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Linking Individual-based Models and Dynamic Energy Budget Theory: Lessons for Ecology and Ecotoxicology

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Chapter 1: Introduction

The hierarchy in levels of biological organisation is one of the most pervasive themes in ecology. This hierarchy influences how ecologists perceived research questions in ecology to such an extent that major disciplines within ecology were often defined by the biological scale of interest (e.g. population ecology, community ecology). In early work within the field of ecology, the natural tendency when confronted by a problem of a given level of organisation was to seek an explanatory mechanism at the same level. For example the early work in population ecology aimed to answer key questions such as the regulation of populations by considering the population itself as the unit of interest. The different branches delineated along levels of biological organisation in ecology have led to important insights in their respective fields (optimal foraging theory at the individual level, exploration of causes of population cycles through use of population models, etc.). However, in recent decades the role of scale in ecology has shifted from that of a delineator of research interests, to that of the critical link for both basic understanding and useful predictions. This shift has been primarily motivated by the realization that patterns observed at one scale are often the emergent result of processes occurring at smaller scales (Levin 1992; Grimm and Railsback 2005). A second reason for the shift in the role of scaling among levels of biological organisation in ecology is based on more pragmatic argumentation. Generally, as one shifts from lower to higher levels of biological organisation, relevant time and spatial scales increase the time and costs required to collect useful data. In most cases, it is much easier to collect data on individuals than populations, and still more challenging to monitor communities. Thus the availability of quality data becomes more rare, necessitating the development of theory and methods to use lower-level data to understand and predict higher-level patterns.

One problem that exemplifies both of these challenges, and the example that serves as the motivation for this thesis, is the risk assessment of chemicals. Currently, most data on the toxicity of chemicals is collected at the individual level or lower. Typically, a series of tests are conducted on individuals to monitor survival or to measure changes in sub-lethal endpoints such as reproductive output in response to exposure to a toxicant. However, the protection directives for most species (at least within the European Union) are aimed at achieving sustainable populations. Thus, relevant questions for risk assessment are: what effects will a given exposure to a chemical have on population density or size structure? How long will it take the population to recover after an exposure? Thus, for risk assessment of chemicals, understanding the link between individuals and populations is critical.

Due to the logistical, financial, and ethical constraints of conducting large-scale population experiments for each pesticide is impractical, ecological modelling has been suggested as a tool to link individual and population levels for chemical risk assessment. With this aim, many models have been developed for chemical risk assessment using a variety of methods: with most either using classical differential equation models, matrix models, or individual-based models (IBMs; Galic et al. 2010, Schmolke et al. 2010, Thorbek et al. 2010). In this thesis I use the latter. Unlike classical population models, which use state variables of populations such as population density, individual-based models consider individuals in the population explicitly. In IBMs, individuals are discrete and unique entities. These individuals follow a set of rules in which their state variables are updated, (e.g. eat, move, reproduce) and the dynamics of the system as a whole emerge from the interactions of individuals with each other and their environment. Thus, IBMs are advantageous when variation between individuals, local interactions, or adaptive behavior of individuals is important for a particular research question (DeAngelis and Mooij 2005, Railsback and Grimm 2012). IBMs are especially useful for chemical risk assessment, where data is available at the individual level, but predictions are needed at the population level.

One criticism of the use of IBMs is that they are often complex and species specific. This creates two major problems. First, in a basic context, the complexity and specificity of many IBMs hinders the development of general theory. Because IBMs differ so widely in structure it is difficult to generalize the finding from one model or species to another (Grimm 1999, Grimm et al. 1999). The fact that IBMs are usually species-specific may reflect their broad use by biologists with more empirical backgrounds. Compared to theoretical ecologists, empirical ecologists often are most interested in what makes species unique rather than what makes them similar. Secondly, for applied research, the time and costs required to develop and test a new model will be prohibitive for most species. This is especially relevant for chemical risk assessment were developing a new model for each species is impossible, and extrapolations among species are needed. While there are several good examples of predictive and useful IBMs (e.g., Railsback and Harvey 2002, Stillman and Goss-Custard 2010), these models were generally the result of up to a decade of guided model development. Thus one major goal of my research in addition to developing methodology for predicting the effects of chemicals on populations using individual-level data, is to generalize the link between individuals and populations. In that respect, I use the generic Dynamic Energy Budget theory (DEB) as a basis for my IBM.

DEB is a generic theory that aims to provide a common framework for understanding the dynamics of individuals (Kooijman 2010). DEB describes the life-history of individuals using a mass-balance approach. Here the processes of energy acquisition through feeding, and allocation to growth and reproduction are represented using a set of coupled differential equations. The use of a common framework for all species is motivated by the observation that key metabolic pathways are highly conserved through evolution, and thus a common set of rules can be used to model how animal gather and use energy. This assumption is supported by the surprising generalities among a diverse range of animal taxa, for example the ubiquity of von Bertalanffy growth at constant environmental conditions. Therefore, rather than using a new model framework for each species, in DEB the framework is conserved and differences between species are represented through variation in parameter values (see Chapter 2 for an broader introduction to DEB theory).

Thus, combining DEB and IBM allows the advantages of using IBMs, but with the potential for generality. However, to date, little work exists combining DEB theory and IBMs to understand the dynamics of higher levels of biological organisation. Additionally, while predictions of DEB have been tested at the individual level, the ability of DEB to accurately scale from the individual to population level has rarely been tested. Thus the goal of my thesis is twofold: first, to develop methodologies to encourage further use of DEB in an IBM context, and secondly to test the ability of DEB to scale from individuals to populations in both basic and applied contexts. Below I give a brief outline of these two themes divided into three research chapters.

First, to motivate the use of DEB and IBMs together, I developed a generic implementation of DEB theory for use in an IBM context in NetLogo (DEB-IBM) (Chapter 2). DEB-IBM serves as a framework for investigating population-level research questions, with DEB serving as the base model for individual performance. The DEB-IBM framework was designed to be easily adaptable to address specific research questions. In addition to the manuscript and code, I have also provided a framework description and user manual with examples of how to adapt the model to a specific research question.

I then use this generic framework to develop a model for the water flea, *Daphnia magna* and test the ability of the model to capture population-level processes (population density and size structure over time) using data at the individual level to parameterise the model (Chapter 3). The goal of this chapter was not only to test the ability of DEB to scale from individual level to the population level, but also to develop theory. Here I use information from the mismatches between model predictions and data to further guide theory development.

Finally, I test the ability of the model adapted for *Daphnia* to predict the population response to chemical stressors using individual-level data (Chapter 4). To accomplish this, I use data sets collected for both individual and population response to 3,4 dichloroaniline. I use the individual-level data to identify the physiological mode of action, calibrate the effect of the toxicant, and to use this information to make predictions for the effect at the population level.

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Chapter 2: Dynamic Energy Budget theory meets individual-based modelling: a generic and accessible implementation

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Abstract

Dynamic Energy Budget (DEB) theory was designed to understand the dynamics of biological systems from cells to populations and ecosystems via a mass balance approach of individuals. However, most work so far has focused on the level of the individual. To encourage further use of DEB theory in a population context, we developed DEB-IBM, a generic individual-based model (IBM) that is based on DEB theory. The generic IBM is implemented as a computer program using NetLogo, a free software platform that is accessible to biologists with little programming background. The IBM uses DEB to represent assimilation, maintenance, growth and reproduction of individuals. The model description follows the overview, design and details (ODD) protocol, a generic format for describing IBMs, and thereby provides a novel and accessible introduction to DEB theory and how it works in a population context. Dynamic Energy Budget-individual-based model can be used to explore properties of both individual life-history traits and population dynamics, which emerge from the set of DEB parameters of a species, and their interaction with environmental variables such as food density. Furthermore, DEB-IBM can be adapted to address specific research questions, for example by including spatial effects. A user manual explains how this can be done. Dynamic Energy Budget-individual-based model is designed to both facilitate use and testing DEB theory in a population context and to advance individual-based modelling by basing the representation of individuals on well-tested physiological principles.

Introduction

Understanding how population dynamics emerge is one of the fundamental challenges in ecology. As the influence of individual variation, local interactions and adaptive behaviour on population dynamics has become more appreciated, individual-based models (IBMs) are playing an increasing role in both basic and applied disciplines (DeAngelis & Mooij 2005; Grimm & Railsback 2005; Stillman & Goss-Custard 2010). IBMs represent individual organisms as unique entities that differ from each other and change over their life cycle. Individuals are characterized by a set of state variables and attributes, which are chosen according to the problem addressed with the model (Grimm *et al.* 2010). Individuals behave as autonomous entities according to behavioural rules. They interact with each other and their abiotic environment, including habitat structure and environmental drivers such as temperature, humidity or disturbances. Population dynamics emerge from these interactions.

Individual-based models have been shown to be powerful and flexible tools. However, they have also been criticized for often being based on *ad hoc* assumptions and representations of individual dynamics and behaviour (Grimm 1999). This makes the development of IBMs inefficient and the field of individual-based modelling incoherent (Grimm & Railsback 2005). To facilitate re-usability of IBMs and their elements and to facilitate distilling general insights from specific IBMs, it is desirable to base IBMs more on standardized and well-tested approaches for individual behaviour (Berger, Hildenbrandt, & Grimm 2002).

Dynamic Energy Budget (DEB) theory (Kooijman 2010) is such an approach. It has been developed with the goal of understanding the dynamics of biological systems, from cells to ecosystems, via a balance approach for mass and energy. As in IBMs, in DEB theory, individuals are considered the key unit of interest for understanding dynamic systems at higher levels of organization. Focusing on the individual is motivated by the fact that mass and energy balances are easier to calculate for individuals than for higher or lower levels of biological complexity. Additionally, natural selection occurs at the level of the individual, which shapes the life-history traits of a species, and ultimately drives dynamics at higher levels of biological organization. DEB theory provides a quantitative framework for modelling the acquisition and use of resources for organisms over the entire life cycle. It thereby generates a quantitative explanation for the time patterns of life-history traits such as growth, maturity and reproduction in dynamic environments.

An overview of DEB theory and its applications can be found in Nisbet *et al.* (2008), Kooijman (2001), Van der Meer (2006) and Sousa, Domingos, & Kooijman (2008). A key assumption in the theory is that the mechanisms governing metabolic organization are similar among species.

Therefore, the same basic model structure can be used for, in principle, all animal species; species differ in life history primarily as a result of differences in their set of DEB parameters, not because of differences in model structure. The generality of DEB facilitates a growing understanding of how life-history traits covary among and within taxa. In spite of DEB's generality, it is an empirically grounded and well-tested theory and has been applied in a range of disciplines, including ecotoxicology (Jager, Heugens, & Kooijman 2006) and aquaculture (Alunno-Bruscia, van der Veer, & Kooijman 2009), and to species from a wide range of taxonomic groups including bacteria, yeast, arthropods, fish and mammals. Yet to understand behaviour at higher levels of biological organization, tools are needed to scale from the individual model to populations.

We believe both DEB and IBMs can benefit each other; however, to date, these approaches have rarely been used in combination. Below, we discuss how each of these approaches can benefit each other and then describe the DEB-IBM framework, which we have developed to facilitate the use of DEB in an individual-based context.

How can DEB benefit IBMs?

A common problem with the application of IBMs is their complexity. IBMs are often developed for very specific research questions, and the structure and parameterization of models defining the life history of organisms differ widely. This creates a problem not only for model developers who often start from scratch when modelling a new species but also for the scientific community, which must try to reconcile different models or try to understand how conclusions for one species relate to another. DEB is appropriate as a building block for IBMs because it is a relatively simple model that translates environmental conditions to individual performance (growth, survival and reproduction) and is consistent with first principles such as conservation of energy. This is important because the trade-offs in life-history traits that DEB specifies (growth vs. reproduction, time and size to maturation) turn out to strongly influence population dynamics (Sæther & Bakke 2000; Denney, Jennings, & Reynolds 2002). Moreover, because DEB is a generic theory, it can be applied to virtually all species, which would facilitate broader insight from specific studies and comparisons between species.

How can IBMs benefit DEB?

Because DEB models specify behaviour of an individual, tools are needed to extrapolate to the population level. So far, most of such population predictions based on DEB theory were made using matrix models (Klok & de Roos 1996; Klanjscek *et al.* 2006; Billoir, Péry, & Charles 2007) or the Euler–Lotka equation (Kooijman & Metz 1984; Jager *et al.* 2004). The disadvantage of these approaches is that only one state variable can be easily considered (age, stage or size), whereas the consistent application of DEB often requires considering more state variables, especially in time-varying environments. Another method for simulating population dynamics based on a model of individual performance is provided by physiologically structured population models (PSPM) [e.g. the escalator boxcar train from De Roos, Diekmann, & Metz (1992)]. PSPMs can be used to model population dynamics in dynamic environments. However, for all of these approaches (Matrix, Euler–Lotka equation, PSPM) as opposed to IBM's, variation among individuals, local interactions or adaptation cannot be easily considered in a rigorous manner. IBMs are the natural link to the population for DEB because both approaches focus on the behaviour of individuals, as a key aspect in understanding higher levels of biological complexity. Additionally, use of DEB in a population context has generally used a deterministic approach. DEB-IBM allows for the inclusion of stochasticity and thus provides a framework to investigate its effect at the population level.

DEB-IBM links DEB theory with IBMs

Despite this potential, so far DEB theory has not been widely used in IBMs. We only know of three published examples (Kooijman, Hoeven, & Werf 1989; Alver, Alfredsen, & Olsen 2006; Bacher & Gangnery 2006). A reason for this might be that to implement DEB theory in IBMs, skills in both mathematics and computer programming are required, which many ecologist lack. Therefore, to encourage further development and use of DEB theory, we have developed a generic framework for DEB-based IBMs using a software platform that is accessible to biologists with little programming background: NetLogo (Wilensky 1999). DEB-IBM is a generic IBM, which can be linked to specific species by using species-specific parameters. It is thus rather a framework than a specific model. We here focus on the general framework, which is designed to facilitate using DEB and IBM in combination for tackling all kinds of generic and specific questions for a wide range of species. We present a transparent and complete yet concise implementation of the DEB model for a generic isomorphic (i.e. organisms retain the same shape during growth) and ectothermic animal (Kooijman *et al.* 2008) within an IBM. In the following, we first briefly describe the DEB-IBM framework and then present the IBM and its scope.

The DEB-IBM Framework

We implemented a scaled version of the standard DEB model as described in Kooijman *et al.* (2008). A full description of the model, following the overview, design and details (ODD) protocol for describing IBMs (Grimm *et al.* 2006, 2010), a user manual and the NetLogo file of DEB-IBM are all included in the supplementary material (http://cream-itn.eu/projects/wp-1/daphnia-2/deb-ibm). In the following, we provide a brief overview of DEB-IBM and describe how it can be used.

Each model individual is characterized by four primary state variables (called 'DEB state variables' hereafter) that describe the energy content of four different compartments: 'structure', which determines actual size, feeding rates and maintenance costs; 'reserves', which serve as a buffer between feeding and metabolic processes that require energy; 'maturity', a continuous state variable that regulates transitions between the three development stages (embryo, juvenile and adult) at fixed maturity levels, and a 'reproduction buffer', into which mature individuals direct energy for reproduction and which is converted into embryos during reproductive events.

In DEB theory, metabolic processes are mechanistically driven by surface/volume ratios. Individuals update their DEB state variables based on a set of differential equations. Individuals assimilate food from the environment, which enters the reserve. Energy is mobilized from the reserve and is distributed to two distinct pathways: somatic growth and maintenance on one side, and maturity maintenance, development (for immature individuals) or reproduction (for mature individuals) on the other (maintenance costs need to be satisfied first). Here, κ is the proportion of the mobilized energy allocated to the soma, and $1 - \kappa$ the proportion allocated to maturity maintenance, development or reproduction. Based on the updated DEB state variables, a set of discrete events may occur. An individual dies when it cannot mobilize enough energy to pay somatic maintenance. At each time step, for each mature individual, it is calculated whether the individual has enough energy for an offspring, if it does, it produces one offspring. In the next time step of the numerical simulation, this individual is added to the population; it will start to feed exogenously when the maturity level reaches the threshold for birth; however, this default reproduction process can be easily adapted to replicate other types of reproduction behaviour. In addition to this standard model, we have included optional submodels for the ageing process, intraspecific variation and simple predator–prey dynamics.

Species in the model are specified by the 8 'scaled' DEB parameters (see user manual), with two additional parameters for the ageing submodel (optional), and two parameters needed for the foraging submodel [you also need the two parameters (r and K) of the logistic growth formula of the prey to run the population dynamics under logistic prey dynamic conditions].

Our implementation is compatible with a database of DEB parameters for a rapidly growing number of species: 'Add_my_pet' (http://www.bio.vu.nl/thb/deb/deblab/add_my_pet/index.php). In the user manual, we provide a detailed explanation of how to obtain parameters from this database and input them into DEB-IBM. The 'Add_my_pet' database is relatively new, with parameters values for approximately 60 species, with varying degree of support. However, users can assess the degree of support for a species in the database, because the data used to derive the parameter set for each species are given in a corresponding data file, and within the file the references from which the data were taken are listed.

Many users still will have to obtain DEB parameters themselves. There are currently two thorough reviews and guides for parameterizing a DEB model for a species (Van der Meer 2006; Kooijman *et al.* 2008). If data are very limiting, a general set of parameters can be estimated from maximum body size of an individual (Kooijman *et al.* 2008). While users can cope with less, generally data for growth and reproduction at multiple food densities provides enough information to get a good set of parameters for use in DEB-IBM. Parameterization tools, DEBtool (available in both Matlab and the free software Octave) and DEBtoxM (specific for toxic stress, Matlab only), can be obtained from http://www.bio.vu.nl/thb/deb/deblab/, which perform the required optimization techniques for varying levels of data availability. This level of use requires deeper investment into DEB theory.

There are two levels of application for our generic framework. First, it can be used to explore properties of both individual life-history traits and population dynamics, which emerge from the set of DEB parameters of a species, and their interaction with environmental variables such as food density. For this, no programming or technical understanding of DEB theory are required. Users need only input DEB parameters and environmental conditions in the graphical user interface, from which they can monitor and record various individual and population-level output such as fecundity, population density and size structure.

The second level of use, involves adapting DEB-IBM to address a specific research question. For this, users must learn how to change the code of the generic model. For example, the research question might be: how are the population dynamics of a species influenced by changes in land use? In this case, the user would adapt the generic DEB-IBM to include space and movement behaviour of individuals, with DEB theory acting as the energetic model for the individual. We provide detailed examples of how the model can be adapted to include both spatial and behavioural aspects. The NetLogo implementation is flexible enough to add all kinds of modules or alter existing ones, including ones that are in DEBtool or DEBtoxM.

This more advanced use of the model requires users to learn programming in NetLogo. However, NetLogo is an exceptionally well-documented software platform that was specifically designed for implementing IBMs; moreover, a recent textbook on individual-based modelling, which is based on NetLogo is available (Railsback & Grimm 2012). NetLogo comes with powerful built-in procedures, leading to a shallow learning curve. This makes both IBMs and DEB more accessible to ecologists without formal training in computer programming.

NetLogo has some limitations, in particular regarding computation time, number of agents and spatial units it can deal with, and the lack of a tool for debugging the software. However, these limitations turn out to not be constricting for many models and problems in population ecology. Moreover, because NetLogo slowly but surely is turning into a standard platform for implementing IBMs, we expect that these limitations will be overcome in the near future (see, for example, the recent link between NetLogo and the computationally more powerful platform RePast: http://repast.sourceforge.net/repast_simphony.html).

For DEB-IBM, we did not chose a general programming language such as C++ or Java because learning these languages to the point were users can implement or modify IBMs would usually be too time-consuming for most ecologists. Likewise, we considered none of the alternative software platforms, e.g. Repast (repast.sourceforge.net) or MASON (Luke *et al.* 2005) suitable because they are much harder to learn and not as thoroughly documented (for comparative reviews of software platform for individual-based or agent-based models, see Railsback, Lytinen, & Jackson 2006; Nikolai & Madey 2009).

Discussion

Dynamic Energy Budget-IBM can be used without modification to make general estimations of population characteristics, such as population growth rate, in simple environments, and as a learning tool for understanding how the physiological properties of individuals can influence population dynamics. While other tools, such as matrix models or the Euler–Lotka equation can be used to estimate population growth rates in constant environments, they cannot as easily be extended to dynamic environments. A further advantage of DEB-IBM is that we can consider the interactions between a predator population and its prey. In the default version of DEB-IBM, we have allowed the option to model dynamic predator–prey population dynamics, assuming the prey follows a logistic growth pattern and is depleted via predation; however, this can be adapted when needed to model prey dynamics of a specific system. Thus, DEB-IBM can be used to estimate carrying capacity of the predator population as a function of its environment. Because DEB-IBM predicts dynamics in time, it lends itself to more rigorous testing with population-level data, which often consist of time series observations of population density and/or size structure. This is important because validation of models against population data is necessary to build confidence in the model for applied uses.

It should be noted that although DEB-IBM facilitates applying DEB theory in individual-based population models, using it still requires commitment. For specific research questions, DEB-IBM merely serves as a starting point. Researchers will have to consider species-specific processes such as the rules for converting the reproduction buffer into offspring. In the generic model, individuals reproduce when they have enough energy to produce one offspring. However, many animals produce clutches of offspring, either at fixed time intervals or when triggered by an environmental cue. These differences in life-history strategy can easily be incorporated into the generic model, and in the user manual, we give examples of how to do so. Additionally, relevant behaviours such as dispersal or habitat selection may have to be considered. Users of DEB-IBM should thus be prepared to learn basic skills in NetLogo, but this requires, owing to the design and excellent documentation of NetLogo, usually not more than a few days.

Like any useful theory, DEB theory is not static, and there are still plenty of open questions within DEB that require dedicated research. A growing international community is currently working with this theory, so we can expect new developments in the near future. One benefit of using DEB in a population context is that it highlights aspects of the individual dynamics, which are especially relevant for population dynamics. Often these are areas that have been overlooked by those focusing solely on individuals. Our own initial use of DEB-IBM has highlighted important questions where further research is needed. For example, within DEB, a general pattern of intraspecific variation in parameter values has been suggested (Kooijman, Hoeven, & Werf 1989); however, little research to date has investigated how DEB parameters (co)vary among individuals within a population. Additionally, little research has so far been carried out on the process of starvation. Kooijman (2010) offers some possibilities to handle starvation within a DEB context, but these rules are probably highly species-specific and require further evaluation.

Nevertheless, the advantage of using a mechanistic framework like DEB is that once these questions are addressed, and the major processes understood, they are more likely to apply in untested conditions, whereas phenomenological approaches can only be applied within the range of tested conditions. Additionally, research on starvation within a DEB context may help shed light on how similar the mechanisms of the starvation process are among a wide range of taxa. DEB has a lot to offer for solving specific problems, but to exploit its benefits as a general theory, it needs to be used and tested more widely at the population level. This would increase confidence in the model, clarify its limitations and possibly lead to further improvement.

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Chapter 3: Predicting population dynamics from the properties of individuals: a cross-level test of Dynamic Energy Budget theory

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Abstract

Individual-based models (IBMs) are increasingly used to link the dynamics of individuals to higher levels of biological organization. Still, many IBMs are data hungry, species specific, and time consuming to develop and analyse. Many of these issues would be resolved by using general theories of individual dynamics as the basis for IBMs. While such theories have frequently been examined at the individual level, few cross-level tests exist which also try to predict population dynamics. Here we perform a cross-level test of DEB theory by parameterizing an individual-based model using individual-level data of the water flea, *Daphnia magna*, and comparing the emerging population dynamics to independent data from population experiments. We found that DEB theory successfully predicted population growth rates and peak densities, but failed to capture the decline phase. Further assumptions on food-dependent mortality of juveniles were needed to capture the population dynamics after the initial population peak. The resulting model then predicted, without further calibration, characteristic switches between small- and large-amplitude cycles, which have been observed for *Daphnia*. We conclude that cross-level tests help detecting gaps in current individual-level theories and ultimately will lead to theory development and the establishment of a generic basis for individual-based models and ecology.

Introduction

A major objective in ecology is to link processes at different scales through an understanding of how behaviour at a macro scales emerges from the behaviour of individual components of the system. This is especially apparent in population ecology, where individual-based modelling (IBM) has been proposed as a tool to cross between scales and unify their associated subdisciplines, for example, physiological and population ecology (Huston et al. 1988; DeAngelis and Mooij 2005; Grimm and Railsback 2005). However, a well-known drawback of IBMs is that they can be complex and data hungry. Consequently, they often are designed for specific species where sufficient data exist. Model designs are then tied to these species and thus lack generality. This makes model development and analysis inefficient because different models are hard to relate to each other, impeding distillation of general insights from IBMs (Grimm 1999; Grimm et al. 1999).

In contrast to this species-specific approach, some theoretical approaches attempt to deduce the diversity among organisms and ecological systems from generic models of individual-level processes, for example, Dynamic Energy Budget (DEB) theory (Kooijman 1993, 2010) or the Ontogenetic Growth Model (OGM) based on metabolic scaling theory (Hou et al. 2008). These approaches are based on first principles of bioenergetics and thus focus on common and species-independent aspects of organisms and their performance. They apply the same generic model structure for all species and use variation in parameter values to explain differences in life-history patterns among species.

Such standardized generic models hold great potential for advancing the field of individual-based ecology (IBE; Berger et al.2002). First, they make model development and communication more efficient. This is important for both theoretical and applied models. Instead of designing models from scratch, standard designs can be used that do not need to be justified in detail, because they have been tested and used before. Second, they facilitate comparing models addressing different species and systems. Differences in model behaviour can be more easily ascribed to differences in species-specific traits or system-specific controls, whereas without standard submodels they could be ascribed to virtually any detail of the models' structure. Conversely, when the same model structure is used to model different species, we can understand the differences in population level output as a function of differences in individual-level parameters.

Despite the great potential of generic individual-level models as the foundation for IBMs, their ability to accurately capture the dynamics of higher levels of biological organization remains largely untested. Here we focus on performing a cross-level test for one general theory, Kooijman's dynamic energy budget theory (Kooijman 2010; Sousa et al. 2010). DEB is a general theory that describes life-history traits over time over a range of environmental conditions. DEB theory has been used to model individual-level processes for a wide range of animal species, for example, molluscs (Ross and Nisbet 1990; van Haren and Kooijman 1993; Saraiva et al. 2011), zooplankton (Nisbet et al. 2010), and fish (Pecquerie et al. 2009, 2011), and to model population-level processes for microorganisms, for example, bacteria (Kooi and Kooijman 1994; Hanegraaf and Muller 2001) and phytoplankton (Muller 2011). Yet, a primary motivation for the development of DEB theory was to explain population dynamics in terms of individual life-history traits, that is, to obtain unified theory across levels of biological organization (Nisbet et al. 2000). Surprisingly, so far tests of DEB theory that link individual and population process have been sparse and of limited scope (literature reviewed in Nisbet et al. 2010) or have focused on modelling equilibria or population growth rates, for example, de Roos (2008). Here we therefore develop an IBM for a cross-level test of DEB theory. Our cross-level test serves two purposes: to test how well individual-based population models based on DEB theory predict population dynamics and structure and to use possible deviations between model output and data to identify elements of DEB theory that might need to be improved to better capture population-level phenomena.

For implementing our IBM, we used the software tool DEB-IBM (Martin et al. 2012), which is a generic IBM-based DEB theory. As a model system, we use laboratory populations of *Daphnia magna*, for which we collected independent data sets on individual performance and population dynamics under different environmental conditions. We first use individual-level data to parameterize a model of individuals that is based on DEB theory. Then we use these DEB individuals to simulate population dynamics and compare them to results from independent population experiments. Our initial comparison of DEB-IBM model output and data revealed a mismatch between the model and data after the initial peak in population density for all population experiments. Specifically, the model did not capture the decline in population density and the subsequent change in density and size structure following the initial population peak. Our conclusion was that the dynamics of the starvation and recovery mechanisms are poorly understood. We therefore discussed and tested several new alternative size-selective submodels of food-dependent mortality and also formulated and tested a new recovery model. Finally, we compared the model's ability to reproduce additional qualitative patterns, for example, the characteristic occurrence of both small- and large-amplitude cycles under certain resource conditions (McCauley et al. 2008).

Methods

DEB theory is designed to capture the energy budget of a wide range of organisms, environments, and questions. Using DEB theory in a specific context requires setting up specific model equations. Here we introduce the core concepts of DEB theory and then briefly explain our model, which includes the "standard" DEB model (see Sousa et al. 2008 for an in-depth introduction) plus specific submodels of processes that are not fully covered by the standard model. A full, detailed description of our model, following the ODD (overview, design concepts, details) protocol for describing individual-based models (Grimm et al.2006, 2010), and the implementation of the model in NetLogo (Wilensky 1999) are provided in the supplementary material.

DEB Theory

Conceptually, DEB theory is based on three elements: the rate of energy acquisition of an individual scaling with surface area while maintenance costs scales with volume; the "kappa rule" of diverting a fixed proportion, κ, of assimilated energy to maintenance and growth, with the remainder used for development and reproduction; and the inclusion of "reserve." What makes the theory look more complicated is its unique notation system, which allows the theory to be consistent in notation across applications involving properties with different dimensions, for example, energy, mass, volume, proportions of elemental matter, and more. The user manual of DEB-IBM (Martin et al. 2012) gives a straightforward introduction to the notation and conversion among the various versions and parameterizations of DEB theory. In the following, the three elements of DEB theory and the corresponding model are briefly explained.

First, DEB theory recognizes different components of the biomass of an organism: structural biomass, reserve, and a reproduction buffer in adults. Only structure requires energy for maintenance; reserve does not but is used to fuel other metabolic processes. A key assumption in the "standard" DEB model is that the rate of energy acquisition is proportional to the structural surface area of the organism, which could relate to, for example, the area of filtering appendages or gut surface. Maintenance costs are linked to body volume, which is proportional to structural biomass. These assumptions for assimilation and maintenance provide a mechanistic explanation for the widely used growth model developed by von Bertalanffy (1957).

Second, regarding reproduction, DEB theory assumes that throughout their life cycle, individuals allocate a fraction, κ, of their mobilized energy to somatic maintenance and growth and the remainder to maturation and reproduction (fig. 1). In juveniles, there is therefore a constant flux of energy to "maturation" (increasing the organism's complexity to enable reproduction), which is switched to the investment in offspring at "puberty."

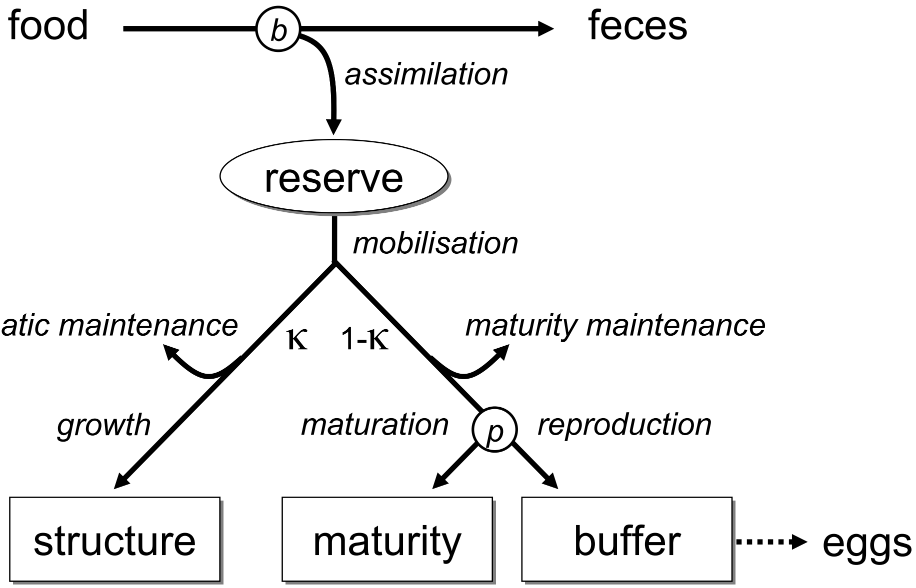

Fig. 1 Schematic diagram of the primary DEB state variables (boxes) and fluxes (italics) of the standard DEB model. The circles containing "b" and "p" denote maturity switches for birth and puberty, where feeding and allocation to reproduction begin respectively.

The kappa rule provides a novel explanation for why organisms do not deviate from von Bertalanffy growth when they begin to reproduce. There are three basic life stages: embryo (feeds on an embryonic reserve, not capable of reproduction), juvenile (feeds exogenously, not capable of reproduction), and adult (feeds exogenously, capable of reproduction). Transitions between these stages are assumed to be marked by fixed maturity thresholds.

Third, DEB theory assumes that assimilated energy first enters a reserve compartment, which serves as a buffer. The rate of energy mobilization depends only on body size and reserve density, that is, the ratio of reserve energy over structural body volume, and is calculated using a homeostasis assumption: at constant food levels, the reserve density should, after some initial equilibration, be constant over the juvenile and adult life stages. The derivation of this argument is the most challenging part of DEB theory (Kooijman 2000, p. 37). DEB theory often uses the term "scaled reserve density," *e*, which is the reserve density relative to the maximum reserve density that is obtained if individuals are fed ad lib. Because mobilization of energy depends on the reserve density and not on the instantaneous assimilation rate, it is to some extent buffered from rapid changes in food level. The capacity for buffering depends on a parameter called "energy conductance," $\dot{v}$, which determines the mobilization of the reserve. At the same feeding rate, a larger value of $\dot{v}$ will lead to lower maximum reserve density and thus less buffering capacity for changes in food availability.

The Model

In the standard DEB model, individuals are primarily characterized by four state variables: structural length, L, which determines actual size, feeding rates, and maintenance costs; scaled reserve, U_E, which serves as an intermediate storage of energy between feeding and mobilization processes; scaled maturity, U_H, a continuous state variable that regulates transitions between the three maturity stages (embryo, juvenile, adult) at fixed maturity levels; and scaled buffer U_R, which is an energy buffer of mature individuals for reproduction; this buffer energy is converted into offspring during reproductive events. Four differential equations specify how these state variables change depending on their current values and environmental conditions, such as food level and temperature. Two additional state variables are needed to characterize the aging process (app. A). We implemented a discretized version of the differential equations using the Euler method. At each time step, individuals forage, then assimilated energy first enters a reserve compartment, from which energy is mobilized to fuel all other processes (see app. A for details). Then, based on the updated DEB state variables, a set of discrete events may occur, such as reproduction or death.

General DEB theory makes no assumptions about how the reproduction buffer is converted into offspring, because too many different strategies exist. We here assumed that *Daphnia* reproduce in clutches, where energy allocated to embryos is accumulated over one molt period (assumed to have a fixed value throughout the life cycle). The embryos develop during the next molt and hatch at the end of that molting period. We augmented the standard DEB model with a submodel describing response to starvation. Within DEB theory, there are several proposed ways to include mortality via starvation (Kooijman 2010), which occurs when the energy mobilized from the reserve and allocated to the soma is not sufficient to pay somatic maintenance costs. A possible starvation submodel assumes that animals can redirect energy from the $(1 - \kappa)$ portion normally allocated to maturation (embryos and juveniles) or reproduction (adults; Kooijman 2010). Our analysis of this set of starvation submodels revealed starvation times far too short (<1 day at 20°C), and they were thus ruled out. This point was previously noted for *Daphnia pulex* (McCauley et al.1990).

We selected an alternative starvation submodel for our simulations, which assumes that when there is not enough energy to pay somatic maintenance costs, individuals can "burn" structure to pay these costs ("shrinking"). *Daphnia* can survive extended periods of starvation, where their body mass can fall to 30%–50% of their previous maximum body mass (Perrin et al. 1990; Bradley et al.1991; Cleuvers et al. 1997; Vanoverbeke 2008). We selected a mortality submodel similar to those of Vanoverbeke (2008) and Rinke and Vijverberg (2005), where death occurs when organisms' mass falls below some threshold of its previous maximum mass. We selected a critical threshold (V_{crit}) of 40% of maximum weight achieved so far, after which individuals experience a high per capita death rate of 0.35 day^{-1} (Rohrlack et al. 1999; Rinke and Vijverberg 2005).

Parameterisation

The scaled DEB model used by DEB-IBM has eight parameters, with two additional parameters needed for the aging submodel and two parameters for the feeding submodel (table 1). The processes in DEB theory are abstractions; therefore, most of the parameter values cannot be measured directly. Rather, parameters influence various fluxes, which determine observable output like body size over time, reproduction, or survival (Kooijman 2010; Nisbet et al. 2012). Thus, DEB model parameters for a species can be obtained by fitting the model to observed life-history traits over time (Lika et al. 2011). We used a data set for *Daphnia magna* comprising individual growth and reproduction data at four food levels (Sokull-Kluettgen 1998; details of parameterization given in app. B).

Simulation Experiments

Simulations were designed to mimic the experimental settings described in Preuss et al. (2009). Population dynamics were driven by "semi-batch" feeding conditions, that is, a normal portion of food was added each day Monday–Thursday to a 900-mL beaker containing a *Daphnia* population, and three times the normal food level was added on Friday. Three times a week the population was counted in three size classes. The experimental data sets consisted of two experiments conducted at a "low" food level (0.5 mg C day^{-1}), starting with either 5 neonates <24 h old (low-N) or 3 adults and 5 neonates (low-NA), and one experiment conducted at "high" food level (1.3 mg C day^{-1}) that began with 3 adults and 5 neonates (high-NA), resulting in three treatments, with 4 replicates each. For each experimental setup, we ran the model for 42 days and 100 replicates and compared the mean, maximum, and minimum of total population abundance and the abundance of three size classes to corresponding experimental observations. For details of the experimental setups in the model, see the ODD model description in appendix A.

Table 1. Parameters of the DEB model for *Daphnia magna* along with confidence intervals determined. The unit for time (t) is days, for structural length of animals (L) in mm, for the abundance of prey (#) in cells, and for length of the environment (l) in cm. A dot over a symbol indicates a rate parameter (two dots represent t-2). Curly brackets around a symbol represent the parameter is per unit surface area (see Martin et al. 2012 for the full explanation of notation).

Symbol	Description	Dimension	Value	95% confidence interval
κ	Fraction of mobilized energy to soma	-	0.678	0.657-0.700
κ_R	Fraction of reproduction energy fixed in eggs	-	0.95	Fixed value
$\dot{k}_m$	Somatic maintenance rate coefficient	t^{-1}	0.3314	0.327 - 0.336
$\dot{k}_j$	Maturity maintenance rate coefficient	t^{-1}	0.1921	0.150-0.236
U_H^b	Scaled maturity at birth	tL^2	0.1108	0.0989 - 0.123
U_H^p	Scaled maturity at puberty	tL^2	2.555	2.36 - 2.844
$\dot{v}$	Energy conductance	Lt^{-1}	18.1	17.89 - 18.3
g	Energy investment ratio	-	10	Fixed value
Ageing parameters				
$\ddot{h}_a$	Weibull ageing acceleration	t^{-2}	3.04E-6	1.70E-6 - 4.60E-6
s_G	Gompertz stress coefficient	-	.019	0.00911-0.0273
Prey dynamics parameters				
$\{\dot{J}_{XAm}\}$	Surface-area-specific max ingestion rate	$\#L^{-2}t^{-1}$	3.80E+05	3.7E+5 - 4.0E+5
K	Half-saturation coefficient	$\#l^{-3}$	1585	1571 - 1600
Daphnia specific parameter values				
Molt-time	Time between reproductive events	t	2.8	-
V_{crit}	Proportion of structural mass below which *Daphnia* experience starvation mortality	-	0.4	-
M	Reserve dependent mortality coefficient	t^{-1}	Varied	-

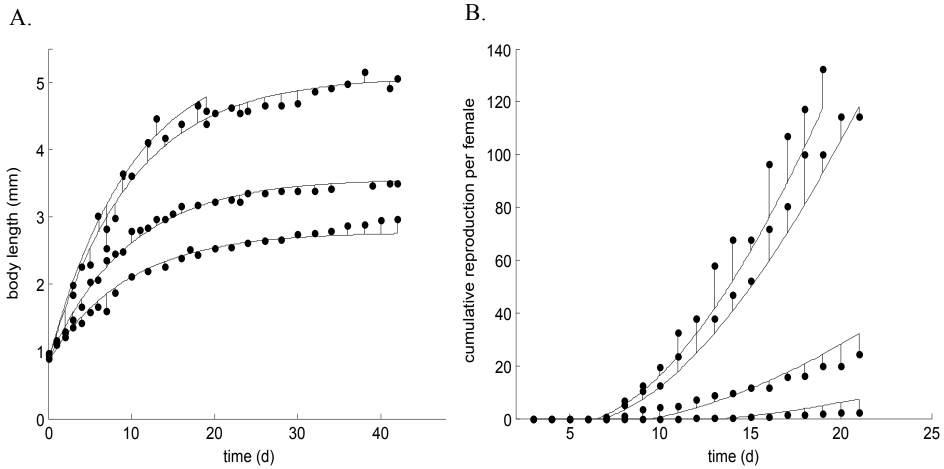

Fig. 2 Data for growth (A) and reproduction (B) at four food levels (100000, 25000, 5000, and 1000 cells/ml) and the DEB model fit. The experiment was conducted in a flow-through system in 500 ml ADAM medium at a flow-through rate of 360 ml h^{-1}.

Stochasticity enters the simulations in three ways. First, all mortality either due to aging or starvation is probabilistic. Second, individuals vary in parameter values. We followed the method used in Kooijman et al. (1989), where individuals have a log-normally distributed scatter multiplier that affects the maximum surface area specific assimilation rate. This parameter is scaled out of the model, but the two maturity threshold parameters, U_H^b and U_H^p (where superscripts b and p denote birth and puberty); the maximum surface-area-specific ingestion rate, $\{\dot{J}_{XAM}\}$; the half-saturation coefficient, *K*; and the compound parameter, *g*, which is the cost of synthesizing one unit of structure over the product of κ and the maximum reserve density, are all affected by the scatter multiplier (Kooijman 1989; Martin et al. 2012; and ODD of this article). Finally, we assume the amount of food added each day varies due to experimental error, with a standard deviation equal to 10% of the desired food concentration.

Results

Individual-Level Parameterization

Parameterization revealed that the parameters g and $\dot{v}$ (table 1) could not be specified individually (app. B; fig. 2). Further analysis revealed that these

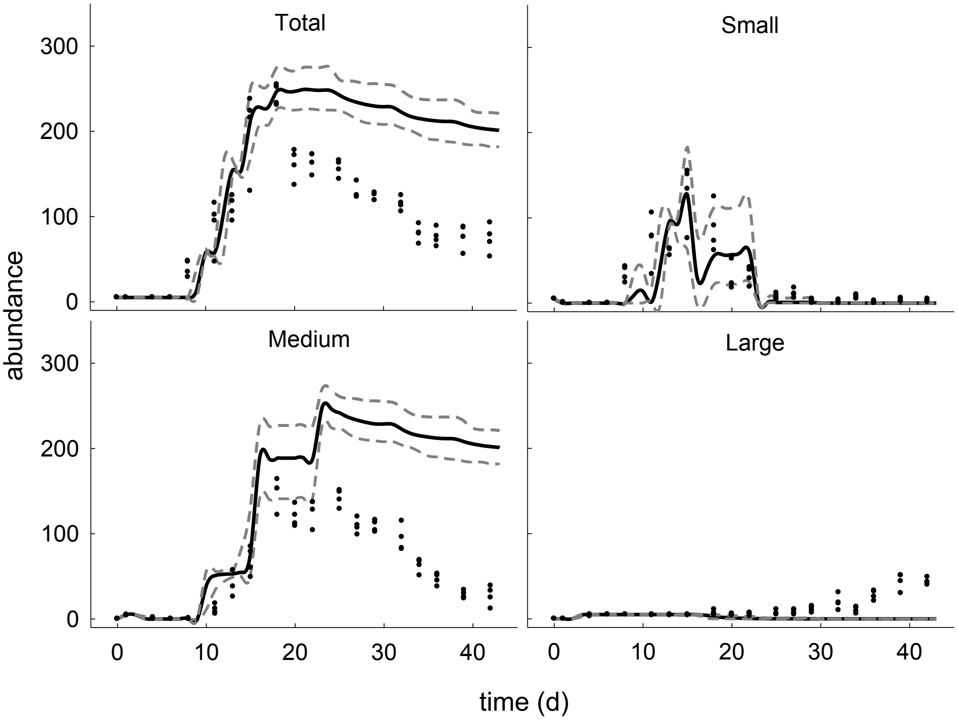

Fig. 3 Comparison of data and DEB-IBM predictions at the population level for the lowN experiment. Experiments were initiated with 5 neonates in a 900ml beaker, and 0.5mgC was added per day. Simulations with DEB-IBM replicated the experimental conditions. Figures show the mean (think black line) and max and min (dashed grey lines) of 50 simulations. Simulations for the lowNA and highNA experiments are shown in figure S1.

parameters positively covaried and their ratio was well determined. This indicates that, at least for *Daphnia* in the given settings, one of these parameters is redundant. An increase in $\dot{v}$ and g together indicates an increasing rate of reserve mobilization and simultaneously a decrease in the size of the reserve. As both parameters increase toward infinity, one ultimately ends up with a “reserveless” DEB model.

To determine the population-level effect of using different values for parameters linked to the reserve dynamics, we ran simulations using parameter sets where the value of g was fixed at incrementally higher values and all other parameter values were estimated (app. B). We found that using fixed values

Table 2. R^2 values for the default DEB-IBM and various adapted models the before (Growth Phase), after (Decline phase) the population peak, and the entire data set for total abundance, and each of the 3 size classes, over 42 day population experiments at 3 experimental setting. Additionally the negative log-likelihood ($-\ell$) is given for the Standard DEB model and the three modified mortality submodels.

	R^2			$-\ell$
	Growth Phase	Decline Phase	Total	Total
Standard DEB model	0.878	-0.2013	0.318	199643
Food-dependent mortality sub-models				
Neutral (all)	0.920	0.873	0.903	28249
Negative (juveniles only)	0.921	0.897	0.916	24358
Positive (adults only)	0.910	0.342	0.618	111757

of *g* within the likely range (10 to infinity) had negligible influence on population level output. Therefore, the results from our analysis would be independent of the value chosen for *g*, and we used the parameter set with *g* fixed at 10 for all further simulations. Using the resulting parameter set, the DEB model explained most of the variation in growth (R^2 = 0.986) and reproduction (R^2 = 0.967; fig. 2).

Population-Level Results for the "Standard" DEB-IBM Daphnia Model

The model closely matched observations during the initial population growth phase, capturing population growth rate, size distribution, and peak population density for all experimental settings (fig. 3 for the low-N setting; low-NA and high-NA shown in fig. S1). However, after the initial population peak, model predictions and data diverged. This mismatch was not resolved by changing the model parameters within their confidence intervals. We quantified the overall fit by dividing each time series into two periods, the population growth phase and the population decline phase. All predictions after the population peak in the simulations were grouped into the decline phase and all before into the growth phase. We then compared overall agreement of the predictions and observations of total density and the three size classes for each of the two periods, for all experimental setups (fig. 4). As a way of comparing goodness of fit, we report "prediction" R^2 values for each period (growth and decline phases), as well as for the data set as a whole (see app. B). Our analysis revealed a much poorer fit between model predictions and observations during the decline phase (table 2).

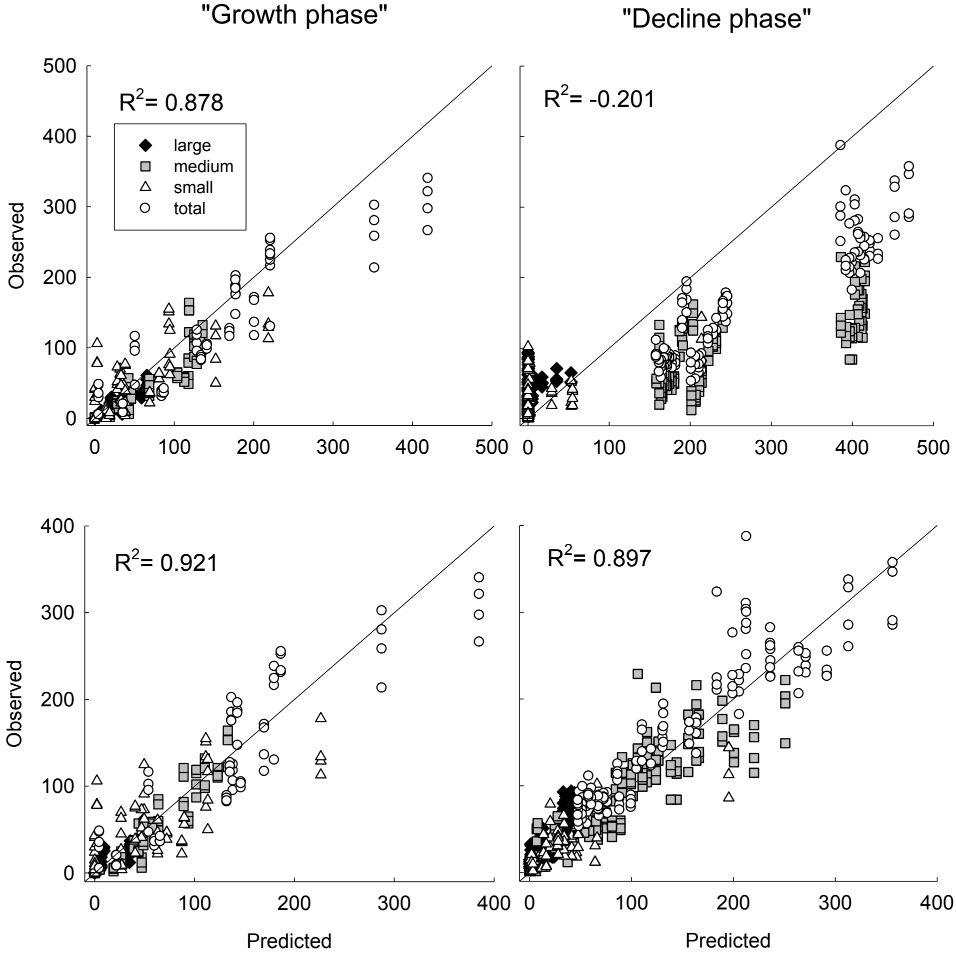

Fig. 4 Observed vs. predicted values for all three population experiments for total abundance (open circles), and three size classes: large (black diamonds), juveniles (grey squares), and neonates (open triangles) for the standard model (a) and the adapted model (NegSS) with the additional juvenile food-dependent mortality submodel (b). The data are divided into two panels, for data before the population peak (Growth Phase), and after (Decline Phase).

Alternative Models of Starvation and Recovery

We implemented an additional starvation submodel (*Daphnia* still have a high probability of dying if they fall below a critical proportion of their previous mass), where mortality was inversely linked to reserve density, *e*, which is a time-weighted average of feeding history (app. A):

$$\Pr(mortality)d^{-1} = M(1-e)$$

where M is the reserve-dependent mortality coefficient. To check whether starvation was size selective in the experimental systems, we compared three versions of this new submodel by applying it only to juveniles (negative size selection [NegSS]), only to adults (positive size selection [PosSS]), or to all *Daphnia* (neutral size selection [NeutSS]).

Because we also wanted some indication of how well the starvation models, once parameterized, were able to capture the dynamics of population in other experimental settings, we restricted our parameterisation data set to one of the population experiments (low-N). We then compared the goodness of fit of the three starvation submodels and to the complete data set (all three population experiment setups; see app. B for details).

Furthermore, standard DEB theory assumes that a *Daphnia* that has shrunk to, for example, 50% of its previous maximum mass behaves physiologically the same as a *Daphnia* with the same state that has not shrunk. This is, however, in disagreement with experimental observations at the individual level, as *Daphnia* recover mass much faster than expected following the standard DEB equations (Perrin et al. 1990; Bradley et al. 1991). One possible explanation is that although *Daphnia* shrink, they maintain their ability to ingest and assimilate energy according to their previous maximum size. This may be due to the fact that *Daphnia* do not shrink in physical length, as they live within a rigid carapace, and thus their feeding appendages keep their previous size even as the mass of the individual shrinks. This can be modelled in DEB by using the maximum achieved value of length in the assimilation formula. By using this modified recovery model, we found (data not shown) a large improvement in predictions for the timing of individual-level recovery compared to data and predictions from Perrin et al. (1990). Although both models underpredict time to recovery compared to the data, the “fast” recovery model predicts a time to recover (4 days) much closer to the data (between 1 and 3 days) than the “default” recovery (7 days).

Population-Level Results for the Modified DEB-IBM Model

Parameterization of the three starvation submodels on the low-N data set resulted in values of 0.085, 0.39, and 0.090 day^{-1} for M, the mortality constant for the NeutSS, PosSS, and NegSS submodels, respectively. The NeutSS ($R^2 = 0.938$) and NegSS ($R^2 = 0.929$) submodels led to substantially better fits on the parameterization data set (low-N) than the PosSS. On the complete data set (all three population experiments), all three modified starvation submodels better

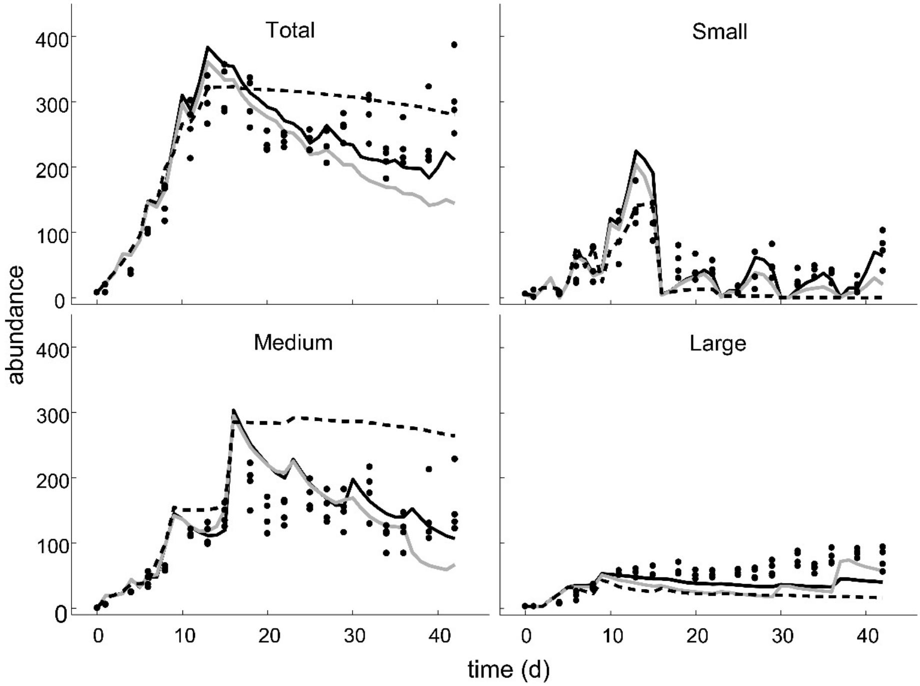

Fig. 5 Comparison of the performance of three starvation submodels with data from the highNA experiment. In each of the three models, a 1 parameter food-dependent mortality submodel, was applied, but models differed in that it was either applied only to juveniles (black solid), only adults (black dashed), or all *Daphnia* (grey solid). Simulations for the lowN and lowNA experiments are shown in figure S2.

matched the data relative to the standard model, and most of this improvement in model fit relates to increased predictive power during the decline phase (table 2). While the NeuSS and NegSS models fit the parameterization data set nearly equally well (fig. S2), the NegSS model provided the best fit to the complete data set (table 2). This was driven by a better agreement of model and data for the independent data sets, specifically for the high-NA experiment (fig. 5).

The results of the starvation recovery submodel showed an improved fit over the standard recovery model (fig. 6; fig. S3). This result is mainly due to the lack of production of offspring for the standard dynamics compared to the revised model and experimental observations. This lack of production of new offspring then ultimately leads to almost no *Daphnia* in the intermediate size class and results in a population dominated by large *Daphnia*.

Discussion

Having a generic model relating population dynamics to the size, maturity, energy reserves, and current food intake of its constituent organisms would raise individual-based ecology (IBE) to a completely new level. IBE would be then based on firm and increasingly tested theory (Grimm and Railsback 2005). Species would still be expected to show different physiological and behavioral strategies, but with IBMs based on DEB theory or any other kind of generic theory, we would have a much better idea of where and when to use standard approaches and where to look for more specific submodels.

Did our attempt to predict population dynamics from what individuals do indicate that DEB theory is such a generic theory for IBE? The answer is both yes and no. On the one hand, the standard DEB model without ad hoc modifications accurately predicted the population growth rate and peak density of laboratory *Daphnia* populations in different conditions from a model parameterized at the individual level. Our study provides at least one point of evidence suggesting that the DEB model with little modification may be used for many applied purposes requiring an understanding of how population growth rate varies as a function of the environment. For example, in ecotoxicology, population growth rate often is proposed as a composite indicator of toxicity of chemicals, which simultaneously takes into consideration reductions in growth, reproduction, and survival (Forbes and Calow2002). DEB theory can easily be used to link individual performance under toxicant stress to effects on the population growth rate (see Jager and Klok 2010), and thus this work further supports its use.

On the other hand, the unmodified model did not accurately capture the dynamics after the population peak, where there was little food per *Daphnia*. In contrast to the model predictions, the experimental observations showed a sharp decline in *Daphnia* density. This decrease in density also decreased competition for food, allowing those *Daphnia* that survived to consume more and thus grow at faster rates. For this reason, we saw a discrepancy not only in the population density between model predictions and observations but also in the size distribution.

The discrepancy between model predictions and observations for declining populations turned out to be highly informative. It was our hope that cross-level testing DEB would lead us to identify potential limitations of standard DEB theory and possibly find ways to overcome these limitations. Due to the lack of data on starvation, we had to do this inversely, that is, infer from population-level patterns to the individual-level process of starvation. We contrasted three phenomenological starvation models, which differed in their size selectivity. We found that if we assumed negative size selection, that is, starvation of smaller

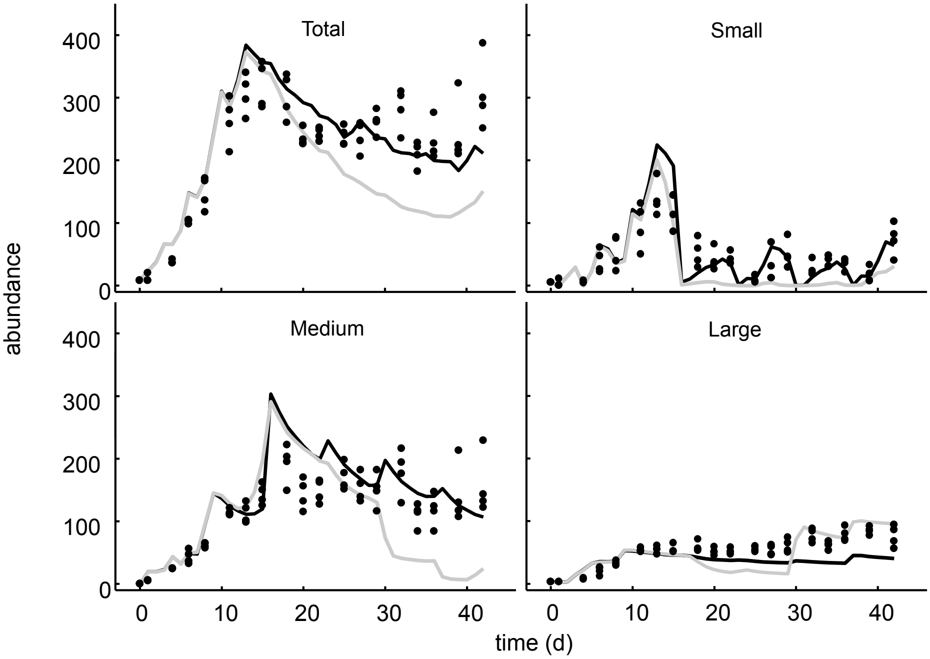

Fig. 6 Comparison of alternate starvation-recovery assumptions against the highNA data set. The grey line show the scenario where individuals feed at a rate proportional to their current length, while the black line shows the average of 100 model simulations when individuals feed at a rate proportional to their maximum length attained. Simulations for the lowN and lowNA experiments are shown in figure S3.

individuals, agreement between predicted and observed population dynamics and structure was improved. One notable contradiction between predictions and observations for the PosSS model was a lack of neonate production after the initial population growth phase. This trend is best observed in the high-food-level experiment (fig. 5). The NeutSS model captured the dynamics and size structure of the population in that it predicted bursts of neonate production; however, compared to the NegSS model, these bursts were too small as there were fewer adults due to the non-size-selective mortality. Consequently, prediction of neonate production in the NegSS model was most appropriate, also leading the more accurate predictions of the total population abundance (table 1; fig. 4*B*).

The outcome of our analysis is supported by the previous work on the same population data set using an empirical individual-based population model (Preuss et al. 2009), in which the decline of the population density after the peak was explained as a mixture of starvation and crowding. Crowding causes negative interference (Goser and Ratte 1994) among daphnids, leading to life-strategy shifts and reduced feeding even at the same level of food (Goser and Ratte 1994; Cleuvers et al. 1997). Within this model a crowding submodel was used, calibrated on individual-level data. One of the main factors in this crowding submodel was the increased mortality of juveniles (Preuss et al. 2009), as was also found in this analysis and attributed to starvation.

Increased juvenile food-dependent mortality also was proposed in a different model and experimental system for capturing another aspect of *Daphnia* populations (McCauley et al. 2008). It has been found in experimental systems (McCauley et al. 1999, 2008) that when *Daphnia* feed on a dynamic prey source, the *Daphnia* population and its algal resource may exhibit either small-amplitude (SA) cycles or large-amplitude (LA) cycles. Replicate populations may exhibit either dynamic pattern and on occasion may alternate between these two multiple attractors. When cycles are observed in the field, the predominant pattern is SA cycles (Murdoch et al. 1998). Besides the magnitude of the fluctuations, the key diagnostic feature of the two cycle types is that in SA cycles, the juvenile development time (time from birth to reproducing adult) is longer than the period of the population cycles, while in the LA cycles, the juvenile development time is shorter then the cycle period (McCauley et al. 2008).

To explore the origin of these dynamics, McCauley et al. (2008) developed a deterministic, two-stage-structured (juveniles and adults) bioenergetic model that includes food-dependent mortality rates estimated separately for adults and juveniles. Their parameterization generated higher food-dependent mortality coefficients for the juvenile stage class than the adults; however, it was not identified as the driver of the bistability. More recently, Ananthasubramaniam et al. (2011) attributed the stabilizing mechanism responsible for generating the small-amplitude cycles to the presence of adults that survived through the population decline phase and were able to reproduce shortly after the algae population began to recover. This is remarkably similar to the pattern we see in the high-food experiment where the bursts of neonate production observed during the decline phase and the subsequent leveling off of the population decline were predicted only by the NegSS model.

To test whether our model captures, without any further calibration or modification, the SA/LA cycle patterns explored by McCauley et al. (2008), we used the NegSS model, but instead of simulating the populations in batch-fed environments, we let them feed on a prey following logistic growth. In agreement with previous models, the populations exhibit exclusively SA cycles when the carrying capacity of prey is low and LA cycles when the carrying capacity of the

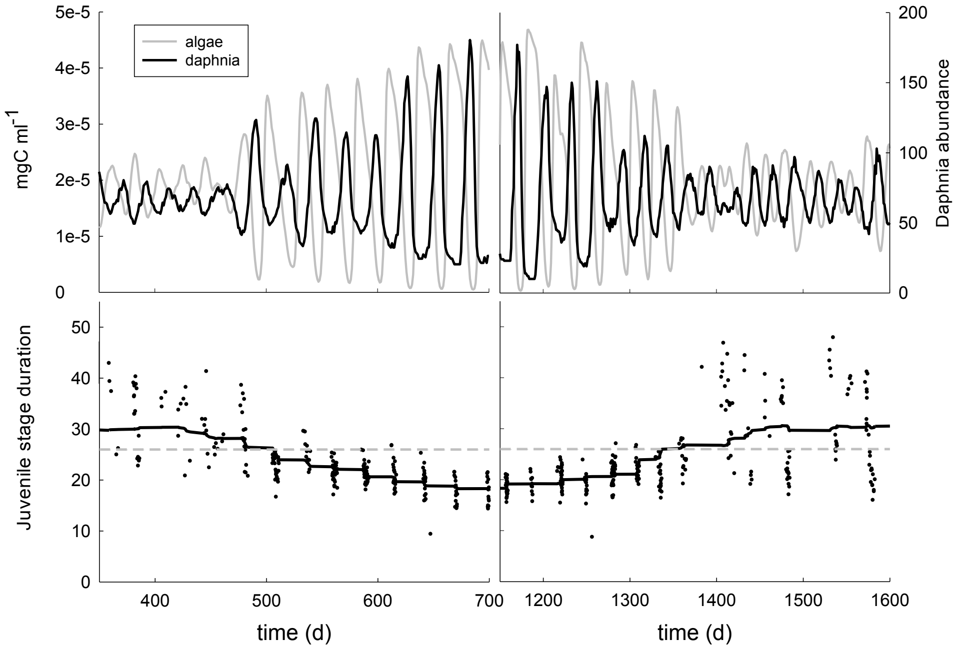

Fig. 7 Two characteristic simulations, showing the switches between multiple attractors of LA and SA cycles. Simulations were run using the NegSS model where the *Daphnia* feed on a prey source following logistic growth (r = 1.5, K = 5e-5 mgC ml^{-1}) in a 30 liter system. Simulations were initiated with 5 neonate *Daphnia*.

prey is high. Most interestingly, the model also captures the dynamic at intermediate prey carrying capacities where the population exhibits the multiple attractors (LA and SA cycles) proposed for previous models and observed in the lab populations. Particularly convincing is that, as in experimental observations, the model also captures the key diagnostic feature, that under SA cycles the mean juvenile development time was longer than the cycle period, while the opposite was found for LA cycles (fig. 7). We take this finding as strong evidence that our modified DEB model is a realistic and comprehensive representation of laboratory *Daphnia* populations and is able to reproduce population-level patterns for a wide range of environmental settings.

Our results highlight the importance of understanding resource-dependent mortality for making accurate cross-level predictions. Surprisingly however, this remains a poorly developed area of research. From our analysis of size-dependent mortality submodels, it is clear that not only the overall starvation tolerance of a species is important but that relative tolerance of small and large individuals in a population greatly influences the dynamics (see also de Roos and Persson 2013).

Our initial assumption was that mortality is triggered when mass falls below some threshold of the previous maximum mass, so the size dependence of resource-dependent mortality is determined largely by how two fluxes, assimilation and maintenance, scale with body mass. The two most popular theories for individual growth, DEB and OGM, always infer either neutral starvation tolerance or a greater starvation tolerance in juveniles depending on the food conditions. In the case of absolute starvation (going from high food to no food immediately), both theories predict that time to starvation will be independent of body size. In partial starvation, when there is some food level available but where the assimilation flux is less than the energy needed to satisfy the maintenance flux, smaller individuals have an advantage over larger ones because both theories assume decreasing mass-specific assimilation rate with size. Thus, both theories contradict our findings.

While there is relatively little information on the ontogeny of starvation tolerance, the few data that do exist support the indirect conclusions, made from population-level analyses, that starvation tolerance increases with size intraspecifically (McCauley et al.2008; this study). For two species of *Daphnia*, adults survived longer without food than neonates (Tessier et al. 1983). Additionally, two separate studies on copepods found a clear monotonic pattern of increasing starvation tolerance with size/development for *Calanoides carinatus* (Borchers and Hutchings 1986) and *Pseudocalanus newmani* (Tsuda 1994). If these observed trends turn out to be general, it would suggest both formulations (DEB and OGM) of individual resource dynamics need revisiting. Several hypotheses could explain increasing starvation tolerance with increasing size within a species: (1) V_{crit} could decrease as a function of size; larger individuals can shrink to a lower proportion of their previous maximum mass before they starve. (2) Specific energy storage may increase with size. (3) Mass-specific maintenance costs may decrease with size. (4) Energy utilization to development may be partially inflexible (smaller individuals continue to catabolize energy stores to continue development for some time after food levels decrease). There are not enough data available to test which if any of these mechanisms may be a valid explanation of the observed trends. What is clear is that due to the importance of the mechanism in determining the types of population dynamics that emerge, no generic theory will be able to capture dynamics at the population level from a generic individual model without accurately capturing the dynamics of how resource-dependent mortality scales with size.

In addition to the size-selective nature of food-dependent starvation risk we also investigated the consequence of assumptions of recovery after a long period of starvation. The standard DEB model does not distinguish between “novel” somatic growth and recovery somatic growth. We tested this assumption against individual-level data (Perrin et al. 1990) and revealed that this assumption grossly underestimated recovery of somatic mass. We thus used an alternate assumption where recovering individuals retain the performance abilities of their previous maximum size. This modified model performed much better at both levels of biological organization tested, although recovery of somatic growth was still underestimated at the individual level. With the new assumption, adult *Daphnia* were able to assimilate food more quickly when food levels began to recover, resulting in neonate production in agreement with observations from the low-NA and, to a greater extent, high-NA experiments. The poor performance of the default recovery submodel highlights the fact that "novel" and "recovery" somatic growth cannot be treated as equivalent. As most animals can survive periods of starvation by burning existing biomass, this conclusion may not be unique to *Daphnia*.

Our results also bring into question the need to include the state variable "reserve" for the purpose of predicting population dynamics from the characteristics of individuals. We found that the parameters associated with the speed of reserve mobilization and hence the size of the reserve are not easily specified using growth and reproduction data at multiple food levels. Thus, parameterizing the reserve accurately would require some additional data or strong assumptions, for example, relating to the duration of the embryonic period. From our analysis for *Daphnia*, it appears allowing individuals to burn structural body mass to pay maintenance costs is an adequate substitute for reserve to capture how fluctuating food levels affect growth and reproduction output at the individual and population level. However, if reserve is not included, our results suggest mortality should be linked to energy assimilation rather than death occurring only when animals fall below some proportion of their previous mass, as was assumed by McCauley et al. (2008).

In the population experiments, variation in food levels during the day were quite extreme, transitioning from ad lib. feeding conditions during the first few hours after food was added to no food. Yet the reserveless model performed nearly identically to the model with reserve without the resource-dependent mortality submodel at all experimental conditions tested (fig. B2), a finding consistent with previous work using biomass-based models (reviewed by Nisbet et al. 2010). Including the resource-dependent mortality term with the parameters derived when reserve dynamics were fixed to be very fast (g fixed to 100) results in negligible deviations in the population dynamics from those resulting from the parameter set used in this study (g fixed to 10; data not shown). This may be because the "true" maximum reserve density for *Daphnia* is small enough that the time lag between changing food levels and changing mobilization is small. There is some limited evidence of this relating to energy allocated to reproduction; see Tessier et al. (1983) and related discussion by McCauley et al. (1990). The interspecific scaling laws of DEB predict that maximum reserve density will increase with the maximum size of the species, and thus, for larger species the inclusion of reserves may be important.

Whether or not a reserveless model is still actually a DEB model is a matter of semantics. Our concern lies more with identifying the most useful general models as a basis for IBE. One may question, without the reserve state variable, how the theory differs from other generic models of individual metabolism such as the OGM. Here the biggest advantage of using DEB as opposed to the OGM is not the inclusion of reserve but other distinctive aspects of DEB. For example, OGM does not consider how or from where energy is allocated for reproduction or what mediates life-stage transitions; clearly these are required for capturing population dynamics. With additional assumptions, the OGM might perform similarly to DEB—but this would mean the two descriptions were themselves converging.

How far we can go with generic theory in an IBM context? It may be that the deviations between model predictions and data at the population level are due to species-specific deviations from the DEB model. If species-specific submodels are unavoidable, having a generic model at least reduces the number of structural differences among models of different species and thus increases their comparability. However, it is also possible that generic theory may be able to account for starvation and recovery, but this theory has not been developed. It seems most likely that the answer is some combination of both; there may always be some situations where species-specific models are needed when highly accurate predictions are required; however, it is also likely that with further testing and development we can vastly improve the predictive capabilities of our generic models. What is promising is that the processes that required modification in our study are not species specific; starvation and recovery from starvation are ubiquitous in natural populations. Further experiments at the individual level to guide theory development, especially relating to starvation and recovery, and cross-level experiments to tests theory at the population level are needed. Until these theories are developed, DEB-IBM still serves as a useful starting point that handles the majority of other relevant aspects of individual life history (growth, development, and reproduction).

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Chapter 3 (Appendix A): DEB-IBM Model Description (ODD)

The model description follows the ODD protocol for describing individual-based models (Grimm et al. 2006, 2010) and is adapted from Martin et al. (2012).

Purpose

The purpose of this model is to perform a cross-level test of DEB theory by parameterizing a DEB model adapted for *Daphnia* at the individual level and comparing the emergent population dynamics to independent experimental data.

Entities, State Variables, and Scales

The model includes two types of entities, *Daphnia* and the environment. Each *Daphnia* is characterized by four primary state variables, henceforth referred to as DEB state variables: structure (L, unit: mm), which determines actual size, feeding rates, and maintenance costs; scaled reserves (U_E, unit: days mm^2), which serve as an intermediate storage of energy between feeding and mobilization processes; scaled maturity (U_H unit: days mm^2), a continuous state variable that regulates transitions between the three development stages (embryo, juvenile, adult) at fixed maturity levels; and finally, a scaled reproduction buffer (U_R, unit: days mm^2) that is converted into eggs during reproductive events. The term "scaled" in reserves, maturity, and buffer refers to the fact that in this "scaled" version of the model the dimension of energy or mass (either as joules or moles of reserve) are scaled out (see Kooijman et al. 2008 and sec. 2 of the DEB-IBM user manual from Martin et al. 2012).

In addition to these DEB state variables, intrinsic variation among individuals is created by including a random component in some of the individuals' eight "DEB-IBM parameters." Each individual has a state variable we refer to as a "scatter multiplier" which is a lognormally distributed number, by which four of the standard DEB parameters are multiplied to get the individual-specific set of DEB parameters (see "Stochasticity").

Additionally, the model includes an aging submodel based on DEB theory that includes two state variables, damage-inducing compounds ($\ddot{q}$) and damage ($\dot{h}$). The aging process is tightly linked to energetics in that the production of damage-inducing compounds is proportional to mobilization (energy utilization). Damage-inducing compounds produce damage and thereby affect survival probability. In addition to directly producing damage, damage-inducing compounds also can proliferate by inducing their own production (see "Aging Submodel").

The second entity in the model is the environment, which is defined by the state variables food density and temperature. The simulations are designed to replicate the “batch-fed” experiments conducted by Preuss (2009), where a specific amount of food (algal cells) is added on fixed days. Food is depleted from the environment via feeding by the *Daphnia*.

All simulations represent dynamics in a 90-mL vessel, and the model is nonspatial, as we assume food and *Daphnia* are well mixed within the container.

Process Overview and Scheduling

Individuals update their DEB state variables based on a discretized form of the differential equations. At each time step, a set of discrete events may occur. If an organism can no longer pay all maintenance costs (the growth equation becomes negative), individuals cover maintenance costs by burning structure (shrink). If individuals shrink below a specific proportion of their previous maximum body size (crit-mass) they have a high probability of dying (0.35 per day). The second source of mortality is death via aging. At each time step, individuals have a probability of dying that is proportional to their damage state variable, $\dot{h}$. Finally, mature individuals reproduce at fixed intervals equivalent to the length of a typical molt period for a *Daphnia* (2.8 days). At the reproduction time step, mature *Daphnia* convert all energy accumulated during the previous molt period to embryos; the number of embryos produced is equal to energy accumulated in the reproduction buffer divided by the cost of producing an embryo (see “Reproduction Submodel” for details).

The following pseudo-code describes the scheduling of events within one time step of the numerical solution of the model equations (see “go” procedure in NetLogo implementation):

```
For each individual
 [
  Calculate change in reserves
  Calculate change in length
  If mature
   [
    Calculate change in reproduction buffer
   [
  Else
   [
    Calculate change in maturity
   [
  Calculate change in ageing acceleration
  Calculate change in hazard
 [
For the environment
 [
  Calculate food depletion
 [
For mature individuals
 [
  Update molt-time
  if molt-time >= time-between-molts
   [
    Release offspring created at last molt
    Create embryos from reproduction buffer that will hatch
    the next brood
    Set molt-time 0
    Set reproduction buffer back to 0
   ]
 ]
Update individual state variables
Update environmental state variables
```

Design Concepts

Basic Principles

The model is based on the dynamic energy budget theory (Kooijman 1993, 2000, 2010). An overview of the concepts can be found in Kooijman (2001) or Nisbet et al. (2000). The theory is based on the general principle that the rates of fundamental metabolic processes are proportional to surface area or body volume and a full balance for mass and energy.

Emergence

Traits of the individual and structure and dynamics of the population emerge from the properties of metabolic organization and indirect interactions of individuals via competition for food.

Adaptation

The framework does not include adaptive behaviour; in particular, DEB parameters vary among individuals but remain constant over an individual's life span. Consequently, the design concepts "objectives," "learning," "prediction," and "sensing" do not apply to this framework.

Interaction

Individuals interact indirectly via competition for food.

Stochasticity

There are three sources of stochasticity in the model. The first source is intraspecific differences in parameter values. We followed the method outlined in Kooijman (1989) where the surface-area-specific maximum assimilation rate of an individual (referred via index *i*) is given by multiplying the corresponding species-specific rate $\{\dot{J}_{EAm}\}$ with the individual-specific "scatter multiplier" SM_i. The scatter multiplier is a lognormally distributed random number with a standard deviation that is user defined. However, since DEB-IBM is based on the scaled and not the standard DEB model where $\{\dot{J}_{EAm}\}$ is scaled out of the model, $\{\dot{J}_{EAm}\}$ is a "hidden" parameter affecting four other scaled and compound parameters. These interrelationships are described in detail in section 2 of the DEB-IBM user manual of Martin et al. (2012). For our simulations, we used a value of 0.05 for the standard deviation for the scatter multiplier. The second source of stochasticity is that all mortality processes are probabilistic. Finally, the last source of stochasticity is in the submodel representing food input. Although in the experiments a fixed amount of cells is added each day, we assume some variation in the actual amount of food added to the experimental vessel by assuming a standard deviation of 10% of the daily food input.

Observation

Over the course of the 42 days of simulation we kept track of both the total *Daphnia* abundance and the abundance of three size classes of *Daphnia*. In the experiments, size classes were grouped by filtering the *Daphnia* through various-sized mesh filters. Size classes were calculated based on the diameter of the mesh size multiplied by a factor of 1.25. Previously it has been assumed *Daphnia* pass through the mesh with their smallest side, so we used value 1.6, which corresponds to the length-to-width ratio of the clone of *Daphnia* used in the study. We calculated the value 1.25 by comparing the number of *Daphnia* in each size class to a replicate experiment where each *Daphnia* was measured (Agatz et al. 2012). Using a conversion factor of 1.25 provided the greatest agreement between the individually measured data (Agatz et al. 2012) set and the grouped-by-mesh-size-class data set (Preuss2009). This corresponds to size classes of small (<1.1 mm), medium (1.1–2.0 mm), and large (>2.0 mm).

Initialization

Simulations are initialized with conditions corresponding to the experimental conditions they are supposed to represent. Our simulation model experiments with two different initial conditions. The first type starts with 5 newborn *Daphnia* (neonates) less than 24 h old. The second starts with 3 adults, in addition to 5 neonates. We mirror these initial conditions for neonates by starting with newly hatched *Daphnia* and simulating a random amount of development time between 0 and 24 h, selected from a uniform distribution. For adults we simulated growth at ad lib. conditions until each was 4 mm in length, as were those used in the experiments. Moreover, as in the experimental setup, each individual was bearing eggs at different levels of development, 1 nearly complete (0.1 days from hatching), 1 with eggs midway through development (1.55 days from hatching), and 1 with eggs just beginning development (2.65 days from hatching). When food level was given as carbon content, we recalculated in cell mL^{-1}, assuming that *Desmodesmus subspicatus* has an average carbon content of 1.95×10^{-8} mg C $cell^{-1}$ (Sokull-Kluettgen 1998; Preuss et al. 2009).

Input Data

The framework does not include input data representing external driving processes.

Submodels

Calculate Change in Reserve

The change in energy reserves U_E of an individual in a time step is determined by the difference in scaled assimilation S_A and mobilization S_C fluxes:

$$\frac{d}{dt}U_E = \left(S_A - S_C\right),$$

The assimilation flux is given by

$$S_A = fL^2,$$

where *f*, the scaled functional response, is assumed to follow a Holling type II functional response for individuals that have surpassed the maturity threshold for birth, U_H^b:

$$f = \frac{X}{K+X} \text{ for } U_H > U_H^b,$$

where *X* is prey density and *K* the half-saturation coefficient. The mobilization flux is given by

$$S_C = L^2 \frac{ge}{g+e}\left(1 + \frac{L\dot{k}_M}{\dot{v}}\right), \text{ where } e = \dot{v}\frac{U_E}{L^3},$$

where *e* is the scaled reserve density (falls between 0 and 1, with 1 representing maximum reserve density), *g* is the energy investment ratio (a compound parameter which is a ratio of the costs to synthesize a unit of structural biomass and the product of the maximum reserve density and the proportion of mobilized energy allocated to the soma, κ), $\dot{k}_m$ is the somatic maintenance rate coefficient, and $\dot{v}$ is energy conductance (see Martin et al. 2012 for detailed discussion of DEB parameters).

Because embryos do not feed exogenously, when

$$U_H < U_H^b \quad f = 0$$

the assimilation flux will be zero and the change in reserves is reduced to:

$$\frac{d}{dt}U_E = -S_C$$

Rationale. DEB theory includes a state variable "reserve" that acts as an intermediate between the feeding and mobilization process. Reserves allow for metabolic memory, that is, the metabolic behavior of individuals is not solely dependent on the current food availability but rather the "recent" feeding history of an individual. For example, animals can continue to grow for a short period of time when food has been removed from their environment.

Calculate Change in Maturity

Individuals begin with a maturity level U_H of 0, which increases each time step according to the differential equation

$$\frac{d}{dt}U_H = (1-\kappa)S_C - \dot{k}_j U_H \text{ when } U_H < U_H^p$$

else

$$\frac{d}{dt}U_H = 0$$

Transitions between development stages occur at set values of maturity. An embryo that feeds exclusively on reserves becomes an exogenously feeding juvenile when $U_H = U_H^b$ and a reproducing adult when $U_H = U_H^p$. Once puberty is reached, maturity is fixed and energy previously directed toward maturity is now allocated to the reproduction buffer. Before *Daphnia* reach puberty, if mobilized energy is not enough to pay maturity maintenance costs, the maturity flux can become negative, and animals decrease in maturity.

Rationale. Immature individuals divert mobilized energy from reserves between competing functions of growth and development, with the proportion $1-\kappa$ of mobilized reserves allocated to development. Individuals first pay maintenance costs associated with maintaining their current level of maturity (the maturity maintenance rate coefficient, $\dot{k}_j$, multiplied by the current level of maturity, U_H) from the fraction of mobilized reserves directed toward development $(1-\kappa)S_C$. The remainder represents the increase in development during a time step.

Calculate Change in Reproduction Buffer

When an individual has reached puberty, energy from the maturity flux is diverted into a reproduction buffer, U_R:

$$\frac{d}{dt}U_R = (1-\kappa)S_C - \dot{k}_J U_H^p \text{ for } U_H > U_H^p$$

else

$$\frac{d}{dt}U_R = 0$$

If mobilized energy is not enough to pay maturity maintenance costs, the reproduction buffer flux becomes negative to pay maturity maintenance costs. If the reproduction buffer flux is negative but there is no energy remaining in the reproduction buffer, maturity maintenance is not paid (U_R cannot be <0).

Rationale. This submodel is basically the same as for the delta maturity calculation but is calculated only for mature individuals whose maturity does not increase. The energy that accumulates in the reproduction buffer in a given time step is the difference between mobilized energy allocated toward reproduction and the fixed maturity maintenance costs.

Calculate Change in Length

During a time step, energy needed for somatic maintenance costs are paid from mobilized energy allocated for soma. The remainder is converted from reserve to structural length. Under non-starvation conditions,

$$\frac{d}{dt}L = \frac{1}{3}\left(\frac{\dot{v}}{gL^2}S_C - \dot{k}_M L\right)$$

The parameter κ, which determines the fraction of mobilized energy directed to the soma, is not explicit in this formula; however, κ, is in the compound parameter *g* (see sec. 2.4 in the user manual of Martin et al. [2012] for a discussion of compound parameters).

If mobilized energy allocated toward somatic growth and maintenance is insufficient to pay somatic maintenance costs, growth becomes negative. Essentially the *Daphnia* pay maintenance costs by “burning” their structure. When an individual shrinks below 40% of its previous maximum mass, the individual then has a mortality rate of 0.35 day^{-1}.

Rationale. When mobilized reserves allocated to the soma are insufficient to pay somatic maintenance costs, animals may respond in many ways, which can be represented in DEB, for example, by shrinking in structure (see Kooijman 2010 for discussion of starvation strategies). Our implementation of the starvation model assumes that *Daphnia* get 100% of the energy invested in growth back to pay maintenance costs when shrinking.

Reproduction Submodel

DEB theory makes no general assumptions about the reproduction buffer handling rules, and these must therefore be defined for each species. *Daphnia* release clutches of embryos during the molt, using energy accumulated over the intermolt period. These embryos develop in the brood chamber over the next intermolt period and are released during the next molt, at which time they begin feeding exogenously. Below we describe how this process is replicated mathematically.

At the time step where *Daphnia* reach maturity ($U_H = U_H^p$), they set a state variable "molt-time" to 0. In each subsequent time step, the state molt-time ticks up by the amount of time transpired until it reaches the parameter "time-between-molts." We estimated the time-between-molts to be 2.8 days from the average time to between reproductive events for individually cultured *Daphnia* kept at 20°C. When molt-time ≥ time-between-molts, the *Daphnia* convert energy accumulated in the reproduction buffer (U_R) into embryos. The number of embryos produced is given by

$$N = \left\lfloor \frac{U_R \kappa_R}{U_E^0} \right\rfloor$$

Here κ_R represents the conversion efficiency of the reproduction buffer to the reserves of the embryo, which is assumed to be high as both in DEB theory are assumed to have the same composition. The cost of producing one embryo, U_E^0, is the amount of energy needed to create one offspring that will reach the maturity for birth threshold ($U_H = U_H^p$) with a reserve density, e, equal to 1. This value is dependent on the DEB parameters of a species and is calculated numerically using the bisection method during the setup procedure. The initial bounds for the bisection method were set to 0 and an unrealistically high number to ensure the true value was contained within the initial bounds. Values of U_E^0 were tested by simulating the embryonic period following the mass balance equations of DEB theory. In DEB theory embryos start out as nearly all reserves and a very small amount of structure. During the embryonic period, embryos mobilize reserves to grow and gain maturity. The selection criteria for the value of U_E^0 was that embryos were within 5% of a reserve density $e = 1$ when the maturity threshold for birth was surpassed. With the parameter values used for *Daphnia* in our simulations, this corresponded with a length at birth of 0.851 mm. This later value falls well within the range of observed hatching sizes of *Daphnia magna*.

In the simulations, after the calibration of the U_E^0 value we do not simulate the embryonic period. Rather we use the U_E^0 value to determine how many offspring are produced, then in the subsequent molt offspring are created equal to the number of embryos produced in the previous molt, and their state variables are set to the values determined in the calibration period ($L_b = 0.851$, $e = 1$, $U_H = U_H^b$).

Prey Dynamics Submodel

Prey dynamics were modelled to replicate the experimental design. In the experiments food was added at the nominal amount Monday–Thursday and at triple the normal amount on Friday, and there was no feeding on Saturday or Sunday. We matched this pattern by updating the food state variable (X) with the appropriate amount. Food is depleted from the environment via feeding of *Daphnia*. The sum of all feeding by *Daphnia* is given as

$$P_X = \sum_i f L_i^2 \{\dot{J}_{XAm}\}_i$$

Aging Submodel

The basic premise of the DEB aging submodel is that damage-inducing compounds are created at a rate proportional to reserve mobilization. Damage-inducing compounds induce more damage-inducing compounds also at a rate proportional to mobilization. The hazard rate for mortality due to aging of an individual is proportional to density of the accumulated damage in the body. Additionally, the concentration of both damage-inducing compounds and damage are assumed to be diluted via growth. The aging submodel includes two new parameters: the Weibull aging acceleration parameter, $\ddot{h}_a$, and the Gompertz stress coefficient, S_G. To reduce the total number of parameters, the equations for damage-inducing compounds, damage and hazard rate are scaled and combined to two ordinary differential equations, for "scaled acceleration" ($\ddot{q}$) and hazard rate ($\dot{h}$):

$$\frac{d}{dt}\ddot{q} = (\ddot{q}\frac{L^3}{L_m^3}s_G + \ddot{h}_a)e(\frac{\dot{v}}{L} - \dot{r}) - \dot{r}\ddot{q} \text{ where } \dot{r} = \frac{3}{L}\frac{d}{dt}L$$

$$\frac{d}{dt}\dot{h} = \ddot{q} - \dot{r}\dot{h}$$

Rationale. In our framework aging processes are linked tightly to energetics as the production of damage-inducing compounds are proportional to mobilization. One interpretation of this assumption is that the production of free radicals or other reactive oxygen species is proportional to the use of dioxygen in metabolic processes. The inclusion of energetics in the aging process allows differences in aging of animals in feeding conditions or physiological phenotypes to be explained without altering aging parameters.

Alternative Models of Starvation and Recovery

In addition to the standard model we tested alternative models of starvation and recovery. These modifications are explained in the main text.

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Chapter 3 (Appendix B): Model parameterization

Parameterization of the DEB model was conducted using the DEB3 version of DEBtox (http://www.debtox.info/debtoxm.php) developed by T. Jager. Overall, the approach compares the model predictions of a parameter set θ for growth, reproduction, and survival over time to data for each of these. This involves calculating the goodness-of-fit indicator for each data type and combining the goodness-of-fit measures for each data type into a maximum likelihood value. We then search the parameter space to find the parameter set that maximizes the likelihood given the data for growth, reproduction, and survival. Below we describe in detail how goodness of fit was calculated for each data type, how they were combined to give the likelihood of a parameter set, and finally how we searched the parameter space to find the most likely parameter set and determine the confidence intervals for each parameter.

The data used for parameterization for all parameters except the surface-area-specific maximum assimilation rate, $\{\dot{J}_{XAm}\}$, and the two aging submodel parameters, consisted of body size and reproduction data at four food levels over the course of 42 days (Sokull-Kluettgen 1998).

DEB-IBM has eight basic parameters, plus two parameters for the foraging submodel and two parameters for the aging submodel. The strategy we employed was to first specify the basic DEB parameters and then specify the parameters of the two submodels. Of the eight basic DEB parameters, we fixed one of the parameters, the conversion efficiency from the reproduction buffer to embryonic reserves, κ_R, at 0.95. The parameter was fixed at a high value because the reproduction buffer and the reserves of an embryo are assumed in DEB theory to have the same composition, and thus, there is a high conversion efficiency. Our parameterization began by simultaneously estimating the remaining seven DEB parameters (κ, $\dot{k}_M$, $\dot{k}_j$, U_H^b ,U_H^p ,$\dot{v}$, and *g*). Additionally we allowed the scaled food density parameter, *f*, to be estimated separately for each food level. The variable, *f*, takes a value between 0 (no feeding) and 1 (feeding at the maximum rate). The value is dependent on the ambient food level and is generally determined by some functional response. When the food levels are known, one can estimate the half-saturation coefficient (*K*) of the scaled Holling type 2 functional response:

$$f = \frac{X}{K + X}$$

While the food levels were known, we instead let *f* be estimated independently for each food level. This is because it is known that over longer time periods *Daphnia* can modify their feeding appendages to forage at higher rates at low food conditions, thus imposing a Holling type 2 functional response would lead to an imperfect fit, and we did not want this lack of fit to be compensated for in the eight DEB parameters. Thus after we determined the eight DEB parameters of an individual, we fixed these values and then parameterized K, with all other parameters fixed. Aging parameters ($\dot{h}_a$, S_G) were determined from survival data of 10 individually cultured *Daphnia* at three food levels (0.2, 0.05, and 0.01 mg C day^{-1}; Preuss et al. 2009). Because aging is dependent on mobilization (utilization of reserves), which is linked to feeding, organisms can age at different rates at different food levels.

Likelihood Estimation of DEB Parameters

The log likelihood of one data type, assuming normal independent errors, is given by (see Jager and Zimmer 2012)

$$\ell\left(\theta \middle| Y, \sigma^2\right) = -\frac{N}{2}\ln\left(2\pi\sigma^2\right) - \frac{1}{2\sigma^2}\sum_{j=1}^{m}\sum_{i=1}^{k_j}\sum_{r=1}^{n_{ij}}\left(Y_{ijr} - \hat{Y}_{ij}(\theta)\right)^2$$

where an observation Y_{ijr} represents the observation at *i*th time point, for the *j*th food level, and for the *r*th individual. However, in our case we do not have data for each individual but rather have the means for the body size and reproduction output for individuals at the *i*th time point of the *j*th food level. Thus, we cannot estimate σ^2 directly from the data. To circumvent this problem, we use a separate data set where individual measures of growth and reproduction were measured. We then estimate the variance of each data type (growth and reproduction) and fix σ^2 in our estimation procedure. When the variance is known, the first term no longer depends on the model parameters, and thus equation (1) reduces to

$$\ell\left(\theta \middle| Y, \sigma^2\right) = -\frac{1}{2\sigma^2}\sum_{j=1}^{m}\sum_{i=1}^{k_j}\sum_{r=1}^{n_{ij}}\left(Y_{ijr} - \hat{Y}_{ij}(\theta)\right)^2$$

Then we can work with the means, $\overline{Y}_{ij}$, instead of individual data points, Y_{ijr}:

$$\ell\left(\theta \middle| Y, \sigma^2\right) = -\frac{1}{2\sigma^2} wSSQ_n(\theta; Y)$$

$$wSSQ_n(\theta; Y) = \sum_{j=1}^{m} \sum_{i=1}^{k_j} n_{ij} \left(\overline{Y}_{ij} - \hat{Y}_{ij}(\theta)\right)^2$$

where wSSQ = the weighted sum of squares. From here, getting the log likelihood of the complete data set, Y_+, is a matter of summing the log likelihoods of each data set, Y_s:

$$\ell\left(\theta \middle| Y_+\right) = \sum_{s} \ell\left(\theta \middle| Y_S\right)$$

For the growth data set we compared the predictions of the model to the mean size of *Daphnia* for each combination of food level and time. For the reproduction data set we compare the average number of offspring produced between observation intervals to the predictions of parameter set θ integrated reproduction rate over that same interval (see Jager and Zimmer 2012):

$$wSSQ_n(\theta; Y) = \sum_{j=1}^{m} \sum_{i=1}^{k_j} \left(\frac{n_{ij} - n_{i-1j}}{2}\right)\left(\int_{t_{i-1}}^{t_i} R_j(\tau, \theta) d\tau - \frac{2Y_{ij}}{n_{ij} + n_{i-1j}}\right)^2$$

However, for reproduction, only the data before 21 days were used because after 21 days (after the fifth brood) there was a significant reduction the reproduction rate of *Daphnia*, which was not accounted for in the DEB model. We did not use these data because we did not want the model fit to be influenced by reproduction data points after the fifth brood, as *Daphnia* in natural contexts rarely survive to produce more than 5 broods.

Survival data used for parameterizing the aging submodel follow a multinomial distribution. The log likelihood is given by (see Jager et al. 2011)

$$\ell(\theta; Y) = \sum_{j=1}^{m} \sum_{i=1}^{k_j} \left(Y_{ij} - Y_{i-1j}\right) \ln\left(S_{ij}(\theta) - S_{i+1j}(\theta)\right)$$

where S_{ij} is the number of individual at time point *i* of food level *j* and S_{i+1j} is the number of survivors at the next observation time.

Optimization and Confidence Intervals

Optimization was conducted using a Nelder-Mead simplex method (Nelder and Mead 1965). Confidence intervals were calculated using the profile likelihood method (Venzon and Moolgavkar 1988; Meeker and Escobar 1995), which is more appropriate for nonlinear models (Pawitan 2000).

Parameterization of $\{\dot{J}_{XAm}\}$

Once these parameters were fixed we estimated the final feeding submodel parameter, the maximum surface-area-specific feeding rate, $\{\dot{J}_{XAm}\}$. This parameter determines at what rate food (algal cells) are depleted from the environment by *Daphnia* predation. To fit this parameter we used a data set of growth and reproduction at three food levels in batch cultures (Coors et al.2004). In batch cultures, in contrast with the flow-through experiments, all or much of the food is removed each day via predation at all but very high food levels. How much food is depleted is highly dependent on the $\{\dot{J}_{XAm}\}$ parameter; therefore, we used these data to estimate this parameter by running simulations replicating the experimental conditions of the Coors experiments, with incrementally increasing values of $\{\dot{J}_{XAm}\}$. Experiments and model were run in 80-mL M4-Elendt medium, and daphnids were daily fed *Desmodesmus subspicatus* at one of three different food levels (0.05, 0.075, and 0.2 mg C day^{-1}). *Desmodesmus subspicatus*has an average carbon content of 1.95 x 10^{-8} mg C cell^{-1}. After an initial range finding test we evaluated values of $\{\dot{J}_{XAm}\}$ ranging from 2.0 to 5.0 x 10^{5} (cells mm^{-2} day^{-1}) with a resolution of 1 x 10^{4}. Maximum likelihood estimation was used to select the appropriate value in the same manner as in the previous section.

Results of Individual Parameterization

Analysis of the confidence intervals for each parameter revealed that most parameters were well specified within a narrow range with the exception of $\dot{v}$ and *g*. For each of these parameters, there was no narrow peak in the profile likelihood. Instead, as the values of $\dot{v}$ and *g* were fixed at higher values, the likelihood increased but at a decreasing rate (fig. B1). An increase in these

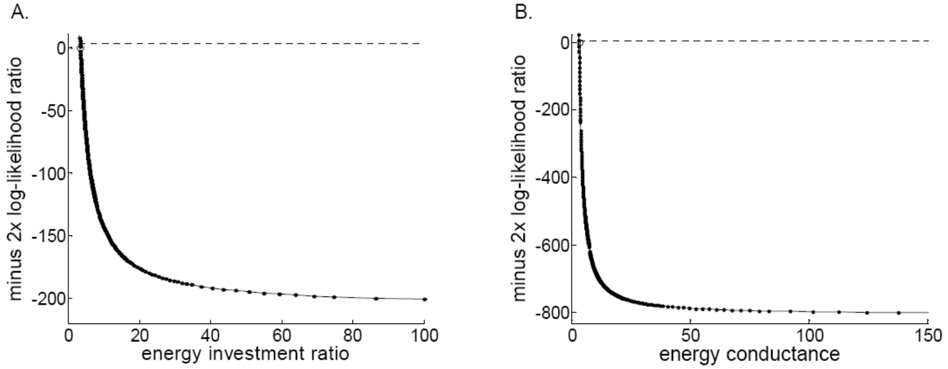

Fig. B1 Confidence intervals for the energy investment ratio, g (A) and energy conductance, $\dot{v}$ (B) using the profile likelihoods method (Meeker and Escobar 1995). For both g and $\dot{v}$ the model fit continued to improve at a decreasing rate as their values increased.

parameters together indicates an increase in speed in the reserve dynamics, as $\dot{v}$ is the mobilization rate of reserves and g is a compound parameter

$$g = \frac{[E_G]}{\kappa[E_M]}$$

where $[E_G]$ is the cost to produce one unit of structure and $[E_M]$ is the maximum reserve density. Thus, an increase in $\dot{v}$ and g together indicates a faster rate of reserve mobilization and a simultaneous decrease in the size of the reserves. As both $\dot{v}$ and g increase toward infinity, you ultimately end up with a "reserveless" DEB model. Here we no longer have the parameters g and $\dot{v}$, but we use maximum length L_M as a primary parameter. The differential equation for length is then reduced to $dL/dt = (\dot{k}_m/3)(L_M f - L)$, and the equations for maturity and reproduction now differ only in that instead of mobilized energy being allocated to each state variable, it is assimilated energy, fL^2.

$$\frac{dU_H}{dt} = (1-\kappa)fL^2 - \dot{k}_j U_H$$

when $U_H < U_H^p$, and

$$\frac{dU_R}{dt} = (1-\kappa)fL^2 - \dot{k}_j U_H$$

when $U_H > U_H^p$. The embryonic stage requires a slight modification. Instead of a reserve we use an embryonic buffer, U_B, from which embryos assimilate energy at their maximum rate: $\frac{dU_B}{dt} = -L^2$. Embryos grow and mature following the same dynamics as juveniles and adults. Mothers allocate enough energy into the embryonic reserve so that the buffer is depleted as embryos reach the maturity threshold for hatching (U_H^b).

Based on the confidence profiles of g and $\dot{v}$, the goodness of fit was not significantly worse to a range down to 10 for g. Because we were unable to specify the value of g and $\dot{v}$ exactly, we instead fixed the parameter g at 10. For computational reasons, having g fixed to a lower value means we need less resolution in the time steps, thus we wanted to select the lowest possible value. To determine the consequence of fixing g to 10 as opposed to higher values, we also parameterized the model with g fixed to 100 and a reduced model with no reserves (table B1). We then ran the population simulations using each of the parameter sets representing increasing speed of reserve dynamics (fig. B2). The resulting comparison indicated that using parameter sets with faster reserve dynamics, or no reserve state variable at all, had negligible effects on the population dynamics.

As the goal was to test DEB theory, we did not want to deviate from the inclusion of reserves. With g fixed to a value of 10 all parameter values were well specified for the standard DEB model (fig. B3), the aging submodel (fig. B4), and the feeding submodel (fig. B5). Additionally for the feeding submodel we show simulations of growth and reproduction at the individual level at the three batch-fed food levels (Coors et al. 2004) with the same assumptions of stochasticity as used in the population simulations (fig. B6).

Parameterization and Analysis at the Population Level

We parameterized the new starvation model by fitting the M parameter using the same "multidata type" likelihood approach used for parameterizing the DEB model. However for parameterizing M at the population level, the data sets used were the total abundance and the abundance of three size classes over time. We used weighted sum of squares to normalize variances within and among data types. Residuals between model and data were first weighted by the square root plus 1 (1 was added to avoid division by 0 for some observations), as there was higher variance for higher population abundances. After this transformation there was still heteroscedasticity among the data types (total population abundance and

Fig. B2 Comparison of mean of 100 simulations of 3 DEB-IBM models parameterized with *g* fixed at 10 (black solid), 100 (grey solid), or the modified reserveless model (black dashed) at the lowN (a), lowNA (b), and highNA (c) population experiments

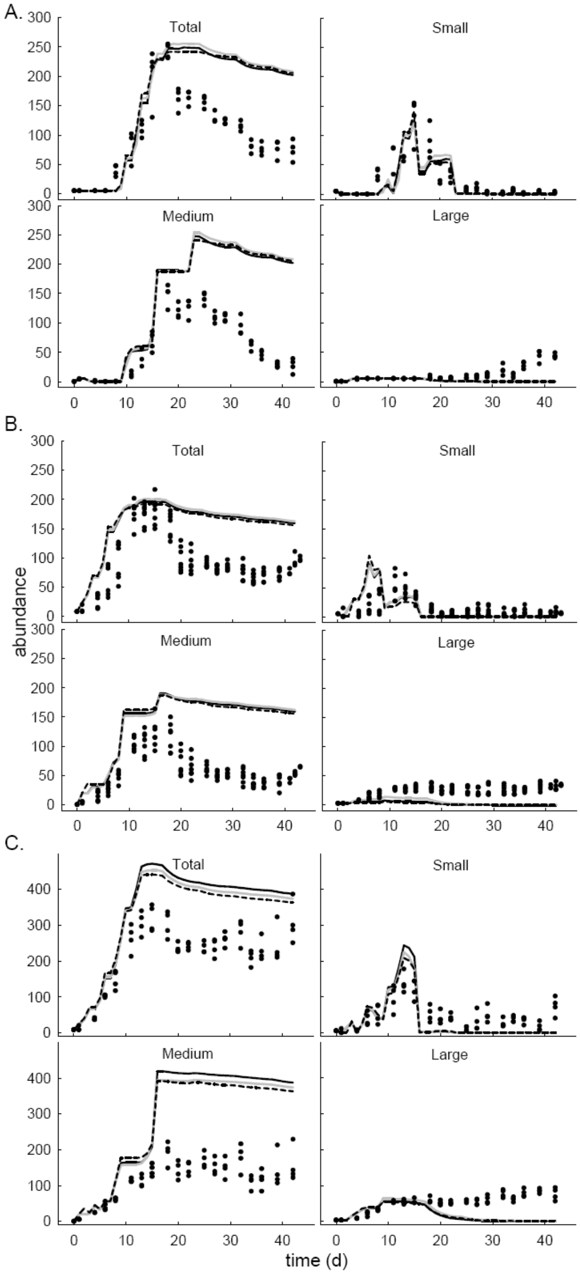

Fig. B3 Confidence intervals for DEB parameters using the profile likelihoods method with g fived at a value of 10 (Meeker and Escobar 1995).

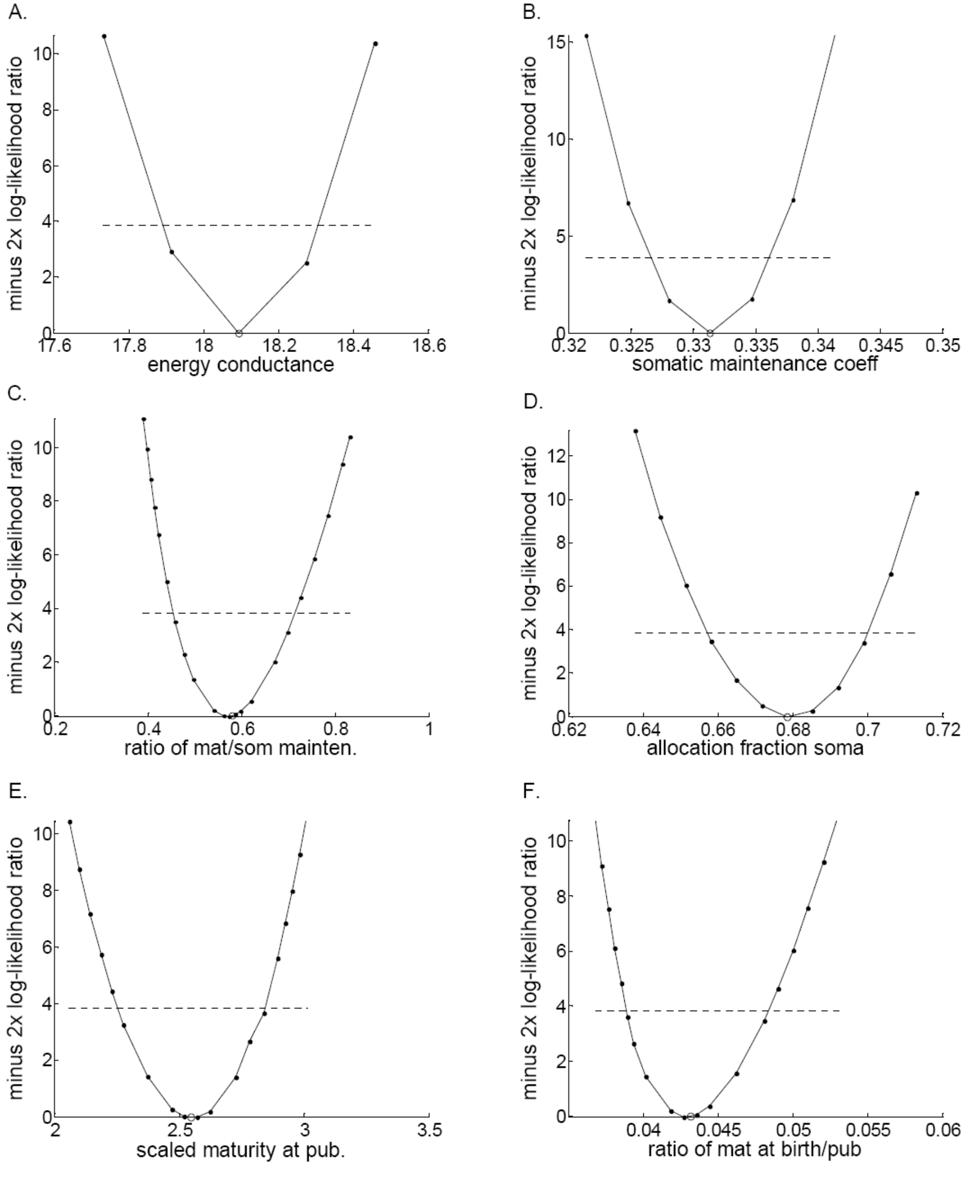

Fig. B4 Confidence interval for Weibull ageing rate, $\dot{k}_W$ (A), and the Gompertz aging rate, $\dot{k}_G$ (B). Note that for use in DEB-IBM we use the aging parameters $\ddot{h}_a$ and s_G, where $\ddot{h}_a = \frac{\dot{k}_W^3}{\dot{k}_m g}$ and $s_G = \frac{\dot{k}_G}{\dot{k}_m g}$.

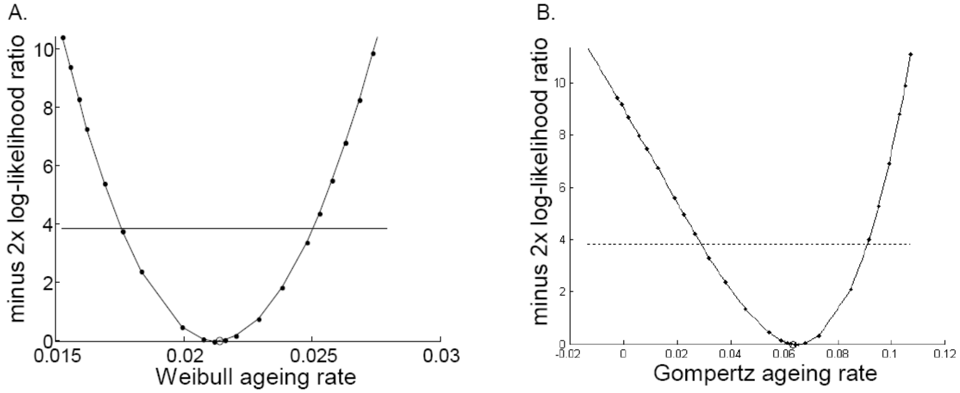

Figure B5. Confidence interval for feeding submodel parameters: the half saturation coefficient (K) and the maximum surface area-specific ingestion rate $\{\dot{J}_{XAm}\}$.

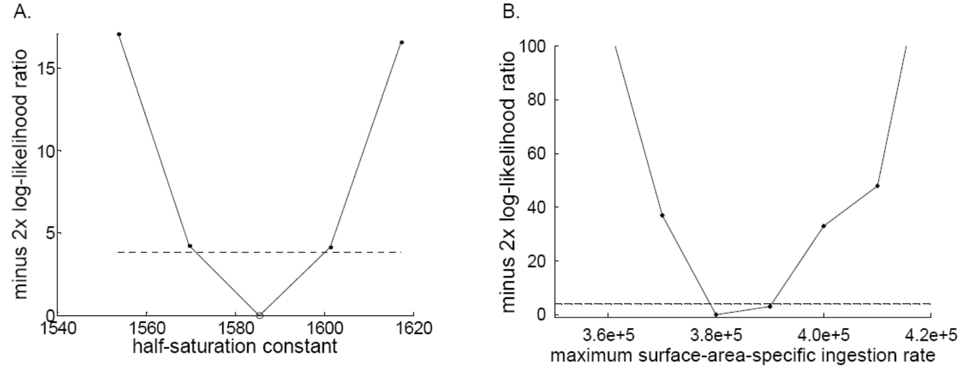

Table B1 Parameter values used in comparing the sensitivity of population dynamics to the speed of reserve dynamics. Increasing values of g mean faster reserve dynamics (i.e. faster turnover of the reserve compartment). For each set we wither fixed g to 10, 100, or removed the reserve compartment completely g = ∞. The unit for time (t) is days, for structural length of animals (L) in mm, for the abundance of prey (#) in cells, and for length of the environment (l) in cm.

DEB parameters

symbol	dimension	g fixed at 10	g fixed at 100	reserveless DEB
κ	-	0.678	0.682	0.645
κ_R	-	0.95	0.95	0.95
$\dot{k}_m$	t^{-1}	0.3314	0.308	0.3054
$\dot{k}_j$	t^{-1}	0.1921	0.207	0.2109
U_H^b	tL^2	0.111	0.118	0.134
U_H^p	tL^2	2.547	2.80	2.876
$\dot{v}$	Lt^{-1}	18.1	177.4	-
g	-	10	100	-
L_M	L	-	-	5.42
		Feeding submodel parameters		
$\{\dot{J}_{XAm}\}$	$\#L^{-2}t^{-1}$	3.80E+05	3.40E+05	3.80E+05
K	$\#l^{-3}$	1585	1511	1505

the abundances of the three size classes for the three population experiment), thus we weighted each data type by its variance. In addition to giving the weighted SSQ for each model type, we also present R^2, which was taken as the 1 − root mean square error, with the root mean square error equal to the wSSQ divided by the weighted variance of the data (Kendall et al. 2005). We parameterized each of the three starvation submodels only using data from the low-N treatment. To compare which model best explained the data, we then compared the three mortality submodels using the complete data set.

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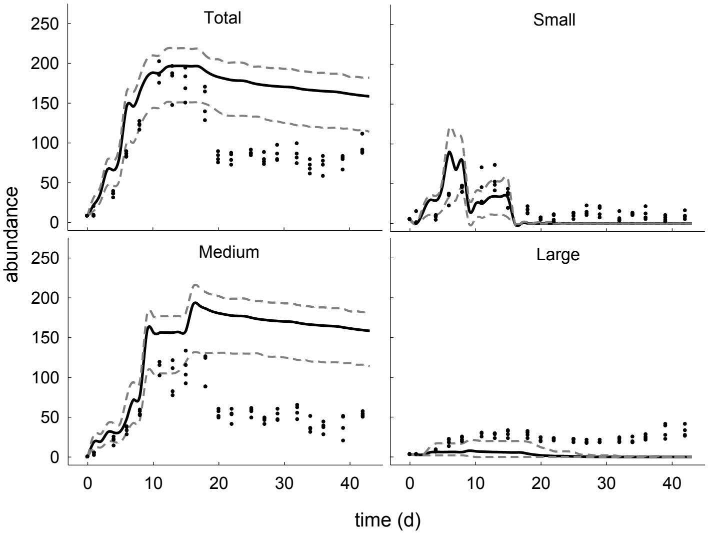
Chapter 3 (Appendix C): Supplementary figures

Fig. S1 Comparison of data and DEB-IBM predictions at the population level for the lowNA (A) and highNA (B) experiments. Simulations with DEB-IBM replicated the experimental conditions. Figures show the mean (think black line) and max and min (dashed grey lines) of 100 simulations.

A.



B.

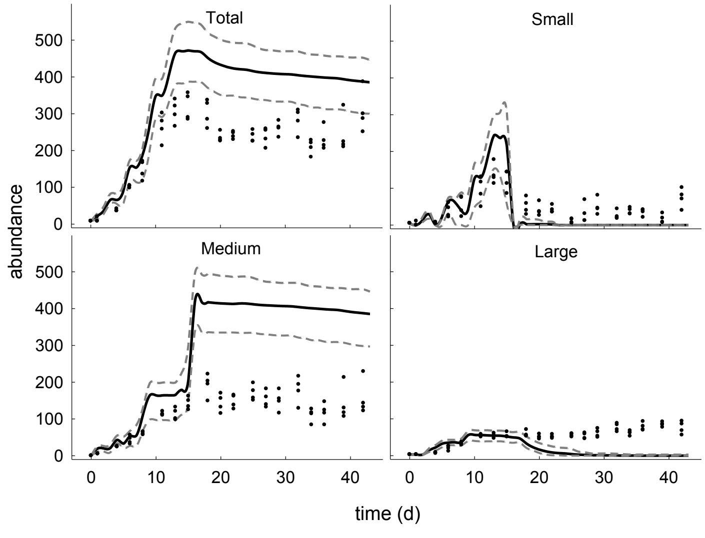
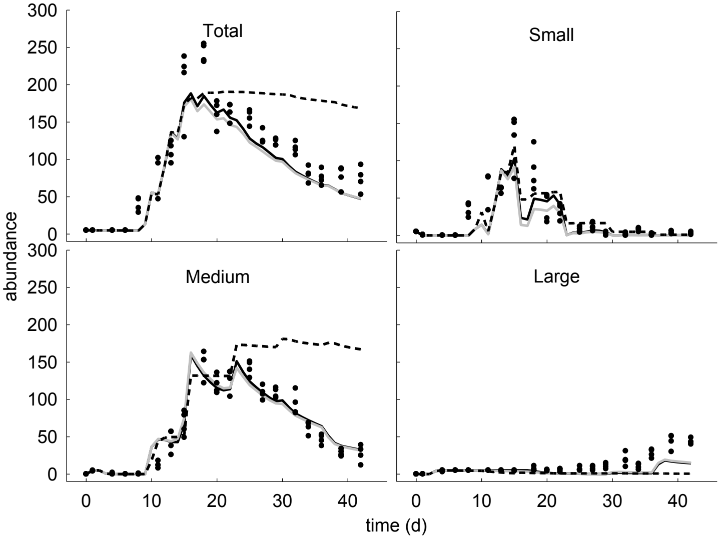


Fig. S2 Comparison of the performance of three starvation submodels with data from the lowN (A) and lowNA (B) experiments. In each of the three models, a 1-parameter food-dependent mortality submodel, was applied, but models differed in that it was either applied only to juveniles (black solid), only adults (black dashed), or all *Daphnia* (grey solid).

A.



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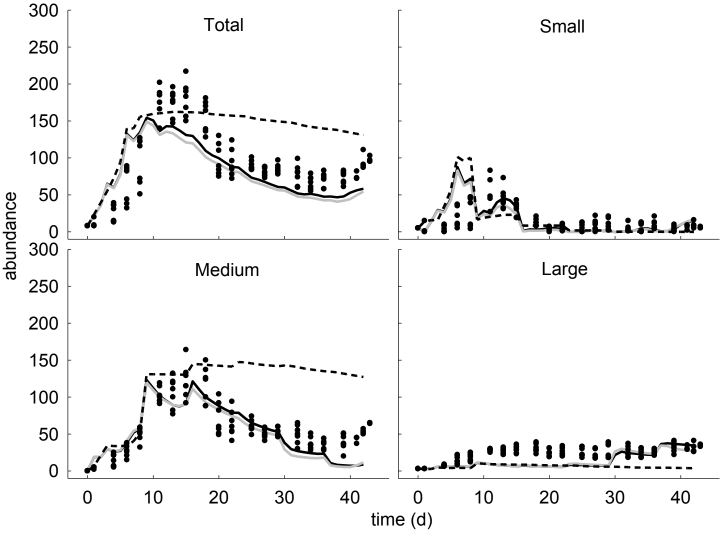
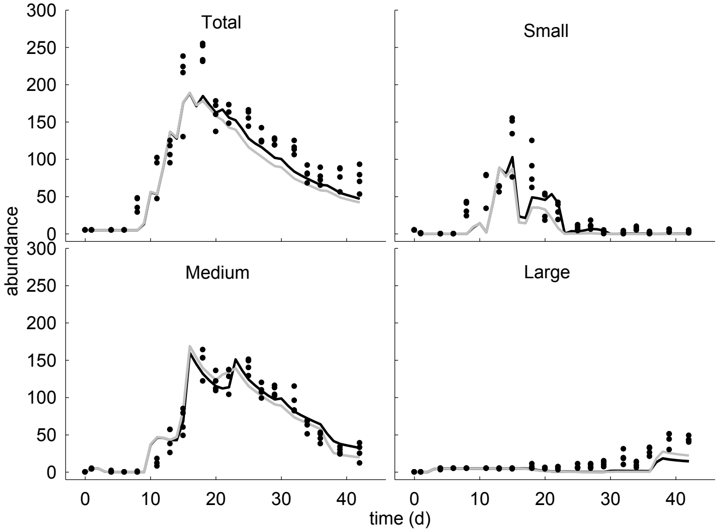


Fig. S3 Comparison of starvation-recovery assumptions at the high food population level for the lowN (A) and lowNA (B) experiments. The grey line show the average of 100 model simulations when individuals feed at a rate proportional to their current length, while the black line represents the average of 100 model simulations when individuals feed at a rate proportional to their maximum length attained.

A.



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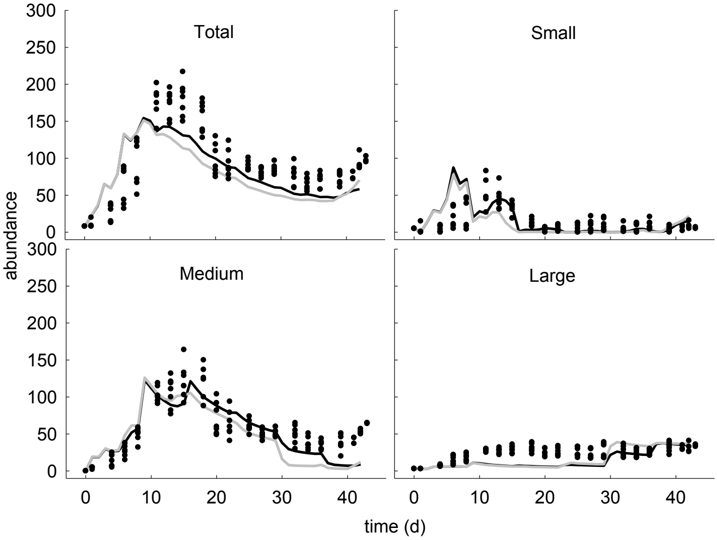

Chapter 4: Extrapolating ecotoxicological effects from individuals to populations: a generic approach based on Dynamic Energy Budget theory and individual-based modeling

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Abstract

Individual-based models (IBMs) predict how dynamics at higher levels of biological organization emerge from individual-level processes. This makes them a particularly useful tool for ecotoxicology where the effects of toxicants are measured at the individual level but protection goals are often aimed at the population level or higher. However, one drawback of IBMs is that they require significant effort and data to design for each species. A solution would be to develop IBMs for chemical risk assessment that are based on generic individual-level models and theory. Here we show how one generic theory, Dynamic Energy Budget (DEB) theory, can be used to extrapolate the effect of toxicants measured at the individual level to effects on population dynamics. DEB is based on first principles in bioenergetics and uses a common model structure to model all species. Parameterization for a certain species is done at the individual level and allows to predict population-level effects of toxicants for a wide range of environmental conditions and toxicant concentrations. We present the general approach, which in principle can be used for all animal species, and give an example using *Daphnia magna* exposed to 3,4–dichloroaniline. We conclude that our generic approach holds great potential for standardized ecological risk assessment based on ecological models. Currently, available data from standard tests can directly be used for parameterization under certain circumstances, but with limited extra effort standard tests at the individual would deliver data that could considerably improve the applicability and precision of extrapolation to the population level. Specifically, the measurement of a toxicants effect on growth in addition to reproduction, and presenting data over time as opposed to reporting a single EC50 or dose response curve at one time point.

Introduction

A central question in ecological risk assessment of chemicals is: how likely are adverse ecological effects if a population is exposed to a toxicant (Munns *2006*)? This is difficult to answer empirically because for most (non-microbial) species of interest population data are scarce and conducting experiments at the population level is usually impossible for logistic, financial, or ethical reasons. Consequently, the effect of a toxicant is commonly measured on individuals as a proxy for the effect on populations, for example by measuring how a given concentration of a chemical affects reproduction, growth, or survival of individuals. However, it is usually hard to determine the implications for populations of a stress-induced change in individual performance. As a tool to help aswer this question, ecological modelling has been discussed for a long time (Kooijman and Metz *1984*; Kendall and Lacher *1994*; Pastorok et al. *2001*), but over the last 5 years or so interest in using this approach for ecological risk assessment has increased considerably (Grimm et al.*2009*; Forbes et al. *2009*; Preuss et al. *2009*; Thorbek et al. *2010*).

This development was probably triggered both by the increasing demand for ecological realism in regulatory risk assessment (Forbes et al. *2009*, *2010*) and by recent advances in predictive ecological modelling. Modern simulation models that can take into account spatial aspects, stochasticity as well as individual differences, interactions, and behaviour, allow for a level of structural realism (Wiegand et al.*2003*; Grimm et al. *2005*; Grimm and Railsback *2012*) which seemed impractical 10 or 20 years ago. Particularly relevant are individual-based models (IBMs), often also referred to as agent-based models, of populations or communities, because they are designed to let population dynamics emerge from what individuals do.

There are an increasing number of successful examples of well-designed and tested IBMs which accurately extrapolate from data on individuals to predict population dynamics (e.g., Railsback and Harvey *2002*; Preuss et al. *2010*; Stillman and Goss-Custard *2010*). However the development of these models required large quantities of data, that even for species which are relatively well-studied and easy to observe, such as *Daphnia* (Preuss et al. *2010*), trout (Railsback and Harvey *2002*), or shorebirds (Stillman and Goss-Custard *2010*), took 5–10 years to gather and use for parameterization and testing. Obviously, we cannot afford to collect such data, and invest so much time, for every species and environment of concern.

Using a generic theory of how individuals perform could help to reduce the amount of data needed and to make model development more efficient (Martin et al. *2012*; Martin et al., in press). Generic models focus on commonalities rather than differences and thus conserve model structure from one species to the next. This allows the modeller to spend less time focusing on basic model structure and to focus on system- and species-specific aspects. For ecological risk assessment of chemicals, we propose using one generic theory, Dynamic Energy Budget theory (DEB) (Kooiman *2010*), which is especially well-suited for extrapolating individual effects of stressors to populations for three main reasons.

First, the major thrust of DEB theory is understanding patterns of growth, reproduction, and mortality of individuals. The theory attempts to define the simplest framework that can explain these patterns as a function of internal states and environmental conditions. The link to classical theoretical population ecology is via the two processes: reproduction and mortality. Because DEB also considers body size, it accounts for size-structured interactions which have been shown to be important at the population level (de Roos and Persson *2013*). Secondly, we have auxiliary theory and tools to fill in the generic framework with species-specific parameter values. Parameterization for a DEB model can be flexible to the amount of data available (Kooijman et al. *2008*; Lika et al. *2011*). Additionally, parameterization software (DEBtoolhttp://www.bio.vu.nl/thb/deb/deblab/debtool/, DEBtox http://www.debtox.info/) is freely available with a growing user community. Once parameterization is complete, there is also a generic implementation of DEB theory (DEB-IBM) in an individual-based population model (Martin et al. *2012*), which is freely available, comes with a user manual and guide for parameterization, and is implemented in NetLogo (Wilensky *1999*), a free software platform which does not require a computer science background to be used (Railsback and Grimm *2011*). Finally, DEB has a strong track record in interpreting data from toxicological tests and other studies on individuals (e.g., Jager et al. *2006* and references therein).

In this paper we present a generic approach for representing effects of chemical stressors at the individual level using a DEB model, and extrapolating these effects to populations via IBMs. We use DEB-IBM to parameterize and represent individual *Daphnia magna* and then predict the population level response to a chemical stressor, 3,4-dichloroaniline (3,4-DCA). We use independent data at the individual level (to parameterize the effect of the toxicant), and at the population level (to test the ability of the model to predict population dynamics from individual level data). Finally we discuss the limitations of standard ecotoxicological tests for extrapolating individual effects to populations and make suggestions to dramatically improve experimental test design for individuals without a large increase in effort.

Methods

The goal of our analysis is to test how well using a DEB-IBM approach can predict the effects of a stressor at the population level based on data measured on individuals. To do this, we parameterized the effect of a toxicant using individual data and compared simulations of an adapted DEB-IBM model for *Daphnia* to population experiments (Preuss et al. *2010*).

DEB-IBM model for Daphnia

We used a DEB model of *Daphnia magna* (Martin et al., in press) adapted from the generic DEB-IBM framework (Martin et al. *2012*). The model for individual animals is non-spatial and consists of a number of coupled differential equations describing the dynamics of state variables which characterize the energetic and developmental state of each individual. It is thoroughly described in Martin et al. (in press), and a full, detailed model description following the ODD protocol (Grimm et al. *2006*, *2010*), a standard format for describing IBMs, is given in Online Resource 1. For a general introduction to DEB theory see Nisbet et al. (*2000*) and Sousa et al. (*2008*).

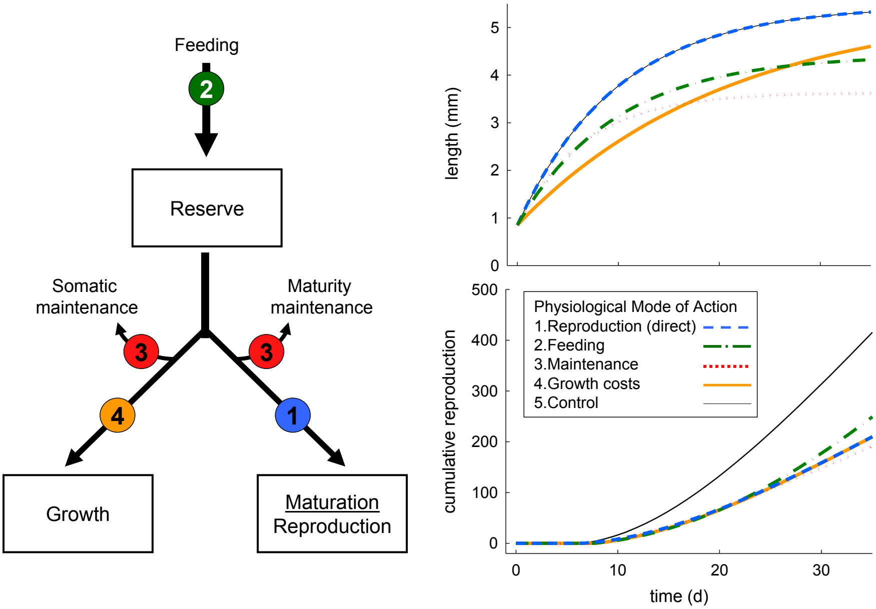
Stress at the individual level

Toxicants once absorbed by an individual are assumed to affect one or more physiological processes. This is manifested in DEB theory via an effect on an individual parameter which in turn alters life-history output over time. Thus the type of sub-lethal effect invoked by a toxicant depends both on the physiological process (which parameter is affected), and the magnitude of the effect on that parameter. We refer to effects on different parameters as different "Physiological Modes of Action" (PMoA) (Álvarez et al. *2006*) (Table 1). The term "stress level", *s*, quantifies the magnitude by which a parameter is altered by a chemical. The stress level is determined by the internal concentration of a toxicant. For all toxicants DEB assumes that there is a concentration below which the chemical will have no effect (No Effect Concentration, *NEC*), and above this, the stress level increases linearly with increasing internal concentration, c_q, with a slope determined by a "tolerance parameter", C_T.

$$s = \max(0, c_q - NEC)C_T$$

The first step in predicting the population response to a stressor is identifying the model parameter that is affected by the toxicant of interest. The parameters of a species, along with the environmental conditions determine the growth or reproductive output over time. Conversely, we can use information on reproduction and growth over time at different levels of toxicant exposure to identify the affected parameter or PMoA (Fig. 1).

Fig. 1 The left panel shows a schematic diagram of energy flow in a DEB model. The parameter values for a species and the state of the environment (characterized here by food density) determine the magnitude of the energy fluxes into, within, and out of the organism. These fluxes specify the change over time of measurable quantities such as growth or reproductive output. Stressors are modelled in DEB as changes in the value of one or more parameters thereby modifying one or more of the energetic fluxes leading to different patterns in growth and or reproduction. The pattern of the stressed life history output depends on the physiological mode of action (PMoA). In the right panel, the *black line* shows the predicted body size and cumulative reproduction for *Daphnia magna* in ad libitum feeding conditions over the course of 35 days, using the DEB model parameterized for *Daphnia* (Martin et al., in press). For all *other lines* in the right panel we calculated the needed stress level for each PMoA shown in the left panel that would result in 50 % reduction in reproduction in a 21 day *Daphnia* reproduction test. Then, for each PMoA in the left panel, we used the stressed values for a parameter to simulate growth and reproduction under the same conditions as the control to compare the patterns of life-history output predicted by the different PMoAs. The *colours* of each line in the right panel correspond the PMoA that is simulated from the left panel. The *vertical black line* represents where the end of a 21 day *Daphnia* reproduction test would occur and data would be recorded.



3,4-dichloraniline (3,4-DCA), has a 48 h LC50 of 220 µg l^{-1} (Preuss et al. *2010*). However, at concentrations an order of magnitude lower, sub-lethal effects on reproduction have been recorded (Sokull-Kluettgen *1998*). Figure 2 shows how reproduction is reduced with increasing concentrations of 3,4-DCA. However these data alone are not enough to deduce the PMoA, as all PMoAs in a DEB context will normally result in a reduction in reproduction (Fig. 1). Previously, it has also been shown that 3,4-DCA has negligible affects on growth and time to first reproduction (Elendt *1990a*, *b*). This ruled out PMoAs with an effect on feeding or assimilation rate, increased maintenance costs, or increased costs of growth, because for each of these PMoAs we should also expect to see an effect on growth, provided the standard DEB model assumptions hold. For example at 40 µg l^{-1} the “Feeding/Assimilation”, “Maintenance costs”, and “Growth Costs” PMoAs would predict a reduction in body length, at the end of a 21 day *Daphnia* reproduction test (OECD 211) of 39, 48 and 46 % respectively, while Elendt (*1990a*, *b*) found no significant differences in the length of *Daphnia* between the control (4.32 mm) and the highest concentration tested, 48 µg l^{-1} (4.28 mm). This leaves only direct effects on reproduction as a possible PMoA (Fig. 1). Assuming rapid toxicokenetics, the stress-induced reduction in reproduction will be constant over time and we can calculate the stress coefficient directly from the cumulative reproduction as a function of the concentration after 21 days.

Table 1. Core DEB parameters of the DEB-IBM model for the DEB-IBM model for *Daphnia magna* (A). And their link to various PMoAs through the stress level (B). The DEB-IBM model is based off the scaled DEB model (Kooijman et al. 2008).

A.

DEB parameters

Symbol	Description	Dimension	Value	PMoA
κ	Fraction of mobilized energy to soma	-	0.678	-
κ_R	Fraction of reproduction energy fixed in eggs	-	0.95	Reproduction costs and embryonic hazard
$\dot{k}_m$	Somatic maintenance rate coefficient	t^{-1}	0.3314	Maintenance costs, growth costs
$\dot{k}_j$	Maturity maintenance rate coefficient	t^{-1}	0.1921	Maintenance costs
U_H^b	Scaled maturity at birth	tL^2	0.1108	-
U_H^p	Scaled maturity at puberty	tL^2	2.555	-
$\dot{v}$	Energy conductance	Lt^{-1}	18.1	-
g	Energy investment ratio	-	10	Growth costs
f	Scaled functional response	-	0-1	Feeding/assimilation

B.

DEB parameters under stress

PMoA	Description	Affected parameter	Stressed value
Feeding / assimilation	Decrease in feeding ability	f	$f_s = f(1-s)$[a]
Maintenance	Increase in maintenance costs	$\dot{k}_m, \dot{k}_j$	$\dot{k}_{M,s} = \dot{k}_M(1+s)$[b] $\dot{k}_{J,s} = \dot{k}_J(1+s)$
Growth costs	Increase in overhead costs of growth	$\dot{k}_m, g$	$\dot{k}_{M,s} = \dot{k}_M/(1+s)$[c] $g_s = g(1+s)$
Reproduction costs	Increase in cost per egg	κ_R	$\kappa_{R,s} = \kappa_R/(1+s)$
Embryonic hazard	Decrease in survival during embryonic period	κ_R	$\kappa_{R,s} = \kappa_R \exp(-s)$

Parameter values in combination with environmental conditions determine the magnitude of energy fluxes as governed by a set of coupled differential equations (given in Online Resource 1). For all parameters with a dimension in time (*t*), the unit is day, and for length (*L*), centimeters, a "–"denotes the parameter is dimensionless

[a] This form assumes the stressor equally impairs the attack rate and the handling time in the context of a Holling type II functional response. Other forms, where either the attack rate, or handling time are affected independently are also possible (see Müller et al. 2010)

[b] Here we show the assumption that both maturity and somatic maintenance costs are both equally affected, however effects on each parameter independently are also possible.

[c] The growth costs PMoA affects the parameter, $[E_G]$ the volume-specific costs of structure. This parameter is indirectly included in the scaled DEB through the two compound parameters $\dot{k}_m$ and g (see Jager and Zimmer 2012 for details).

Within DEB there are two different PMoAs that can act directly on reproduction (Table 1). First the effect can be on the conversion efficiency of reproduction buffer into new offspring ("Reproduction Costs" PMoA) or it can be an effect on mortality of offspring ("Embryonic Hazard" PMoA, EH). The Reproduction Costs and Embryonic Hazard PMoAs differ subtly in the relationship between the stress level and reproductive output under stress, that is

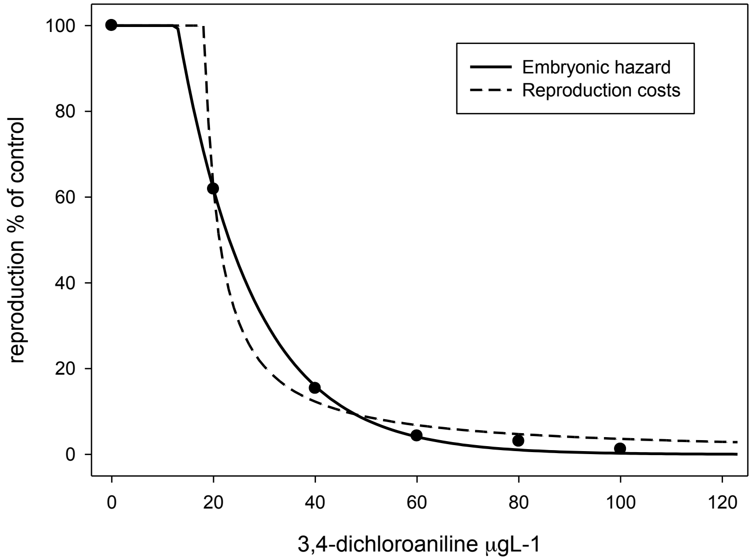


Fig. 2 Comparison of the fitted dose responses "embryonic hazard" and the "reproduction costs" PMoA for 3,4 DCA. For each model the No Effect Concentration (*NEC*), and the Tolerance (C_T) were fitted to the dose response curves.

captured in both cases by changes in the reproduction efficiency parameter, κ_R (Kooijman and Bedaux *1996*; Jager et al. *2010*) and are given by:

$$\kappa_{R,s} = \frac{\kappa_R}{(s+1)}$$

and

$$\kappa_{R,s} = \kappa_R \exp(-s)$$

respectively.

At the population level, the only difference between the two is that the Reproduction Costs PMoA is a deterministic reduction in reproduction, while Embryonic Hazard PMoA is stochastic, with each *Daphnia* having a certain probability of surviving the embryonic period (see Online Resource 1 for details). To determine the PMoA we fit the two parameters (NEC and $C\,T$), for each PMoA. These two parameters in combination with the exposure concentration determine the stress level and ultimately predict reproductive output as a function of exposure concentration. We compared the resulting dose response curve to the output from a 21 day *Daphnia* reproduction test and selected the model with the highest likelihood. Parameterisation was conducted using a Nelder-Mead simplex in MATLAB.

Population experiments and simulations

The simulations of the DEB-IBM for *Daphnia* were run using conditions that matched exactly the experimental setup of population experiments conducted by Preuss et al. (*2010*). These experiments were initiated with 5 newly hatched *Daphnia* (<24 h), and 3 adult *Daphnia* (>4 mm). Feeding dynamics in the experiment were "semi-batch", i.e. food was added each day Monday–Thursday (0.5 mg C d^{-1}, and 3× the normal food level on Friday to a 900 ml beaker. Three times a week the total population density and the number of *Daphnia* in three size classes were counted. The experiments were carried out for 42 days. Each population experiment was conducted with either no 3,4-DCA (control), or at continuous exposure to a concentrations of 2.5, 5.0, 10.0, 20.0, and 40 µg l^{-1}. We ran 100 population simulations with DEB-IBM for each concentration and compared the model results to independent experimental data.

Results

Of the two PMoAs tested for fitting the dose response curve for 3,4-DCA, the Embryonic Hazard PMoA resulted in the highest likelihood, however both PMoAs resulted in relatively good fits to the dose–response curve (Fig. 2). Before continuing with our analysis we compared the two PMoAs at the population level to test the population consequences of assuming one PMoA over the other. We thus tested individual reduction in reproduction of 25, 50 and 75 % via each PMoA and compared the results of the simulations for total population density and size structure over the simulated 42 day experiments. At the population level, for the same level of effect, each PMoA resulted in the same expected reproductive output for *Daphnia*. The results from this analysis revealed negligible differences between the two PMoAs (Fig. 3), and therefore we used the Embryonic Hazard PMoA for all further analysis. However we observed a slightly increased variation among simulation runs for the Embryonic Hazard PMoA relative to the Reproduction Costs PMoA at the 50 and 75 % effect levels, with a 28 and 32 % higher average standard deviation in daily population abundance at the 50 and 75 % effect levels respectively, as might be anticipated from the extra stochasticity associated with this PMoA. There were negligible differences in the average standard deviation of daily abundance at the lowest effect level (<1 % difference).

Fig. 3 Comparison of predictions at the population level for total population density, and the three size classes by the "Embryonic hazard" and the "Reproduction costs" parameterized for ECx values of 25 (A.), 50 (B.), and 75 (C.) in a standard 21 day *Daphnia* reproduction test. Each data point represents the mean value of 100 simulations at a point in time for either total population abundance, or abundance of the size classes of *Daphnia* (data recorded once per day over the 42 day simulations) for each of the two submodels.

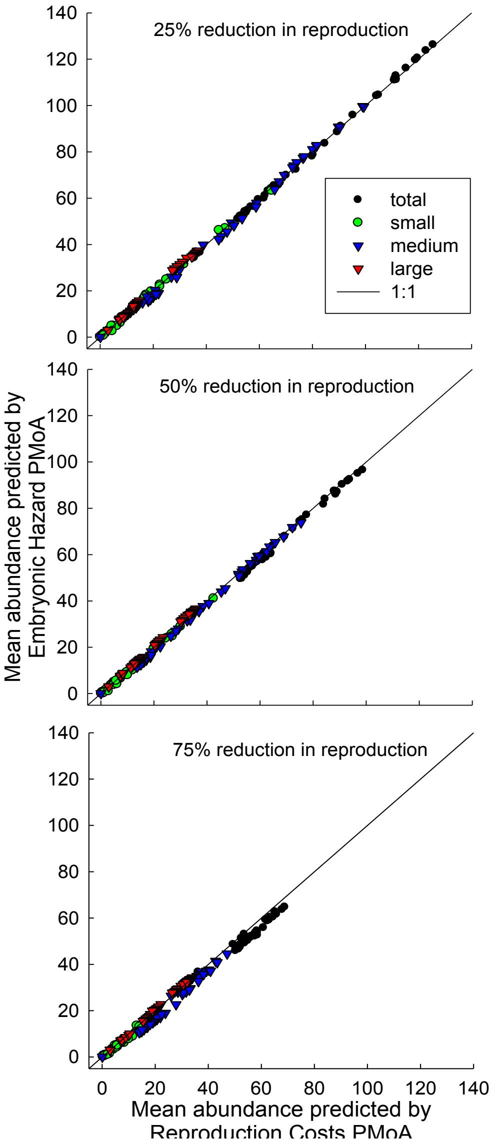
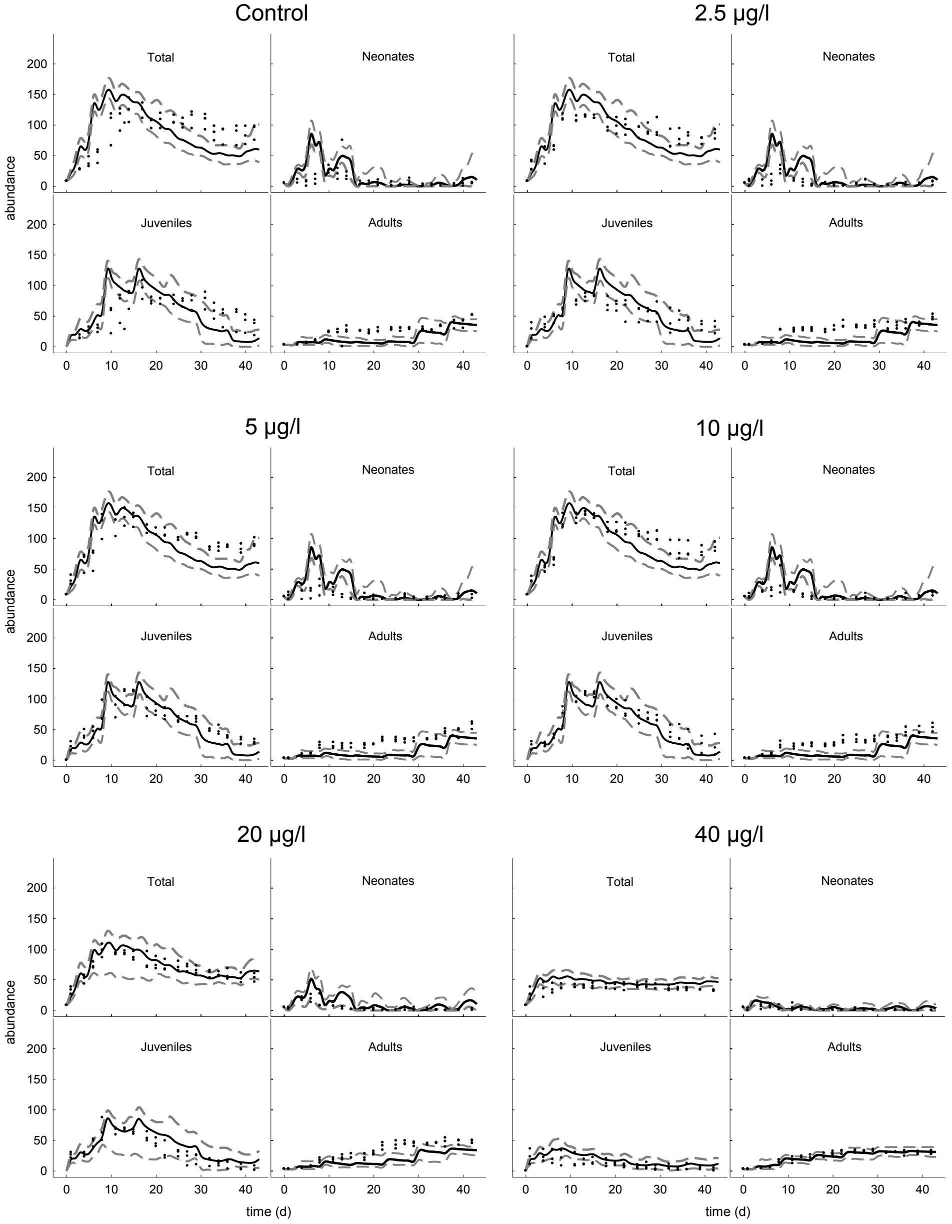


Fig. 4 Comparison of the mean (black solid line) and the maximum and minimum of 100 simulations (dashed gray lines) and experimental data from 42 day population experiments with *Daphnia magna* exposed continuously to increasing concentrations of 3,4-DCA. For each exposure concentration the predicted and observed total population density (upper left panel) and the abundance of three size classes (neonates [upper right], juveniles [lower left], and adults [lower right]) are shown.



The model predictions for the population dynamics showed the same patterns as were observed in the experimental population data sets (Fig. 4). First both model and data showed that for 3,4-DCA concentrations up 10 μg l^{-1} there were no differences in the population dynamics among the treatments. The model predictions for the control, 2.5, 5, and 10 were identical, as the concentration of 3,4-DCA is below the NEC as determined from individual data (Fig. 2). The experimental data confirmed this prediction. The model predicted for the highest two concentrations a deviation from control conditions, which was also observed in the experiments. Most notably the shape of the dynamics over time and the size structure of the population were altered at the highest two concentrations where the differences between the low concentration treatments and the higher two were greatest during the early phase of the test (between 8 and 14 days) in both the model predictions and the experimental data.

Discussion

Using DEB theory gave us a coherent framework for extrapolating the effects of stress from the individual to population level. The strength of having a generic framework was that we were able to use existing theory and methods for identifying the Physiological Mode of Action and quantifying how individuals responded to increasing concentrations of a toxicant. While we were not able to differentiate between two PMoAs, Embryonic Hazard and Reproduction Costs, the differences between these two modes of action are negligible at the population level. Therefore it seems appropriate that in future studies, where identifying population responses to stressors is the major aim, these two PMoAs should be grouped together as “direct reproduction effects”. One point of caution in grouping these PMoAs is that the Embryonic Hazard predicts higher variability in population response compared the Reproduction Costs PMoA, likely reflecting the additional source of stochasticity inherent to the Embryonic Hazard PMoA. This increase in stochasticity may be relevant in cases involving species with low fecundity at low population densities.

Because DEB is a model of individuals, extrapolation to the population level was straightforward using IBM simulations. We have shown that with little modification of the generic approach and by using DEB-IBM it was possible to accurately predict population-level effects of a stressor using only data obtained at the individual level. Not only was the model able to capture the total density, the model also captures the altered dynamics of the size structure. We would like to stress that this was achieved without any further fitting or calibration at the population level. Additionally, the model was able to make extrapolations to environmental conditions not included in the parameterization process. Specifically, in the 21-day *Daphnia* reproduction test, *Daphnia* are fed ad libitum. Conversely, in the population experiments, while the amount of algal food given to each population remained constant, the amount of food per *Daphnia* fluctuated dramatically throughout the duration of the experiments as the population densities increased and decreased due to reproduction and mortality. This highlights a significant benefit of using well constructed, process-based models: the ability to extrapolate to untested scenarios.

Although DEB theory has proven to be a useful framework for extrapolating toxic stress from individuals to populations, there are still open questions, and more development is needed to increase and facilitate its broader use for ecological risk assessment. One notable challenge is the size dependence of resource-dependent mortality. Martin et al. (in press) found that the "standard" DEB model does not accurately capture the size dependence of resource-dependent mortality for *Daphnia*, thus the relative starvation tolerance of juveniles and adults had to be estimated from population level data. This analysis revealed that contrary to the predictions of many generic energetic models, juveniles are more sensitive to starvation than adults. Using the size-dependent starvation submodel parameterised at one population-level experiment, Martin et al. (in press) were able to predict the dynamics at other food levels and initial conditions. Additionally we were able to use the model in novel contexts without further modifications such as the presence of multiple attractors in *Daphnia* consumer resource systems (Martin et al., in press) or the population response of *Daphnia* to a toxicant (this study). However because of the importance of resource-dependent mortality in shaping the dynamics of populations, further work is needed both experimentally and theoretically to develop generic model for resource-dependent mortality.

We were able to parameterize the effect of 3,4-DCA using a data from a single point in time, however for all other PMoAs this would not be possible as the ECx values for both reproduction and growth vary as a function of time (Baas et al. *2010*). This leads to two main challenges. First, many PMoAs can lead to the same ECx for reproduction, and secondly for most PMoAs the effect is time dependent.

Currently, body size is not measured in any standard OECD biotest conducted for risk assessment (Table 1 in Ashauer et al. *2011*). Only in the *Daphnia* reproduction test (OECD 211) size is mentioned as optional endpoint, which, due to cost reduction, is rarely measured. This leads to a problem, as illustrated by Fig. 1, in identifying the PMoA, because most PMoAs will lead to an effect on reproduction, and thus additional data on body size is required to differentiate between possible PMoAs. For example, in addition to direct effects on reproduction, stressors can affect reproduction indirectly through via a decrease in feeding rate, an increase in maintenance costs, and/or an increase in costs for growth. If body size is not measured over time, differentiating between these

PMoAs is impossible as each of these modes of action can lead to the same ECx for reproduction at a given point in time. Simultaneously measuring a second endpoint, such as growth, would require some extra work, however the increase in information it would provide is necessary to identify the PMoA; a critical step in linking the individual and population levels of biological organization. Also, having data for effects on body size and growth eventually may even help to identify patterns across chemicals and species for the PMoA.

Even if the PMoA is known, the parameterization of the effect of the toxicant is dependent on when the measurement was recorded in time (Baas et al. *2010*). In other words, for most PMoAs, a 21 day EC50 is typically the not same as a 14 day EC50. This problem is further complicated as slow toxicokenetics can add an additional source of variation in effects through time. The time-dependence of effects creates a huge barrier for purely statistical approaches, because unique ECx values need to be calculated for every biologically relevant time point. Fortunately, alternative process-based approaches exist, such as DEB, which use the information over time, to quantify time-independent effects (Baas et al. *2010*; Heckmann et al. *2010*). Often as in the *Daphnia* 21 day reproduction test, the data over time is collected but not reported. Thus reporting the data over time can already vastly improve our understanding of sub-lethal effects without additional time or effort.

We have shown a simple example where generic theory allows extrapolation of information on toxic effects from the individual level to the population level. However this represents only one species and one physiological mode of action. The assumption that there is a single PMoA operating over the entire range of exposures requires further exploration. For example, Muller et al. (*2010*) fitted data from several organisms considering two possible PMoAs, a combination of the two but with a single stress parameter and a combination with different stress parameters. In most cases, the individual data could be adequately described by any of the representations, but no population consequences beyond long term population growth rate were modelled or tested. There are strong hints in the theoretical ecology literature that differences in priorities for energy allocations and in energetic costs may profoundly affect population dynamics (e.g., Gurney et al. *1996*; de Roos and Persson *2013*) Further testing of DEB predictions against population data is needed. This will require conducting individual and population level experiments for stressors with different PMoAs, or patterns of effects on life history over time. There is also a challenge for theorists—to develop further generic theory relating different PMoAs to qualitative change in population dynamics.

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Chapter 5: General conclusions

In this thesis, I developed a generic implementation of DEB theory in an IBM context, DEB-IBM (Chapter 2). Using DEB-IBM as a starting point, I parameterized a model for *Daphnia* and then tested the ability of the model to capture dynamics at the population level (Chapter 3). The result of this comparison revealed that while DEB was able to accurately predict the population density and size structure during the population growth phase, and to predict the peak population achieved in experiments with multiple food-levels and initial conditions, after this population peak, when the population began to decline, the model predictions and data diverged. In the experiments, the daily dose of algae cells given to an experimental tank remained constant, thus when the number of *Daphnia* in a tank reached high levels the amount of food per *Daphnia* was very low. This suggests that DEB currently does not capture the relevant processes for *Daphnia* when resources are very low. Our preliminary analysis revealed that the population dynamics during the population decline phase were very sensitive to the size selectivity of resource-dependent mortality. I therefore tested several hypotheses where either the juveniles, adults, or all *Daphnia* were subjected to an additional source of resource-dependent mortality, where the probability of dying is inversely related to the reserve density of the *Daphnia*. Our analysis revealed that the best agreement with the data was given by the model where only juveniles had increased resource-dependent mortality. Using this adapted model I was able to correctly predict population dynamics during the population growth and decline phase for multiple food levels and initial conditions. Additionally I was able to predict, without further calibration, an additional qualitative pattern exhibited by *Daphnia*: the presence of bistability in intermediate prey carrying capacities.

The next goal of this thesis was to test the ability of the model to extrapolate chemical stress measured at the individual level to populations. For this I used information on the effect of 3,4-dichloroanailine at the individual level (Chapter 4). The individual data suggested a direct effect on reproduction, as previous individual-level data sets found no significant effects on growth. Assuming direct effects on reproduction, the model was able to accurately predict the population response to increasing concentrations of 3,4-dichloroaniline.

Individual performance at low food levels

A major result of this thesis is the importance of how resource-dependent mortality scales with size. Currently, starvation is one of the least studied aspects of DEB theory, and of population ecology in general. There have been several suggestions made for how starvation can be included in a DEB context, however most of these possibilities have not been experimentally tested (Kooijman 2010).

The ambiguity about which starvation rules should be used and when, makes accurate *a priori* extrapolation from individuals to populations unlikely. Thus, critical for DEB or any generic model hoping to link the individual and population levels of biological organization, is an understanding of individual dynamics at low food levels.

Below I discuss several of the starvation hypothesis outlined in Kooijman (2010), and discuss their plausibility for *Daphnia*.

Starvation rule 1:

Do not deviate from standard rules. If an individual cannot mobilize enough energy to pay somatic maintenance then the individual dies. This condition is met when scaled reserve density (e) falls below scaled length (length as a proportion of maximum length):

$$e < \frac{L}{L_M}$$

This rule has the consequence that fully-grown individuals will die immediately if feeding is not *ad libitum*. I rejected this hypothesis for *Daphnia* and likely all other species, as adult *Daphnia* can survive days without food (Tessier et al. 1983).

Starvation rule 2:

The second starvation rule described in Kooijman (2010) is one where the individual deviates slightly from standard rules by using energy previously allocated to reproduction to pay maintenance (κ is the allocation fraction to somatic maintenance and growth). This buys individuals extra time and the new threshold for death is given by:

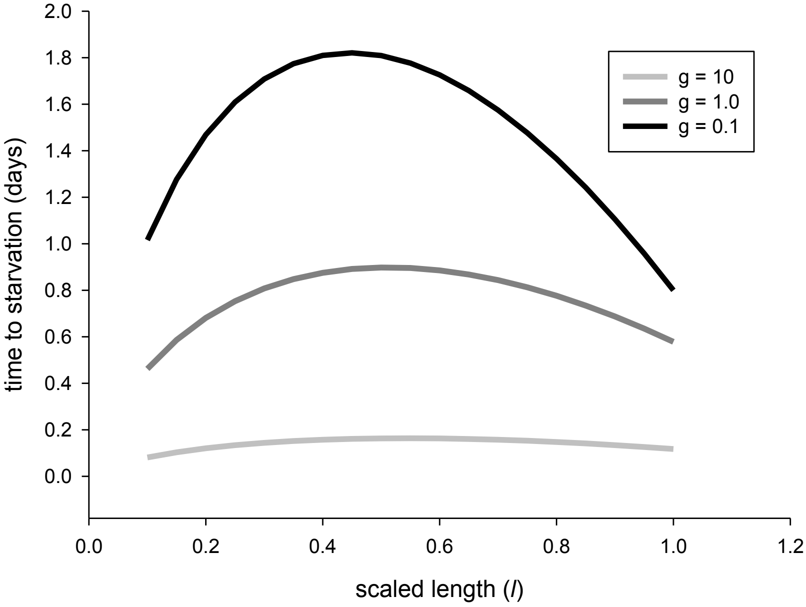
$$e < \kappa \frac{L}{L_M}$$

Assuming no changes in size, the time to starvation is given by:

$$time\_to\_starve = \frac{-l \log(\kappa l)}{g\dot{k}_m} \qquad eq.1$$

(Kooijman 2010). This results in a hump-shaped relationship between the time to starvation and body size, with intermediate-sized individuals having the greatest starvation resistance. However, with the parameter set used for *Daphnia*, energy investment ratio, g, was fixed to 10, which results in extremely short starvation times (Figure 1). This is because a g of 10 corresponds with a high value for the

Fig. 1 Predicted time to starvation for *Daphnia* after being switched from ad libitum food to no food as a function of scaled length (length/ maximum length) by *eq 1*. The three lines represent the predicted starvation times using parameter values where g was fixed to 0.1, 1.0, or 10 (Chapter 3; Table B1).



energy conductance parameter $\dot{v}$, which makes reserve turnover, and thus reserve depletion, very rapid. Fixing *g* or $\dot{v}$ to a lower value increases the time to starvation, however *g* needed to be fixed to values below 0.1 to generate starvation times consistent with those observed for *Daphnia magna*. With *g* fixed at such a low value, resulting parameter sets do not provide satisfactory fits to the growth and reproduction data. Thus, *g* can be fixed to produce either good fits to dynamics under high food conditions, or low food conditions, but not both simultaneously.

Because the starvation times were too short when using reserve as a trigger for starvation, I invoked another mechanism, by allowing individuals to burn somatic mass to pay maintenance costs. Mortality now was triggered by shrinking below a critical proportion (*VCrit*) of the individual's previous maximum structural volume. I chose a threshold of 40% of the previous maximum mass based on the midpoint of the range observed for *Daphnia magna* (Perrin et al. 1990; Bradley et al. 1991). This assumption leads to starvation times within the range observed for

Daphnia (mean time to starvation was approximately 5 days with negligible differences among sizes). However, at the population level, this model led to poor agreement between model and data. The resulting dynamics were sensitive to the value of *VCrit*, but no value of *Vcrit* led to qualitatively similar patterns between model and data. At lower values of *Vcrit*, very few individuals die, and for higher values there was very high mortality but in choppy phases. This may be because the state variables of individual *Daphnia* tended to converge during resource-poor conditions (small individuals kept growing for some time while larger individual could not grow). Additionally, because starvation was not absolute (going from *ad libitum* food to no food instantaneously) but rather gradual, the balance of starvation tolerance was shifted in favor of juveniles, and thus larger individuals were the first to starve. *Daphnia* that died from starvation in the simulations were on average more than 90% of the length of the largest *Daphnia* in the simulation for all three experimental conditions simulate.

One possibility I have not investigated in this thesis is that maintenance costs are not fixed, but they rather decrease during starvation, possibly at the expense of decreased probability of survival. This could allow for starvation tolerance curves similar to those in Figure 1 while still providing a satisfactory fit to growth and reproduction. The challenge however, is knowing exactly by how much and in what manner maintenance costs are reduced, and how this trades off with survival. Unfortunately, while this still remains a plausible explanation, currently the data needed to answer these questions are not available.

Because of these data challenges I worked the other way around, and tried to test various hypotheses about starvation tolerance in *Daphnia* at the population level to infer something about how individuals perform. I tested three submodels where either juveniles, adults or all *Daphnia* were subjected to mortality with a probability inversely related to reserve density. The result of our analysis revealed that only assuming the additional mortality sub-model for juveniles resulted in the best agreement at the population level. This is also in agreement with studies of individual *Daphnia*. Although in our study we linked starvation probability to reserve density, reserve in this context merely played the role as an aggregate measure of feeding history. Qualitatively identical results were achieved when starvation probability was dependent on recent feeding history (e.g. average f experienced by the *Daphnia* over the molt period). Thus below I broaden the discussion by considering starvation in the context of a reserveless model.

When the speed of reserve turnover increases toward infinity, reserve becomes infinitely small and falls out of the model resulting in a simple model for growth:

$$\frac{dm}{dt} = \kappa\left(fam^{2/3} - bm\right) \qquad eq.2$$

where a is related to surface area-specific assimilation rate, b is related to the mass-specific maintenance costs, and f denotes the scaled functional response. Under constant conditions the model is equivalent to the von Bertalanffy growth equation. This is also strikingly similar to the ontogenetic growth model, with the exception that energy allocation to maturation and reproduction is not considered in the OGM model (assumed $\kappa = 1$) and in the power of the first term which is 3/4 rather than 2/3 (Hou et al. 2008). Here, body mass serves as a "reserve" during starvation and when the assimilation flux cannot meet maintenance costs the individual will shrink, with death occurring when an individual falls below a certain threshold of its previous maximum mass.

Under these assumptions and due to the proportionality of maintenance costs with body mass, both models predict that starvation tolerance will be independent of size. In the case that food availability decreases from high food to no food more gradually, the advantage shifts toward smaller individuals which will continue to grow at food levels where larger individuals are already beginning to shrink in mass.

These two predictions seem to go against the limited data available on starvation. For individual data sets, where individuals underwent absolute starvation (*ad libitum* to complete starvation), the majority of studies have found that larger individuals of a species survive longer than smaller individuals (Tessier et al. 1983; Borchers and Hutchings 1986; Tsuda 1994). Additionally at the population level, the presence of small amplitude cycles observed for *Daphnia* in dynamic consumer resource systems, driven by the survival of adults through the decline phase of the population cycle, seems to indicate that often adults maintain a survival advantage during periods of gradual food reduction (Ananthasubramaniam et al. 2011).

In Chapter 3, I outlined several potential mechanisms that could confer an advantage toward larger individuals:

1) The proportion of the previous maximum mass that an individual can shrink to before death could decrease as a function of size (larger individuals can shrink to a lower proportion of their previous maximum mass before they starve).

2) Specific energy storage or reserves may increase with size.

3) Mass specific metabolic rates may decrease with size.

4) Energy utilization may be partially inflexible (smaller individuals continue to catabolize energy stores to continue to develop for some time after food levels decrease).

Currently there are not enough data available to test these hypotheses, but well designed experiments to test these hypotheses may lead to critical insight needed to understand and predict the ontogeny of starvation tolerance. Even more needed are multi-species studies examining starvation tolerance over the range of body sizes observed for a species. Because so few studies have examined how size affects starvation tolerance within a species, it is currently unknown if general patterns exist. If general patterns do exist, measuring over a continuous range of body sizes is critical to identify the shape of the relationship (e.g., is the relationship hump-shaped, or monotonically increasing or decreasing).

Our results have highlighted how critical it is to correctly understand patterns in resource-dependent mortality for predicting population dynamics. Because different assumptions about starvation tolerance can lead to quite different dynamics, and because currently so little is known about which assumption is correct in a specific situation, this remains an important but overlooked area of research in population ecology. It remains to be seen if generic models will be able to predict patterns of starvation for various species without extensive experimentation for each species, but the role of generic models in connecting the individual and population level depends on it. One hope is that the ubiquity of von Bertalanffy growth under constant resource conditions will be mirrored by another general pattern during poor resource conditions.

Is representing reserve necessary?

Another significant outcome of this thesis is that parameters relating to the speed of reserve turnover, specifically $\dot{v}$ (which tightly covaries with g), are difficult to specify using growth and reproduction data alone. Additionally I showed that for at least one species, fixing g or $\dot{v}$ to given parameter values within the range that still provides satisfactory fits to individual growth and reproduction data sets has negligible affects at the population level. This is due to the fact that the most likely parameter sets based on fits to individual growth and reproduction data produced values of $\dot{v}$ in which reserve dynamics were so rapid that the resulting model predictions could hardly be distinguished from infinitely rapid reserve dynamics at neither the individual or population level. With either g or $\dot{v}$ fixed, or in a reserveless model in general, all other parameters could be well specified by the individual data sets. Our results call into question the practicality and utility of including a reserve state variable in a population context (at least for *Daphnia*).

In a population context, the most compelling argument for the inclusion of reserve as a state variable set apart from structure is its capacity to act as a metabolic memory. Obviously, there is a time lag between consumption of a resource and its allocation to growth or reproduction. If this lag time is significant, this could lead to important consequences at the individual level when food is variable. Because food availability is rarely ever constant in natural environments and because populations generally have strong feedbacks on their environment, these consequences could translate to significant effects at the population level. Additionally, if the function of reserve as a metabolic memory extends to prolonged periods of starvation, reserve dynamics can be used to understand and predict size dependence of starvation tolerance, which is so critical to understanding population dynamics. Both of these arguments would be convincing reasons for the inclusion of a reserve. However, the work from this thesis challenges both of these points.

The first problem is that for *Daphnia* at least, the time lags in relation to changing feeding conditions seem to be rather insignificant. Figure 2 shows a dataset for individual growth where individual *Daphnia* were raised at a high (a) or low (b) food level (data from Kooijman 1986). The remainder of the experiments started out with one of the two food levels and then was switched at either day 7, 14, or 21 to the other food level. The lines in each of these figures represent the fit of the DEB model using the same parameter set as used in Chapter 3 and 4, where g was fixed to 10. The only datasets used to parameterize the model were the experiments where food was kept constant at either the high or low algal density. These datasets were used to estimate the scaled functional response (f) for each food concentration. These values were then used to predict body sizes in the remaining experiments where *Daphnia* were switched from one algal density to another.

With this parameter set, reserve turnover is extremely fast and thus there is negligible lag time in response to changing food. Therefore, if delays between food level and allocation to growth are important, a poor match between model and data should be expected. However, this does not seem to be the case as the model and data are in fairly good agreement. The largest discrepancy between model and data can be accounted for by the fact that I assumed a constant f for each food level. However, these were semi-batch experiments where a fixed amount of food was given to each *Daphnia* at the beginning of the day. Because of this, food is depleted throughout the day, and thus the food level experienced throughout the day may change. As *Daphnia* grow we should expect food depletion to be larger, due to increasing assimilation abilities. Thus, even when algae cells given per day is constant, the actual f experienced by a *Daphnia* decreases with size. Therefore, when fitting a model assuming a fixed f, we should expect an underestimation of growth at small sizes, and an overestimation at larger sizes. This is in fact the exact pattern observed in the experiment under constant food conditions, that also explains the deviation in the changing food treatments in Figure 2d.

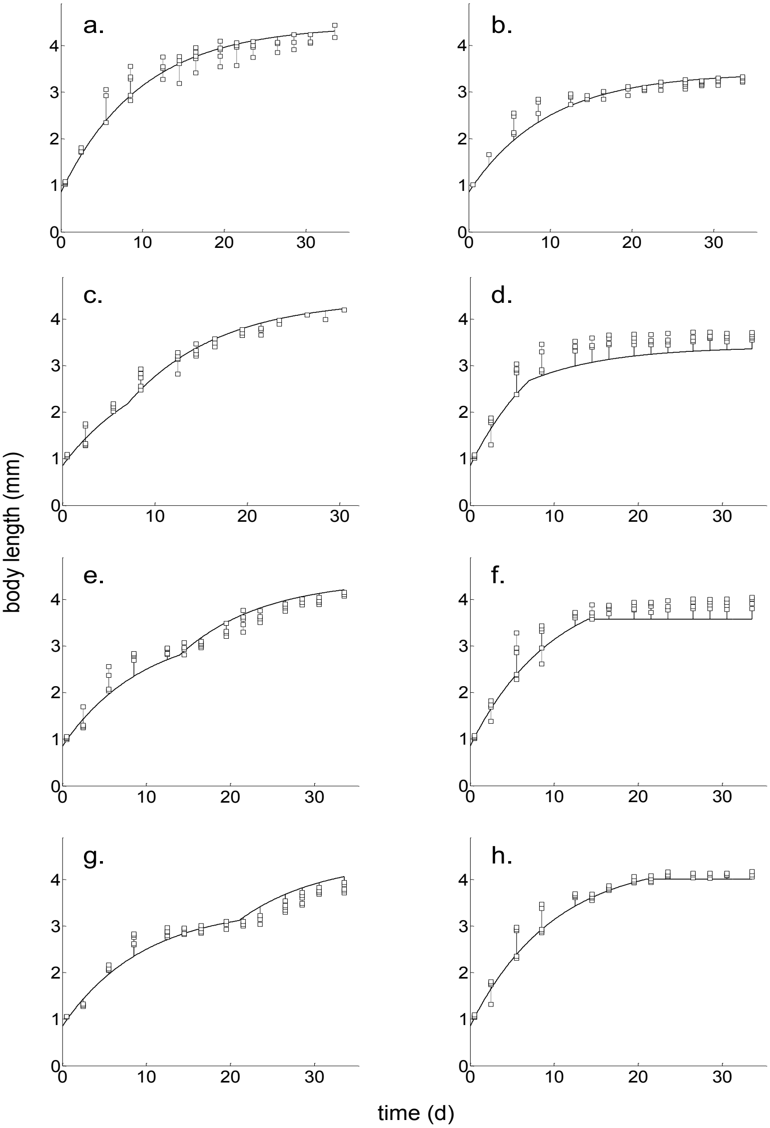


Fig. 2 Observed (open squares) and predicted (lines) body sizes over time for *Daphnia magna* at 20C fed either a constant daily dose of green algae at either a high (a.) or low (b.) density, or switched from one feeding level to another (c.-h.). Panels c., g., and e. show the scenario where *Daphnia* were switched from the low food concentration to the high food concentration at 7, 14, or 21 days after birth, respectively. Panels d., f., h., show the scenario were *Daphnia* were initially feed at the high daily food density and switched to the low food density on days 7, 14, or 21 respectively. The model predictions used parameter values from Table 1, in Chapter 3. Only panels a. and b. were used to estimate *f* for each food concentration.

This highlights an even stronger argument for not including reserves. As *Daphnia* approach larger sizes in non-*ad libitum* conditions, depletion of food becomes quite severe throughout the day (from *ad libitum* to no food in a 24 hr period), yet the model is still able to capture patterns in growth and reproduction in batch-fed conditions (Appendix 3B, Figure 6). The same dynamics occurred at the population experiments (Chapter 3 and 4), which were also semi-batch experiment. Throughout the population growth phase, individuals in the population experienced feeding conditions ranging from complete starvation to *ad libitum* feeding, yet the predictions at the population level remained accurate even in the reserveless model. This seems to highlight that using somatic mass rather than reserve as a form of metabolic memory seems equally capable of handling changing feeding conditions. One caveat is that for my analysis I used *Daphnia*, a relatively small species. According to DEB theory maximum reserve density scales with length. Therefore, for larger species, the importance of reserve may be more significant, and for smaller species reserveless models more appropriate.

In addition to not being necessary to capture short-term changes in food conditions, reserve dynamics, for *Daphnia* at least, is not able to capture patterns in long-term starvation-induced mortality. As discussed previously, parameter values of g and $\dot{v}$ that gave reasonable fits to growth and reproduction data, grossly underpredicted starvation times using the two common DEB starvation rules. Thus, the reserve concept alone (death occurs when reserve mobilization is not enough to match maintenance costs) without further modification of the starvation rules, is not sufficient to explain patterns of resource dependent-mortality. Because to date, the combination of reserve with more complex starvation rules has not been systematically tested for a wide range of species, including reserve currently provides little predictive capabilities for modelling population dynamics.

I have shown that for at least one species including a reserve compartment has little benefit in modelling short-term responses to changing feeding conditions, or predictions for when starvation should occur. These two points, in addition to the difficulty in specifying the parameter values associated with reserve turnover rates, call into question the practicality of including reserve in a population context. I found that using growth and reproduction data alone was not enough to specify reserve parameters for *Daphnia*. Other approaches use information about the length of the embryonic period to specify the value of $\dot{v}$.However for many species DEB does not make accurate predictions for embryonic development time, and this has been attributed to either diapause (Jager et al. 2010) or metabolic acceleration (Augustine et al. 2011). If reserve is to be used, further work is needed in accurately specifying the parameters $\dot{v}$ and g without a large increase in data requirements and in identifying the relative contribution of reserve and structure during prolonged periods of starvation.

Implications for risk assessment

The work from this thesis represents the first combined use of IBM and DEB to predict the effect of a toxicant at the population level using only individual level data. The strong agreement between model predictions and data show the strength of the approach. However, for this approach to be used in standard risk assessment, more comprehensive data collection and reporting is needed. As I outlined in Chapter 4, reproduction data at one time point is not enough to specify the Physiological Mode of Action, PMoA, which is a critical step in extrapolating from the individual to population level. The first and easiest problem to solve in using DEB and IBM for risk assessment is thus reporting data over time. For the 21 day *Daphnia magna* reproduction test, reproductive output is measured every 2 to 3 days, thus the only change required is reporting cumulative reproduction over time rather than at one time point. This is critical because toxicity is a dynamic process in time (Baas et al.2010; Heckmann et al. 2010). The effect over time can be due to slow toxicokinetics where the internal concentration is not constant over time, or additionally due to the changes in the individual (i.e. change in body size over the duration of the exposure). In both DEB and real individuals, the magnitude of various energy fluxes changes over time. For example, the proportion of energy allocated to growth or maintenance costs changes with body size. Thus the percentage reduction compared to a control in a measurable quantity, such as growth is not constant over time. Because in DEB different fluxes change differently with respect to body size, this information is very useful when specifying the most likely PMoA. Measuring body size in addition to reproduction is critical to identifying the most likely PMoA. First, the effects for the various PMoAs on body size are much more differentiated than on reproduction (Chapter 4, Figure 1). Additionally because energy acquisition, and therefore energy availability for reproduction, is highly dependent on body size, effects on reproduction in isolation are impossible to interpret from an energy budget perspective.

Lastly, although our model made accurate predictions for one chemical-species combination, if linking DEB and IBMs is to be a truly generic approach, we need further testing of chemicals and models at both the individual and population level. Specifically, it is important to test chemicals with different PMoAs that result in effects on both body size and reproduction.

Concluding remarks

Overall this thesis shows the potential for developing generic representations of individuals that in combination with IBMs can be used to link the individual and population levels. The results of this thesis give some promise for standardizing the link between individuals and populations, however further work is needed in investigating patterns of resource-dependent mortality. When I included a submodel to account of patterns of size-dependent, resource-dependent mortality, we were able to use the DEB to accurately predict population dynamics in laboratory experiments. I also demonstrated the potential power of the approach for applied contexts, such as extrapolating chemical stress from the individual to population level. Using cross-level tests, I was able to identify areas where theory development and experimentation are needed. Further research identified by our cross-level tests may allow for both generic and accurate extrapolations between the individual and population level.

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Summary

Understanding how the structure and dynamics of populations emerge is one of the fundamental challenges in ecology. As the influence of individual variation, local interactions, and adaptive behaviour on population dynamics have become more appreciated, individual-based models (IBMs) are playing an increasing role in both basic and applied disciplines. IBMs represent individual organisms as unique entities that differ from each other and change over their life cycle. Individuals are characterized by a set of state variables and attributes that are chosen according to the problem addressed with the model. Individuals behave as autonomous entities according to behavioural rules. They interact with each other and their abiotic environment, including habitat structure and environmental drivers such as temperature, humidity, or disturbances. Population dynamics emerge from these interactions.

IBMs have been shown to be powerful and flexible tools. However, they have also been criticized for often being based on ad hoc assumptions and representations of individual dynamics and behaviour. This makes the development of IBMs inefficient and the field of individual-based modelling incoherent. To facilitate re-usability of IBMs and their elements, and to facilitate distilling general insights from specific IBMs, it is desirable to base IBMs more on standardized and well-tested approaches for individual behaviour.

Dynamic Energy Budget (DEB) theory is such an approach. It has been developed with the goal of understanding the dynamics of biological systems, from cells to ecosystems, via a balance approach for mass and energy. As in IBMs, in DEB theory individuals are considered the key unit of interest for understanding dynamic systems at higher levels of organisation. Focusing on the individual is motivated by the fact that mass and energy balances are easier to calculate for individuals than for higher or lower levels of biological complexity. DEB theory provides a quantitative framework for modelling the acquisition and use of resources for organisms over the entire life cycle. It thereby generates a quantitative explanation for the time patterns of life-history traits such as growth, maturity, and reproduction in dynamic environments.

Thus, the use of IBMs in combination with DEB theory has the potential to strengthen the field of population ecology. Because DEB theory provides a generic framework for modelling the life-history of an individual, the same modelling framework can be used for all species. This increases the generality

of model results, as the differences in the behaviour of models of different species can be ascribed to differences in parameter values, rather than to differences in any part of the model structure. IBMs, in turn, allow those working with DEB theory at the individual level to test the consequences of individual-level processes at the population level via simulations.

Despite the great potential of Dynamic Energy Budget theory as the foundation for IBMs, their use together has been limited. To facilitate their combination, I developed a framework for using DEB theory in connection with IBMs: DEB-IBM. DEB-IBM is an accessible implementation of DEB in which a user can enter the DEB parameters of a species and evaluate their dynamics at the population level under various resource conditions. More importantly however, users can adapt the code to address specific research question, for example, how the distribution of resources over space alters the stability of populations in time, or how stressors, such as pesticides alter the dynamics of populations.

Using the DEB-IBM framework I tested the ability of the DEB theory to predict population-level dynamics from the properties of individuals. I used *Daphnia magna* as a model species, where data at the individual level was available to parameterise the model, and population-level predictions were compared against independent data from controlled population experiments.

I found that DEB theory successfully predicted population growth rates and peak densities of experimental *Daphnia* populations in multiple experimental settings, but failed to capture the decline phase, when the available food per *Daphnia* was low. Thus, the analysis revealed that correctly representing resource-dependent mortality is critical for linking individual and population levels. The fact that the standard DEB model was unable to capture patterns of resource-dependent mortality reflects the fact that most work on individuals has been conducted under relatively favourable food conditions. Further assumptions on food-dependent mortality of juveniles were needed to capture the population dynamics after the initial population peak. Specifically, the assumption that juveniles were more vulnerable to resource dependent mortality than adults. The resulting model then predicted, without further calibration, characteristic switches between small- and large-amplitude cycles, which have been observed for *Daphnia* populations. I conclude that cross-level tests help detecting gaps in current individual-level theories and ultimately will lead to theory development and the establishment of a generic basis for individual-based models and ecology.

In addition to theoretical explorations, I tested the potential of DEB theory combined with IBMs to extrapolate effects of chemical stress from the individual to the population level. For this I used information at the individual level on the effect of 3,4-dichloroaniline on *Daphnia*. The individual data suggested direct effects on reproduction but no significant effects on growth. Assuming such direct effects on reproduction, the model was able to accurately predict the population response to increasing concentrations of 3,4-dichloroaniline. Interestingly, the model was able to make extrapolations to environmental conditions not included in the parameterization process. Specifically, in the 21-day *Daphnia* reproduction test, *Daphnia* are fed *ad libitum* however, in the population experiments the food amount of food per *Daphnia* fluctuated dramatically. This highlights a significant benefit of using well-constructed, process-based models: the ability to extrapolate to untested scenarios.

In addition to showing the potential for linking individual and population levels, our result also highlight several shortcomings of current standard risk assessment tests. The practice of measuring chemical effects on reproduction without concurrently measuring body size is insufficient to predict population level effects. This is because stress on many physiological processes can result in a reduction in reproduction (reduced feeding, increased maintenance costs, mortality of embryos, etc.). However, these processes can have very different effects at the population level. With limited extra effort, standard tests at the individual level could deliver data that could considerably improve the applicability and precision of extrapolation to the population level. Specifically, the measurement of a toxicants effect on growth in addition to reproduction, and presenting and analysing data over time as opposed to relying on a single number to represent the toxicity at the end of the test (such as NOEC or EC50).

In conclusion, this thesis shows the potential of DEB and IBMs in combination to help illuminate the links between individual and population levels in both basic and applied contexts. The advantage of using a generic approach is that the lessons learned are directly transferable to other species.

Zusammenfassung

Für die ökologische Risikobewertung von Chemikalien sind individuenbasierte Populationsmodelle ein vielversprechendes Werkzeug um heutige Bewertungen ökologisch realistischer zu gestalten. Allerdings ist die Entwicklung und Parametrisierung derartiger Modelle zeitaufwendig und oft wenig systematisch. Standardisierte, geprüfte Untermodelle, die Einzelorganismen beschreiben, würden die individuenbasierte Modellierung effizienter und kohärenter machen. In meiner Dissertation habe ich daher untersucht, inwieweit sich die *Dynamic Energy Budget*-Theorie (DEB) als Standardmodell innerhalb individuenbasierter Populationsmodelle eignet, und zwar sowohl für die ökologische Risikobewertung als auch für die theoretische Populationsökologie.

Zunächst habe ich eine generische Implementierung der DEB-Theorie im Rahmen individuenbasierter Modellen (IBM) erstellt: DEB-IBM. Dieses Werkzeug nutzend habe ich dann untersucht, ob es mit Hilfe der DEB-Theorie gelingt, ausgehend von den Eigenschaften und Aktivitäten einzelner Individuen, Populationsdynamik vorherzusagen. Wir nutzten dabei *Daphnia magna* als Modellart, für die Daten auf der Individuenebene verfügbar waren, um das Modell zu parametrisieren, sowie Populationsdaten, mit denen Modellvorhersagen verglichen werden konnten.

DEB-Theorie war in der Lage, beobachtete Populationswachstumsraten sowie die maximalen Abundanzen korrekt vorherzusagen, und zwar für verschiedene Umweltbedingungen. Für Phasen des Rückgangs der Population allerdings, wenn die für die *Daphnien* verfügbare Nahrungsmenge gering war, kam es zu Abweichungen. Es waren deshalb zusätzliche Annahmen über nahrungsabhängige Sterblichkeit von juvenilen *Daphnien* erforderlich, um die gesamte Populationsdynamik korrekt vorherzusagen. Das resultierende Modell konnte dann, ohne weitere Kalibrierungen, den für *Daphnien* charakteristischen Wechsel zwischen Populationszyklen mit großen und kleinen Amplituden richtig vorhersagen. Wir folgern daraus, daß Ebenen

übergreifende Tests dabei helfen, Lücken in aktuellen Theorien über Einzelorganismen aufzudecken Dies trägt zur Theorieentwicklung bei und liefert Grundlagen für individuenbasierte Modellierung und Ökologie.

Über diese Grundlagenfragen hinaus haben wir überprüft, ob DEB-Theorie in Kombination mit IBMs es ermöglicht, den Effekt von chemischem Streß auf Individuen auf die Populationsebene zu extrapolieren. Wir nutzten Daten über die Auswirkungen von 3,4 Dichloroanalin auf einzelne *Daphnien*, die zeigten daß im Wesentlichen die Reproduktion, nicht aber das Wachstum beeinträchtigt ist. Mit entsprechenden Annahmen konnte unser Modell den Effekt auf Populationsebene, für den unabhängige Daten vorlagen, korrekt vorhersagen. DEB-Theorie in Kombination mit individuenbasierter Modellierung birgt somit großes Potential für einen standardisierten modellbasierten Ansatz in der ökologischen Risikobewertung von Chemikalien.

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