

Appendix 1

Malishev, M & Civitello, DJ. When should we expect predator biocontrol of human schistosomes to backfire?

Schistosome Individual-Based Dynamic Energy Budget (SIDEB) model description

The SIDEB model contains three main components: a bioenergetics within-host model, a transmission model, and a resource production model. Here we outline the full model structure.

DEB-Infection (within host) model

The within-host bioenergetics model builds on the “standard” model of Dynamic Energy Budget (DEB) theory (Kooijman 2010). It uses ordinary differential equations to track changes in the abundance of food resources in the environment, F , and multiple host traits: physical length, L (maximum shell diameter; proportional to the cube root of structural biomass); the scaled density of energy reserves, e ; and resources invested in development, D , and in reproduction, R_H . We previously added two modules to this standard DEB model to track a within-host population of parasites and host survival, respectively. Within each host, we track the change in parasite biomass, P , and the resources invested in parasite reproduction, R_P . To model mortality we introduced a variable representing the scaled density of repairable “damage”, δ , with instantaneous host hazard rate, H , assumed proportional to damage. The model structure is presented in Eqs. 1–10, state variables and parameters listed in Table S1, subscripts H and P distinguish host and parasite variables and parameters, and parameter values used in this simulation study are defined in Table S2.

$$\frac{dF}{dt} = -i_M L^2 f_H \quad (\text{Eq. 1})$$

$$\frac{dL}{dt} = \frac{g_{VE}}{3\chi} \left(\frac{\kappa^* a_M e - (m_V + m_R E_M \delta) \chi L}{g + e} \right) \quad (\text{Eq. 2})$$

$$\frac{de}{dt} = \frac{a_M}{\chi E_M L} (f_H - e) - \frac{i_{PM} f_P P}{E_M \chi L^3} \quad (\text{Eq. 3})$$

$$\frac{dD}{dt} = \begin{cases} (1 - \kappa^*)C - m_D D & \text{if } D < D_R \\ \min((1 - \kappa^*)C - m_D D, 0) & \text{if } D \geq D_R \end{cases} \quad (\text{Eq. 4})$$

$$\frac{dR_H}{dt} = \begin{cases} 0 & \text{if } D < D_R \\ \max((1 - \kappa^*)C - m_D D, 0) & \text{if } D \geq D_R \end{cases} \quad (\text{Eq. 5})$$

$$\frac{dP}{dt} = (Y_{PE}i_{PM}f_P(1 - r_P) - m_P)P \quad (\text{Eq. 6})$$

$$\frac{dR_P}{dt} = \gamma_{RP}Y_{PE}i_{PM}f_Pr_PP \quad (\text{Eq. 7})$$

$$\frac{d\delta}{dt} = \frac{\Theta}{\chi L^3} \frac{dR_P}{dt} + k_R(1 - e) - k_R\delta - \frac{3\delta}{L} \frac{dL}{dt} \quad (\text{Eq. 8})$$

$$\frac{dH}{dt} = h_b + h_\delta \max(\delta - \delta_0, 0) \quad (\text{Eq. 9})$$

$$\text{Prob}(\text{Survival})[t] = e^{-H(t)} \quad (\text{Eq. 10})$$

Hosts consume food, F , from the environment at a rate determined by the product of their maximum surface area-specific ingestion rate, i_M , a type-II functional response, f_H , with half saturation constant, F_h , and their physical length squared (i.e., proportional to surface area; Eq. 1). Hosts assimilate energy from food into an energy “reserve”, with yield of reserves on food Y_{EF} . The maximum assimilation rate, a_M , is the product of the maximum ingestion rate and the yield of reserves on food. Hosts use reserves to build two types of biomass: structure (which performs vital functions and requires maintenance at rate m_V), and reproductive material (reserve biomass that has been permanently committed to offspring). Reserve dynamics in the absence of parasitism follow from an assumption of “weak homeostasis” (Kooijman 2010). Hosts allocate a constant portion, κ , of mobilized reserves, C , to somatic (vs. reproductive) processes. Hosts grow in length based on the energetic costs of growing structural biomass, determined by the yield of structure on reserves, Y_{VE} , and the difference between energy mobilized for somatic processes and the costs of somatic maintenance and repair (Eq. 2). Juveniles use energy nominally allocated to reproduction for development, D (Eq. 4). Reproduction begins after reaching the developmental threshold for reproduction, D_R , and developmental status is maintained at the rate m_D .

If hosts are infected, then a population of parasites can consume host reserves (Eq. 3), perturb the host’s energy allocation strategy, accumulate biomass (Eq. 6), and produce propagules (human infectious cercariae; Eq. 7). Parasite biomass (Eq. 6) increases through the ingestion and assimilation of host reserves, following a type-II functional response, f_P , with a half saturation coefficient, e_h , maximum mass-specific ingestion rate, i_{PM} , and yield of parasite biomass on host reserve, Y_{PE} . Parasite biomass also decreases through maintenance at a specific rate m_P . A proportion, r_P , of the assimilated reserve is allocated to parasite reproduction, while the rest, $(1 - r_P)$, is allocated to parasite biomass growth.

The allocation proportion r_P itself is assumed to increase as a sigmoid function of parasite density within the host, with an inflection point at p_h (Table S1). This parasite allocation function

reflects within-host density dependence in parasite growth and limitations of physical space. Further, it influences the timing of parasite reproduction and the maximum density of parasite biomass within host tissue (Gérard *et al.* 1993). Parasite offspring biomass increases from parasite allocation to reproduction, with the relative yield of parasite reproduction biomass on assimilated reserve, γ_{RP} . In addition, infection can modulate the host's realized allocation between soma and reproduction, κ^* , with parasite density dependent manipulation rate, α , yielding an effective allocation rule, $\kappa^* = \min(\kappa + \alpha P, 1)$. Thus, parasites may affect the host's energy budget in two direct ways: direct consumption of host reserves and by modulating the host's energy allocation rule. If infection diverts host allocation from reproduction to growth, then it can cause parasitic castration, the rapid reduction/cessation of reproduction by infected hosts, and host gigantism, increased growth of infected hosts relative to uninfected hosts (Hall *et al.* 2007; Lafferty & Kuris 2009).

When starved, snails lose tissue biomass (shrink) and cease reproduction. Thus, when allocation by snail hosts is insufficient to meet somatic or developmental maintenance costs, they lose structural mass or developmental status, respectively (Civitello *et al.* 2020). The growth dynamic can become negative when allocation to soma is insufficient to pay maintenance costs, $(m_V + m_R * E_M * \delta) \chi L^3 > \kappa^* C$. A similar situation exists for development and reproduction. If allocation to reproduction is insufficient to cover developmental maintenance costs, $m_D D > (1 - \kappa^*) C$, then reproduction ceases ($dR_H/dt = 0$) and development regresses at a rate equal to the deficit in allocation. Although hosts can shrink, we note that snail shells do not. Thus, the degree to which a snail's current structural volume differs from its maximum structural volume reflects its degree of starvation-induced shrinkage.

We assume that hosts die from damage caused by low energy reserve density, “reserve depletion”, or harm caused by emerging parasite offspring. We incorporated these drivers of mortality by adapting the stochastic death model of the Generalized Unified Threshold model of Survival (GUTS) framework (Gergs & Jager 2014). Scaled damage density, δ , increases due to the release of parasite offspring with damage intensity, Θ . The damage repair rate, k_R , determines the rate of damage caused by reserve depletion and the damage repair. Damage density also decreases through dilution by growth (Eq. 8). Damage repair by hosts may be energetically costly, and we assume that these costs, m_R , are a specified component of somatic maintenance for the host. The cumulative hazard, H , experienced by hosts increases with the background hazard rate, h_b , and a linear function of damage density beyond a threshold, δ_0 , with hazard coefficient h_δ (Eq. 9). Host survival probability, $P(\text{Survival}[t])$ is a negative exponential function of cumulative hazard, H , (Eq. 10).

Several derived parameters and functions simplify the presentation of the model or the statistical analysis (Table S1). A full derivation of the survival submodel as well as additional discussion and justification of the parasitism submodel are presented by Civitello *et al.* (2018) and (2020).

Transmission model

Snail hosts become infected after density-dependent contact with free-living miracidia following a model that separates the transmission process into two components: irreversible exposure to parasites in the water (i.e., host tissue invasion) and infection probability given an exposure (Civitello *et al.* 2013; Civitello and Rohr 2014). We assume that miracidia are

introduced into the aquatic environment by humans at a constant rate, M_{in} , and they contact snails at a per capita exposure rate, ε . Upon exposure, each invading parasite has a probability of successful infection, σ . Infection adds the carbon biomass of a single miracidium (2.85×10^{-5} mg C) to the parasite biomass compartment within the host's DEB submodel (Eq. 6). If the host was previously uninfected, this event effectively “turns on” the parasite submodel (Eqs. 6 and 7) as well as individual terms throughout the host's energy budget that depend on parasite biomass. Miracidia that invade hosts or die due to background mortality are removed from the environment. Given a density of snail hosts, S , and miracidia, M , the transmission model implies the following probability of infection for each snail in a given time interval, with duration t :

$$Prob(Infection)[t] = 1 - e^{-\frac{\sigma M}{S}(e^{-\varepsilon S t} - 1)} \quad (\text{Eq. 11})$$

Resource production model

Our model simulations considered two scenarios of food resource production. Snails could consume (1) logistically growing periphyton algae or (2) detritus produced at a constant rate, e.g., by aquatic macrophytes that are inedible for snails while they are alive, representing a resource subsidy. Therefore, resources in the environment, F , can be separated into algae, F_a , and detritus, F_d .

Algal dynamics follow a logistic growth equation with losses from host feeding:

$$\frac{dF_a}{dt} = rF_a \left(1 - \frac{F_a}{K}\right) - f_H(i_M \sum L^2) \quad (\text{Eq. 12})$$

with intrinsic algal growth rate, r , carrying capacity, K , and scaled Type II functional response, f , maximum food intake rate, i_M , and host length, L , representing the total uptake surface area of the host population.

Detritus dynamics follow a constant supply rate, det , and similar losses from host feeding:

$$\frac{dF_d}{dt} = det - f_H(i_M \sum L^2) \quad (\text{Eq. 13})$$

Simulation process

On each day, the infection submodel runs first, adding parasite biomass to infected hosts. Next, a daily step of the bioenergetics model is run for every snail. Resource density updates on each time step based on equations 12 or 13 (depending on the resource scenario), reflecting consumption by the entire snail population. The final phase of each daily step updates the host population and environmental variables. Dead snails are removed from the population and eggs

hatch after a 10-day delay. Free-living cercariae die at background rate m_Z and miracidia are introduced at rate M_{in} at this time.

Table S1. Parameters and compound functions for the bioenergetic model of within-host infection dynamics.

(A) State variables		
Quantity	Description	Units
F	Environmental resource abundance	mg C
L	Physical host length	mm
e	Scaled density of host energy reserves	dimensionless
D	Host reserve invested in maturity/development	mg C
R_H	Host reserve invested in reproduction	mg C
P	Parasite biomass	mg C
R_P	Parasite biomass invested in reproduction	mg C
(B) Primary parameters (Host)		
Quantity	Description	Units
i_M	Surface area-specific maximum host ingestion rate	mg C d ⁻¹ mm ⁻²
F_h	Host (Type-II) foraging half saturation constant	mg C
Y_{EF}	Yield of reserve on resources	dimensionless
Y_{VE}	Yield of structure on reserve	dimensionless
κ	Proportion of mobilized reserve allocated to soma	dimensionless
m_D	Maintenance rate for maturity	d ⁻¹
L_M	Maximum physical host length	mm
χ	Ratio of structural biomass to physical length cubed	mg C mm ⁻³
E_M	Maximum host reserve biomass relative to structural biomass	dimensionless
D_R	Host maturity threshold for reproduction	mg C
ε_H	Carbon content of host offspring	mg C
(C) Primary parameters (Parasite)		
Quantity	Description	Units
Y_{AE}	Yield of parasite assimilate on host reserve	dimensionless
Y_{PA}	Yield of parasite biomass on assimilate	dimensionless
Y_{RP}	Yield of parasite offspring biomass on assimilate	dimensionless
i_{PM}	Parasite maximum mass-specific ingestion rate	mg C d ⁻¹
e_h	Parasite ingestion half saturation constant	dimensionless

p_h	Parasite allocation half-saturation constant	dimensionless
α	Parasite manipulation of host allocation rule	mg C ⁻¹
m_P	Mass-specific maintenance rate for parasites	d ⁻¹
ε_P	Carbon content of parasite offspring	mg C

(D) Primary parameters (Damage, hazard, and survivorship)

k_R	Damage repair rate constant	d ⁻¹
Θ	Intensity of parasite-induced damage	dimensionless
h_b	Background hazard rate	d ⁻¹
h_δ	Hazard coefficient of damage	d ⁻¹
m_R	Scaled energy expenditure rate for damage repair	d ⁻¹
δ_0	Damage density threshold	dimensionless

(E) Derived parameters and functions

Equation	Description	Units
$a_M = i_M Y_{EF}$	Maximum host assimilation rate	mg C d ⁻¹ mm ⁻²
$g = \frac{1}{\kappa^* Y_{VE} E_m}$	Cost of structural growth relative to maximum possible allocation to soma	dimensionless
$p = \frac{P}{\chi L^3}$	Parasite density in host structural tissue	dimensionless
$r_P = \frac{p^2}{p_h^2 + p^2}$	Proportional allocation of parasite assimilate to reproduction	dimensionless
$Y_{PE} = Y_{PA} Y_{AE}$	Yield of parasite biomass on host reserve	dimensionless
$\gamma_{RP} = \frac{Y_{RP}}{Y_{PA}}$	Relative yield of parasite reproduction on parasite assimilate	dimensionless
$c = \left(\frac{ge}{g+e} \right) \left(a_M L^2 + \frac{(m_V + m_R E_M \delta) \chi L^3}{\kappa^* g} \right)$	Commitment/mobilization rate of reserve	mg C d ⁻¹
$m_V = \frac{\kappa a_M}{\chi L_M}$	Mass-specific maintenance rate for structure	d ⁻¹
$\mu_D = \frac{m_D}{m_V}$	Scaled maturity maintenance rate	dimensionless

$$M = \chi(1 + E_M)$$

Volume-biomass coefficient for hosts mg C mm⁻³

$$\kappa^* = \min(\kappa + \alpha P, 1)$$

Realized proportion of mobilized reserve allocated to soma dimensionless

$$f_H = \frac{F}{F_h + F}$$

Scaled host functional response dimensionless

$$f_P = \frac{e}{e_h + e}$$

Scaled parasite functional response dimensionless

Table S2. Parameter estimates used in this simulation study

Parameter	Description	Estimate ¹	Units
<u>Host parameters</u>			
κ	Proportional allocation to soma	0.908	—
M	Mass:volume relationship	5.17×10^{-3}	mg C mm ⁻³
E_M	Maximum host reserve biomass relative to structural biomass	1.40	mg C
L_M	Maximum physical host length	53.6	mm
i_M	Surface area-specific maximum host ingestion rate	3.04×10^{-2}	mg C d ⁻¹ mm ⁻²
F_h	Host (Type-II) foraging half saturation constant	5.31×10^{-4}	mg C L ⁻¹
Y_{EF}	Yield of reserve on resources	0.269	—
Y_{VE}	Yield of structure on reserve	0.261	—
μ_D	Maintenance rate for maturity	0.133	—
D_R	Host maturity threshold for reproduction	0.617	mg C
ε_H	Carbon content of host offspring	0.015	mg C
<u>Parasite parameters</u>			
α	Parasite manipulation of host allocation rule	2.20	mg C ⁻¹
i_{PM}	Parasite maximum mass-specific ingestion rate	0.583	mg C d ⁻¹
Y_{PE}	Yield of parasite biomass on reserve	0.937	—
e_h	Parasite ingestion half saturation constant	0.220	—
m_P	Mass—specific maintenance rate for parasites	0.311	d ⁻¹
p_h	Parasite allocation half-saturation constant	0.128	—
Y_{RP}	Yield of parasite offspring biomass on assimilate	0.921	mg C
ε_P	Carbon content of parasite offspring	4×10^{-5}	mg C
<u>Damage, hazard, survival, and repair parameters</u>			
k_R	Damage repair rate constant	3.09×10^{-2}	d ⁻¹
δ_0	Damage density threshold	2.61×10^{-2}	—
h_δ	Hazard coefficient of damage	4.73×10^{-3}	d ⁻¹
h_b	Background hazard rate	3.09×10^{-4}	d ⁻¹
Θ	Intensity of parasite-induced damage	79.3	—
m_R	Scaled energy expenditure rate for damage repair	8.06×10^{-6}	d ⁻¹
<u>Transmission model</u>			
ε	Snail-miracidia contact rate	20	L d ⁻¹
σ	Miracidia infection probability given contact	0.5	—
M_{in}	Miracidial input rate	10	d ⁻¹
m_M	Mortality rate of miracidia	1	d ⁻¹
<u>Environmental/Resource parameters</u>			
ENV	Volume of environment	500	L
r	Algal maximum growth rate	Varied	d ⁻¹
K	Algal carrying capacity	5	mg C L ⁻¹
det	Detritus subsidy rate	Varied	mg C L ⁻¹ d ⁻¹

M_Z

Mortality rate of cercariae

1

d^{-1}

-
1. Host, parasite, and damage, hazard, survival, and repair parameters derived from Civitello et al. 2020 and rounded to three significant figures.
 2. Transmission model parameters rounded from estimates in Civitello and Rohr 2014
 3. Environmental/resource parameters chosen to reflect a $1\text{m}^2 \cdot 0.5\text{ m}$ deep volume of habitat, realistic quantities of algal growth or detrital input, and rates of parasite mortality.