the parasite will (successfully) kill the host.

"Castrators" presumably alter allocation of energy of the host indirectly, as do "consumers" (by lowering energy reserves and starving the host), but they also influence it directly. This direct influence may result from the release of hormones or from interference with the endrocrine glands of the host (Baudoin 1975; Ebert et al. 2004). As a first approximation, we assume that parasites influence the κ-function monotonically with density of parasites. Several possible functions capture the essence of such a phenomenon (Fig. 2):

$$\kappa_{\mathrm{I}}(N) = \min\left(1, \left(\frac{1-\kappa_0}{2N_{\mathrm{k}}}\right)N + \kappa_0\right) \tag{16.a}$$

$$\kappa_{\mathrm{II}}(N) = \left(\frac{1-\kappa_0}{N_{\mathrm{k}}+N}\right)N + \kappa_0 \tag{16.b}$$

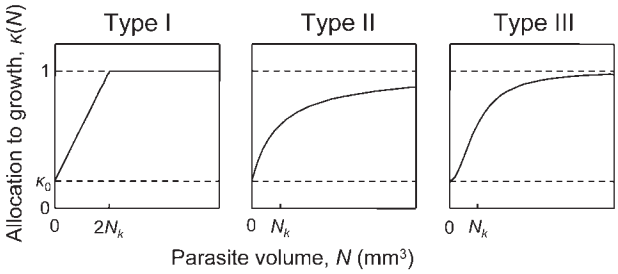

Fig. 2 Three different variations linking parasite density to allocation of energy to reproduction by the host, $1-\kappa(N)$ versus growth, $\kappa(N)$. Ordinarily, without parasitism, the DEB model assumes that hosts allocate a fixed proportion of energy to growth, κ_0. When infected by a castrator, the model assumes that allocation to growth (and away from reproduction) increases as density of the parasite, N, increases according to phenomenological functions resembling the classic type-I (piece-wise linear), type-II (hyperbolic), or type-III (sigmoid) curves. In these functions, parameter N_k is the density of parasite at which the reproduction-allocation function reaches the half-way point between κ_0 and one.

$$\kappa_{\mathrm{III}}(N) = \left(\frac{1-\kappa_0}{N_{\mathrm{k}}^2+N^2}\right)N^2 + \kappa_0, \tag{16.c}$$

where now the kappa function, $\kappa_j\ (N)$, follows a modified version of the type I (eqn. 16.a), II (16.b), and III (16.c) functional responses common to consumer-resource theory (Fig. 2). Here, κ_0 is the value of kappa without parasites, and N_{k} is the volumetric abundance of parasites at which $\kappa_j\ (N)$ reaches the half-way point between κ_0 and one. All three functions predict that allocation of reserve energy to growth, $\kappa_j\ (N)$, should approach one as parasite density (N) increases. For illustrative purposes, we chose the type-II-based version (eqn. 16.b), but our results do not qualitatively depend upon this choice. As one might expect, the castrator can shut down reproduction as the parasite population grows. To be specific, for animals in decent energetic status, reproduction stops once $\mathrm{d}R/\mathrm{d}t=0$, or from equation (7), when:

$$(1-\kappa(N))\frac{\mathrm{d}C}{\mathrm{d}t} = m\left(\frac{1-\kappa_0}{\kappa_0}\right)\min(V_P, V) \tag{17}$$

which occurs when proportion of energy allocated to reproduction (left-hand side eqn. 17) equals costs for maturity maintenance (right hand side, eqn. 17). For animals that had stopped growing but still were reproducing (i.e., "moderate" starvation), the parasite shuts off reproduction when:

$$\frac{\mathrm{d}C}{\mathrm{d}t} = mV - m\left(\frac{1-\kappa_0}{\kappa_0}\right)V_P, \tag{18}$$

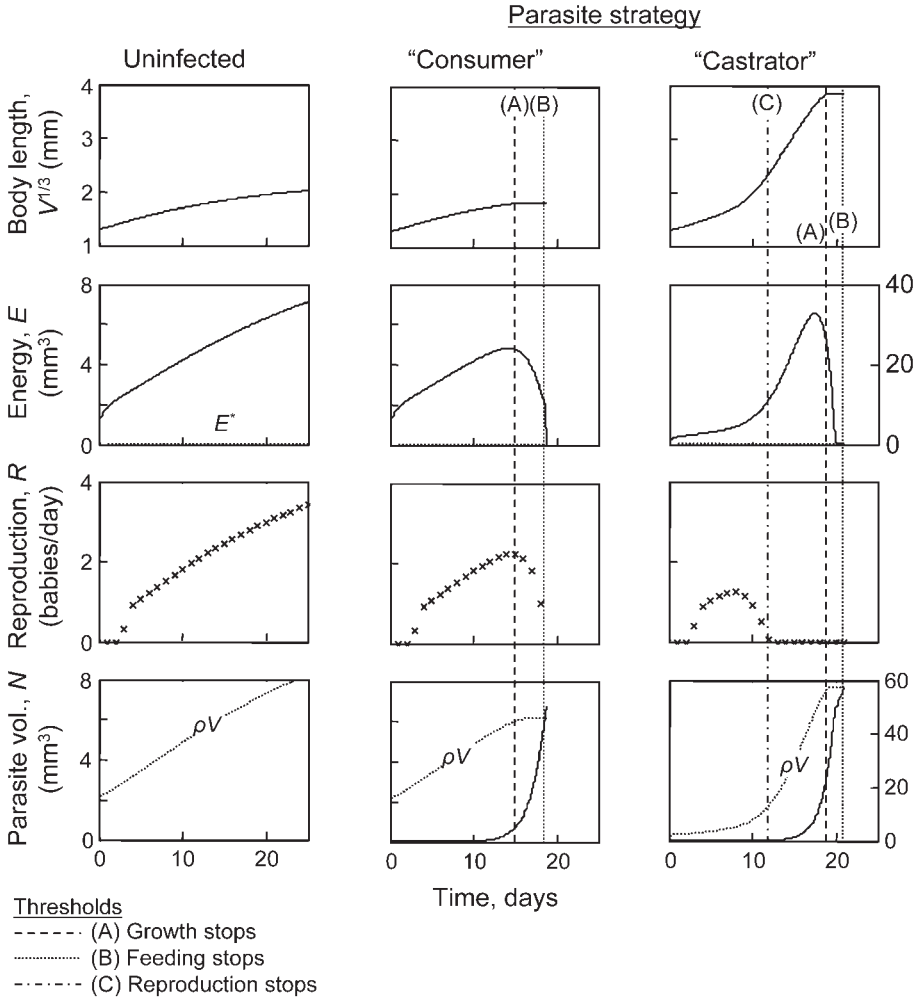

Fig. 3 Example simulations of the DEB model, contrasting scenarios with an uninfected host, a juvenile host infected with a parasite showing a "consumer" strategy, and a juvenile infected with a parasite using a "castrator" strategy. The consumer parasite steals energy, *E*, of the host, but does not directly alter allocation of the host's energy to growth and reproduction. Meanwhile, the castrator steals this energy but increasingly shuts off allocation to reproduction. Both types of parasite influence growth of the animal's structural volume (*V*), energy volume (*E*), and reproduction (R). The consumer can first shut off growth (first vertical dashed line) and then stop reproduction (data not shown) before a mechanical threshold is reached (where volume of the parasite, *N*, equals some proportion of structural mass, ρ*V*, second vertical dashed line). At this point, the host stops feeding and dies shortly thereafter. The castrator typically first stops reproduction (first dashed line), then stops growth (second line) before the mechanical threshold is reached (third line). Parameters used in these simulations follow Table 2 with food levels, F_0/c, set daily at 1.0 mg C/l, and initial volume of consumed parasite, N_0, set at 0.0001 mm^3.

as is the case with the run-of-the-mill "consumer" parasite. Of course, with "severe" starvation, the animal was neither growing nor reproducing anyway, regardless of infection status. Therefore, the parasite does not influence fecundity at that point.

Results

This model readily captures the essence of the "castrator" strategy. One can first appreciate this result by examining representative samples of model dynamics (Fig. 3) with healthy hosts and those parasitized by "consumers". The baseline DEB model readily captures the increasing but decelerating growth of the healthy (uninfected) host's structural volume (V) through time. As the animal grows, its energy density (e) quickly plateaus (not shown); since total energy reserve, E, equals e times V, energy reserve increases with body volume (Fig. 3). Growth rate decelerates because energy assimilation increases with surface area of the host ($\propto V^{2/3}$), while maintenance costs are paid on volumetric basis ($\propto V$). The animal begins reproducing once it reaches a threshold size at maturity (V_P).

The "consumer" parasite alters this scheme by starving and eventually killing the host. In the

example illustrated (Fig. 3), the infected juvenile host enjoys ample food supply. Regardless, as parasite growth increases, the parasite causes the host to stop growing. In this moderate, parasite-induced state of starvation, both energy density and total reserve energy drop. Not surprisingly, reproduction rate also plummets. In this illustrated example (Fig. 3), however, the parasite kills the host before it also shuts down reproduction. The host dies once that mechanical threshold ($N = \rho V$) is crossed. At $N = \rho V$, the animal stops eating, and without incoming energy derived from food, the host's energy reserve drops to zero, while fueling the final growth of the parasite before the host dies. In an environment with less plentiful food, the parasite first shuts down growth, then reproduction, before it kills the host at the key mechanical threshold (data not shown). Importantly, in both cases (low and high food), this mechanical threshold was crossed before the parasite depleted energy reserve to its own energy requirement, E_N^*. Had this threshold been reached first, the parasite would have persisted with the host at equilibrium.

With a "castrator", we see a rather different scenario (Fig. 3). In this case, the parasite directly shuts down reproduction (by manipulating the allocation function) while promoting growth of large hosts—much larger than would have been achieved by even healthy hosts. Reproduction does not cease immediately when parasite volume is low. Not surprisingly, the gigantism-induced host can contain a very large amount of reserve energy (Fig. 3). This stockpile of energy, in turn, fuels growth of very large amounts of parasite—much more than would have been produced by the "wasteful" consumer strategy. In the example illustrated, the host does eventually stop growing in structural volume (V) before the mechanical threshold is crossed. Note, however, the difference in timing; the castrator first shuts down reproduction, then growth, before ultimately killing the host (Fig. 3).

These differences between the strategies of the castrator and consumer also readily appear after characterizing the end-points from similar simulations over a gradient of resource supply to the hosts (Fig. 4). With increasing food supply, we see that hosts infected with castrators achieve larger size at death and reproduce at a lower mean rate [averaged over time from infection to time of death; lifetime reproduction rate closely mirrors these patterns for mean reproduction rate (data not shown)]. Furthermore, given an initial dose of parasite, hosts infected with castrators can live longer than do those infected with consumers; still, for both strategies,

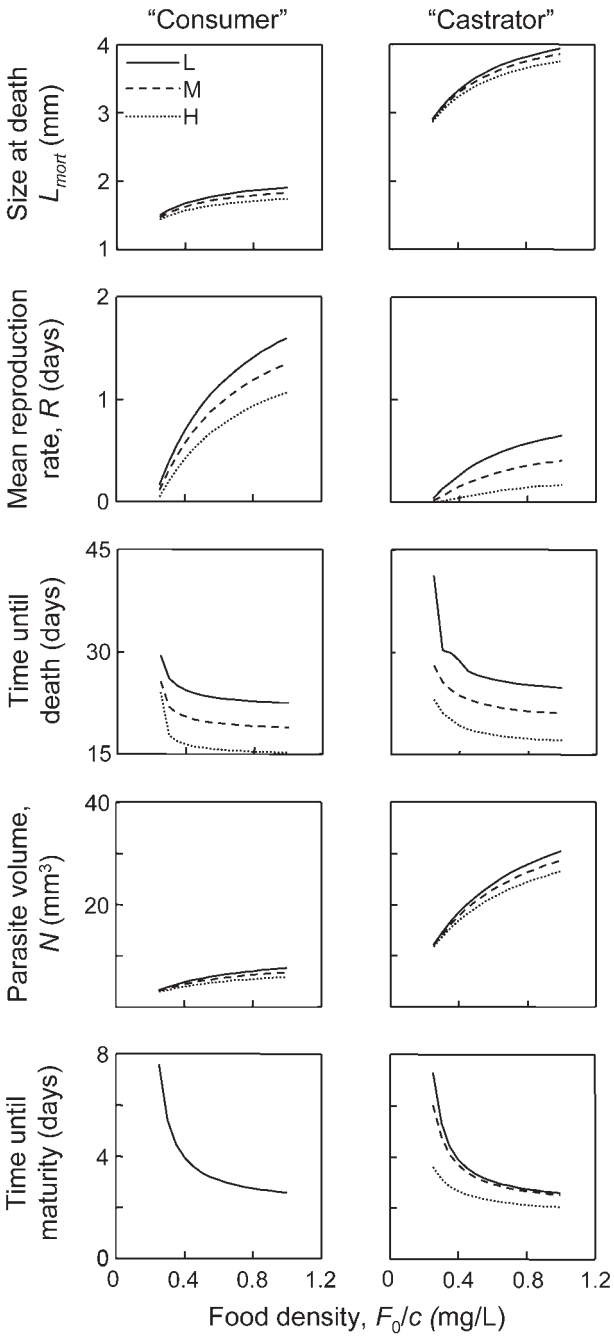

Fig. 4 End-points of simulations of the DEB model incorporating a parasite showing the "consumer" or the "castrator" strategy over a gradient of food resources supplied to hosts which are infected as juveniles. "Consumers" steal host resources but do not influence allocation of host energy, while "castrators" steal energy and can shunt the host's energy from reproduction to growth. Quantities are calculated once the host dies (i.e., when its internal energy volume, E, equals zero). Note that for age at first reproduction of the host infected with a "consumer" the three curves differ so slightly as to appear nearly congruent. Three different initial sizes of parasites ($N_0 = 0.00001$ ["L"], 0.0001 ["M"], and 0.001 ["H"] mm^3).

higher intake of energy by the host translates into faster death over a gradient of environmental food supply. Once they die, gigantism-induced hosts yield relatively large amounts of parasite (as much as an order of magnitude more than for the consumer, given the same parameters for growth and losses of the parasite). The logic involved behind this suite of results seems simple: ''giant'' hosts ingest much more food per unit time and thus yield more energy resources for parasites, all else being equal. Remember that feeding rate of the host increases with the square of body length (Fig. 1B). At a given level of food supply in the environment, this difference in actual food intake per unit time translates into higher spore production for the castrator. However, the castrating parasite may take longer to kill its host (Fig. 4) because the all-important mechanical threshold increases rapidly as the host devotes more and more energy to growth rather than to reproduction (Fig. 3). Over a gradient of food supply, higher availability of assimilated energy, in turn, yields faster death but enhanced growth of hosts sick with either parasite (Fig. 4). Furthermore, the dose of the parasite influences each of these four aspects of the host–parasite interaction. Higher doses of spores results in earlier death of the host, smaller size reached at death, and lower mean reproduction (Fig. 4). These results emerge because the larger initial populations of parasites within hosts more quickly grow to that critical mechanical threshold.

Furthermore, hosts infected with the castrator can reach ''puberty'' and reproduce at an earlier time than do uninfected hosts and those infected with consumer parasites, particularly with higher doses of spores (Fig. 4). The intuition behind this result involves the castrator's influence on growth rate of the host. Higher doses of spores exerts a greater initial influence on the kappa (κ) function, the regime that the host uses to allocate energy reserve to growth versus reproduction. As the parasite directly elevates κ, it encourages faster growth towards puberty in the host. In contrast, the consumer-style parasite does not directly influence κ, only energy available to be partitioned by the host. Therefore, animals infected with this type of parasite reach age-at-first-reproduction at a relatively similar (but slightly longer) time than would a healthy host at a given food supply; the curves for different doses of spore are virtually congruent (Fig. 4). For both parasites, higher food supply in the environment yields earlier age at first reproduction of the host because well-fed animals grow more quickly and therefore reach size-at-maturity (V_P) more rapidly.

Discussion

Adding a parasite to a standard model of a host's DEB captured the essence of two parasitic life-history strategies: ''consumers'' and ''castrators''. It complements recent characterization of these strategies by Bonds (2006). In that model, evolution of virulence of parasites on survivorship and fecundity of hosts emerged using a population-level framework assuming fixed resource supply to hosts. Here, the DEB-parasite models take a more physiologically-based perspective. They assume that energy assimilated by individual hosts are first stored, then used for growth, reproduction, and associated energy costs, as governed by the κ-rule (Kooijman 1993; Nisbet et al. 2000). Like assumed in the Bonds (2006) model, both types of parasites steal from that pool of reserve energy and use it for their own growth, reproduction, and metabolism. In doing so, they cause reductions in growth, survivorship, and reproduction of their hosts. Thus, in a mechanistically justifiable and rigorous manner, these models confirm that virulent effects of parasites on survivorship and reproduction naturally emerge as a consequence of the consumption of resources by the parasite (Bull 1994; Ebert et al. 2004; Bonds 2006). However, castrators also alter the allocation of energy reserves by the host away from reproduction and directly towards growth. We captured that phenomena by making the allocation function, κ, depend upon parasite density.

To be more specific, in both variations of the DEB-parasite model, parasites shunt energy away from the growth and reproduction of the host, functionally starving the host by dropping its energy reserves (Hurd 1990, 2001; Polak 1996). Then, both variations either predict that the parasite can persist with the host or can kill it outright, depending on which of two key thresholds are reached first. The parasite persists with the host if it reaches a minimal requirement for its own reserve energy (called here E_N^*). Analogous to the R^* prediction of many consumer-resource models familiar to ecologists (Tilman 1982; Grover 1997), parasites need this level of food supplied to them by the host in order to just offset mortality and metabolic costs. It emerges as a consequence of density-dependent growth of the parasite. Thus, the model can certainly accommodate the observation that many parasitic castrators greatly reduce fecundity but not survivorship of the host (Lafferty and Kuris 2002)—such parasites likely have large E_N^*. However, the parasite kills its host if it reaches a mechanical threshold first. At this threshold, the physical burden of enormous

parasite load prohibits the host from physically acquiring food. After this point, parasites lower the energy reserves of the host to zero, and the host dies. This scenario is more likely for parasites that are more efficient (i.e., lower E_N^*). Since many parasites of *Daphnia*, our focal host, are ''obligate killers'' (Ebert and Weisser 1997; Ebert 2005), we devoted our attention to this latter scenario.

A comparison between ''consumers'' and ''castrators'' encapsulates much of the essence of the strategy of parasitic castration. In that comparison, we imagined parasites with similar traits (e.g., feeding rate, assimilation rate, loss rate) but allowed the castrators to directly alter allocation. It should not surprise readers that castrated hosts should show ''gigantism''. Gigantism occurs in a variety of host–castrator systems (including snail–trematodes, zooplankton–bacteria, fish–fungus, and plant–ants) (Table 1), and it probably seems advantageous to the parasite from a resource-ecology standpoint. After all, larger hosts acquire resources at a rate (in this model) proportionate to surface area of the host (Kooijman 1993). Therefore, larger hosts assimilate more energy per unit time, all else being equal. As a related benefit, larger hosts can also store more reserve energy (Ebert et al. 2004), in essence stocking a warehouse with resources for future growth of the parasites well above their minimal requirement (E_N^*). Both avenues (higher acquisition rate, more storage) ultimately fuel higher production of parasites before the host dies. Despite such a favorable environment for the parasite, castrated hosts can live longer than do hosts infected by ordinary ''consumers''. This result occurs because fast growing parasites can continually push the mechanical threshold that catalyzes death of the host to increasingly high levels, thereby delaying death. Eventually, of course, the host dies. Furthermore, the model predicts that, by starving the host, ''consumer'' parasites typically first shut down growth of the host, then its reproduction. Cessation of reproduction by consumers relates to ''nutritional castration'' (Baudoin 1975) that should not be confused with active castration. In contrast, active ''castrators'' typically first shut down reproduction, then growth. The timing of these events (and whether they even occur) depends upon supply of resources to the host.

Actually, our model for castrators makes key points related to suboptimal evolution of parasites and fecundity compensation. Simple theory can predict that parasites should completely sterilize their host (Ebert and Herre 1996; Jaenike 1996; Gandon et al. 2002; O'Keefe and Antonovics 2002; Bonds 2006). Therefore, one might point to incomplete sterilization as evidence for suboptimal performance by the parasite (Janeike 1996). The model for castrators here suggests that incomplete sterilization may reflect a time lag between initial infection of the host at low spore doses and strong control over the host's allocation of energy. Simply put, small initial populations of parasites might not completely squelch reproduction until later during the infectious period. In fact, the model predicts that hosts can reproduce earlier when infected by castrators than when uninfected or infected by a ''consumer''. This phenomenon (fecundity compensation) is typically believed to reflect active modification of allocation schemes by infected hosts (Ebert et al. 2004; Chadwick and Little 2005; Bonds 2006 explored this phenomenon theoretically by allowing hosts to evolve in response to parasitism). Remarkably, evidence for fecundity compensation surfaced from our model without any such active modification by the host; instead, it emerges here purely as a consequence of the allocation of resources. The model predicts that, paradoxically, castrators accelerate age at first reproduction by encouraging faster growth from the juvenile to the adult stage (assuming that reproduction commences once a key body size is reached). Of course, our postulated mechanism for fecundity compensation does not mean that hosts do not actively alter their allocation of energy in response to such things as parasitism and predation—certainly, evidence suggests that they can (De Jong-Brink 1995; Hurd 1999; Webb and Hurd 1999) and theory indicates that they should under certain situations (Bonds 2006). Instead, one can perhaps consider our results as a null model of sorts: fecundity compensation does not necessarily imply active reallocation schemes by infected hosts.

The model for both ''consumer'' and ''castrator'' parasites also predicts a strong signal of resource ecology on virulence. In fact, in both cases, greater supply of resources causes quicker death of the host (i.e., stronger mortality virulence), higher production of parasites, and faster growth, earlier age at first reproduction and larger size at death of the host. Such patterns emerge as a result of variation in acquisition of resources by hosts and feature prominently in studies of *Daphnia* and their parasites (Ebert 2005). They also contribute to a small, but growing, sense that resource ecology may influence virulence of parasites, even holding genetic identity of both host and parasite constant (Smith and Holt 1996; Smith 2002; Smith et al. 2005; Lively 2006). This point about ecology of virulence should not seem surprising, given that much discussion of parasitism and castration implicitly assumes that

virulence arises as the consequence of within-host dynamics and competition for limited resources. Still, it is fair to say that much interest in variation of virulence currently involves genetic match–mismatch mechanisms between host and parasite (''gene-for-gene'' and ''matching allele'' models) (Agrawal and Lively 2002). Clearly, such genetic mechanisms deserve much attention. Our complementary message highlights that supply of resources to hosts may explain additional variation in nature, particularly when there is fluctuation in the amount of resource available to hosts.

Despite a strong qualitative match between core results of the castrator variant of the DEB-parasite model and *a priori* predictions (Table 2), we should point out one apparent shortcoming. Ebert et al. (2004) found that higher initial doses of spores should induce stronger gigantism and yield greater production of spores, a phenomenon also seen in other castrator systems (Zakikhani and Rau 1999; Sorensen and Minchella 2001). In contrast, our model predicts opposite patterns, at least for values of the parameter considered here: higher initial doses of spores led to smaller (but still gigantic) hosts and lower production of parasites. Higher initial doses also promoted earlier age at first reproduction. These results largely reflect the mechanism by which parasites actually kill hosts in the model. If one assumes that parasites kill their host once a critical ''mechanical'' threshold is reached, a higher initial dose of spores might promote faster death of the host if initially-larger populations of parasites reach the mechanical threshold more rapidly. Actually, Ebert et al. (2004) suggested that host–castrator systems might respond non-monotonically to initial spore dose—with high initial doses, density-dependence may prevent hosts from producing as many spores. Our model seems to capture that latter aspect.

To be fair, we cannot expect the DEB-parasite model to capture all aspects of host–parasite interactions because it does not include some key components. Instead, we suggest that it should be viewed as a compelling template on which to add more complicated, yet interesting, biology. In one variation hosts might manipulate their allocation parameter (κ) in response to parasitism. (Here, the allocation strategy showed no plasticity but instead remained fixed). Such an addition might allow for more analogous comparisons to other related models (Bonds 2006). Additionally, it might be fascinating to explicitly add immune function to this DEB framework. Energetic requirements for immunity, including up-regulation of immune defenses, can become quite costly (Demas et al. 1997; Moret and Schmid-Hempel 2000). If such costs were added to this model, it would not be surprising to see reduction in fecundity and/or greater mortality following infection (Day and Burns 2003). After all, energy used for defense cannot be used for reproduction or growth. We intend to add such details in the future.

In the meantime, even without such features, the models studied here provide a more mechanistic explanation for resource-dependent virulence of ''consumer'' and ''castrator'' strategies than existed previously. It complements the more evolutionary perspective developed by Bonds (2006). In particular, the ''castrator'' variation provides a mechanistic explanation for most of the interesting and bizarre features of parasitic castration: gigantism, severe reductions in fecundity, long infectious periods, and early fecundity compensation. Each of these results naturally emerged as the net result of simple assumptions about competition for energy reserves that the host would otherwise allocate to growth, reproduction, and associated maintenance. Furthermore, the models suggest a strong, predictable signal linking environmental supply of resources and the degree of virulence exhibited by consuming and castrating parasites. This resource-ecology-of-virulence signal merits more attention as the field of disease ecology continues to develop and mature.

Acknowledgments

Many thanks go to the organizers of the SICB symposium (Ecology and Evolution of Disease Dynamics; Y. Kuang, V. Smith, J. Elser, J. Nagy, T. Newman) for providing the invitation and forum for us to share this work and to SICB for financial support. R. Nisbet (UCSB) provided guidance in formulating the model for ''consumers,'' and the Lively Lab and participants in the ''Disease Ecology and Evolution Discussion'' group at Indiana University and two anonymous reviewers provided helpful feedback. Also, we thank NSF (DEB 06-13510) for additional financial support.

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