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Transient sensitivity analysis for nonlinear population models

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Summary

1. Performing sensitivity analyses for deterministic multi-stage, multi-parameter population models that include nonlinearity presents a significant computational challenge.

2. We implement a standard forward sensitivity analysis to evaluate partial derivatives of population state variables with respect to parameters at all times for which the solution is known. We present a hybrid MATLAB/Maple software package, SENSAI, which automates the steps required to calculate sensitivities and elasticities. We focus on sensitivities of transient states of populations. Our analysis therefore differs from the more common analysis of linear systems where sensitivities are computed for the asymptotic stable-stage distribution assuming unbounded population growth. The method generalizes the matrix calculus methods for nonlinear, stage-structured matrix models previously developed by Caswell (2009, *Journal of Difference Equations and Applications*, **15**, 349–369).

3. We present an example of a nonlinear, discrete-time population model in the form of a stage-structured Lefkovitch matrix, and another multi-stage, continuous-time SIR disease model in the form of a system of ordinary differential equations. In addition, we extend the framework for composite nonlinear maps of population demography to include single-locus genetics with natural selection discriminating among genotypes.

4. SENSAI allows for the analysis of a quantity of interest (an arbitrary function of variables and parameters, e.g. the proportion of infected individuals in a disease model), and sensitivity to combinations of model parameters. For example, we can compute sensitivities with respect to parameters and initial conditions at all times during an outbreak in a disease model, before a steady state of disease prevalence is attained. Similarly, in population genetic models, we can compute sensitivity of a response to natural selection (e.g. the change in allele frequencies) in relation to fitness differences among genotypes.

5. We illustrate the capabilities of SENSAI through a series of canonical models with relatively few variables and parameters. However, SENSAI has the capability to analyse significantly more complex models.

Key-words: elasticity, matrix population models, partial dominance, $\mathscr{R}_0$, sensitivity, single-locus genetics, SIR model, transience

Introduction

Analysis of multi-stage population models remains a challenge, especially for the nonlinear models that commonly arise in studies of ecological and evolutionary processes. Examples of these nonlinearities include density dependence acting differently on juvenile versus adult life stages, infection rates of susceptibles depending on the numbers of infected individuals in disease models, and the strength of natural selection in genetic models being influenced by the number, survival and mating success of genotypes. Analytical tools and methods for linear systems are well-developed (e.g. Caswell 2001) and allow for the estimation of both the asymptotic state of the population (in the limit as $t \to \infty$) and changes in asymptotic population structure when parameters are perturbed (i.e. sensitivity). However, with the uncertainty known to exist in natural populations, analysis of asymptotic behaviour may not accurately

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or reliably assess model predictions, especially in the short term. Thus, analyses that examine near-term transience and sensitivity analysis have been called for by numerous authors (e.g. Caswell 2007, 2008; Fox & Gurevitch 2000; Koons *et al.* 2005; Yearsley 2004; Caswell 2009; Ezard *et al.* 2010; Townley *et al.* 2007).

Nonlinearity in population projection models changes the focus away from the analysis of the asymptotic stage structure and asymptotic growth rate and towards the study of equilibrium solutions. While a population model with nonlinear feedbacks will generally result in an equilibrium solution that does not change over time, or one that exhibits periodic oscillations (such as the classical predator-prey model), a population with linear growth will asymptotically grow to infinity or decline to extinction. The stage structure of this asymptotic solution is determined by the eigenvector corresponding to the dominant eigenvalue (λ_1). Sensitivity analyses of linear systems examine the rate of change of the dominant eigenvalue with respect to model parameters when stable age- or stage-structure of the population is reached. Thus, sensitivity analyses of linear systems are unrealistic, given the assumption of unbounded growth. Examining short-term transience of linear systems provides one alternative (Fox & Gurevitch 2000), but methods for examining sensitivity and transience of nonlinear systems are clearly required.

Transience in a nonlinear demographic model will arise after disturbance of populations away from a stable equilibrium. We distinguish between (i) perturbations, changes in model parameters like survival, transition or birth rates, and (ii) disturbances, which we consider to be changes in the values of the model variables (cf. Townley & Hodgson 2008). An example of disturbance would be when adults above a certain size are removed by disease or harvesting (model sensitivity considers the effects of changes in the model itself). In a disturbed population, the birth rate may temporarily decline after the loss of adults, or in cases where adults suppress juveniles, birth rates may race ahead of those before the disturbance. Sensitivity to disturbances may be studied via sensitivities with respect to initial conditions (Caswell 2007; Fox & Gurevitch 2000). As pointed out by Fox & Gurevitch (2000), the effects of disturbances, expressed as changes in initial conditions, are common and important in both ecology (e.g. composition of ecological communities and invasion of exotic species) and evolutionary biology (e.g. probability of spread of novel alleles within populations).

Transience following a disturbance that does not change the stable equilibrium solution may take the form of oscillatory or monotonic decay back to the equilibrium solution. Disturbances may also change the qualitative nature of the equilibrium solution attained if the disturbance is large enough to move the system into the basin of attraction of a different stable equilibrium point. For example, a large enough disturbance can force a population to become extinct.

Transience is also expected after the model parameters are perturbed. Changes in the parameters of the model, such as probability of transition between stages in a stage-structured model, may change the quantitative nature of the equilibrium solution. Changes in parameters may also change the stability of equilibria and may therefore change the qualitative nature of the equilibrium point attained after a period of transience.

Sensitivity analysis during transience provides valuable insight into the most important parameters and initial conditions in models and may highlight which parameters must be estimated accurately and which may be estimated roughly with relative impunity. A sensitivity analysis can also help to identify key processes in models, and determine which others, while intriguing, contribute relatively little to specific outcomes of the model.

Here, we provide methods for calculating sensitivities of transient solutions of population models with respect to parameters and to initial conditions. We introduce a hybrid MATLAB/Maple package, SENSAI, that performs forward sensitivity analyses for parametrized nonlinear maps and systems of nonlinear, first-order, ordinary differential equations (ODEs). The method calculates derivatives of variables with respect to all parameters at each time step as the population evolves with time. Initial conditions of the population may be included as parameters so that sensitivity to particular disturbances can be evaluated. For instance, in a stage-structured population model, the state variables will be the number of individuals in each stage class, and the parameters will be the transition probabilities between stages or survivorship within stages. The initial conditions would be the starting number in each stage. Quantities of interest (*QoI*) may be defined as functions of the system variables and parameters, and their trajectories and sensitivities can be determined. For example, sensitivities of the frequencies of alleles in genetic models or the prevalence of infected individuals in disease models may be computed. Finally, sensitivities may be computed with respect to combinations (functions) of the original model parameters, which we call user-defined 'parameters'. Elasticities (sensitivities evaluated on a relative scale) of all variables with respect to all parameters including initial conditions may also be computed simultaneously.

Our mathematical framework is appropriate for significantly more complicated models than the examples presented here, but we illustrate the approach and the capabilities of SENSAI with canonical models containing a modest number of variables and parameters. For discrete-time maps, in 'Parametrized nonlinear maps' we examine a simple two-stage population model described by Caswell (2008), and in 'Generalized single-locus genetics stage-structured models' (also see Appendix A) we extend this simple model to include single-locus population genetics with selection (e.g. Charlesworth 1994). For continuous-time models based on ODEs in 'Systems of nonlinear, first-order, ODEs', we explore a SIR disease model that includes susceptible (S), infected (I) and recovered (R) individuals (e.g. Anderson & May 1979). For the SIR model, in Appendix B, we contrast the equilibrium concept of the basic reproductive ratio for infectious disease, $\mathscr{R}_0$, with the understanding that comes from calculating transient sensitivities. We draw conclusions and comparisons with other approaches in 'Conclusions' and 'Comparison to Other Methods', respectively, and discuss available software, including SENSAI, in 'Software'.

Parametrized nonlinear maps

The basic iterative process we consider is the parameterized nonlinear map

$$\left.\begin{aligned} \boldsymbol{x}(t+1,\boldsymbol{p}) &= \boldsymbol{h}(\boldsymbol{x}(t,\boldsymbol{p}),\boldsymbol{p}),\\ \boldsymbol{x}(0) &= \boldsymbol{z}, \end{aligned}\right\} \qquad \text{eqn 1}$$

where the vector of variables $\boldsymbol{x} \in \mathbb{R}^{\mathrm{M}}$, and the vector of parameters $\boldsymbol{p} \in \mathbb{R}^{\mathrm{K}}$, and the vector of initial conditions $\boldsymbol{z} \in \mathbb{R}^{\mathrm{M}}$. This includes classes of maps with both linear and nonlinear Leslie and Lefkovitch matrices. However, rather than writing the maps as matrix-vector products and using matrix calculus as in Caswell (2009), we represent the right-hand side as a general nonlinear function. At an equilibrium solution $\boldsymbol{x}^*(\boldsymbol{p})$,

$$\boldsymbol{h}(\boldsymbol{x}^*(\boldsymbol{p}),\boldsymbol{p}) = \boldsymbol{x}^*(\boldsymbol{p}). \qquad \text{eqn 2}$$

Component-wise, we write equation (1) as

$$\left.\begin{aligned} x_i(t+1,\boldsymbol{p}) &= h_i(\boldsymbol{x}(t,\boldsymbol{p}),\boldsymbol{p}),\\ x_i(0) &= z_i, \end{aligned}\right\}, i = 1,\ldots,\mathrm{M}. \qquad \text{eqn 3}$$

We define the sensitivity of the ith variable with respect to the kth parameter, $S_{i,k}$, as

$$S_{i,k} = \frac{\partial x_i}{\partial p_k}. \qquad \text{eqn 4}$$

The standard forward sensitivity analysis approach (in contrast to an adjoint-based approach; see Buzby *et al.* 2008) is to differentiate equation (3) with respect to the kth parameter p_k providing an expression for the sensitivities of all variables with respect to all parameters,

$$\left.\begin{aligned} \frac{\partial x_i}{\partial p_k}(t+1) &= \left(\sum_{m=1}^{\mathrm{M}} \frac{\partial h_i}{\partial x_m}\frac{\partial x_m}{\partial p_k}(t)\right) + \frac{\partial h_i}{\partial p_k}(t),\\ \frac{\partial x_i}{\partial p_k}(0) &= 0,\\ i &= 1,\ldots,\mathrm{M}, k = 1,\ldots,\mathrm{K}. \end{aligned}\right\}, \qquad \text{eqn 5}$$

An expression for the sensitivity of the ith solution variable x_i with respect to the jth initial condition z_j can be obtained by differentiating equation (3) with respect to z_j, i.e.

$$\left.\begin{aligned} \frac{\partial x_i}{\partial z_j}(t+1) &= \left(\sum_{m=1}^{\mathrm{M}} \frac{\partial h_i}{\partial x_m}\frac{\partial x_m}{\partial z_j}(t)\right) + \frac{\partial h_i}{\partial z_j},\ j = 1,\ldots,\mathrm{M},\\ \frac{\partial x_i}{\partial z_j}(0) &= \delta_{ij},\\ i &= 1,\ldots,\mathrm{M}, \end{aligned}\right\} \qquad \text{eqn 6}$$

where the Kronecker delta $\delta_{ij} = 1$ if $i = j$ and 0 otherwise. For notational convenience in SENSAI, we consider the jth initial condition z_j to be a parameter which we label $p_{\mathrm{K}+j}$. Re-writing equation (6) we have

$$\left.\begin{aligned} \frac{\partial x_i}{\partial p_{\mathrm{K}+j}}(t+1) &= \left(\sum_{m=1}^{\mathrm{M}} \frac{\partial h_i}{\partial x_m}\frac{\partial x_m}{\partial p_{\mathrm{K}+j}}(t)\right) + \frac{\partial h_i}{\partial p_{\mathrm{K}+j}},\ j = 1,\ldots,\mathrm{M},\\ \frac{\partial x_i}{\partial p_{\mathrm{K}+j}}(0) &= \delta_{ij},\\ i &= 1,\ldots,\mathrm{M}. \end{aligned}\right\} \qquad \text{eqn 7}$$

To solve for both the variables and their sensitivities with respect to the parameters and initial conditions, we evolve equations (3), (5) and (7) simultaneously. This is a system of size M·(1 + K + M). SENSAI evaluates the Jacobian $\partial h_i/\partial x_j$, $i, j = 1,\ldots,\mathrm{M}$ and all partial derivatives of the right-hand side $\partial h_i/\partial p_k$, $i = 1,\ldots,\mathrm{M}$, $k = 1,\ldots,\mathrm{K}$ symbolically using Maple, which is also used to automatically write the MATLAB routines necessary to evaluate these derivatives.

We note that we can recover the analysis of Caswell (2007) for linear systems with a parametrized Lefkovitch matrix $\boldsymbol{A}(\boldsymbol{p}) = a_{ij}(\boldsymbol{p}), i,j = 1,\ldots,\mathrm{M}$, as a special case of our construction. Let

$$\left.\begin{aligned} x_i(t+1,\boldsymbol{p}) &= a_{ij}(\boldsymbol{p})x_j(t),\\ x_i(0) &= z_i, \end{aligned}\right\}, i = 1,\ldots,\mathrm{M}. \qquad \text{eqn 8}$$

Differentiating equation (8) with respect to the kth parameter p_k provides an expression for the sensitivities of all variables with respect to all parameters,

$$\left.\begin{aligned} \frac{\partial x_i}{\partial p_k}(t+1) &= \left(\sum_{m=1}^{\mathrm{M}} a_{im}\frac{\partial x_m}{\partial p_k}(t)\right) + \left(\sum_{m=1}^{\mathrm{M}} \frac{\partial a_{im}}{\partial p_k}x_m(t),\right)\\ \frac{\partial x_i}{\partial p_k}(0) &= 0,\\ i &= 1,\ldots,\mathrm{M}, k = 1,\ldots,\mathrm{K}, \end{aligned}\right\}, \qquad \text{eqn 9}$$

The first two terms on the right-hand side of equation (9) correspond to the first two terms on the right-hand side of equation (5). Note how the second term on the right-hand side of equation (9) depends *explicitly* on $\boldsymbol{x}(t)$, while the second term on the right-hand side of equation (5) depends *implicitly* on $\boldsymbol{x}(t)$.

This construction simplifies the approach of Hodgson, Townley & McCarthy (2006), Yearsley (2004) and Fox & Gurevitch (2000) because it does not rely on computing the sensitivities of eigenvalues, eigenvectors and initial conditions with respect to parameters. Indeed, we can obtain sensitivity with respect to initial conditions through equation (6) as above. However, our approach does not encompass the low-rank perturbations of the entire projection matrix that are considered in Hodgson *et al.* (2006).

Elasticities are defined in terms of relative sensitivities. Let

$$\Delta\xi = \frac{\Delta x}{x} \text{ and } \Delta\kappa = \frac{\Delta p}{p},$$

then the elasticity of x with respect to p

$$\frac{\partial \xi}{\partial \kappa} = \lim_{\Delta\kappa\to 0}\frac{\Delta\xi}{\Delta\kappa} = \frac{p}{x}\lim_{\Delta p\to 0}\frac{\Delta x}{\Delta p} = \frac{p}{x}\frac{\partial x}{\partial p}.$$

We define the elasticity of the ith variable with respect to the kth parameter, $E_{i,k}$, as

$$E_{i,k} = \frac{p_k(t)}{x_i(t)} \frac{\partial x_i}{\partial p_k}(t). \qquad \text{eqn 10}$$

Elasticities with respect to initial conditions are defined in a similar fashion.

QUANTITIES OF INTEREST

In many instances, the outcome of greatest interest is the sensitivity of a function of the solution with respect to model parameters. SENSAI provides a convenient method to evaluate such *QoI*s and to illustrate, we consider three examples in 'Quantities of Interest', 'Two-Stage Discrete Time Model with Single-Locus Two-Allele Genetics' and 'A SIR Model with Logistic Growth', the proportion of juveniles in a population (Q_1), the frequency of a particular allele in a population (Q_2) and the prevalence of infected individuals in a population (Q_3).

In general, let the *QoI* be a scalar valued function of time, such that

$$Q(t) = Q(\boldsymbol{x}(t, \boldsymbol{p}), \boldsymbol{p}). \qquad \text{eqn 11}$$

The sensitivities of the quantity of interest can be computed via the chain rule, namely

$$\frac{\mathrm{d}Q}{\mathrm{d}p_k}(t) = \left(\sum_{m=1}^{\mathrm{M}} \frac{\partial Q}{\partial x_m} \frac{\partial x_m}{\partial p_k}(t) \right) + \frac{\partial Q}{\partial p_k}(t), \; k = 1, \ldots, \mathrm{K} + \mathrm{M}. \qquad \text{eqn 12}$$

As described above, some analyses require an output variable that is some combination of the state variables. Conversely, on some occasions, the user may wish to define a new 'parameter', $\zeta = \zeta(\boldsymbol{p})$, that is a combination of the existing parameters. The sensitivities and elasticities of the variables $\boldsymbol{x}(t)$ and the quantity of interest $Q(t)$ can be computed with respect to this new 'parameter'. Thus, SENSAI provides the ability to evaluate user-defined *QoI* and calculate their sensitivity with respect to user-defined 'parameters', at all time steps (t).

TWO-STAGE, DISCRETE-TIME MODEL

We first demonstrate the capabilities of SENSAI by extending the results reported by Caswell (2008) for a two-stage, nonlinear population model in which x_1 is the number of juveniles in the population and x_2 is the number of adults. Only adults are capable of mating. Let

$$\boldsymbol{h}(\boldsymbol{x}(t, \boldsymbol{p}), \boldsymbol{p}) = \begin{pmatrix} \sigma_1(1-\gamma)x_1 + bx_2 \\ \sigma_1\gamma x_1 + \sigma_2 x_2 \end{pmatrix}, \text{where } \sigma_1 = \tilde{\sigma} e^{-\rho(x_1+x_2)}, \qquad \text{eqn 13}$$

with initial conditions

$$\boldsymbol{z} = \begin{pmatrix} 0{\cdot}2 \\ 0{\cdot}2 \end{pmatrix}. \qquad \text{eqn 14}$$

Parameter values are given in Table 1. The parameter ρ was added to the model of Caswell (2008) to scale the equilibrium population size. For the values of the parameters given in Table 1, the equilibrium population is

$$x_1^* \approx \frac{0{\cdot}1487}{\rho}, \quad x_2^* \approx \frac{0{\cdot}2586}{\rho}. \qquad \text{eqn 15}$$

This model is in the general form of a (non-constant) Lefkovitch matrix,

$$\boldsymbol{A}(\boldsymbol{x}) = \begin{pmatrix} \sigma_1(1-\gamma) & b \\ \sigma_1\gamma & \sigma_2 \end{pmatrix}, \qquad \text{eqn 16}$$

that includes a nonlinear term σ_1 that models density-dependent survival and prevents unbounded growth of the population. We define the *QoI* as the relative abundance of the juvenile class

$$Q_1(t) = \frac{x_1(t)}{x_1(t) + x_2(t)}, \qquad \text{eqn 17}$$

and provide all sensitivities and elasticities as a function of time step. All figures represent graphical output produced by SENSAI, but the package also creates binary and ascii output files that can be used as input to other graphics packages. The quantity of interest, $Q_1(t) = \frac{x_1(t)}{x_1(t)+x_2(t)}$, and the sensitivities of $Q_1(t)$ with respect to the five model parameters and with respect to the initial conditions are plotted as a function of time in Fig. 1(a) and (b), respectively. Sensitivities at equilibrium are the same as originally reported by Caswell (2008). Further, SENSAI provides sensitivities for each time step of the population's trajectory. Sensitivities and elasticities of the solutions $x_1(t)$, $x_2(t)$, and of $Q_1(t)$ with respect to the user-defined 'parameter' $\zeta = \frac{b}{\tilde{\sigma}}$, the ratio of birth to survival probabilities, are plotted in Fig. 1(c) and (d), respectively.

Further, the sensitivity of the quantity of interest with respect to ρ is zero because it is simply a scaling, as is obvious

Table 1. Parameter values for the two-stage, discrete-time model

	Fecundity of adults	Transition probability from juvenile to adult	Survivorship of juvenile class	Survivorship of adult class	Parameter determining size of equilibrium population
Parameter number	1	2	3	4	5
Parameter label	b	γ	$\tilde{\sigma}$	σ_2	ρ
Parameter value	0·25	1/15	0·98	0·95	1·0

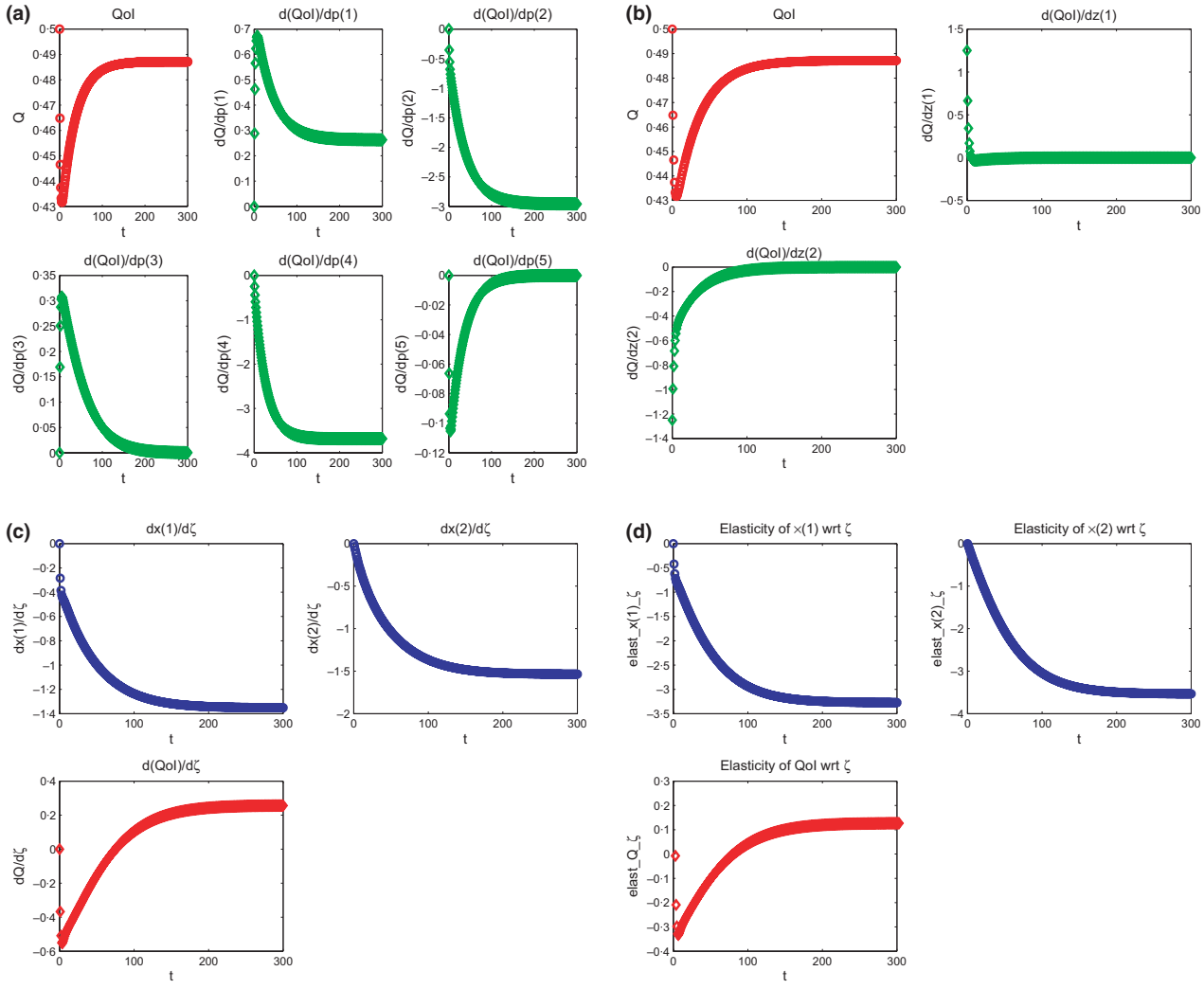

Fig. 1. Two-stage, discrete-time model with the proportion of juveniles in the population as the quantity of interest $Q_1(t) = x_1(t)/(x_1(t) + x_2(t))$. (a) Sensitivities of $Q_1(t)$ with respect to parameters $b, \gamma, \tilde{\sigma}, \sigma_2$ and ρ. (b) Sensitivities of $Q_1(t)$ with respect to initial conditions z_1 (juveniles) and z_2 (adults). (c) Sensitivities of juveniles, adults and $Q_1(t)$ with respect to the user-defined 'parameter', the ratio of adult fecundity to juvenile survival ($\zeta = b/\tilde{\sigma}$), (d) Elasticities of juveniles, adults and $Q_1(t)$ with respect to the user-defined 'parameter' (ζ).

from equation (15). Figure 1(a) illustrates how the sensitivities with respect to parameters evolve with time before approaching a constant value as the equilibrium solution is approached. Sensitivities rapidly change initially as the solution changes over the first few time steps before the gradual monotonic approach to the equilibrium solution. Notice in Fig. 1(b) that, as expected, the sensitivities with respect to initial conditions decay and approach zero as the equilibrium solution is reached. Similar behaviour is observed for the user-defined 'parameter' (ζ), with an initial rapid change before slow approach to equilibrium.

Generalized single-locus genetics stage-structured models

Inheritance and mating systems, modelled as population genetic processes, add nonlinearities to population models. Let the elements of $\boldsymbol{x}_{\{n\}}(t,\boldsymbol{p}) \in \mathbb{R}^n$ contain the populations in each stage of an n-stage structured model at time t. We use the subscript notation $\boldsymbol{x}_{\{mn\}}(t,\boldsymbol{p})$ to denote the size of the state vector, because we will construct genetic models that contain mn classes where m is the number of genotypes. We assume a given population model in the form of a nonlinear map

$$\boldsymbol{x}_{\{n\}}(t+1,\boldsymbol{p}) = \boldsymbol{h}_{\{n\}}(\boldsymbol{x}_{\{n\}}(t,\boldsymbol{p}),\boldsymbol{p}),\ \boldsymbol{x}_{\{n\}}(0,\boldsymbol{p}) = \boldsymbol{x}_{\{n\},0}, \quad \text{eqn 18}$$

and construct a single-locus genetics model from equation (18). Applying population genetic analyses to stage-structured models allows multiple fitness components (e.g. survival, fecundity and growth) to be simultaneously examined for many life stages. Genetic models can also be easily extended to cases with multiple alleles and, with greater difficulty, to multiple loci.

TWO-STAGE, DISCRETE-TIME MODEL WITH SINGLE-LOCUS TWO-ALLELE GENETICS

We extend the two-stage, discrete-time model in 'Two-Stage Discrete Time Model' (detailed in Appendix A) by including

the effect of genotype on survivorship of both juveniles (x_1) and adults (x_2). We assume a single locus with two alleles (A, a) and three genotypes (AA, Aa, aa). For simplicity, fecundity is assumed to be independent of genotype, but this extension would be trivial within our mathematical framework. We order the six classes ($m = 3, n = 2$) as below

$$x_1 = \text{Juvenile}^{AA},\ x_2 = \text{Adult}^{AA},$$
$$x_3 = \text{Juvenile}^{Aa},\ x_4 = \text{Adult}^{Aa},$$
$$x_5 = \text{Juvenile}^{aa},\ x_6 = \text{Adult}^{aa}.$$

and let

$$N(t) = \sum_{i=1}^{6} x_i(t). \qquad \text{eqn 19}$$

Let the effect of genotype on survivorship and transition be implemented via the relative fitnesses of the three genotypes AA, Aa and aa,

$$w_1 = 1, \quad w_2 = 1 - hs, \quad w_3 = 1 - s, \qquad \text{eqn 20}$$

respectively, which is the usual form for *partial dominance*, where s is the selection coefficient and h determines the degree of dominance (Hedrick 2009). We label h and s parameters 6 and 7, respectively. When $h = 0$, allele a is completely recessive, when $h = 0{\cdot}5$, alleles A and a are co-dominant, and when $h = 1$, the allele a is completely dominant (see Appendix A).

We define the quantity of interest, $Q_2(t)$, to be the frequency of the deleterious allele a in the population, i.e.

$$Q_2(t) = \frac{x_5(t) + x_6(t) + 0{\cdot}5(x_3(t) + x_4(t))}{N(t)} = q(t). \qquad \text{eqn 21}$$

We present results for the same parameter values provided in Table 1 except that we now choose $\rho = 10^{-4}$ to increase equilibrium population size to several thousands. In the absence of genetics, using equation (15), the equilibrium populations are $x_1^* \approx 1487$ and $x_2^* \approx 2586$.

The initial populations in each genotype were distributed equally between juveniles and adults, such that $z_{2i-1} = z_{2i}$, $i = 1, 2, 3$. The initial population and frequency of the deleterious allele were

$$N(0) = N_0 = \sum_{i=1}^{6} z_i, \quad \text{and}$$
$$q(0) = q_0 = \frac{z_5 + z_6 + 0{\cdot}5(z_3 + z_4)}{N_0}, \qquad \text{eqn 22}$$

respectively. Specifically, when $N_0 = 32$, we chose the values given in Table 2. Initial population sizes for different values of N_0 were appropriately scaled.

In Fig. 2(a–c), we plot the frequency of the a allele $Q_2(t)$ for a range of values of q_0 and N_0 for $h = 0$, $h = 0{\cdot}5$ and $h = 1$, respectively. In Fig. 2(d), we fix $N_0 = 3200$ and compare the quantity of interest as a function of time for a range of values of q_0 and h. In Figs 4–6, the x-axis (q_0) labels 1,…,3 correspond to initial deleterious allele frequencies $q_0 = 0{\cdot}094$, $0{\cdot}5$ and $0{\cdot}906$, respectively. The y-axis (N_0) labels 1,…,4 correspond to initial population sizes $N_0 = 32{\times}10^{(l-1)}$, for $l = 1,\ldots,4$ where l is the axis label (i.e. $l = 1,2,3$, corresponds to $N_0 =$ 32, 320, 3200, 32 000, respectively), resulting in a total of 12 parameter combinations per panel.

Table 2. Parameters and initial conditions for extending the two-stage, discrete-time model to include single-locus, two-allele genetics, when the initial population size is fixed ($N_0 = 32$) but initial allele frequencies differ. See Figs 4–6

	Parameter number	8	9	10	11	12	13	
	Parameter label	z_1	z_2	z_3	z_4	z_5	z_6	q_0
Case 1	Parameter value	14	14	1	1	1	1	0·094
Case 2	Parameter value	4	4	8	8	4	4	0·5
Case 3	Parameter value	1	1	1	1	14	14	0·906

DELETERIOUS RECESSIVE ALLELE: $h = 0, s = 0{\cdot}1$

In Fig. 2(a), we plot the frequency of the a allele, $Q_2(t)$, for the three different initial values of $q_0 = 0{\cdot}094$, $0{\cdot}5$, $0{\cdot}906$ and four different values of $N_0 = 32$, 320, 3200, 32000. In initial populations, each genotype is distributed equally between juveniles and adults. As expected, the proportion of the deleterious allele in the population declines with time for all values of q_0, but the reduction (i.e. allele purging) is most rapid for populations with $q_0 = 0{\cdot}5$ and $q_0 = 0{\cdot}906$. For $0 < t \leq 50$, $Q_2(t)$ is strongly dependent upon q_0 and relatively independent of N_0.

In Fig. 3, we plot the elasticities of the frequency of the a allele, $Q_2(t)$, with respect to the parameters and with respect to the initial conditions for $N_0 = 3200$, $q_0 = 0{\cdot}906$, $h = 0$ and $s = 0{\cdot}1$ for $t = 0,\ldots,50$.

The sensitivities and elasticities of the frequency of the a allele, $Q_2(t)$, with respect to the initial conditions at $t = 50$ are given in Fig. 4(a) and (b), respectively. The qualitative information provided in Fig. 4(a) is largely as expected. The quantitative behaviour, both at a fixed time and as a function of time, can only be determined through computation. To summarize:

1. The sensitivities $\frac{\partial Q_2}{\partial z_1}|_{t=50} < 0$ and $\frac{\partial Q_2}{\partial z_2}|_{t=50} < 0$ because a small increase in z_1 or z_2 (initial number of AA juveniles and AA adults respectively) would decrease q_0, which would decrease $Q_2(50)$.

2. The sensitivities $\frac{\partial Q_2}{\partial z_5}|_{t=50} > 0$ and $\frac{\partial Q_2}{\partial z_6}|_{t=50} > 0$ because a small increase in z_5 or z_6 (initial number of aa juveniles and aa adults, respectively) would increase q_0, which would increase $Q_2(50)$.

3. The signs of $\frac{\partial Q_2}{\partial z_3}|_{t=50}$ and $\frac{\partial Q_2}{\partial z_4}|_{t=50}$ depend upon q_0.

(a) The sensitivities $\frac{\partial Q_2}{\partial z_3}|_{t=50} > 0$ and $\frac{\partial Q_2}{\partial z_4}|_{t=50} > 0$ when $q_0 < 0{\cdot}5$, because a small increase in z_3 and z_4 (initial number of heterozygote Aa juveniles and adults, respectively) would increase q_0, which would increase $Q_2(50)$.

(b) The sensitivities $\frac{\partial Q_2}{\partial z_3}|_{t=50} < 0$ and $\frac{\partial Q_2}{\partial z_4}|_{t=50} < 0$ when $q_0 > 0{\cdot}5$, because a small increase in z_3 and z_4 would decrease q_0 which would decrease $Q_2(50)$.

(c) When $q_0 = 0{\cdot}5$, a small increase in z_3 or z_4 would leave q_0 unchanged and its effect needs to be computed!

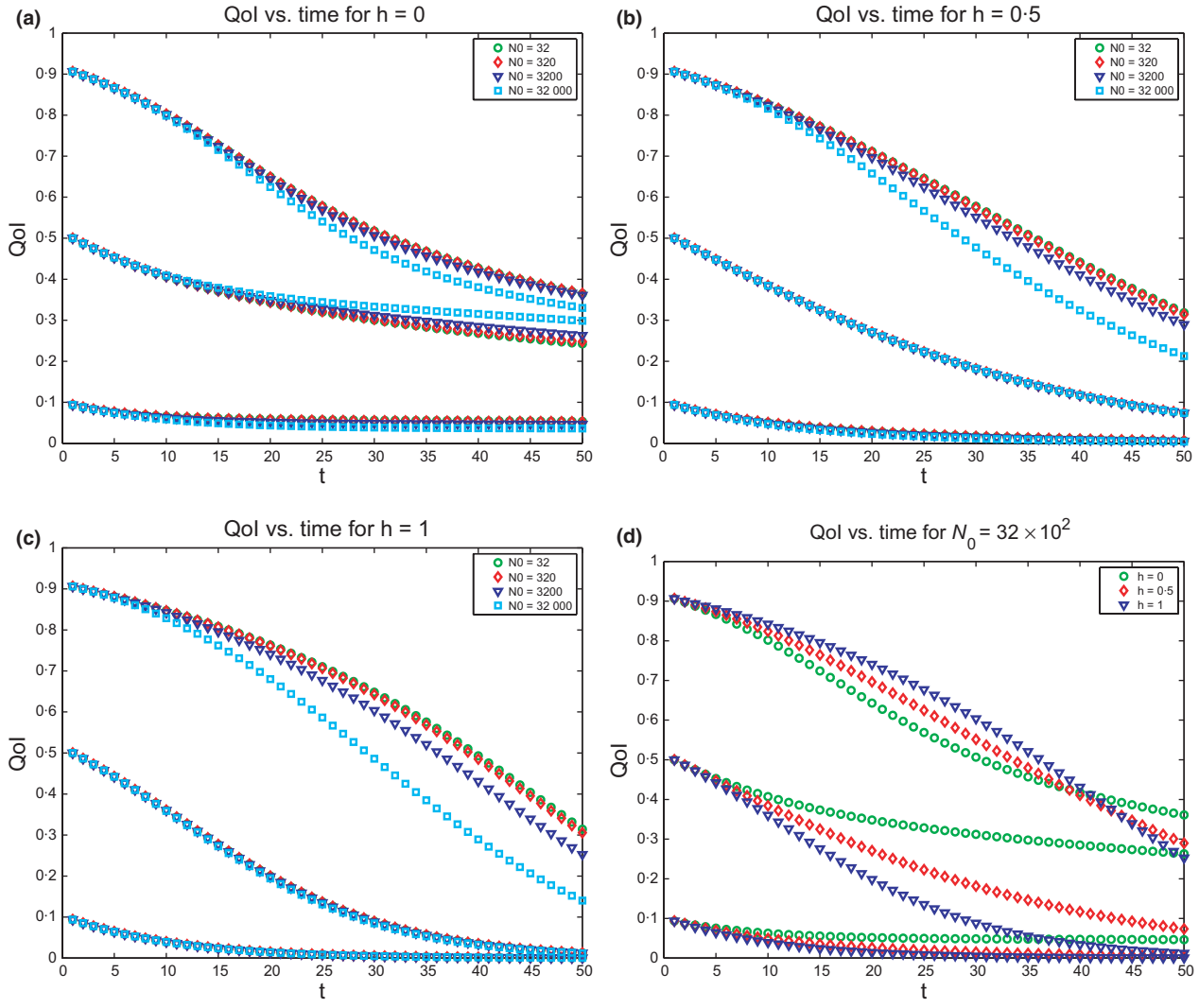

Fig. 2. Quantity of interest, the frequency of the deleterious allele a, $Q_2(t)$, for $t = 0,\ldots,50$ for $s = 0{\cdot}1$ and $q_0 = 0{\cdot}094, 0{\cdot}5, 0{\cdot}906$. (a) Deleterious recessive: $h = 0$, $N_0 = 32, 320, 3200, 32\,000$ (circles, diamonds, triangles and squares, respectively). (b) Co-dominance: $h = 0{\cdot}5$, $N_0 = 32, 320, 3200, 32\,000$ (circles, diamonds, triangles and squares, respectively). (c) Deleterious dominant: $h = 1$, $N_0 = 32, 320, 3200, 32\,000$ (circles, diamonds, triangles and squares, respectively). (d) $N_0 = 3200$, $h = 0, 0{\cdot}5, 1$ (circles, diamonds and triangles, respectively).

4. The magnitudes $|\frac{\partial Q_2}{\partial z_1}|$ and $|\frac{\partial Q_2}{\partial z_2}|$ increase with q_0 because small increases in z_1 and z_2 have a larger effect on q_0 when q_0 is large. (The effect on q_0 of adding the allele A to the population is large when the proportion of the allele A in the population is small.)

5. The magnitudes $|\frac{\partial Q_2}{\partial z_5}|$ and $|\frac{\partial Q_2}{\partial z_6}|$ decrease with q_0 because small increases in z_5 and z_6 have a smaller effect when on q_0 when q_0 is large. (The effect on q_0 of adding the allele a to the population is small when the proportion of the allele a in the population is large.)

6. The magnitudes $|\frac{\partial Q_2}{\partial z_j}|$ for all $j = 1,\ldots,6$ decrease with increasing N_0 because small changes in the initial conditions z_j have a smaller effect when the total population N_0 is large. This parallels the well known phenomenon of *genetic drift* in small populations.

7. The magnitudes of the sensitivities for juveniles $|\frac{\partial Q_2}{\partial z_j}|, j = 1, 3, 5$ are smaller than those for the corresponding adult populations $|\frac{\partial Q_2}{\partial z_j}|, j = 2, 4, 6$, because juveniles must survive first before they reproduce and affect the next generation.

The elasticities in Fig. 4(b) are computed by rescaling the corresponding sensitivities by $\frac{z_j}{q_0}, j = 1, \ldots, 6$, and as all parameters and class sizes are positive, the signs of the elasticities are the same as those of the sensitivities. However, this rescaling changes the relative magnitudes of elasticities for both fixed initial population size, N_0, when varying initial allele frequencies q_0 and for fixed initial allele frequency, q_0, when varying N_0. This demonstrates that the effect of rescaling sensitivities to elasticities is not always intuitive and requires a computation.

CO-DOMINANT ALLELES: $h = 0{\cdot}5, s = 0{\cdot}1$

In Fig. 2(b), we plot the frequency of the a allele, $Q_2(t)$, for the three different values of q_0=0·094, 0·5, 0·906 and four different values of $N_0 = 32, 320, 3200, 32000$. When compared to

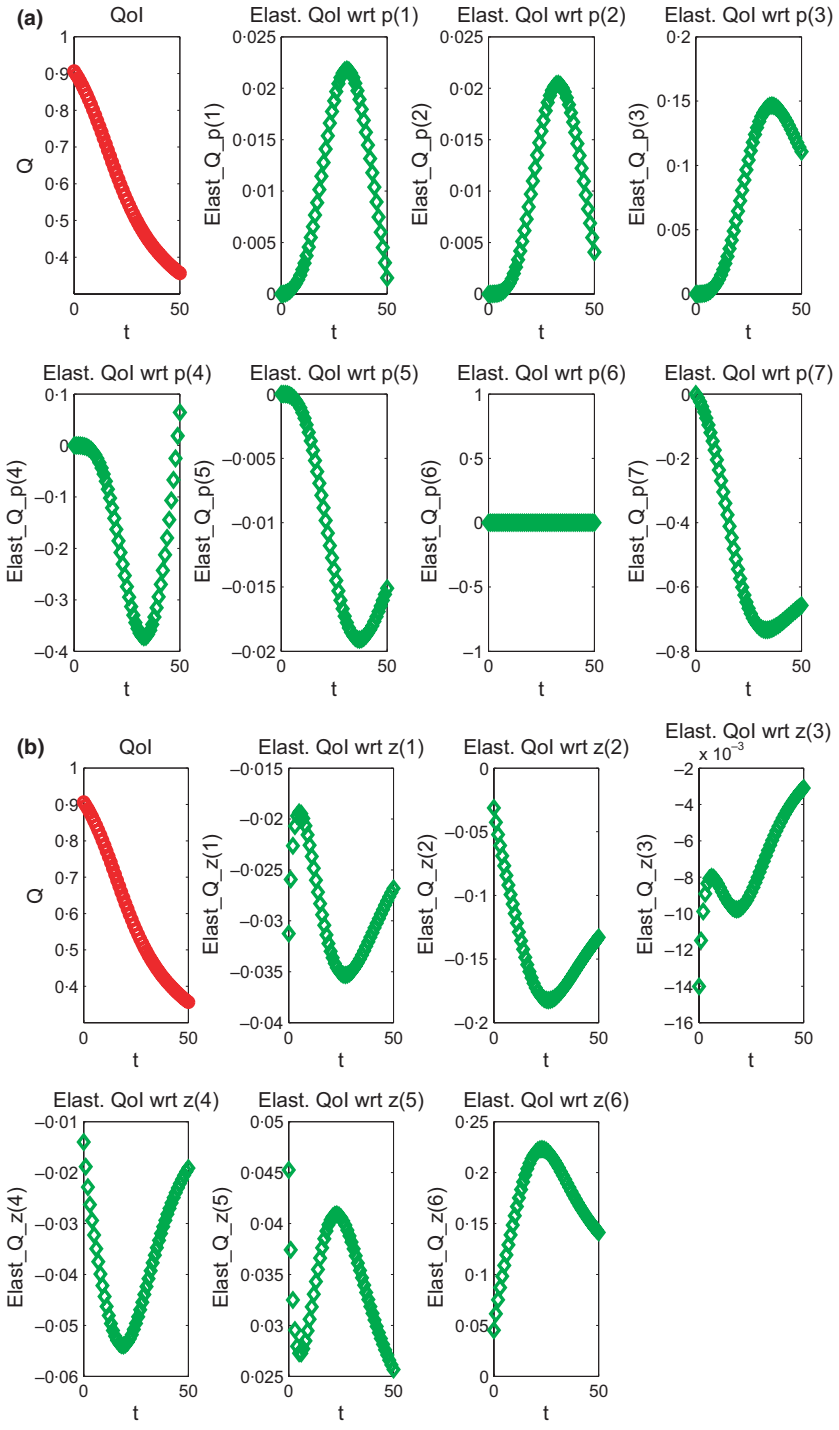

Fig. 3. Elasticities for the frequency of the deleterious alleles, $Q_2(t)$, for $t = 0,\ldots,50$ with $q_0 = 0{\cdot}906$, $N_0 = 3200$ and $h = 0, s = 0{\cdot}1$. (a) Elasticities with respect to the parameters. (b) Elasticities with respect to the initial conditions.

Fig. 2(a), it is clear that the purging of deleterious alleles in the population is faster when heterozygote individuals also experience negative selection.

The elasticities with respect to initial conditions at $t = 50$ are given in Fig. 5. The elasticities in Fig. 5 are qualitatively similar to those in Fig. 4(b). The most significant difference is the magnitude of the elasticities with respect to z_5 and z_6 (the initial number of *aa* juveniles and adults), which is approximately twice that when the deleterious allele is recessive. Selection now acts on both the homozygous *aa* and heterozygous *Aa* individuals (albeit unequally).

DELETERIOUS DOMINANT ALLELE: $h = 1, s = 0{\cdot}1$

In Fig. 2(c), we again plot the frequency of the *a* allele, $Q_2(t)$, for the three different values of $q_0 = 0{\cdot}094$, $0{\cdot}5$, $0{\cdot}906$ and four

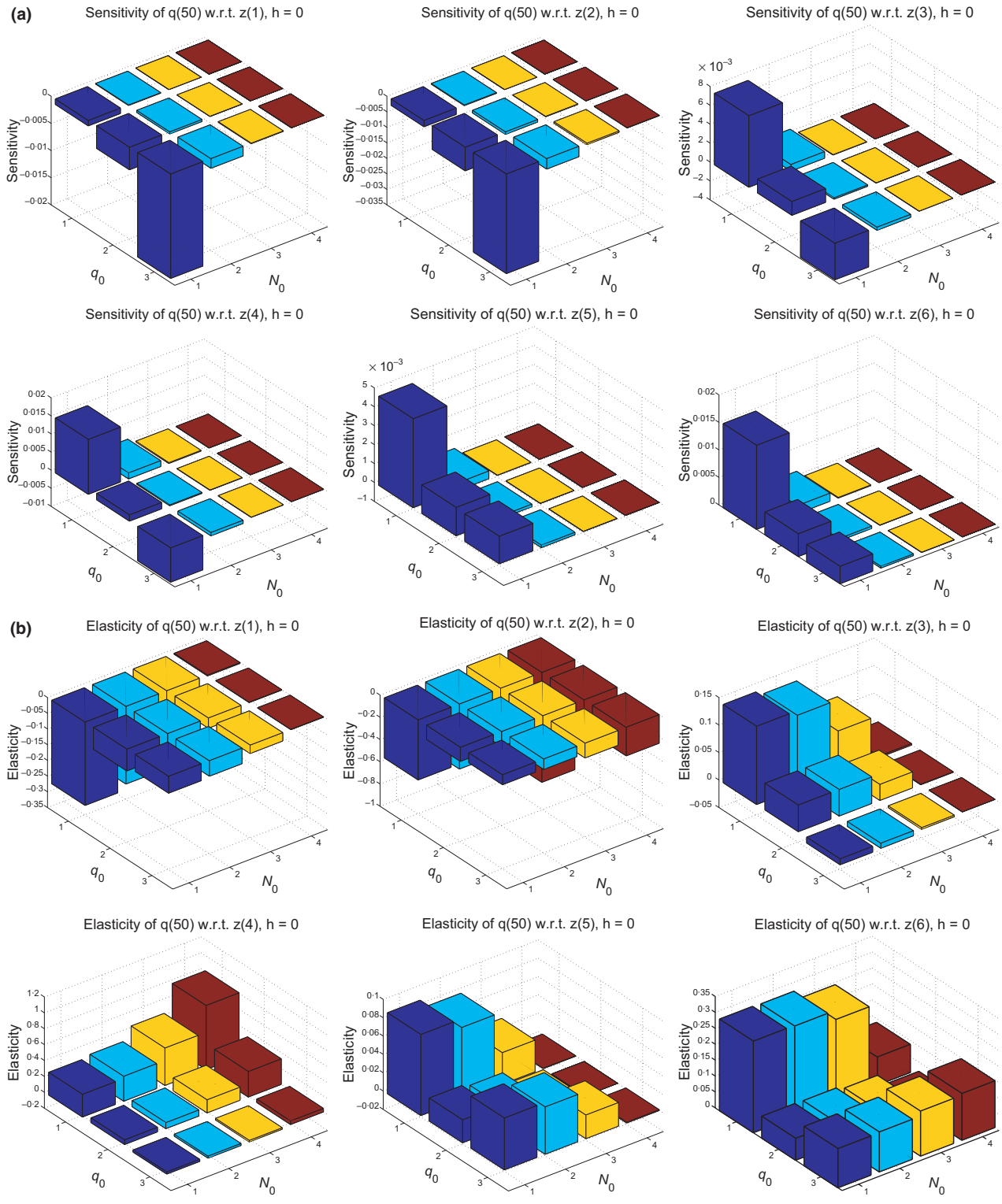

Fig. 4. Sensitivities and elasticities of the frequency of the deleterious allele a, $Q_2(t)$, with respect to initial conditions at $t = 50$ for $h = 0$ and $s = 0{\cdot}1$ (deleterious recessive) plotted against q_0 where $q_0 = 0{\cdot}094, 0{\cdot}5, 0{\cdot}906$ for $i = 1, 2, 3$, respectively, and against $N_0 = 32 \times 10^{(l-1)}$ for $l = 1,\ldots,4$. (a) Sensitivities. (b) Elasticities.

different values of $N_0 = 32, 320, 3200, 32000$. Notice both the value of $Q_2(50)$ and the slope of the trajectory $\mathrm{d}Q_2/\mathrm{d}t$ at $t = 50$ in Figs 2(a–c). These both suggest that the efficiency with which selection removes the deleterious allele (i.e. purging) improves with increasing h (dominance coefficient), as the deleterious allele essentially becomes 'unmasked' to negative

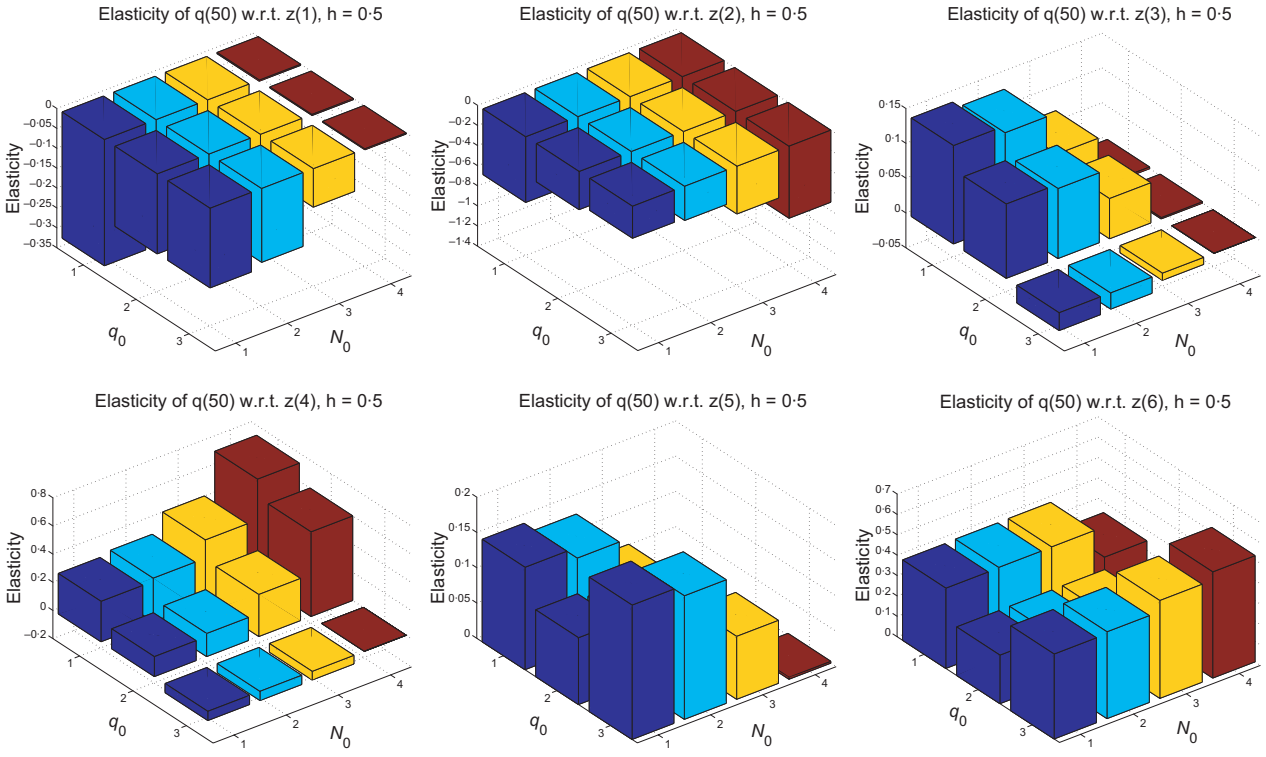

Fig. 5. Elasticities of the frequency of the deleterious allele a, $Q_2(t)$, with respect to the initial conditions at $t = 50$ for $h = 0{\cdot}5$ and $s = 0{\cdot}1$ (co-dominant alleles) plotted against q_0 where $q_0 = 0{\cdot}094, 0{\cdot}5, 0{\cdot}906$ for $i = 1, 2, 3$, respectively, and against $N_0 = 32 \times 10^{(l-1)}$ for $l = 1,\ldots,4$.

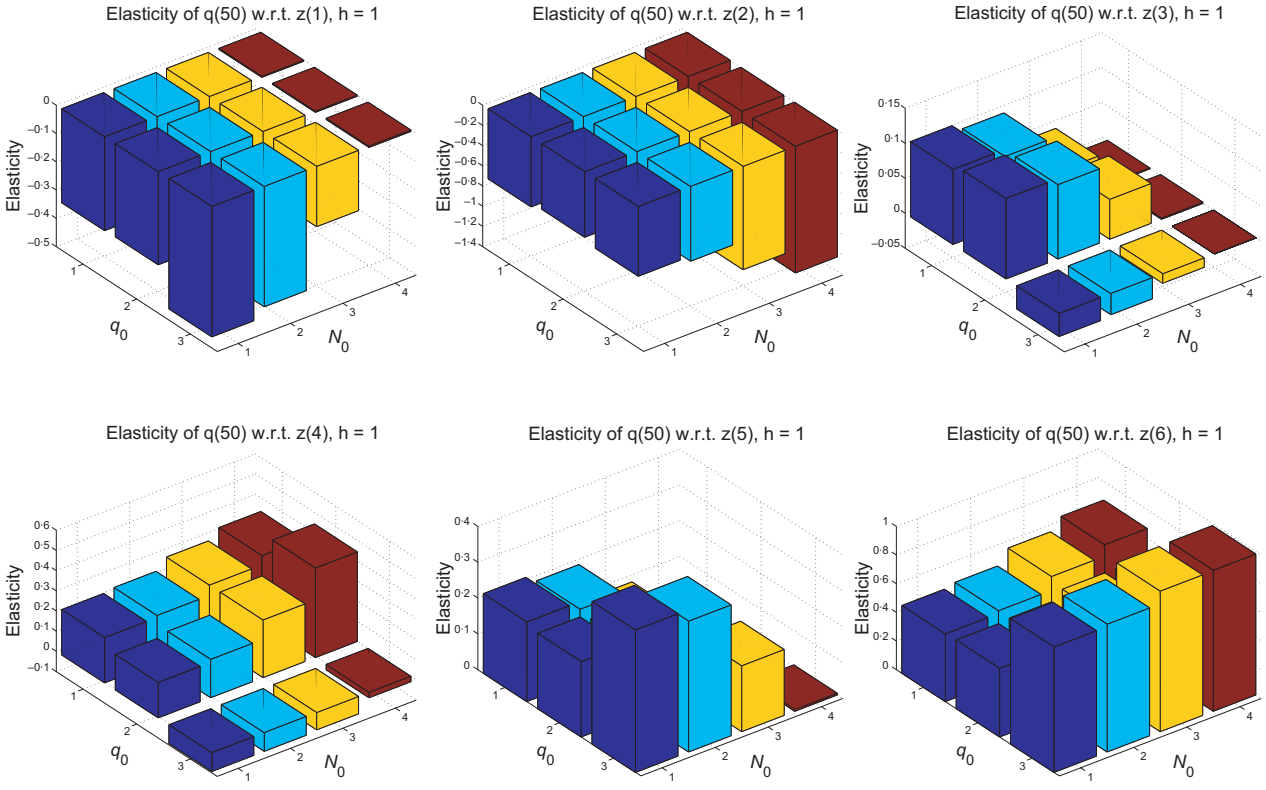

Fig. 6. Elasticities of the frequency of the deleterious allele a, $Q_2(t)$, with respect to initial conditions at $t = 50$ for $h = 1$ and $s = 0{\cdot}1$(deleterious dominant) plotted against q_0, where $q_0 = 0{\cdot}094, 0{\cdot}5, 0{\cdot}906$ for $i = 1, 2, 3$, respectively, and against $N_0 = 32 \times 10^{(l-1)}$ for $l = 1,\ldots,4$.

selection. This effect is particularly apparent for $q_0 = 0{\cdot}5$ in Fig. 2(d) where we show results for all three values of h for a single value of N_0.

Elasticities with respect to initial conditions at $t = 50$ are given in Fig. 6. The elasticities in Fig. 6 are qualitatively similar to those in Fig. 5. The most significant difference is the magnitude of the elasticities with respect to z_5 and z_6, which is approximately twice that of the co-dominant case. Selection acts *equally* against homozygous *aa* and heterozygous *Aa* individuals.

Systems of nonlinear, first-order, ODEs

We now consider continuous-time, stage-structured population models in the form of nonlinear systems of first-order, ODEs,

$$\left.\begin{aligned} \frac{d\boldsymbol{x}}{dt}(t,\boldsymbol{p}) &= \boldsymbol{h}(\boldsymbol{x}(t,\boldsymbol{p}),\boldsymbol{p}),\\ \boldsymbol{x}(0) &= \boldsymbol{z}, \end{aligned}\right\} \qquad \text{eqn 23}$$

where $\boldsymbol{x} \in \mathbb{R}^{\mathrm{M}}, \boldsymbol{p} \in \mathbb{R}^{\mathrm{K}}$ and the initial conditions $\boldsymbol{z} \in \mathbb{R}^{\mathrm{M}}$. At an equilibrium solution $\boldsymbol{x}^*(\boldsymbol{p})$,

$$\boldsymbol{h}(\boldsymbol{x}^*(\boldsymbol{p}),\boldsymbol{p}) = 0. \qquad \text{eqn 24}$$

A derivation of sensitivities and elasticities for systems of nonlinear first-order ODEs is analogous to that for nonlinear maps in 'Parametrized nonlinear maps'. We construct and solve a system of first-order differential equations of size M·(1 + K + M) to compute the population and its stability with respect to parameters and initial conditions.

A SIR MODEL WITH LOGISTIC GROWTH

Consider the following variation on the classic SIR disease model Anderson & May (1979) in which we have a logistic growth term to curb unbounded growth,

$$\left.\begin{aligned} \frac{\mathrm{d}S}{\mathrm{d}t} &= rN(t)\left(1-\frac{N(t)}{K}\right) - \beta S(t)I(t) - \mu S(t),\\ \frac{\mathrm{d}I}{\mathrm{d}t} &= \beta S(t)I(t) - \gamma I(t) - \mu I(t) - \nu I(t),\\ \frac{\mathrm{d}R}{\mathrm{d}t} &= \gamma I(t) - \mu R(t), \end{aligned}\right\} \qquad \text{eqn 25}$$

where $N(t) = S(t) + I(t) + R(t)$. We choose initial conditions

$$\boldsymbol{z} = (5,5,5)^{\top}. \qquad \text{eqn 26}$$

Solutions and sensitivities are provided for the parameter values given in Table 3. Our *QoI* is disease prevalence, the fraction of the population that is infected,

$$Q_3(t) = \frac{I(t)}{S(t)+I(t)+R(t)}, \qquad \text{eqn 27}$$

and defines a function of the parameters, the *basic reproductive ratio for infectious disease*,

$$\mathscr{R}_0 = \frac{\beta}{\gamma+\mu+\nu}. \qquad \text{eqn 28}$$

Solutions for $t \in [0,100]$ are provided in Fig. 7(a). The elasticities of the quantity of interest with respect to the initial conditions are given in Fig. 7(b), where (as expected) these decay to zero as the stable equilibrium solution is approached. At equilibrium, approximately 90% of the population is infected. The sensitivities and elasticities of the quantity of interest $Q_3(t)$ with respect to the user-defined parameters are given in Fig. 7(c) and (d), respectively.

The signs (if not the precise magnitudes) of the sensitivities and elasticities of S and I with respect to $\mathscr{R}_0$ in Fig. 7(c) and (d) are readily explained. From equation (28), an increase in the ratio of infection rate (β) relative to the rate of removal of infected individuals ($\gamma + \mu + \nu$) should increase the number of infected individuals and decrease the number of susceptible individuals. However, there are two plausible arguments that lead to different conclusions regarding the sign of the elasticity of the number of recovered individuals. At first glance, an increase in $\mathscr{R}_0$ produces an increase in infected individuals, which should result in an *increase* in the number of recovered individuals. A second argument suggests that an increase in $\mathscr{R}_0$ can occur as a result of a decrease in γ, which should result in a *decrease* in the number of recovered individuals. A computation is required to determine which of the two competing processes dominates. For example, increasing the size of γ from 0·02 to 0·3 reverses the sign of the elasticity. For $\gamma = 0{\cdot}02$, the elasticity of the number of recovered individuals with respect to $\mathscr{R}_0$ at the new equilibrium population is positive. For $\gamma = 0{\cdot}3$, the elasticity of the disease prevalence with respect to $\mathscr{R}_0$ also changes sign, and the fraction of infected individuals decreases with increasing $\mathscr{R}_0$.

Table 3. Parameter values for SIR model using ordinary differential equations with logistic growth

	Intrinsic growth rate	Carrying capacity	Infection rate	Death rate	Recovery rate	Additional death rate (disease)
Parameter number	1	2	3	4	5	6
Parameter label	r	K	β	μ	γ	ν
Parameter value	0·5	1000	0·1	0·2	0·02	0·1

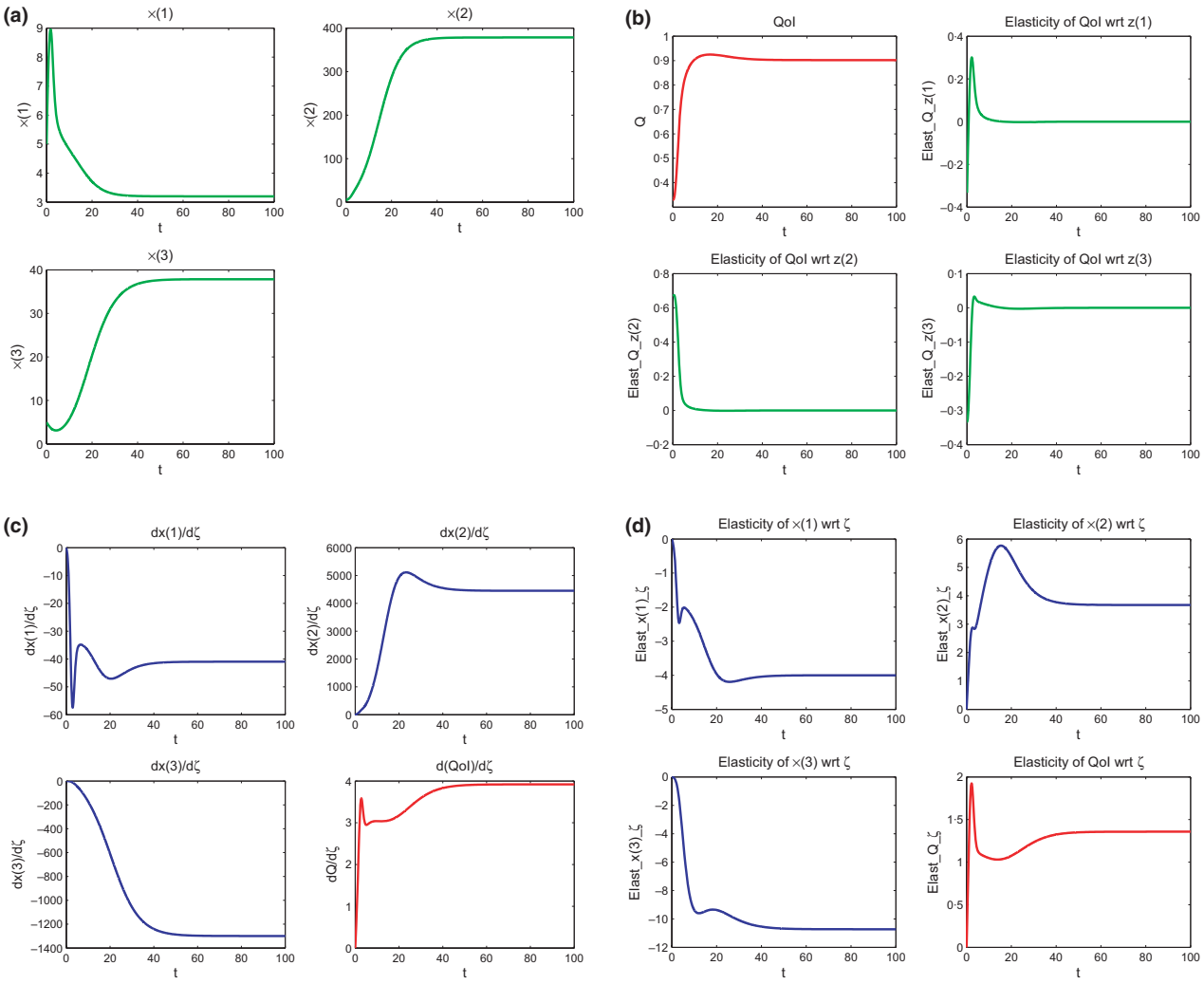

Fig. 7. SIR model with the quantity of interest as the prevalence of infection, $Q_3(t) = I(t)/(S(t) + I(t) + R(t))$ and the user-defined parameter, $\mathscr{R}_0 = \beta/(\gamma + \mu + \nu)$. (a) Solutions $S(t)$, $I(t)$, $R(t)$ for $t = 0,\ldots,100$. (b) Elasticities of $S(t)$, $I(t)$, $R(t)$ and $Q_3(t)$ with respect to the initial conditions for $t = 0,\ldots,100$. (c) Sensitivities of $S(t)$, $I(t)$, $R(t)$ and $Q_3(t)$ with respect to the user-defined parameter $\mathscr{R}_0$ for $t = 0,\ldots,100$. (d) Elasticities of $S(t)$, $I(t)$, $R(t)$ and $Q_3(t)$ with respect to the user-defined parameter $\mathscr{R}_0$ for $t = 0,\ldots,100$.

Conclusions

Deterministic nonlinear systems of ODEs and nonlinear maps provide convenient and powerful mathematical models to gain insight into population dynamics and demographic processes. Transient analysis of these models is enhanced by the ability to compute sensitivities and elasticities of variables and user-defined functions of variables and parameters with respect to all parameters (including initial conditions) at all points of the trajectory. For example, the ability to compute sensitivities *during* an outbreak or epidemic in a disease model may be more useful than a single measure ($\mathscr{R}_0$) governing the (linear) stability or instability of a disease-free equilibrium solution (see Appendix B).

SENSAI provides a convenient framework in which to develop and analyse complex, nonlinear population models by allowing models to be developed within a Maple environment and then coupled to MATLAB solver routines to compute sensitivities and elasticities with respect to parameters and initial conditions. As one example, we generalized the mathematical framework to include nonlinear, deterministic, single-locus genetic models in which extensions to different forms of selection (e.g. frequency-dependent selection) or mating systems (e.g. separate sexes) are straightforward.

COMPARISON TO OTHER METHODS

The relatively straightforward approach used in SENSAI for calculating sensitivities of solutions of deterministic parameterized nonlinear population models provides just one method for evaluating processes in ecology and evolutionary biology. The sensitivities we compute differ from those calculated for linear, stage-structured models, e.g. Caswell (2001), Grant & Benton (2003) and Haridas & Tuljapurkar (2007). These concern the sensitivity of the asymptotic solution, which has a stable-stage distribution for which the *relative* sizes of stages

remain constant with time (corresponding to the dominant eigenvector). We address the sensitivity of *solutions*, rather than the sensitivity of *eigenvalues* and *eigenvectors* with respect to changes in parameters.[1] Similarly, our approach differs from that of Hodgson *et al.* (2006) who seek to quantify the effect of low-rank matrix perturbations to the eigenvalues of Lefkovitch matrices.

Significant transient population growth can occur for solutions of linear systems with highly non-normal Lefkovitch matrices. See Trefethen & Embree (2005) for examples from a comprehensive discussion of transient growth arising because of non-normal matrices across a wide range of applications. Transient growth phenomena can be bounded by various matrix norms. Townley *et al.* (2007) suggest the Kreiss matrix bound as providing a useful lower *bound* on transient growth in systems modelled by Lefkovitch matrices and low-rank perturbations of these matrices. In SENSAI, we consider transient sensitivities along specific solution trajectories rather than providing bounds on the transient behaviour for whole classes of trajectories.

The transient analysis conducted by SENSAI is in contrast to the linearized (asymptotic) stability analysis of the equilibria of nonlinear systems more commonly performed for population models, especially in population genetics (e.g. Charlesworth 1994; Ellner 1996). Bifurcation theory, e.g. Golubitsky & Schaeffer (1985) and Kuznetsov (2004), is the study of the equilibria of parameterized nonlinear differential equations and maps, and bifurcation analysis partitions parameter space into regions of qualitatively similar behaviour, for instance stable or unstable nodes versus stable or unstable spiral equilibrium points. Sensitivity of equilibrium solutions may also be evaluated using our techniques, but numerical methods for bifurcation analysis are well developed, e.g. Govaerts (2000) and Mei (2000), and several software packages are freely available, e.g. AUTO (http://cmvl.cs.concordia.ca/auto/) and MATCONT (http://www.matcont.ugent.be/). Examples of insights obtained by studies of population models in ecology using bifurcation theory include Dennis *et al.* (1997), Wikan (2001) and Govaerts & Ghaziani (2006).

It should be recognized that nonlinear models may have multiple equilibria, and sensitivity with respect to parameters may differ in different regions of parameter space. Buzby *et al.* (2008) present an adjoint-based approach to examine sensitivity for ODEs over entire regions of parameter space by systematically examining sensitivities in the vicinity of reference values of the parameters and adaptively constructing a piecewise linear approximation to the sensitivity surface. Similar adjoint-based techniques have been developed for nonlinear maps.

[1]Sensitivity with respect to initial conditions is not typically considered when analysing linear systems. In linear, stage-structured models, the stable-stage distribution is independent of the initial conditions, except in the very special circumstances when the initial condition lies in an invariant subspace that is orthogonal to the dominant eigenvector.

Stage-structured Markov chain models provide another common approach to studying population dynamics, see e.g. Caswell (2001), Tuljapurkar (1989) and Ellner (1996). Stability, sensitivities and elasticities for stochastic models typically concern expected values and higher moments of probability distributions and an assessment of the uncertainty of these quantities owing to finite sampling. Recently, stochastic collocation techniques, see e.g. Xiu (2010), have been developed to provide an efficient way to solve differential equations with stochastic parameters.

Individual-based or agent-based models, see e.g. Grimm & Railsback (2005), provide another popular alternative that is also complementary to the analysis of stage-structured models. Understanding the effects of complicated nonlinear interactions, determining the sensitivities and elasticities of the expected value and higher moments (variances, skewness, and kurtosis) of the solution with respect to parameters, and locating the values of parameters at which qualitative changes in the expected value of the solutions occur all present significant challenges when using these models.

RESEARCH CAPABILITIES

The ability to study transience and transient sensitivities is particularly important when studying long-lived species. The authors are engaged in a study of disease in high-altitude Whitebark Pine, a species which takes decades to reach maturity and hundreds of years to achieve an equilibrium population. An understanding of the effects of a major environmental disruption such as fire, the introduction of disease or the introduction of a resistant genotype is desired over time intervals measured in years and decades, not in centuries. Sensitivities of the equilibrium population under these circumstances are of limited utility. SENSAI is able to provide transient solutions, their sensitivities and elasticities with respect to parameters and initial conditions for complex disease models. This capability has allowed us to reinterpret field observations that are available for only a limited number of years in the context of the transient behaviour of our model and identified the critical components of the disease pathway which require better understanding and parametrization.

Software

SENSAI is a hybrid MATLAB/Maple package that uses the symbolic differentiation capabilities of Maple to differentiate the right-hand side function of the ODE or map and automatically write the MATLAB subroutines to compute the derivatives with respect to the system variables and with respect to the parameters, including user-defined function of parameters. The right-hand side of the nonlinear map or ODE model, its parameters and initial conditions, quantity of interest and user-prescribed parameter may be defined either by using a graphical user interface for simple models or by adapting Maple templates for more sophisticated models. By default, the package uses the stiff solver ODE13s to integrate initial value problems.

The code is freely available from the website http://www.fescue.colostate.edu/SENSAI. Other examples and Maple templates are available at this site.

Several other software packages are also available for the construction and analysis of deterministic and stochastic matrix population models, including Poptools in Excel, (see http://www.poptools.org/) and Popbio in R (see http://cran.r-project.org/web/packages/popbio/popbio.pdf). These packages also support the analysis of data to construct deterministic models and stochastic models. Sophisticated software for computing sensitivities of systems of differential equations can be found in CVODES, a component of the SUNDIALS package Hindmarsh *et al.* (2005).

Acknowledgements

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(A) Details of the genetics model

Details of the single-locus population genetic model are described, including simplifying assumptions that may be changed or relaxed to modify the model.

Assumption 1 Fecundity occurs after survivorship and transition

and let

$$\boldsymbol{x}_{\{n\}}(t+1,\boldsymbol{p}) = \boldsymbol{g}_{\{n\}}(\boldsymbol{x}_{\{n\}}(t,\boldsymbol{p}),\boldsymbol{p}) + \boldsymbol{f}_{\{n\}}(\boldsymbol{g}_{\{n\}}(\boldsymbol{x}_{\{n\}}(t,\boldsymbol{p}),\boldsymbol{p}),\boldsymbol{p}) \quad \text{eqn 29}$$

where $\boldsymbol{f}$ denotes fecundity and $\boldsymbol{g}$ denotes survivorship and transition. We make this distinction as survivorship and transition occurs *within* genotypes while fecundity occurs *across* genotypes. We consider only a single locus with two alleles A and a and let

$$\boldsymbol{x}_{\{3n\}}(t,\boldsymbol{p}) = \begin{pmatrix} \boldsymbol{x}^{AA}_{\{n\}}(t,\boldsymbol{p}) \\ \boldsymbol{x}^{Aa}_{\{n\}}(t,\boldsymbol{p}) \\ \boldsymbol{x}^{aa}_{\{n\}}(t,\boldsymbol{p}) \end{pmatrix}. \quad \text{eqn 30}$$

Noting that survivorship and transition occur independently *within* each genotype, we define

$$\boldsymbol{g}_{\{3n\}}(\boldsymbol{x}_{\{3n\}}(t,\boldsymbol{p}),\boldsymbol{p}) = \begin{pmatrix} \boldsymbol{g}_{\{n\}}(\boldsymbol{x}^{AA}_{\{n\}}(t,\boldsymbol{p}),\boldsymbol{p}) \\ \boldsymbol{g}_{\{n\}}(\boldsymbol{x}^{Aa}_{\{n\}}(t,\boldsymbol{p}),\boldsymbol{p}) \\ \boldsymbol{g}_{\{n\}}(\boldsymbol{x}^{aa}_{\{n\}}(t,\boldsymbol{p}),\boldsymbol{p}) \end{pmatrix}. \quad \text{eqn 31}$$

Random mating is applied through the action of the nonlinear vector-valued function

$$\boldsymbol{f}_{\{3n\}}(\boldsymbol{x}_{\{3n\}}(t,\boldsymbol{p}),\boldsymbol{p}), \quad \boldsymbol{f}_{\{3n\}} : \mathbb{R}^{3n} \times \mathbb{R}^{\mathrm{K}} \mapsto \mathbb{R}^{3n}. \quad \text{eqn 32}$$

We further assume

Assumption 2 Genotype affects survivorship and fecundity independently.

Assumption 3 We can model the role of genotype through two fitness functions $\boldsymbol{V}(\cdot,\boldsymbol{p})$ and $\boldsymbol{W}(\cdot,\boldsymbol{p})$ where $\boldsymbol{V}(\cdot,\boldsymbol{p})$ is the effect on fecundity and $\boldsymbol{W}(\cdot,\boldsymbol{p})$ is the effect on survivorship and transition.

As $\boldsymbol{x}(\cdot,\boldsymbol{p})$, $\boldsymbol{g}(\cdot,\boldsymbol{p})$, $\boldsymbol{f}(\cdot,\boldsymbol{p})$, $\boldsymbol{V}(\cdot,\boldsymbol{p})$ and $\boldsymbol{W}(\cdot,\boldsymbol{p})$ all depend explicitly on $\boldsymbol{p}$, we suppress this dependence for clarity. Thus,

$$\begin{aligned}\boldsymbol{x}_{\{3n\}}(t+1) = {} & \boldsymbol{W}(\boldsymbol{g}_{\{3n\}}(\boldsymbol{x}_{\{3n\}}(t))) \\ & + \boldsymbol{V}(\boldsymbol{f}_{\{3n\}}(\boldsymbol{W}(\boldsymbol{g}_{\{3n\}}(\boldsymbol{x}_{\{3n\}}(t)))))\end{aligned} \quad \text{eqn 33}$$

To simplify this expression, let

$$\widehat{\boldsymbol{x}}_{\{3n\}} = \boldsymbol{W}(\boldsymbol{g}_{\{3n\}}(\boldsymbol{x}_{\{3n\}}(t))) \quad \text{eqn 34}$$

where $\widehat{\boldsymbol{x}}_{\{3n\}}$ represents the population after survivorship and transition and prior to mating, then

$$\boldsymbol{x}_{\{3n\}}(t+1) = \widehat{\boldsymbol{x}}_{\{3n\}} + \boldsymbol{V}(\boldsymbol{f}_{\{3n\}}(\widehat{\boldsymbol{x}}_{\{3n\}})). \quad \text{eqn 35}$$

THE TWO-STAGE POPULATION MODEL WITH SINGLE-LOCUS GENETICS

We now describe an extension of the two-stage Caswell model in 'Quantities of Interest' to produce a model that describes selection at a single locus.

Assumption 4 The population consists entirely of hermaphrodites.

Extending the model to include separate sexes is straightforward but doubles the number of classes, so we restrict this example to the simpler hermaphrodite case.

We order the six classes ($m = 3, n = 2$) as below

$$\begin{aligned} x_1 &= \text{Juvenile}^{AA},\ x_2 = \text{Adult}^{AA}, \\ x_3 &= \text{Juvenile}^{Aa},\ x_4 = \text{Adult}^{Aa}, \\ x_5 &= \text{Juvenile}^{aa},\ x_6 = \text{Adult}^{aa}. \end{aligned}$$

and let

$$N(t) = \sum_{i=1}^{6} x_i(t). \quad \text{eqn 36}$$

Here, we assume that fitnesses of genotypes are partially dominant and affect survivorship and transition only (and not fecundity), and that allele a is deleterious. Further, we assume that the function $\boldsymbol{W}(\boldsymbol{x},\boldsymbol{p})$ is simply multiplication $\boldsymbol{W}\boldsymbol{x}$ where $\boldsymbol{W} \in \mathbb{R}^{3n\times 3n}$and that the function $\boldsymbol{V}(\boldsymbol{x},\boldsymbol{p})$ is the identity map $\boldsymbol{I}\boldsymbol{x}$ where $\boldsymbol{I}$ is the $3n \times 3n$ identity matrix. Other modelling assumptions, such as when the genotype affects fecundity only, when survivorship, transition and fecundity depend upon genotype, or when fecundity occurs before survivorship and transition, are all readily handled within this general mathematical framework (and within SENSAI).

SURVIVORSHIP AND TRANSITION

We define survivorship and transition as

$$\left.\begin{aligned} g_{2i-1} &= w_i\left[\sigma_1 e^{-N}(1-\gamma)x_{2i-1}\right] \\ g_{2i} &= w_i\left[\sigma_1 e^{-N}\gamma x_{2i-1} + \sigma_2 x_{2i}\right] \end{aligned}\right\}, \quad i = 1,2,3, \qquad \text{eqn 37}$$

where parameters γ, σ_1 and σ_2 are as defined in Table 1. Let the effect of genotype on survivorship and transition be implemented via the relative fitnesses of the three genotype AA, Aa and aa, respectively

$$w_1 = 1, \quad w_2 = 1 - hs, \quad w_3 = 1 - s, \qquad \text{eqn 38}$$

i.e.

$$\boldsymbol{W}(h,s) = \begin{pmatrix} w_1 & 0 & \vdots & 0 & 0 & \vdots & 0 & 0 \\ 0 & w_1 & \vdots & 0 & 0 & \vdots & 0 & 0 \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ 0 & 0 & \vdots & w_2 & 0 & \vdots & 0 & 0 \\ 0 & 0 & \vdots & 0 & w_2 & \vdots & 0 & 0 \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ 0 & 0 & \vdots & 0 & 0 & \vdots & w_3 & 0 \\ 0 & 0 & \vdots & 0 & 0 & \vdots & 0 & w_3 \end{pmatrix}$$

$$= \begin{pmatrix} 1 & 0 & \vdots & 0 & 0 & \vdots & 0 & 0 \\ 0 & 1 & \vdots & 0 & 0 & \vdots & 0 & 0 \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ 0 & 0 & \vdots & 1-hs & 0 & \vdots & 0 & 0 \\ 0 & 0 & \vdots & 0 & 1-hs & \vdots & 0 & 0 \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ 0 & 0 & \vdots & 0 & 0 & \vdots & 1-s & 0 \\ 0 & 0 & \vdots & 0 & 0 & \vdots & 0 & 1-s \end{pmatrix}, \qquad \text{eqn 39}$$

which is the usual form for *partial dominance* where s is the selection coefficient and h determines the degree of dominance (Hedrick 2009). When $h = 0$, allele a is completely recessive, when $h = 0{\cdot}5$, alleles A and a are co-dominant, and when $h = 1$, the allele a is completely dominant.

FECUNDITY AND MATING

We define the proportion of each class of adults in the mating population, y_{2i}, as

$$y_{2i}(t) = \frac{x_{2i}(t)}{M(t)}, \quad i = 1,2,3, \quad M(t) = \sum_{i=1}^{3} x_{2i}(t), \qquad \text{eqn 40}$$

where $M(t)$ is the mating population. Next, we define the proportion of new juveniles of each genotype AA, Aa, aa expected from random mating of an adult population. Dropping the explicit dependence on t, let

$$\begin{aligned} \varphi_1(t) &= y_2y_2 + 0{\cdot}5y_2y_4 + 0{\cdot}5y_4y_2 + 0{\cdot}25y_4y_4 \\ &= y_2^2 + y_2y_4 + 0{\cdot}25y_4^2 \\ \varphi_2(t) &= 0{\cdot}5y_2y_4 + y_2y_6 + 0{\cdot}5y_4y_2 + 0{\cdot}5y_4y_4 \\ &\quad + 0{\cdot}5y_4y_6 + y_6y_2 + 0{\cdot}5y_6y_4 \\ &= y_2y_4 + 2y_2y_6 + 0{\cdot}5y_4^2 + y_4y_6 \\ \varphi_3(t) &= 0{\cdot}25y_4y_4 + 0{\cdot}5y_4y_6 + 0{\cdot}5y_6y_4 + y_6y_6 \\ &= 0{\cdot}25y_4^2 + y_4y_6 + y_6^2. \end{aligned}$$

and

$$f_{2i-1}(\boldsymbol{x},t) = b\varphi_i(t)M(t), \quad i = 1,2,3. \qquad \text{eqn 41}$$

Combining equations (37), (39) and (41), and using the notation of equation (18),

$$\boldsymbol{h}(\boldsymbol{x}) = \boldsymbol{W}\boldsymbol{g}(\boldsymbol{x}) + \boldsymbol{I}\boldsymbol{f}(\boldsymbol{W}\boldsymbol{g}(\boldsymbol{x})) = \boldsymbol{W}\boldsymbol{g}(\boldsymbol{x}) + \boldsymbol{f}(\boldsymbol{W}\boldsymbol{g}(\boldsymbol{x})). \qquad \text{eqn 42}$$

(B) A comment on $\mathscr{R}_0$

The popular index $\mathscr{R}_0$, the *basic reproductive ratio for infectious disease*, is a measure of the linear stability (or instability) of *disease-free* equilibrium solutions. For this reason, $\mathscr{R}_0$ is considered a measure of the spread of a disease in a wholly susceptible population after the introduction of a single infected individual. For our example in 'A SIR Model with Logistic Growth'

$$\mathscr{R}_0 = \frac{\beta}{\gamma + \mu + \nu} = \frac{0{\cdot}1}{0{\cdot}02 + 0{\cdot}2 + 0{\cdot}1} = 0{\cdot}3125.$$

The following standard argument shows that the disease-free equilibrium population $S(t) = S^*$, $I^* = R^* = 0$ is unstable if $S^* > \frac{1}{\mathscr{R}_0} = 3{\cdot}2$.

Assume the values of S, I and R are fixed at their equilibrium values and consider a small disturbance $\mathscr{I} > 0$ in the number of infected individuals (from an equilibrium value of zero). Substituting into the differential equation for the number of infected individuals,

$$\begin{aligned} \frac{d\mathscr{I}}{dt} &= \beta S^*.\mathscr{I} - (\gamma + \mu + \nu).\mathscr{I} = (\beta S^* - (\gamma + \mu + \nu)).\mathscr{I} \\ &> 0 \quad \text{if} \quad \beta S^* - (\gamma + \mu + \nu) > 0, \\ \text{i.e.} \quad \frac{d\mathscr{I}}{dt} &> 0 \quad \text{if} \quad S^* > \frac{\gamma + \mu + \nu}{\beta} = \frac{1}{\mathscr{R}_0}. \end{aligned}$$

The complete linear stability picture for the disease-free equilibrium solution is provided by the eigenvalues and eigenvectors of the Jacobian $\partial\boldsymbol{h}/\partial\boldsymbol{x}$ (using the notation of equation (23)) evaluated at the equilibrium solution. For the parameter values chosen here, the disease-free equilibrium solution is $S^* = 600$, $I^* = R^* = 0$ and the Jacobian evaluated at this point has two stable and one unstable eigenvalues, $-0{\cdot}3$, $-0{\cdot}2$ and $59{\cdot}7$, respectively. The eigenvector corresponding to the most stable eigenvalue ($-0{\cdot}3$) has a non-zero S-component, but zero I and R components. The eigenvector corresponding

to the other stable eigenvector (−0·2) has non-zero S and R components, but zero I component. This is to be expected because the disease-free equilibrium is stable when the population contains only susceptible and recovered individuals (i.e. is stable within the subspace of disease-free solutions). The unstable eigenvector has a nonzero I component, because the disease-free equilibrium is unstable in the presence of disease.

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Supporting Information

Additional Supporting Information may be found in the online version of this article.

Appendix S1. The tar file SENSAI_code.tar contains the Matlab and Maple files that comprise the package SENSAI. The software required and instructions for using the code, as well as a discussion of examples provided appear in the file README/README.pdf.

[Correction made after online publication 1 April 2011: addition of Supporting Information section].

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