**Robustness Analysis of Extension Reaction**

**Objective**

The main focus of this study is to determine the distribution of the state vector of the extension model based on given estimated distribution of the model uncertainties. The distribution of the model uncertainties should be estimated once the model parameters are estimated. Therefore the following are the two main objectives f this study.

1. Estimate the distribution of the model parameter uncertainties.
2. Using the distribution of the model parameter uncertainty, estimate the distribution (time dependent) of the state vectors and hence estimate the expected value, *E*(*x*) and the variance, , for the state variables.
3. Based on the observation from point 2, comment on the robustness of the model parameter.

**Theory - Model parameter Uncertainty description**

Temperature dependent uncertainty model

Let *k* be a vector of rate of constants and the true or nominal estimate of the these parameters is , then the uncertainty associated with the model parameter can be written as



We assume that the model uncertainties lies within a hyperellipsoid. The hyperellipsoid can be constructed based on the normal distribution of the model parameters that can be computed from the experimental data. The dimensions of the hyperellipsoid can be fixed by choosing a confidence level for the distribution function. As we know not all the rate constants are in the same order of magnitude and therefore, the elements of the parameter uncertainty vector, will also be in different order of magnitude. For an efficient robustness analysis, the elements of vector should be normalized so that they will be in a same order of magnitude. Therefore, the covariance matrix of the model uncertainty needs to be included to normalize the uncertainties and hence the model uncertainty can be described as follows



 - Covariance matrix of the model uncertainties. If the model uncertainties are uncorrelated then, this matrix is a diagonal matrix and the diagonal elements are the variance of the model uncertainties.

*r*- Distribution function.

*α* - Confidence interval.

Distribution of state variables.

Assuming that model parameter uncertainties distributed based on the normal distribution,



From the experimental data of the rate constants, the mean and variance need to be calculated.

Now, using the Taylor's series first order expansion, the deviation in the state variables *x* with respect to the deviation in the model parameters from its nominal values can be written as follows



Here, *J* is a Jacobian matrix and its elements can be defined as



Thus, the deviation in the state variables can be estimated for a given deviation in the model parameters. It should be noted that since the state variables are a function of time (it's nominal values) *x*(*t*), the Jacobian matrix will also be a function of time. Using this, the following distribution for the state variables can be written.





As mentioned above, since the state variables and hence the Jacobian matrices are a function of time, the above derived distribution will also be a function time. It is also possible to include the temperature dependent time evolution of the *f*(*x*).

Robustness of the model parameters:

Though it is possible to comment the robustness of the model parameters based on the variance of the state variables, it would be great if we can experimentally verify the robustness of the model parameter.

1. At a fixed reaction condition, experimentally estimate the evolution of a specific state variables (DNA concentration). This can be done in the PCR machine.
2. Once the mean and variance of the state variables are obtained with respect to time, it is possible to comment on the robustness of model parameters by comparing the simulated state variables with the experimentally estimate state variables.