Sensitivity analysis for nonlinear population models

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1 Introduction

In this paper we introduce a package hybrid MATLAB/Maple package called SENSAI in order to perform a forward sensitivity analyses for parametrized nonlinear maps and for parametrized systems of nonlinear first-order ordinary differential equations. Sensitivities of all variables with respect to all parameters and with respect to all initial conditions are evaluated. Sensitivities may also be computed with respect to a user-defined quantity of interest that can be a nonlinear function of the variables and parameters and with respect to a user-defined parameter. We use this tool to investigate the sensitivities of nonlinear models for selection of traits coded by a single pair of alleles. We demonstrate the distinct sensitivity differences for the common selection mechanisms of partial dominance, over dominance and frequency dependent selection.

Needs another introductory paragraph laying out why sensitivity of models is important in population biology, especially in nonlinear systems, and that sensitivity analyses in genetic models have been limited to examining stability of equilibrium points.

2 Parametrized nonlinear maps

The basic iterative process we consider is the parametrized nonlinear map

\[
\begin{align*}
  x(t + 1, \theta) &= g(x(t, \theta), \theta) \\
  x(0) &= z
\end{align*}
\]

(1)

where \( x \in \mathbb{R}^{\text{xdim}} \), \( \theta \in \mathbb{R}^{\text{kdime}} \), and with initial conditions \( z \in \mathbb{R}^{\text{xdim}} \) or component-wise,

\[
\begin{align*}
  x_i(t + 1, \theta) &= g_i(x(t); \theta) \\
  x_i(0) &= z_i 
\end{align*}
\]

\( i = 1, \ldots, \text{xdim} \). (2)

Differentiating equation (2) with respect to the \( k \)th parameter \( \theta_k \) gives

\[
\begin{align*}
  \frac{\partial x_i}{\partial \theta_k}(t + 1) &= \sum_{m=1}^{\text{xdim}} \left( \frac{\partial g_i}{\partial x_m} \frac{\partial x_m}{\partial \theta_k}(t) + \frac{\partial g_i}{\partial \theta_k} \right) \\
  \frac{\partial x_i}{\partial \theta_k}(0) &= 0
\end{align*}
\]

(3)
To determine the sensitivity of the solution variable $x_i$ with respect to the initial condition $z_j$, we differentiate (2) with respect to $z_j$, i.e.,

$$\frac{\partial x_i}{\partial z_j}(t+1) = \sum_{m=1}^{\text{xdim}} \left( \frac{\partial g_i}{\partial x_m} \frac{\partial x_m}{\partial z_j}(t) \right) + \frac{\partial g_i}{\partial z_j}, \quad i = 1, \ldots, \text{xdim}, j = 1, \ldots, \text{xdim}, \quad (4)$$

$$\frac{\partial x_i}{\partial z_i}(0) = 1, \quad \frac{\partial x_i}{\partial z_l}(0) = 0, \quad l = 1, \ldots, \text{xdim}, l \neq i,$$

For notational convenience we consider the $j$th initial conditions $z_j$ to be a parameter which we label $\theta_{\text{kdim}+j}$. Re-writing equation (4) we have

$$\frac{\partial x_i}{\partial \theta_{\text{kdim}+j}}(t+1) = \sum_{m=1}^{\text{xdim}} \left( \frac{\partial g_i}{\partial x_m} \frac{\partial x_m}{\partial \theta_{\text{kdim}+j}}(t) \right) + \frac{\partial g_i}{\partial \theta_{\text{kdim}+j}}, \quad i = 1, \ldots, \text{xdim}, j = 1, \ldots, \text{xdim}. \quad (5)$$

$$\frac{\partial x_i}{\partial \theta_{\text{kdim}+i}}(0) = 1, \quad \frac{\partial x_i}{\partial \theta_{\text{kdim}+l}}(0) = 0, \quad l = 1, \ldots, \text{xdim}, l \neq i,$$

To solve for both the variables and their sensitivities with respect to the parameters and initial conditions we evolve equations (2), (3) and (5) simultaneously. This is a system of size $\text{xdim}^*(1+k_{\text{dim}+\text{xdim}})$.

Observe that to evolve (3) and (5) in order to determine the sensitivity of variable $x_i$ where $i = 1, \ldots, \text{xdim}$ with respect to parameters $\theta_k, k = 1, \ldots, k_{\text{dim}+\text{xdim}}$ at any $t > 0$ we need to evaluate all partial derivatives of the right-hand-side function $g$ with respect to the variables $\theta$, i.e., to evaluate the Jacobian $\partial g_i/\partial x_j, i, j = 1, \ldots, \text{xdim}$ and all the partial derivatives of the right-hand-side function $g$ with respect to the parameters $\theta$, i.e., $\partial g_i/\partial \theta_k, i = 1, \ldots, \text{xdim}, k = 1, \ldots, k_{\text{dim}}$. The essential feature of SENSAI is that it computes these derivatives using Maple and automatically writes the MATLAB routines necessary to evaluate these derivatives.

In many instances the outcome of greatest interest is a (possibly nonlinear) function of the solution and the parameters. Let the quantity of interest (QoI) the a scalar valued function of time, such that

$$Q(t) = Q(x(t, \theta), \theta). \quad (6)$$

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

$$\frac{\partial Q}{\partial \theta_k}(t) = \sum_{m=1}^{\text{xdim}} \left( \frac{\partial Q}{\partial x_m} \frac{\partial x_m}{\partial \theta_k}(t) \right) + \frac{\partial Q}{\partial \theta_k}, \quad k = 1, \ldots, k_{\text{dim}+\text{xdim}}. \quad (7)$$

[Note: The QoI cannot depend explicitly on time $t$, nor explicitly on the initial conditions $z$.]

On rare occasions the user may wish to define a new “parameter” $p(\theta)$ that is a function of existing parameters. The sensitivities of the variables $x(t)$ and the quantity of interest $Q(t)$ can be computed with respect to this new “parameter”.
3 Systems of nonlinear first order o.d.e.s

The above argument is completely analogous for systems of nonlinear first-order ordinary differential equations, namely

\[
\dot{x}(t, \theta) = g(x(t, \theta), \theta)
\]
\[x(0) = z\]  \hspace{1cm} (8)

where \( x \in \mathbb{R}^{xdim}, \theta \in \mathbb{R}^{kdim} \) and the initial conditions \( z \in \mathbb{R}^{xdim} \). Using index notation, we rewrite equation (8) as

\[
\dot{x}_i(t, \theta) = g_i(x(t); \theta), \quad x_i(0) = z_i
\]  \hspace{1cm} (9)

Differentiating equation (9) with respect to the \( k \)th parameter \( \theta_k \) gives

\[
\frac{d}{dt} \left( \frac{\partial x_i}{\partial \theta_k} \right) = \sum_{m=1}^{xdim} \left( \frac{\partial g_i}{\partial x_m} \frac{\partial x_m}{\partial \theta_k} + \frac{\partial g_i}{\partial \theta_k} \right), \quad i = 1, \ldots, xdim, \quad k = 1, \ldots, kdim.
\]  \hspace{1cm} (10)

Differentiating equation (9) with respect to the \( j \)th initial condition \( z_j \) gives

\[
\frac{d}{dt} \left( \frac{\partial x_i}{\partial z_j} \right) = \sum_{m=1}^{xdim} \left( \frac{\partial g_i}{\partial x_m} \frac{\partial x_m}{\partial z_j} + \frac{\partial g_i}{\partial z_j} \right), \quad i = 1, \ldots, xdim, \quad j = 1, \ldots, xdim,
\]
\[
\frac{\partial x_i}{\partial z_i}(0) = 1,
\]
\[
\frac{\partial x_i}{\partial z_l}(0) = 0, \quad l = 1, \ldots, xdim, \quad l \neq i.
\]  \hspace{1cm} (11)

To solve for both the population and its stability with respect to parameters and initial conditions we solve equations (9), (10) and (11) simultaneously using the MATLAB solver \texttt{ode45}. This is a system of first-order differential equations of size \( xdim*(1+kdim+xdim) \).

4 Examples

4.1 Population models as nonlinear maps

4.1.1 Caswell (2008), example 1, page 67

In this two stage example, in which \( x_1 \) is the number of juveniles in the population and \( x_2 \) is the number of adults. Let

\[
g = \begin{pmatrix}
\sigma_1(1 - \gamma)x_1 + r x_2 \\
\sigma_1 \gamma x_1 + \sigma_2 x_2
\end{pmatrix}, \quad \text{where} \quad \sigma_1 = \tilde{\sigma} e^{-(x_1 + x_2)},
\]  \hspace{1cm} (12)

with initial conditions

\[
z^T = (0.2 \ 0.2)^T,
\]  \hspace{1cm} (13)

and parameters

\[
r = 0.25, \quad \gamma = 1/15, \quad \tilde{\sigma} = 0.98, \quad \sigma_2 = 0.95.
\]  \hspace{1cm} (14)

We choose \( Q(x, \theta) = x_1 + x_2 \).
To specify the model, parameters and quantity of interest, please see Examples/MAP_examples/Caswell08/Caswell08.mw or enter the information directly from the GUI.

Figure 1: Caswell (2008): Solutions $x_1$ and $x_2$

Figure 2: Caswell (2008): Sensitivities of variable $x_1$ with respect to parameters $\theta_1, \ldots, \theta_4$
Figure 3: Caswell (2008): Sensitivities of variable $x_2$ with respect to parameters $\theta_1, \ldots, \theta_4$

Figure 4: Caswell (2008): Sensitivities of variables $x_1$ and $x_2$ with respect to initial conditions $z_1$ and $z_2$
Figure 5: Caswell (2008): Sensitivities of the quantity of interest with respect to parameters $\theta_1, \ldots, \theta_4$

Figure 6: Caswell (2008): Sensitivities of quantity of interest with respect to initial conditions $z_1$ and $z_2$
Figure 7: Caswell (2008): Sensitivities of variables and quantity of interest with respect to the “new” parameter, $p = (\theta_2, \theta_3)$

4.1.2 Caswell model with single locus genetics

We now consider the effect of selection on a phenotype determined by a single pair of alleles. The number of classes triples from just two, juveniles and adults to six classes. We order these six classes (somewhat arbitrarily) as below.

$x_1 = \text{Juvenile}_{AA}, \quad x_2 = \text{Adult}_{AA},$
$x_3 = \text{Juvenile}_{AB}, \quad x_4 = \text{Adult}_{AB},$
$x_5 = \text{Juvenile}_{BB}, \quad x_6 = \text{Adult}_{BB}.$

Let the breeding population $M$ be the total number of adults, i.e.,

$$M = \sum_{i=1}^{3} x_{2i}$$  \hspace{1cm} (15)

and the proportion of each class of adults in the breeding population, $y_{2i}$ be

$$y_{2i} = \frac{x_{2i}}{M}, \quad i = 1, 2, 3.$$  \hspace{1cm} (16)

The total population $N$, i.e., the total number of individuals is

$$N = \sum_{i=1}^{6} x_i.$$  \hspace{1cm} (17)

Next we define the proportion of new juveniles of each genotype AA, AB, BB expected from randomly mating the adult population, assuming that adults are hermaphrodites (i.e., we do not consider the case of separate sexes, although extension to a mating system with separate sexes
would be trivial). Let

\[ f_1 = y_2y_2 + 0.5y_2y_4 + 0.5y_4y_2 + 0.25y_4y_4 \]
\[ = y_2^2 + y_2y_4 + 0.25y_4^2 \]
\[ f_2 = 0.5y_2y_4 + y_2y_6 + 0.5y_4y_2 + 0.5y_4y_4 + 0.5y_4y_6 + y_6y_2 + 0.5y_6y_4 \]
\[ = y_2y_4 + 2y_2y_6 + 0.5y_4^2 + y_4y_6 \]
\[ f_3 = 0.25y_4y_4 + 0.5y_4y_6 + 0.5y_6y_4 + y_6y_6 \]
\[ = 0.25y_4^2 + y_4y_6 + y_6^2. \]

**Partial Dominance:** Let selection be implemented via the relative fitnesses

\[ w_1 = 1, \quad w_2 = 1 - hs, \quad w_3 = 1 - s, \]

the usual form for *partial dominance* where \( s \) is the selection coefficient and \( h \) determines the degree of dominance \((h = 0: \text{B allele is completely recessive}, \ h = 0.5: \text{A and B alleles codominant}, \ h = 1: \text{B allele completely dominant})\). The extension of the Caswell two-stage model to include single locus genetics with partial dominance is

\[
\begin{align*}
g_{2i-1} &= w_i \left[ \sigma_1 e^{-N} (1 - \gamma)x_i + r f_i M \right], \\
g_{2i} &= w_i \left[ \sigma_1 e^{-N} \gamma x_i + \sigma_2 x_{2i} \right], \quad i = 1, 2, 3. \tag{18}
\end{align*}
\]

For an implementation of partially dominant selection, please see Examples/MAP_examples/Caswell_genetics/PartialDominance/PartialDominance.mw.

*** Calculations need to be repeated ***

**Over Dominance:** Alternatively, the effect of genetics be implemented via the fitnesses

\[ w_1 = 1 - s_1, \quad w_2 = 1, \quad w_3 = 1 - s_2 \]

so-called *over dominance*. For an implementation of over dominant selection, please see Examples/MAP_examples/Caswell_genetics/OverDominance/OverDominance.mw.

**Frequency Dependence:** The effect of genetics may also be implemented via the fitnesses

\[ w_1 = 1 - sp^2, \quad w_2 = 1, \quad w_3 = 1 - sq^2 \]

where \( p \) and \( q \) are the frequencies of \( A \) and \( B \) alleles in the *adult (breeding)* population,

\[ p = y_2 + 0.5y_4, \quad q = 0.5y_4 + y_6 \]

so-called *frequency dependence*. For an implementation of over dominant selection, please see Examples/MAP_examples/Caswell_genetics/FrequencyDependence/FrequencyDependence.mw.

*** Calculations need to be repeated ***

### 4.1.3 Doebeli model with single locus genetics

We now consider the effect of single allele genetics with partial dominance. Let

\[ x_1 = x_{AA}, \quad x_2 = x_{AB}, \quad x_3 = x_{BB}; \]
and

\[ M = \sum_{i=1}^{3} x_i \quad \text{and} \quad y_i = \frac{x_i}{M}, \quad i = 1, 2, 3. \]  

The fitness function \( \xi_i \) for each class is given by

\[ \xi_i = \frac{\lambda_i}{(1 + a_i M)^{b_i}}, \quad i = 1, 2, 3. \]

We define

\[ f_1 = y_1 y_1 + 0.5 y_1 y_2 + 0.5 y_2 y_1 + 0.25 y_2 y_2 \]
\[ = y_1^2 + y_1 y_2 + 0.25 y_2^2 \]
\[ f_2 = 0.5 y_1 y_2 + y_1 y_3 + 0.5 y_2 y_1 + 0.5 y_1 y_3 + y_3 y_1 + 0.5 y_3 y_2 \]
\[ = y_1 y_2 + 2 y_1 y_3 + 0.5 y_2^2 + y_2 y_3 \]
\[ f_3 = 0.25 y_2 y_2 + 0.5 y_2 y_3 + 0.5 y_3 y_2 + y_3 y_3 \]
\[ = 0.25 y_2^2 + y_2 y_3 + y_3^2 \]

**Partial Dominance:** Let the effect of genetics be implemented via the fitnesses

\[ w_1 = 1, \quad w_2 = 1 - hs, \quad w_3 = 1 - s \]

i.e., partial dominance. We now define

\[ g_i = w_i \xi_i f_i M, \quad i = 1, 2, 3 \]

and choose

\[ \lambda_i = 10, \quad a_i = 0.1, \quad b_i = 2.25, \quad i = 1, 2, 3 \]

so that the equilibrium solution has a periodic orbit of period two. As our quantity of interest, we choose the fraction of the population with AA genotype, i.e.,

\[ Q(x, \theta) = \frac{x_1}{x_1 + x_2 + x_3} \]

For an implementation of partially dominant selection, please see

Examples/MAP_examples/Doebeli_genetics/PartialDominance/PartialDominance.mw
Figure 8: Doebeli (1999): No selection, $h = 0.5$ and $s = 0$. Solutions $x_1, x_2, x_3$. Note that the equilibrium solution is a periodic orbit with period two.

Figure 9: Doebeli (1999): No selection, $h = 0.5$ and $s = 0$. Quantity of interest, $Q = x_1/(x_1 + x_2 + x_3)$ and its sensitivities of with respect to the parameters, $\theta_1, \ldots, \theta_{11}$. Note that despite the fact that the variables are periodic, the quantity of interest is a constant.
Figure 10: Doebeli (1999): Partial Dominance, \( h = 0.5 \) and \( s = 0.075 \). Solutions \( x_1, x_2, x_3 \). Note that the equilibrium solution is a periodic orbit with period two.

Figure 11: Doebeli (1999): Partial Dominance, \( h = 0.5 \) and \( s = 0.075 \). Quantity of interest, \( Q = x_1/(x_1 + x_2 + x_3) \) and its sensitivities of with respect to the parameters, \( \theta_1, \ldots, \theta_{11} \). At equilibrium, the AA genotype comprises the entire population.
**Frequency Dependence:** The effect of genetics may also be implemented via the fitnesses

\[ w_1 = 1 - sp^2, \quad w_2 = 1, \quad w_3 = 1 - sq^2 \]

where \( p \) and \( q \) are the frequencies of \( A \) and \( B \) alleles in the population,

\[ p = y_1 + 0.5y_2, \quad q = 0.5y_2 + y_3 \]

so-called *frequency dependence*. As our quantity of interest, we choose the fraction of the population that are heterozygous with \( AB \) genotype, i.e.,

\[ Q(x, \theta) = \frac{x_2}{x_1 + x_2 + x_3} \]

For an implementation of frequency dependent selection, please see Examples/MAP_examples/Doebeli_genetics/FrequencyDependence/FrequencyDependence.mw

Figure 12: Doebeli (1999): No selection. Solutions \( x_1, x_2, x_3 \). Note that the equilibrium solution is a periodic orbit with period two.
Figure 13: Doebeli (1999): No selection. Quantity of interest, \( Q = \frac{x_2}{(x_1 + x_2 + x_3)} \) and its sensitivities of with respect to the parameters, \( \theta_1, \ldots, \theta_{10} \). Note that despite the fact that the variables are periodic, the quantity of interest is a constant.

Figure 14: Doebeli (1999): Frequency Dependence, \( s = 0.1 \). Solutions \( x_1, x_2, x_3 \).
Figure 15: Doebeli (1999): Frequency Dependence, $s = 0.1$. Quantity of interest, $Q = x_2/(x_1 + x_2 + x_3)$ and its sensitivities of with respect to the parameters, $\theta_1, \ldots, \theta_{10}$. Note that despite the fact that the variables are periodic, the quantity of interest is a constant.

Figure 16: Doebeli (1999): Frequency Dependence, $s = 1$. Solutions $x_1, x_2, x_3$. 
Figure 17: Doebeli (1999): Frequency Dependence, $s = 1$. Quantity of interest, $Q = x_2/(x_1 + x_2 + x_3)$ and its sensitivities of with respect to the parameters, $\theta_1, \ldots, \theta_{10}$. Note that despite the fact that the variables are periodic, the quantity of interest is a constant.

Figure 18: Doebeli (1999): Frequency Dependence, $s = 2.5$. Solutions $x_1, x_2, x_3$. 
Figure 19: Doebeli (1999): Frequency Dependence, \( s = 2.5 \). Quantity of interest, \( Q = x_2/(x_1 + x_2 + x_3) \) and its sensitivities of with respect to the parameters, \( \theta_1, \ldots, \theta_{10} \). Note that despite the fact that the variables are periodic, the quantity of interest is a constant.

Another interesting choice for the quantity of interest is

\[
\frac{dp}{dt} = \frac{d}{dt} \left( \frac{x_1 + 0.5x_2}{x_1 + x_2 + x_3} \right) = \frac{(g_1 + 0.5g_2)(x_1 + x_2 + x_3) - (x_1 + 0.5x_2)(g_1 + g_2 + g_3)}{(x_1 + x_2 + x_3)^2} \equiv 0
\]

for this choice of parameters.

**Over Dominance:** For an implementation of over dominant selection, please see Examples/MAP_examples/Doebeli_genetics/OverDominance/OverDominance.mw.

### 4.2 Population models as nonlinear ODEs

#### 4.2.1 SIR

The classic SIR disease model is the system of ordinary differential equations below,

\[
\begin{align*}
\dot{S} &= bN \left(1 - \frac{N}{K}\right) - \beta SI - dS \\
\dot{I} &= \beta SI - \gamma I - dI - cI \\
\dot{R} &= \gamma I - dR
\end{align*}
\]

where \( N = S + I + R \). We choose

\[
b = 0.5, \ K = 100, \ \beta = 0.1, \ d = 0.0, \ \gamma = 0.02, \ c = 0.
\]
As our quantity of interest, we choose the fraction of the population that is infected, i.e.,

$$Q(x, \theta) = \frac{x_2}{x_1 + x_2 + x_3}.$$ 

To specify the model, parameters and quantity of interest, please see Examples/ODE_examples/SIR/SIR.mw or enter the information directly from the GUI.

Figure 20: SIR. Solution, $x_1, x_2, x_3$.

Figure 21: SIR. Quantity of interest, $Q = x_2/(x_1 + x_2 + x_3)$ and its sensitivities with respect to the parameters $\theta_1, \ldots, \theta_6$. 

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4.2.2 Predator Prey with genetics

The basic predator prey model is the coupled pair of ordinary differential equations.

\[
\begin{align*}
\frac{dx}{dt} &= rx - \gamma xy \\
\frac{dy}{dt} &= c\gamma xy - dy - ey^2
\end{align*}
\]

This system has a fixed point at

\[
(x_{eq}, y_{eq}) = \left( \frac{1}{c\gamma} \left[ d + \frac{er}{\gamma} \right], \frac{x_i}{M}, i = 1, 2, 3 \right)
\]

We choose \(r = 0.2, \gamma = 0.05, c = 0.5, d = 0.1\). When \(e = 0\) the fixed point at \((x_{eq}, y_{eq})\) is a center. When \(e > 0\), the fixed point is a stable spiral.

We now consider the effect of selection of the prey population only based on a phenotype determined by a single pair of alleles. We now have three prey populations. Let

\[
x_1 = x_{AA}, \quad x_2 = x_{AB}, \quad x_3 = x_{BB}, \quad M = \sum_{i=1}^{3} x_i, \quad \text{and} \quad y_i = \frac{x_i}{M}, \quad i = 1, 2, 3.
\]

Similarly to the previous examples we define

\[
\begin{align*}
f_1 &= y_1^2 + y_1y_2 + 0.25y_2^2 \\
f_2 &= y_1y_2 + 2y_1y_3 + 0.5y_2^2 + y_2y_3 \\
f_3 &= 0.25y_2^2 + y_2y_3 + y_3^2.
\end{align*}
\]

**Frequency Dependence:** We let the effect of genetics be implemented via the fitnesses

\[
w_1 = 1 - sp^2, \quad w_2 = 1, \quad w_3 = 1 - sq^2
\]

where \(p\) and \(q\) are the frequencies of \(A\) and \(B\) alleles in the population, i.e., frequency dependent selection. Then

\[
\begin{align*}
\frac{dx_i}{dt} &= rf_iM - \gamma w_i x_i y, \quad i = 1, 2, 3 \\
\frac{dy}{dt} &= c\gamma M y - dy - ey^2
\end{align*}
\]

For an implementation of frequency dependent selection, please see

Examples/ODE_examples/predator_prey/FrequencyDependence/FrequencyDependence.mw.

*** Calculations need to be repeated ***

In the results shown below, we fix \(h = 0.5\) and consider \(s = 0\) and \(s = 0.075\), and \(e = 0\) and \(e = 0.005\). We choose the quantity of interest to be the ratio of the number of BB prey individuals to the predator population,

\[
Q(x, \theta) = \frac{x_3}{x_4}.
\]
Figure 22: Predator-Prey: No selection. Quantity of interest, $Q = x_3/x_4$ and its sensitivities with respect to the parameters $\theta_1, \ldots, \theta_6$ for $e = 0$.

Figure 23: Predator-Prey: No selection. Quantity of interest, $Q = x_3/x_4$ and its sensitivities with respect to the parameters $\theta_1, \ldots, \theta_6$ for $e = 0.005$. 
Figure 24: Predator-Prey: Frequency Dependence, \( s = 1 \). Quantity of interest, \( Q = x_3/x_4 \) and its sensitivities with respect to the parameters \( \theta_1, \ldots, \theta_6 \) for \( \epsilon = 0 \).

Figure 25: Predator-Prey: Frequency Dependence, \( s = 1 \). Quantity of interest, \( Q = x_3/x_4 \) and its sensitivities with respect to the parameters \( \theta_1, \ldots, \theta_6 \) for \( \epsilon = 0.005 \).
Another interesting choice for the quantity of interest is

$$\frac{dp}{dt} = \frac{d}{dt} \left( \frac{x_1 + 0.5x_2}{x_1 + x_2 + x_3} \right) = \frac{(g_1 + 0.5g_2)(x_1 + x_2 + x_3) - (x_1 + 0.5x_2)(g_1 + g_2 + g_3)}{(x_1 + x_2 + x_3)^2}$$

for this choice of parameters.

We begin the initial value problem with $z_1 = 5, z_2 = 10, z_3 = 1$ and $z_4 = 2$ so that $p \neq 0.5$ and $q \neq 0.5$. Frequency dependent selection creates an equilibrium population (or periodic orbit) such that $p = q = 0.5$ and $dp/dt = 0$.

Figure 26: Predator-Prey: Frequency Dependence, $s = 1$. Quantity of interest, $Q = p$ and its sensitivities with respect to the parameters $\theta_1, \ldots, \theta_6$ for $e = 0$. 
Figure 27: Predator-Prey: Frequency Dependence, $s = 1$. Quantity of interest, $Q = p$ and its sensitivities with respect to the initial conditions $z_1, \ldots, z_4$ for $e = 0$.

Figure 28: Predator-Prey: Frequency Dependence, $s = 1$. Quantity of interest, $Q = dp/dt$ and its sensitivities with respect to the parameters $\theta_1, \ldots, \theta_6$ for $e = 0$. 
Figure 29: Predator-Prey: Frequency Dependence, \( s = 1 \). Quantity of interest, \( Q = dp/dt \) and its sensitivities with respect to the initial conditions \( z_1, \ldots, z_4 \) for \( e = 0 \).

Finally for the stable spiral...

Figure 30: Predator-Prey: Frequency Dependence, \( s = 1 \). Quantity of interest, \( \text{QoI}=p \) and its sensitivities with respect to the parameters \( \theta_1, \ldots, \theta_6 \) for \( e = 0.005 \).
Figure 31: Predator-Prey: Frequency Dependence, $s = 1$. Quantity of interest, QoI=$p$ and its sensitivities with respect to the initial conditions $z_1, \ldots, z_4$ for $e = 0.005$.

**Partial Dominance:** We let the effect of genetics be implemented via the fitnesses

$$w_1 = 1, \quad w_2 = 1 - hs, \quad w_3 = 1 - s$$

(36)

i.e., partial dominance. For an implementation of frequency dependent selection, please see Examples/ODE\_examples/predator\_prey/PartialDominance/PartialDominance.mw.
Figure 32: Predator-Prey: Frequency Dependence, $s = 1$. Quantity of interest, $Q = x_3/x_4$ and its sensitivities with respect to the parameters $\theta_1, \ldots, \theta_6$ for $e = 0$.

Figure 33: Predator-Prey: Frequency Dependence, $s = 1$. Quantity of interest, $Q = x_3/x_4$ and its sensitivities with respect to the parameters $\theta_1, \ldots, \theta_6$ for $e = 0.005$. 

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Figure 34: Predator-Prey: Partial Dominance, $h = 0.5, s = 0.1$. Quantity of interest, $Q = x_3/x_4$ and its sensitivities with respect to the parameters $\theta_1, \ldots, \theta_6$ for $e = 0$.

Figure 35: Predator-Prey: Partial Dominance, $h = 0.5, s = 0.1$. Quantity of interest, $Q = x_3/x_4$ and its sensitivities with respect to the parameters $\theta_1, \ldots, \theta_6$ for $e = 0.005$. 
4.2.3 Plague model

A five variable, 11 parameter model can be handled with ease. Consider

\[
\begin{align*}
\dot{S}_R &= r_R S_R \left(1 - \frac{T_R}{K_R}\right) + r_R R_R (1 - p) - d_R S_R - \frac{S_R}{T_R} F(1 - \exp(-a T_R)), \\
\dot{I}_R &= \beta_R S_R F(1 - \exp(-a T_R)) - (d_R + m_R) I_R \\
\dot{R}_R &= r_R S_R \left(p - \frac{T_R}{K_R}\right) + m_R g_R I_R - d_R R_R \\
\dot{N} &= r_F \left(1 - \frac{T_R}{K_F}\right) + \frac{d_R}{T_R} F(1 - \exp(-a T_R)) \\
\dot{F} &= (d_R + m_R(1 - g_R)) I_R N - d_F F.
\end{align*}
\]

with parameter values

\[
\begin{align*}
r_R &= 5, \quad p = 0.975, \quad K_r = 2500, \\
d_R = 0.2, \quad \beta_R = 4.7, \quad m_R = 20, \quad g_R = 0.02, \\
a = 0.004, \quad r_F = 20, \quad d_F = 10, \quad K_F = 6.57
\end{align*}
\]

In the results shown below we choose the quantity of interest to be the fraction of infected rats, i.e.,

\[
Q(x, \theta) = \frac{x_2}{x_1 + x_2 + x_3}.
\]

For an implementation of the plague model, please see

Examples/ODE_examples/plague/plague.mw.

![Plague model: Solutions](image)

Figure 36: Plague model: Solutions $x_1, \ldots, x_5$. 

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Figure 37: Plague model: Quantity of interest, \( Q = \frac{x_2}{(x_1 + x_2 + x_3)} \) and its sensitivities with respect to the parameters \( \theta_1, \ldots, \theta_{11} \).

A Appendix: The SENSAI package

A.1 Software requirements

1. MATLAB 7.8.0 (R2009a)
2. Maple 13
3. “Maple toolbox for MATLAB” which is freely available from http://www.maplesoft.com/products/MapleMatlab/index.asp (Need to create an account etc...)

A.2 Executing the GUI

1. Open MATLAB
2. Change directory to SENSAI directory
3. Type >> sensai to open GUI
4. Select check box “Input from GUI?” if equations etc are to be entered from the GUI
5. Select check box “Iterated nonlinear map?” if the model is in the form of a map
6. Assuming “Input from GUI?” selected (maximum of four equations and six parameters)

   (a) Enter data using [.] to denote vector elements, i.e., Maple syntax
(b) Select “Create MATLAB files using Maple” which creates gvec.m, dgvec_dxvec.m, dgvec_dparam.m, qoi.m and dcp_dparam.m

(c) Select “Execute MATLAB file created by Maple” which runs gtype.m

7. Assuming “Input from GUI?” is not selected

(a) Create Maple worksheet user_input.mw using templates e.g., Examples/MAP_examples/caswell_ex1/caswell_ex1.mw, or Examples/ODE_examples/SIR/SIR.mw

(b) Execute Maple worksheet user_input.mw creating MATLAB files user_equations.m, user_input.m, user_plotdata.m, user_qoi.m and user_parameters.m

(c) Select “Create MATLAB files using Maple” which creates gvec.m, dgvec_dxvec.m, dgvec_dparam.m, qoi.m and dcp_dparam.m using input from the user_* .m files created above

(d) Select “Execute MATLAB file created by Maple” which runs gtype.m

### A.3 How the GUI works

#### A.3.1 MATLAB files

Check the box “Input from GUI”

On pressing the button “Create Maple files” the GUI reads the right-hand-sides specified in the GUI boxes and calls the MATLAB file mm_interface.m. The MATLAB file mm_interface.m reads and then executes the Maple files listed in §A.3.2 below. The Maple files compute the required derivatives of the right-hand-sides and then write five MATLAB files, gvec.m, dgvec_dxvec.m, dgvec_dparam.m, dqoi_dxvec.m and dcp_dparam.m.

On pressing the button “Run MATLAB files” the GUI reads the initial conditions and parameter values from the GUI boxes and then calls the MATLAB file gtype.m. The MATLAB file gtype.m evolves the nonlinear map or integrates the system of ordinary differential equations and computes the stability of the solutions with respect to the parameters and initial conditions using the routines gvec.m, dgvec_dxvec.m, dgvec_dparam.m, dqoi_dxvec.m and dcp_dparam.m.

#### A.3.2 Maple files

These files are located in the MapleRoutines subdirectory.

1. The Maple files gvec_top.mpl, gvec_middle.mpl and gvec_bottom.mpl create the MATLAB file gvec.m which evaluates the right hand side

2. The Maple files dgvec_dxvec_top.mpl, dgvec_dxvec_middle.mpl and dgvec_dxvec_bottom.mpl create the MATLAB file dgvec_dxvec.m which computes the Jacobian

3. The Maple files dgvec_dparam_top.mpl, dgvec_dparam_middle.mpl and dgvec_dparam_bottom.mpl creates the MATLAB file dgvec_dparam.m which computes derivatives with respect to the parameters

4. The Maple files qoi_top.mpl, qoi_middle.mpl and qoi_bottom.mpl creates the MATLAB file qoi.m which computes the quantity of interest and its derivatives with respect to the variables and the parameters
5. The Maple files dcp_dparam_top.mpl, dcp_dparam_middle.mpl and dcp_dparam_bottom.mpl creates the MATLAB file dcp_dparam.m which computes derivatives of the user defined parameter with respect to the original parameters.

The *_top.mpl and *_bottom.mpl files write MATLAB statements at the top and bottom of each of these MATLAB files. The *_middle.mpl files use the Maple “Matlab” command to write the derivatives computed using Maple to a file in MATLAB syntax. ¹

A.3.3 Post Processing

SENSAI uses the MATLAB save command to create the .mat file PostProcess/gtype_output.mat containing t, x, dxdp, xdim, kdim and tfinal. Here t is a (1 × nt) vector, x is an (xdim × nt) array, dxdp is a (xdim × kdim × nt) array. This information is easily retrieved using the MATLAB load command and manipulated as required, see for example PostProcess/allele_frequency.m.

A.3.4 The key technology

A Maple procedure can (apparently) not receive a vector of strings as an input. To overcome this restriction all right hand sides are concatenated and sent to the Maple files as a single string in which each right hand side is separated by a semicolon. This is achieved in usemaple.m by the commands

```
gtotal=gvec(1,1:length(gvec(1,:)))
for i=2:xdim
    gtotal=strcat(gtotal,';',gvec(i,1:length(gvec(i,:))))
end
gtotal=strcat(' " ',gtotal,' " ')
```

This single string is passed to the Maple procedures in the argument list where it is split using the commands

```
gs:=StringTools[Split](gtotal,";");
for i from 1 to xdim do:
    gx[i]:=parse(gs[i]);
end do:
```

¹One of the quirks of Maple is that this (apparently) cannot be accomplished with a single *.mpl file.