To the PNAS editorial board,

Our initial submission of this manuscript (MS. #2016-14116) in August 2016 received mixed reviews, and though both reviewers thought the motivation of the paper was exciting, it seems that it was rejected primarily due to the concerns of Reviewer 2, who had doubts about the basic formulation of the Nutritional State-structured Model (NSM). Although we acknowledge that we were not invited to resubmit, we feel that the referee’s critiques are easily met and we have addressed all of the reviewers concerns, in addition to making substantial improvements to the formulation of our model. Our revised model now includes a full mechanistic description, which we show leads to a simple non-dimensional form. The structure of our model has changed only slightly and the qualitative results remain the same. However, the dimensional form of the model now allows us to make several novel quantitative predictions of empirical data. Given that our response to the referee has not significantly altered our model or it’s predictions, and has added predictions of data, we ask that this submission be reconsidered for review by PNAS. We believe that this submission makes substantial contributions to our understanding of the physiological constraints that drive both the population dynamics of mammalian species as well as the forces that influence changes in body size over evolutionary time. In short, our revised manuscript makes several important contributions:

* Across the observed body size range, terrestrial mammals occupy a region of parameter space where sustained cyclic dynamics are not permitted.
* Even transient cyclic dynamics increase the probability of extinction, and we argue that mammals should have energetic rates that avoid parameter regions close to transient oscillatory regimes. Moreover, regions of parameter space with small steady-state population sizes also increase the extinction probability. Thus we define a “refuge” of parameter space where the extinction probability is minimized between high probabilities of extinction via transience and high probabilities of extinction via low steady state densities, and show that mammals have allometrically constrained rates of starvation and recovery that place them squarely within this lower-risk space.
* Steady-state population sizes in the NSM support the energy equivalence hypothesis (equal energy use across populations of species with different individual body size) for a wide range of body sizes. We show that our model accurately predicts both observed steady state population densities of mammals as well as the energy equivalence rule against empirical data.
* We investigate dynamical constraints on the range of mammalian body sizes by considering the invasion of a steady-state population by mammals with altered amounts of endogenous energetic reserves. We show that mammals with greater amounts of endogenous reserves are able to invade up to the size of the largest recorded mammal (7.4x107g) above which leaner individuals can invade, such that this maximum body size bound serves as an evolutionary attractor. This suggests that the dynamics of starvation and recovery described in the NSM may provide a within-lineage mechanism for the evolution of larger body size among terrestrial mammals, a well-documented phenomenon known as Cope’s rule.

Thank you for considering this request,

Justin Yeakel, Chris Kempes, Sidney Redner

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Responses to the Reviewers’ Comments:

We thank the reviewers for the valuable insight, suggestions, and critiques of our prior submission to *PNAS* (MS. #2016-14116). We have carefully considered the feedback supplied by the reviewers and have revised the model by considering a dimensional and mechanistic counterpart, from which we derive a non-dimensional form for analysis that is presented in our revised contribution. The reviewers raised both major and minor issues related to our methodology and model description. We have addressed all of their points and believe that the revisions made greatly increase the value of our manuscript. *Importantly, these changes do not alter the primary results, and in all cases increase the significance of our findings.* Moreover, we have included additional comparisons of our model results against empirical data to demonstrate the relevance and potential application of our approach to natural population of animals. We thank the reviewers for their insights and hope that our changes and clarifications satisfy their concerns. Our responses to reviewer comments are detailed below. Please let us know if any clarification in required.

General response to the criticisms of model formulation:

We agree with the referees that the original model lacked certain important features and was presented in a non-dimensional form, where the motivating mechanisms were insufficiently described. We have thus introduced a revised model that is fully mechanistic and dimensional along with it’s non-dimensional version in the main text. The key mechanistic additions include the explicit treatment of biosynthesis and maintenance metabolism, resource growth rates and density, an explicit carrying capacity for the resource dynamics, and the saturating dynamics for resource consumption and reproduction for the consumer. This more explicit treatment integrates concepts from ontogenetic growth, resource dynamics, and growth physiology. We then provide an explicit derivation of the non-dimensionalization of this mechanistic model and show that the resulting form is very similar to our previous model, differing only slightly in the resource consumption equation. This new mechanistic model and its non-dimensionalization produce results that are qualitatively similar to our previous analysis, but additionally allow us to make a set of quantitative predictions for data that we have added to the paper. In particular, these revisions clarify many of the concerns raised by Reviewer 2, which we address point-by-point below.

**Reviewer Comments:**

Reviewer #1:

Suitable Quality?: Yes

Sufficient General Interest?: Yes

Conclusions Justified?: Yes

Clearly Written?: No

Procedures Described?: Yes

Comments :

This is a remarkable contribution to the understanding of ecological allometries. It does seems to be an step in the right direction, as the proposed Nutritional models accomplish a lot with rather little in therms of assumptions. However, there are a couple that may be important to discuss in a more explicit way in the manuscript. First, the model assumes that only hungry individuals die, while allometric data shows that mortality rate (e.g. Azbel 1994 PNAS 91, Brown et al 2004). More importantly, however, the authors assume that reproductive rate is independent of resources, and that reproducing individuals require less energy than that required to recover from the starving state. In part this generates the odd result that when there are no resources then (lambda > sigma) the population of well nourished individuals grows exponentially (lines 149-153).

We thank Reviewer 1 for their assessment of our contribution. Our revised model clarifies the dependency of the system on the lambda > sigma criterion. By accounting for the added maintenance term for individuals in the hungry state as well as individuals in the full state, which we have developed in our revised model, biologically plausible values for both consumers and the resource (such that all have densities > 0) is dependent on this criterion. In other words, the lambda=sigma condition now represents a true transcritical bifurcation, not dissimilar from many other consumer-resource models, across which (R\*,H\*,F\*)<0.

In lines 410-415. In relation to the ecological constraints upon body size and how resources in particular can limit extreme sizes see (Marquet and Taper 1998 Evolutionary Ecology, 12(2), 127-139.). This result and a later paper by Burness in PNAS highlight that area exerts important constraints upon persistence, since energy and resources area spatially distributed.

The Reviewer is correct to point out that area is an important determinant of body size constraints. We now explicitly account for resource limitation via an explicit resource density and specific resource growth rate in the dimensional formulation of the model and show that the resulting steady states of the consumer match nearly perfectly against empirical data. We aim to investigate the effects of area in future efforts which we believe are outside of the scope this paper.

Lines 440-452. Although R\* theiry predicts that those species able to maintain populations under low resource concentrations will out-compete those with higher R\* it is important to realize that as populations decrease in size several other factor affect viability (e.g demographic and genetic stochasticity) such that thresholds (e.g.Allee effects) are common.

We agree with the Reviewer, and investigate the effects of stochastic extinction due to lower steady states and cyclic dynamics in the paper (illustrated in Fig. 5). In general, we have shifted our assessment of survival to focus on R\* theory.

Minor comments

Line 80. delete "many"

Line 460 change linneage to lineage

Several references need amendment (initial for authors in 36, 38 incomplete in 42 etc.

It would be interesting to see what the model can say regarding the scaling of extinction risk.

We have corrected the above errors and thank the Reviewer for pointing out these issues. We agree that exploring additional issues regarding mass-specific extinction risks would be a fruitful line of inquiry, though we believe it is beyond the scope of this particular contribution. However, to address the overall question of extinction risk as dependent on size, we have provided three plots in Figure XXX which show the extinction likelihood based on sigma and rho for three different body sizes that span the range of mammals considered. This plot shows that the parameter space where extinction is unlikely is shrinking in area with increased body size.

Reviewer #2:

Suitable Quality?: No

Sufficient General Interest?: No

Conclusions Justified?: No

Clearly Written?: Yes

Procedures Described?: Yes

Comments:

This paper proposes a nutritional-state structured model of consumer-resource interaction and uses the scaling rules resulting from metabolic theory to make inferences about expected types of population dynamics, the risk of extinction as well as the outcome of an evolutionary process in maximum body size. The paper is overall written with a lot of enthusiasm and a clear use of language and therefore has quite a bit of appeal. However, a more careful and critical read of the manuscript shows me that the starting point of the model development and analysis is seriously flawed when considered form a biological point of view. I therefore do not think this is a publishable paper.

• To start with, I fail to see how the proposed model is related to the authors motivation of the study as explained in the introduction. The motivation centers around the trade-off between investment in maintenance and growth on the one hand and reproduction on the other hand, as also emphasised in the significance statement. However, in my opinion the model that the authors propose has little or nothing to do with maintenance and certainly not with somatic growth.

We have now included a more complete treatment of maintenance as detailed below, and also agree that the original model lacked an explicit treatment of maintenance processes. The goal of the original model was to describe the simplest dynamics for starvation, recovery, and reproduction, however we realize that the original formulation lacked an explicit treatment of important biological characteristics and was not clearly described in its original form. We have now included an explicit dimensional and mechanistic model which we non-dimensionlize into a form which is only slight different than the original equations. It should be noted that this is an important improvement to the model because it allows us to make new quantitative predictions and to interact with additional data which we have added to the paper. However, the qualitative results are largely the same as the original model and the two models reduce to the same equations within certain regimes.

• However, my most fundamental problem with the model is not its motivation but its formulation. The authors model a consumer class that is hungry or starving and a consumer class that is full, satiated and reproducing. Both classes of consumers feed on the resource. The resource grows via a logistic growth equation and the authors off-handedly mention that its carrying capacity equals 1. This innocuous remark has huge implications as it means the resource density has to be interpreted as a scaled resource density. In turn, the authors assume that the transition from a full state to a hungry state is proportional to the absence of resource, which they identify with 1−R, where R is resource density. To define the difference between current resource density and its carrying capacity as “absence of resource” is in my opinion not correct, but biologically it is also an absurd assumption as in an unscaled version of the model (where the carrying capacity is not set equal to 1 and hence the term 1 − R, would read K − ˜R with K the carrying capacity of the resource and ˜R the unscaled density) it would imply that an individual consumer would more quickly end up in a hungry state if the maximum density of its resource increases. This makes no sense to me. I have tried to see whether there is some magic scaling of the resource density that would justify this choice of functional form. I failed, so I have come to the conclusion that the term σ(1−R)F describing the rate at which consumer transition from the full to the hungry state is not based on any sensible biological mechanism. It is a mathematical construct that has little or no connection with biological realism.

In our treatment of the dimensional model we have added an explicit treatment of carrying capacity and the saturation of the resource to an upper bound, thus including terms of the form (1-R\_d/C). We also show that within our dimensional system there is a choice of non-dimensionalizations that leads to a form for resource dynamics that depends on (1-R) where R is the non-dimensionalized resource that has been rescaled by the carrying capacity. We agree that the non-dimensional model is not complete without a presentation of the fully dimensional form that we have now added to the supplement along with our explicit non-dimensionalization procedure. Again, it should also be noted that the adjusted mechanisms of the dimensional model lead to a non-dimensional form that differs from the original model for the resource dynamics (dR/dt) equation.

• A second issue arising from this assumption has to do with dimensions: the authors completely overlook the problem of dimensionality that results from the assumption about the starvation rate σ(1−R)F as well as the recovery rate ρRH. In a later section they derive estimates for the parameters σ and ρ, which they give the dimension time−1. This derivation, however, totally ignores that the parameters σ and ρ represent proportionality constants in terms that also involve the resource density. Again in an unscaled version of the model the product ρR should have the dimension time−1 when we only consider the ODE for H, which would suggest that ρ should have a dimension time−1 . resource−1. However, if in an unscaled version of the model we consider the ODE for R, it can be inferred that the product ρH should have the dimension time−1 and hence that ρ should have a dimension 1 time−1 . consumer−1. In short, considering the dimensions of the different terms the model does not make much sense either.

We agree with the Reviewer that our original formulation - without a dimensional counterpart - was not clear in how we accounted for unit transformations. Our reformulation accounts for these issues and allows us to include additional specific information regarding the description of rate laws, specifically those accounting for consumer maintenance. This changes the last two terms in the non-dimensional dR/dt equation to (rho R + delta)H + beta F instead of the previous R(rho H + beta F).

• Further biological issues with the model formulation are more subtle. For example, implicit in the model formulation is that the changes between the hungry and satiated state are taking place at the same time scale as consumer and resource population growth. In my opinion, this assumption is not very convincing as reproduction takes place at a lifetime scale, but individuals are hardly ever hungry for their entire life. It is for this difference in time scale that classic models usually involve a consumer functional response to account for the difference in time scale of the process of hungry/satiated switches and population dynamics.

The reformulation of the rate laws controlling starvation and reproduction now explicitly detail the fact that they are operating on different timescales: the starvation rate occurs on shorter timescales, whereas reproduction is specifically defined as taking place over larger timescales. This is evident in the graphical depiction of the reproduction rate vs. the starvation rate as a function of body mass as shown in Figure 3. We note that individuals in the model can transition back and forth between hungry and full states - on average - many times within an average lifespan.

• Apart from the biological issues with the model, there are also mathematical issues with its analysis. The authors report that for σ = λ a transcritical bifurcation occurs, but this statement is evidently wrong. A transcritical bifurcation indeed involves a real eigenvalue turning positive, as the authors explain, but apart from that a transcritical bifurcation involves 2 different fixed points, one that turns from stable to unstable, while the other turns from unstable to stable. Two different equilibria are hence necessarily involved in a transcritical bifurcation. Inspection of the expressions for the consumer and resource density in the internal equilibrium (equations [2]) shows however that neither the (0, 0, 0, ) nor the (0, 0, 1) equilibrium is involved in the TC. Although for λ ↑ σ R∗ approaches 0, F∗ and H∗do not. What happens around σ = λ is therefore mathematically unclear.

We thank the Reviewer for taking the time and effort to look into these details, and acknowledge that our original formulation had a condition that we mistakenly identified as a transcritical bifurcation, and it was indeed much less clear than we originally thought. However, our reformulation of the model makes this transition point clear and consistent with other consumer-resource models. Accordingly the condition σ = λ is now a true transcritical bifurcation where the internal steady state crosses (0,0,0), as the factor (σ - λ) appears in the numerator for the steady state equations of R, H, and F. This is due to the modifications of the dR/dt equation.

• Along the same lines, in figure 1 it is shown that a parameter region with cycles is bordering the line where σ = λ, where a real eigenvalue turns from negative to positive. From a mathematical point of view I do not understand the dynamics in this region, as the real eigenvalue turning positive relates to the already unstable non-trivial equilibrium. What happens at that border to the limit cycle? It should be explained for which parameter values the limit cycle is stable or unstable, the fact that the already unstable equilibrium becomes infeasible is unrelated to the fate of the limit cycles. Because of the more fundamental problems with the underlying model I will only shortly comment on the later sections, which deal with the parameterisation of the model based on the scaling rules from metabolic theory and with evolution of body size.

We believe that our reformulated model avoids some of the mathematical issues of the original, though in the reformulation, there are again three regions of interest… if we hold the recovery rate constant, and begin with a very low starvation rate, as the starvation rate is increased, the interior fixed point of the system moves from an unstable state to a cyclic regime (as the transcritical bifurcation is crossed), and then to a stable state (as the Hopf bifurcation is crossed). In the unstable state, there are three negative eigenvalues with no imaginary part; in the cyclic regime there is one negative eigenvalue with no imaginary part and two positive eigenvalues with imaginary parts; in the steady state regime there are three negative eigenvalues, two with imaginary parts.

• The authors derive estimates for the recovery rate ρ from the ontogenetic growth model. Implicitly, the authors equate here the process of fattening up following starvation to the process of body size growth after birth. I find this also a questionable assumption, the latter has to do with developing body tissues and structures, whereas the former is a process of replenishing storage compartments. I hence disagree with the starting point that recovery from- starvation parameters can be deduced from the ontogenetic growth model.

We agree with the referee and did not make this clear enough in the first iteration of the paper, but we do in fact employ different energetics for the recovery which is only accounting for refilling fat storage. This is encapsulated in our a^prime estimate which we employ for recovery along the ontogenetic curve. The ontogenetic growth curve encapsulates a wide variety of shapes largely controlled by a and so a^prime leads to replenishment along a different trajectory. We didn’t draw this in the original growth curve schematic because we felt that it was confusing to the reader. It should also be noted that differences in a of XXXX percent in a^prime lead to differences in the timescale of XXXX and the overall scaling across organisms is preserved, and so this is a relatively small effect.

• In the last section on evolution of body size, the authors identify the ESS with the consumer body size with the highest steady-state density of consumers. This assumption is in contrast to any other theory in consumer-resource interaction, in which it invariably holds that the consumer type with the lowest equilibrium resource density is the winner over evolutionary time. Unfortunately, in the model that the authors develop this is the non-sensical consumer with σ = λ as is made clear in figure 6 of the paper. In summary, I can only conclude that I am not at all convinced by this manuscript, which involves a lot of (mathematical) reasoning, but is founded on a flawed biological basis. I apologise for this harsh judgement, but I fail to see an alternative.

We have now reformulated our analysis of competitive advantage (or invasibility) by comparing the steady states of the resource for both resident and invading populations. According to R-star theory, the consumer that can push its resource to the lower steady state will have a competitive advantage. Moreover, we avoid ESS terminology to prevent confusion of our analysis with game-theoretic methods, and focus instead on addressing potential competitive advantages/disadvantages of an invading consumer with modified body mass. We also note that although starvation rates are modified by changing the body mass of the invading consumer, the extent to which mass can be added or removed are strictly constrained by 1) at the small end, the proportion of body mass that is fat (chi = -f\_0\*M^(gamma-1), and 2) at the large end, the reproductive body mass (which we assume is 0.95 the asymptotic mass, such that chi cannot be greater than 0.05). Because of these constraints, the σ > λ condition is always held, and our analysis does not disobey the fundamental laws dictated by our formulation. This revised approach (comparing R-star’s of the invader and resident population) indicates that the maximum size of mammalian body mass is 1.73x10^7g, which is very close to the observed maximum mammalian body size of 1.74x10^7g value reported by Smith et al. (Science) 2010.