Mth 610: Topics in Model-Constrained Optimization

HW #2 - due on May 11, in class

Solution to ODEs with Simultaneous Sensitivity Analysis (ODESSA)

Mathematical models of dynamical systems are often represented as systems of differential equations that require the specification of various input parameters. In practice, the reliability of the model and the predictive uncertainty are often assessed through a *sensitivity analysis*: analyze how the model output will respond to small variations (uncertainty) in the model parameters.

Consider, for example, the basic SIR model in the mathematical theory of epidemics[1]

$$\frac{dS}{dt} = -\frac{\beta S I}{N} \tag{1}$$
$$\frac{dI}{dt} = \frac{\beta S I}{N} - \gamma I \tag{2}$$
$$\frac{dR}{dt} = \gamma I \tag{3}$$

The significance of the state variables $S(t), I(t), R(t)$ is as follows:

- $S(t)$ the number of individuals susceptible to the disease (not yet infected) at time t.
- $I(t)$ the number of individuals who are infected with the disease at time t and are capable of spreading the disease to those in the susceptible category.
- $R(t)$ the number individuals who have been infected and then removed from the disease, either due to immunization or due to death.

The model parameters are assumed to be constant in time: $\beta > 0$ denotes the contact or infection rate of the disease and $\gamma > 0$ denotes the recovery or death rate of the disease. The total size of the population, constant in time, is $N = S(t) + I(t) + R(t)$. Given a set of initial conditions,

$$S(t_0) = S_0, \quad I(t_0) = I_0, \quad R(t_0) = R_0 \tag{4}$$

the solution to (1-4) is used to predict (forecast) the evolution of the state variables over a time interval $[0, t_f]$.

We may view the state variables as functions of time and model parameters: $S(t,\beta,\gamma), I(t,\beta,\gamma), R(t,\beta,\gamma)$ and in this assignment, we are interested to investigate how small variations in the parameters will impact the time-evolution of the state variables. To a first order approximation (linearization),

$$\Delta I(t) \stackrel{def}{=} I(t, \beta+\delta\beta, \gamma+\delta\gamma) - I(t,\beta,\gamma) \approx \delta I \stackrel{def}{=} \frac{\partial I(t,\beta,\gamma)}{\partial \beta}\delta\beta + \frac{\partial I(t,\beta,\gamma)}{\partial \gamma}\delta\gamma \tag{5}$$

and for the mean value of $I(t)$ over the time interval $[0, t_f]$,

$$J = \frac{1}{t_f}\int_0^{t_f} I(\tau,\beta,\gamma)\,d\tau \tag{6}$$

a first order estimate of the impact of parameter variations may be obtained as

$$\Delta J \stackrel{def}{=} J(\beta+\delta\beta, \gamma+\delta\gamma) - J(\beta,\gamma) \approx \delta J \stackrel{def}{=} \frac{\delta\beta}{t_f}\int_0^{t_f} \frac{\partial I(\tau,\beta,\gamma)}{\partial\beta}\,d\tau + \frac{\delta\gamma}{t_f}\int_0^{t_f} \frac{\partial I(\tau,\beta,\gamma)}{\partial\gamma}\,d\tau \tag{7}$$

Notice that expressions such as (5) and (7) require the evaluation of the time-evolving partial derivatives of the state to parameters (sensitivities)

$$\frac{\partial S(t,\beta,\gamma)}{\partial(\beta,\gamma)}, \quad \frac{\partial I(t,\beta,\gamma)}{\partial(\beta,\gamma)}, \quad \frac{\partial R(t,\beta,\gamma)}{\partial(\beta,\gamma)} \tag{8}$$

[1] Kermack, W. O.; McKendrick, A. G. (1927). "A Contribution to the Mathematical Theory of Epidemics". Proceedings of the Royal Society A: Mathematical, Physical and Engineering Sciences. **115**, 700–721.

In a general framework, consider the system of differential equations

$$
\begin{aligned}
\frac{d\,\mathbf{x}}{d\,t} &= \mathbf{f}(t, \mathbf{x}, \mathbf{u}), \quad t > 0 && (9)\\
\mathbf{x}(0) &= \mathbf{x}_0 && (10)
\end{aligned}
$$

The model $\mathbf{f}$ is assumed to be a regular function (for example, a polynomial expression as in the SIR model); $\mathbf{x}(t) \in \mathbb{R}^n$ denotes the state vector, $\mathbf{u} \in \mathbb{R}^m$ is a vector of time-independent model parameters, and $\mathbf{x}_0 \in \mathbb{R}^n$ is the vector of initial conditions. We view the solution as $\mathbf{x} = \mathbf{x}(t, \mathbf{u})$.

The first order sensitivities of the state vector $\mathbf{x}(t)$ with respect to the parameters $\mathbf{u}$ are defined as

$$
\frac{\partial \mathbf{x}(t)}{\partial u_i} = \lim_{\epsilon \to 0} \frac{\mathbf{x}(t, \mathbf{u} + \epsilon \mathbf{e}_i) - \mathbf{x}(t, \mathbf{u})}{\epsilon} \in \mathbb{R}^{n \times 1}, \quad i = 1, 2, \dots m \tag{11}
$$

and are obtained by solving the $n \times m$ ODE system

$$
\begin{aligned}
\frac{d}{d\,t}\frac{\partial \mathbf{x}}{\partial \mathbf{u}} &= \frac{\partial \mathbf{f}}{\partial \mathbf{x}}(t, \mathbf{x}, \mathbf{u})\frac{\partial \mathbf{x}}{\partial \mathbf{u}} + \frac{\partial \mathbf{f}}{\partial \mathbf{u}}(t, \mathbf{x}, \mathbf{u}) && (12)\\
\frac{\partial \mathbf{x}}{\partial \mathbf{u}}(0) &= \mathbf{0} \in \mathbb{R}^{n \times m} \quad (n \times m \text{ zero matrix}) && (13)
\end{aligned}
$$

In (12 - 13), the sensitivity matrix is

$$
\frac{\partial \mathbf{x}}{\partial \mathbf{u}}(t) = \left[\frac{\partial \mathbf{x}(t)}{\partial u_1}\ \frac{\partial \mathbf{x}(t)}{\partial u_2}\ \dots \frac{\partial \mathbf{x}(t)}{\partial u_m}\right] \in \mathbb{R}^{n \times m}, \quad \left[\frac{\partial \mathbf{x}}{\partial \mathbf{u}}(t)\right]_{i,j} = \frac{\partial x_i(t)}{\partial u_j}, \quad i = 1:n,\ j = 1:m \tag{14}
$$

and the right side terms are as follows:

$$
\frac{\partial \mathbf{f}}{\partial \mathbf{x}}(t, \mathbf{x}, \mathbf{u}) \in \mathbb{R}^{n \times n}, \quad \left[\frac{\partial \mathbf{f}}{\partial \mathbf{x}}(t, \mathbf{x}, \mathbf{u})\right]_{i,j} = \frac{\partial f_i}{\partial x_j}, \quad i = 1:n,\ j = 1:n \tag{15}
$$

denotes the Jacobian matrix of the model with respect to the state $\mathbf{x}(t)$ and

$$
\frac{\partial \mathbf{f}}{\partial \mathbf{u}}(t, \mathbf{x}, \mathbf{u}) \in \mathbb{R}^{n \times m}, \quad \left[\frac{\partial \mathbf{f}}{\partial \mathbf{u}}(t, \mathbf{x}, \mathbf{u})\right]_{i,j} = \frac{\partial f_i}{\partial u_j}, \quad i = 1:n,\ j = 1:m \tag{16}
$$

denotes the Jacobian matrix of the model with respect to the parameters $\mathbf{u}$.

For any quantity of interest (QoI) expressed as a function of state variables,

$$
J = \int_0^{t_f} g(\mathbf{x}(\tau))\, d\tau \quad \in \mathbb{R} \tag{17}
$$

where $g : \mathbb{R}^n \to \mathbb{R}$, the sensitivity to parameters is the m-dimensional vector of partial derivative,

$$
\frac{\partial J}{\partial \mathbf{u}} = \int_0^{t_f} \frac{\partial g}{\partial \mathbf{x}} \frac{\partial \mathbf{x}}{\partial \mathbf{u}}(\tau)\, d\,\tau \quad \in \mathbb{R}^{1 \times m} \tag{18}
$$

and a first order estimate to the impact of a parameter variation $\delta \mathbf{u} \in \mathbb{R}^m$ is obtained as

$$
\Delta J = J(\mathbf{u} + \delta \mathbf{u}) - J(\mathbf{u}) \approx \frac{\partial J}{\partial \mathbf{u}} \delta \mathbf{u} \tag{19}
$$

In the context presented here, your task is to perform a sensitivity analysis of the SIR model with respect to the parameters β and γ, as explained next.

Reference setup:

- Set the parameter values to $\beta = 0.4$, $\gamma = 0.04$;
- Set the size of the population to $N = 1000$, and set the initial conditions (4) to $S_0 = 997, I_0 = 3, R_0 = 0$.

Homework tasks (70 points)

Part A (30 points)

- Integrate the ODE system consisting of the model equations (1-4) and the corresponding sensitivity equations (12 - 13) using the Euler method with a step size $h = 0.01$ in the time interval $[0, 100]$ (that is for $K = 10,000$ time steps), to advance simultaneously in time the state and the state sensitivities to parameters,

$$
\begin{aligned}
&for\ k = 1 : K \\
&\qquad \mathbf{x}_k = \mathbf{x}_{k-1} + h * \mathbf{f}(\mathbf{x}_{k-1}, \mathbf{u}) \\
&\qquad \left[\frac{\partial \mathbf{x}}{\partial \mathbf{u}}\right]_k = \left[\frac{\partial \mathbf{x}}{\partial \mathbf{u}}\right]_{k-1} + h * \left(\left[\frac{\partial \mathbf{f}}{\partial \mathbf{x}}\right]_{k-1} \left[\frac{\partial \mathbf{x}}{\partial \mathbf{u}}\right]_{k-1} + \left[\frac{\partial \mathbf{f}}{\partial \mathbf{u}}\right]_{k-1} \right)
\end{aligned}
$$

- Provide the graphs of the state variables (3 plots, same figure) and the sensitivities (8) (6 plots, use separate figures, as necessary to convey the results). Provide a listing of your code/implementation.

Part B (40 points)

(10 points) Use (5) to provide *a priori* estimates $\pm\delta I$ of the impact on the time evolution of the infected population $I(t)$ associated with 10% variations in the parameter β, $\delta\beta = \pm 0.04$, while keeping fixed $\gamma = 0.04$. Provide the graphs of the state $I(t)$ together with the estimated impact of parameter variations, $I(t) \pm \delta I(t)$.

(10 points) Use the $\beta-$ sensitivities to provide an *a priori estimate* of the parameter $\delta\beta$-impact on the mean value functional (6) evaluated with a simple quadrature method,

$$
J = \frac{h}{100} \sum_{k=1}^{K} I_k
$$

(10 points) Validate the *a priori* impact estimates using nonlinear model integrations with β value set to 0.4 ± 0.04.

(10 points) Repeat the steps above for a 10% variation in the parameter γ, $\delta\gamma = 0.004$, while keeping fixed $\beta = 0.4$.

10 bonus points: Repeat the estimation/validation steps above for variations of $\pm 10\%$ in *both parameters.*