

Estimation of time-varying mortality rates using continuous models for *Daphnia magna*

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Abstract

Structured population models that make the assumption of constant demographic rates do not accurately describe the complex life histories seen in many species. We investigated the accuracy of using constant versus time-varying mortality rates within discrete and continuously structured models for *Daphnia magna*. We tested the accuracy of the models we considered using density-independent survival data for 90 daphnids. We found that a continuous differential equation model with a time-varying mortality rate was the most accurate model for describing our experimental *Daphnia magna* survival data. Our results suggest that differential equation models with variable parameters are an accurate tool for estimating mortality rates in biological scenarios in which mortality might vary significantly with age.

Key Words: Structured population model, Leslie matrix model, Sinko-Streifer model, *Daphnia magna*, time-dependent mortality rate

1 Introduction

The most widely used structured population models in ecology are those in which the structured variable is discrete, i.e., a Leslie matrix model [1, 11, 14, 15, 20, 27]. In such discrete models, one typically assumes (i) constant parameter rates, (ii) that individuals can be lumped into discrete classes, (iii) that time can be divided into discrete intervals. Although these model attributes enable fast computation and the application of tools for steady state analysis, they can also lead to instabilities in the data fitting process [5, 29]. Moreover, computation with discrete models can become intractable when using more

realistic time-dependent parameters rather than constant parameters. As an alternative approach, it has previously been suggested that the Sinko-Streifer population model, which uses partial differential equations (PDEs) with a continuously structured variable, is more amenable to describing time-varying parameters and that its use significantly increases accuracy in fitting population data [3, 7].

In this work we compared the accuracy of a discrete matrix model versus a differential equation model in describing density-independent survival data. With both models we also tested the accuracy of using constant versus time-varying parameters. All models we considered were tested using survival data collected for *Daphnia magna*. Daphnids are a compelling system for investigating the accuracy of assumptions about the estimation of age-varying rates because their life history parameters vary with age [1, 16, 18, 23]. Moreover, daphnids are an important species in the context of evolution, ecology, and environmental toxicology. Ecological risk assessments that use daphnids are most commonly performed at the organismal response level. Structured population models can be used to quantitatively propagate organismal level risk assessment information, such as density-independent survival data, to the population level. Thus, improving the estimation of density-independent mortality rates for daphnids may consequently increase the accuracy with which organismal response data is used to predict adverse effects on populations. Here we show that a differential equation model with time-varying parameters best describes our daphnid survival data. This work paves the way for the construction of a validated continuously structured population model for daphnids, which we expect will provide an improvement to previously published models [1, 16, 17, 18, 23, 24].

2 Data and Methods

2.1 Density-independent *Daphnia magna* survival data

Ninety daphnids were longitudinally observed and survival was recorded daily. All daphnids were maintained in individual isolation using previously described protocols and conditions [28]. The daphnids were kept in media reconstituted from deionized water [2] and maintained in an incubator at 20 degrees celsius with a 16-h light, 8-h dark cycle. The daphnids used in our study came from a colony that was maintained at North Carolina State University for over 20 years (clone NCSU1 [25]). Less than 2-h old female neonates were placed individually each into 50mL beakers containing 40mL of media which was changed daily. Daphnids were fed daily with 7.0×10^6 cells of algae (*Pseudokirchneriella subcapitata*) and 0.2 mg (dry weight) TetrafinTM fish food suspension prepared as described previously [21]. Each beaker was checked daily for the presence of new offspring and these neonates were removed daily. The ninety daphnids came from three equally sized groups: thirty daphnids were exposed daily to a .3nM concentration of pyriproxyfen (“Pyriproxyfen + Carrier” group), thirty daphnids were exposed daily to .2 μ L ethanol (“Carrier” group), and thirty daphnids were not treated with any chemicals (“No treatment” group). The amount of

ethanol used in the carrier group is the amount that was used to dilute the pyriproxyfen for the “Pyriproxyfen + Carrier” group. Since no statistically significant difference in survival was found between the three daphnid groups (see Section 3 below), data from all three groups were combined into a single data set for ninety daphnids (“Combined” group) for all subsequent analysis.

2.2 Mathematical models

To test the accuracy of continuous models for describing daphnid survival data, we used a density-independent form of the Sinko-Striefer PDE model [26]:

$$\begin{aligned} u_t(t, x) + (g(t, x)u(t, x))_x &= -\mu(t, x)u(t, x) \\ g(t, x_0)u(t, x_0) &= \int_{x_0}^{x_1} k(t, \xi)u(t, \xi)d\xi, \end{aligned}$$

where x_0 is the minimum age (0 days) and x_1 is the maximum age (the maximum observed age was 91 days). The state variable $u(t, x)$ is the population density at age x and time t , $g(t, x)$ represents the rate at which daphnids age, $\mu(t, x)$ is the mortality rate, and $k(t, x)$ is the fecundity rate. The individual level survival data in the combined data set were time shifted so that the age of all the daphnids was zero at time zero. Hence, age and time progress at the same rate in the survival data and $g(t, x) \equiv 1$. We also assume that $k(t, x) \equiv 0$ since newly born neonates were removed daily. This allows us to simplify our PDE model to

$$\begin{aligned} u_t(t, x) + u_x(t, x) &= -\mu(t, x)u(t, x) \\ u(t, x_0) &= 0. \end{aligned}$$

Using the method of characteristics with $t(s) = x(s) = s$, $\tilde{u}(s) = u(t(s), x(s))$, and $\tilde{\mu}(s) = \mu(s, s)$, we can show that the PDE can be written

$$\begin{aligned} \frac{d\tilde{u}}{ds} &= -\tilde{\mu}\tilde{u}, \\ \tilde{u}(s_I) &= 90, \end{aligned}$$

where $s_I = t_I$ is the time at which the initial 90 daphnids (neonates) are introduced. To test the accuracy of discrete models for describing daphnid survival data, we also used a Leslie matrix model [20] with zero fecundity and mortality $\tilde{\mu}$.

2.3 Inverse problem methodology

In order to estimate $\tilde{\mu}$, we employed an ordinary least squares framework that is widely used to estimate model parameters from data [10, 12]. This technique, which, under well known assumptions on the statistical error model of the data observations, is equivalent to

maximum likelihood estimation [10, 12]. Formally, this technique minimizes the residual sum of squares

$$J(\tilde{\mu}) = \sum_{i=1}^n (\tilde{u}(s_i; \tilde{\mu}) - y_i)^2$$

where y_i is data for the number of living daphnids at time s_i and n is the number of data points. For more information on this estimation framework, see [10, 12].

For both the Leslie and PDE models we used multiple forms of $\tilde{\mu}$. To model a constant mortality rate, we used $\tilde{\mu} \equiv \bar{\mu}$ for some constant $\bar{\mu}$. To model an age-dependent mortality rate, we described $\tilde{\mu}$ using a piecewise constant function for the Leslie model and a piecewise linear spline function for the PDE model.

2.4 Model comparisons

We used the Akaike Information Criterion (AIC) score to compare the accuracy of different models to the combined survival data set for ninety daphnids; a lower AIC score indicates higher accuracy. The AIC score gives an approximately unbiased form of the Kullback-Leibler Distance, or a measure of the distance between a model and the corresponding data [10, 13]. The AIC score we used was corrected for small sample size ($n/p < 40$, n = number of data points, p = number of parameters) and is given by the formula $AIC_C = n \ln \left(\frac{RSS}{n} \right) + 2p + \frac{2p(p+1)}{n-p-1}$, where RSS is the residual sum of squares and p is the number of estimated parameters. We note that we also used the (AIC_C) score to determine how many nodes to use for the piecewise linear spline and piecewise constant functions. We added more nodes to the estimation procedure until it did not provide a significant improvement to the AIC_C score.

3 Results

To test the accuracy of several mathematical models to daphnid survival data, we first generated an experimental data set consisting of survival numbers for ninety daphnids. We used a log-rank test on the Kaplan-Meier survival distributions [19] from the “No treatment”, “Carrier”, and “Pyriproxyfen + Carrier” data sets (Figure 1, left) to determine if there was a statistically significant difference in mortality between the three corresponding experimental groups. The Kaplan-Meier method provides an estimate of the survival distribution for each experimental group, and the log-rank test is a hypothesis test for the null hypothesis that there is no difference between these distributions [22]. The log rank test shows that the null hypothesis cannot be rejected for the “No treatment” vs “Pyriproxyfen + Carrier” groups ($P = 0.3783$), for the “Pyriproxyfen + Carrier” vs “Carrier” groups ($P = 0.7335$), nor for the “Carrier” vs “No treatment” groups ($P = 0.7657$). This suggests that *there is no statistically significant difference in mortality between any of the three groups*. Similarly, we found no statistical difference between the “No treatment” and “Combined”

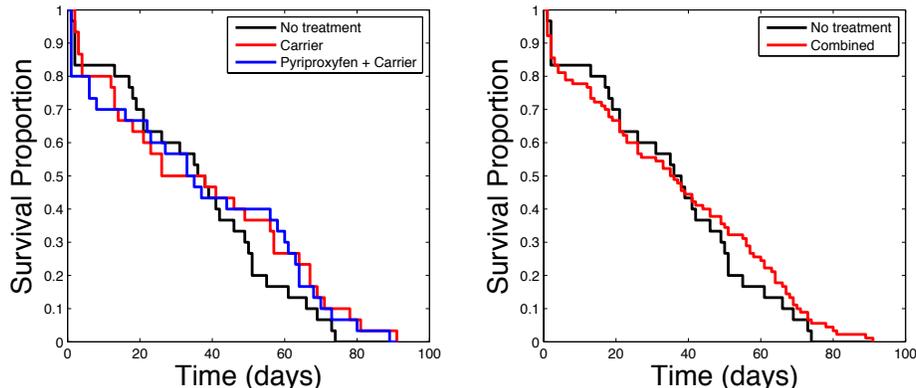


Figure 1: Left: The proportion of surviving daphnids from three groups: no exposure (No treatment), exposure to ethanol (Carrier), or exposure to pyriproxyfen and ethanol (Pyriproxyfen + Carrier). Right: The proportion of surviving daphnids from the no exposure group (No treatment) and the combined set of daphnids from all three groups (Combined).

groups (Figure 1, right, $P = 0.4725$). Hence, we used the “Combined” group data set for all subsequent analysis.

For both the PDE and Leslie models, a constant mortality rate drastically misrepresented the decline in the daphnid population at most ages, while a time-varying mortality rate was better able to capture the survival dynamics at all ages (see Figure 2). The AIC_C values for the Leslie model with constant and time-varying mortality rates (using 18 nodes) were 327.12 and 62.39, respectively. The AIC_C values for the PDE model with constant and time-varying mortality rates (using 12 nodes) were 329.38 and 3.71, respectively. These results confirm that the Sinko-Streifer model with a time-varying mortality rate provides the best fit to the daphnid survival data.

4 Discussion

As seen in this study (Figure 2), a constant mortality model will overestimate survival in the first 11 days, underestimate survival between days 11 and 60, and overestimate survival after 60 days, while a time-varying rate can accurately capture the changing survival dynamics. The non-monotone form of the estimated linear spline function for $\tilde{\mu}(t)$ suggests that the set of daphnids we observed might be composed of at least three subpopulations (Figure 3). The first subpopulation experiences rapid mortality, dying within 8 days. The second subpopulation experiences gradual mortality at a logistic rate within 72 days. The third subpopulation lives up to 90 days. The mortality seen in these subpopulations cannot

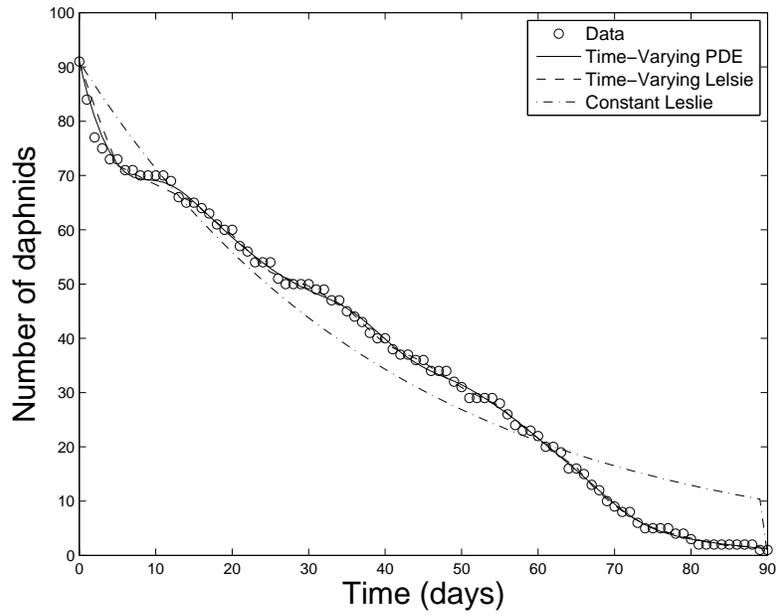


Figure 2: Results from fitting different functional forms for the mortality rate in the PDE and Leslie models.

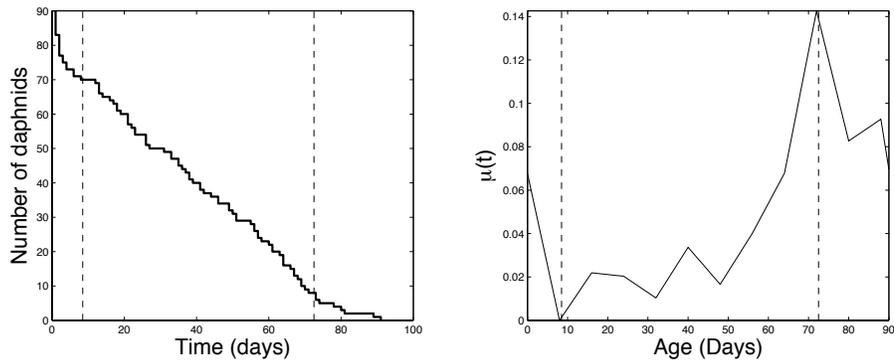


Figure 3: Left: Daphnid survival data. Right: The estimated time-varying mortality function $\tilde{\mu}(t)$ for the Sinko-Streifer model using piecewise linear splines. Both plots are shown with dashed vertical lines representing the division between three possible subpopulations.

accurately be described by a constant mortality rate, and thus, in addition to providing more accurate fits to the data, we suggest that a time-varying mortality rate might also be used to capture the distribution of mortality rates among a population. In theory, time-varying mortality rate distributions can be estimated from our daphnid survival data using continuous structured population models and a Prohorov metric estimation framework [10]. This framework has previously been used to estimate growth rate distributions from longitudinal size-structured data for shrimp and mosquitofish populations [4, 5, 6, 8, 9].

The improved performance of the Sinko-Streifer model over the Leslie model in describing density-independent survival data confirms similar results previously seen for other species [3]. We postulate that incorporating time-varying mortality rates into a density-dependent population model for *Daphnia magna* might enable more accurate descriptions of density-dependent population data by improving the biological assumptions and allowing for better integration of organismal level data.

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