**Motivation**

Parametric sensitivities in nonlinear regression describe the impact of perturbations in model parameter estimates on predicted responses. Poor precision in parameter estimates leads to poor precision in predicted responses when sensitivities are large.

- Identification of influential parameters
- General further experimentation to reduce uncertainties

**Sensitivities are in the context of**
- Specified model formulation: structure and parameterization
- Specified dataset: run conditions & designed experiments

**Multiparameter Regression Models**

**Univariate Model**

- N runs
- \( y_j = \theta_1 x_j + \theta_2 x_j + \theta_3 + \varepsilon_j \)

- Multivariate Model
  - N runs, M responses
  - \( y_{ij} = \theta_1 x_{ij} + \theta_2 x_{ij} + \theta_3 + \varepsilon_{ij} \)

**Profile-Based Sensitivity Coefficient (PSC)**

- Motivated by profiling algorithms of Bates and Watts (1988) for predicting profile plots

\[ f(\theta_0) = \frac{\partial}{\partial \theta} \left[ \frac{1}{N} \sum_{i=1}^{N} \left( y_i - \theta_0 x_i \right)^2 \right] \]

- Profile traces - plots of conditional estimate of one parameter vs another parameter, with parameters held at their conditional estimates
- Profile plots - plots of \( y_{ij} \) vs \( \theta_0 \) show the extent of the parameter nonlinearities in the model
- Indicates both nonlinearity and extent of correlation between parameter estimates

**Profile-Based Sensitivity Coefficient - Unresponse**

**Definition - Unresponse Case**

(Sullivan, 1994; Saltarelli et al., 2000)

\[ \text{PSC} = \frac{\partial y_{ij}}{\partial \theta_0} \]

- Margin sensitivity coefficient: \( \partial y_{ij}/\partial \theta_0 \)
- Connection: accounts for correlation between parameter estimates & sensitivity

**Profile traces**

- Graphical summaries of PSC values

**Example - Unresponse PSC**

- Michaelis-Menten model
- Dataset from Bates and Watts (1988)
- Model equation: \( \frac{f(x, \theta)}{\theta_0} - x_0 \)

**Example - Unresponse PSC**

- Graphical summaries of PSC values

**Multiresponse PSC**

In this case, the parameter estimates are determined to minimize the Box-Draper determinant criterion.

- \( \text{det}(D - \theta_0 R) = \text{det}(D - \theta_0 R) \)

The vector of predicted responses at a nominal run condition is denoted as:

- \(\theta_0(x) = \left\{ \theta_1(x), \theta_2(x), \ldots, \theta_m(x) \right\} \)

The PSC is again defined as a total derivative, yielding a vector of PSC values in this instance:

- \( \text{PSC}(x) = \left\{ \frac{\partial y_{ij}}{\partial \theta_0}, \frac{\partial y_{ij}}{\partial \theta_1}, \ldots, \frac{\partial y_{ij}}{\partial \theta_m} \right\} \)

**Example - Multiresponse PSC**

- Dow Chemical regrowth benchmark
- Isothermal batch reactors
- Dataset consists of concentration profiles over time for batches run at 3 different temperatures
- Data for 3 species used - 3 response variables, \( y_1, y_2, y_3 \)

Model structure included:
- 8 unknown parameters
- 32 system matrices for sensitivity equations
- Measurement times differ for each profile, and are sampled at non-uniform intervals
- Considered by Biegler et al. (1986), Biegler et al. (1991), Guay and McLean (1995)

**Example - Multiresponse PSC**

- Dow Chemical regrowth benchmark example - model
- \( \frac{\partial y_{ij}}{\partial \theta_0} = \frac{y_{ij} - \theta_0 x_{ij}}{1 + y_{ij}} \)

**Summary and Conclusions**

- Reliability of parameter sensitivity results greatly depends on:
  - Prediction schemes used to vary parameter values
  - Using a reduced number of parameters
  - Sensitivity coefficients (PSC) adjust the marginal sensitivity coefficients to account for the effect on model parameter estimates
- Nonlinear in multi-parameter models
- PSCs can be defined as a total derivative of predicted response with respect to parameter of interest
  - For multi-response, use determinant criterion
- PSCs provide more accurate indication of impact of parameter perturbation than other parameters are adjusted to provide best fit quantitatively that can be correlated with graphical summaries - profile traces

**References**