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## 1. Sloppy-Stiff

In general, perturbing parameter values in a model can have different effects on the output. Parameters upon which perturbations cause large (small) changes to output are referred to as stiff (sloppy). If one considers small perturbations to a predetermined reference set of parameters the entire information of sloppy-stiffness is contained within the parametric Hessian matrix, where the ijth element is commonly defined in a unitless fashion (cite gutenkunst):

$$H_{ij} = \sum_{n} \frac{\partial \log y_n}{\partial \log \theta_i} \bigg|_{\vec{\theta}^*} \frac{\partial \log y_n}{\partial \log \theta_j} \bigg|_{\vec{\theta}^*} = \sum_{n} \frac{\theta_i^* \theta_j^*}{(y_n^*)^2} \frac{\partial y_n}{\partial \theta_i} \bigg|_{\vec{\theta}^*} \frac{\partial y_n}{\partial \theta_i} \bigg|_{\vec{\theta}^*}. \tag{1}$$

Above, there are a total n total variables in the model and the reference parameters are represented by a vector  $\vec{\theta}$ . The bar notation emphasizes that the partial derivatives are evaluated at the reference parameter set. The argument of the sum is made unitless by a prefactor involving the reference parameter set and the respective equilibrium values of the variables,  $\vec{y}^*$ . Each element of the hessian is interpreted as the sum of the relative changes of each variable due to relative changes of the respective parameters.

Eigenvalues of the Hessian quantify the total amount of change to all variables given a perturbation to a combination of parameters defined by the respective eigenvector. The eigenvalue spectrum shows that perturbations to some combinations of parameters cause a majority of the effect on variables. The following figure shows the eigenvalue spectrum for the maximum 10 eigenvalues where the largest value is normalized to 1. For our analysis, we considered perturbations to all parameters except  $p_g$ ,  $p_{on}$ , and  $p_{in}$  due to the algebraic constraint imposed by conservation of mass.

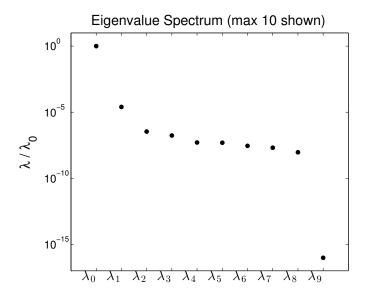


Figure 1: Eigenvalue Spectrum of parametric Hessian matrix. Values are normalized relative to the principle eigenvalue. Only the first 10 eigenvalues of the spectrum are shown. Analysis done by considering perturbations to all parameters except  $p_g$ ,  $p_{on}$ , and  $p_{in}$ .

Each eigenvalue corresponds to some combination of parameters. In our case, the eigenvalue spectrum is dominated by the principle eigenvalue. To get a sense of which parameters are stiff and sloppy we look at the orientation of principle eigenvector in parameter space. The following figure shows the values of the eigenvector in raw parameter space in order of decreasing stiffness.

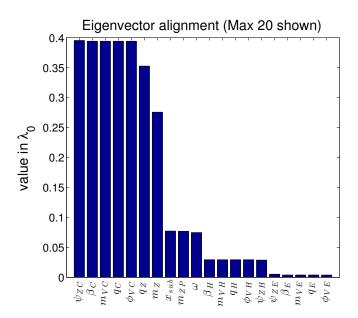


Figure 2: Entries of eigenvector. The higher values correspond to stiffer parameters. Only the 20 stiffest parameters are shown. Analysis done by considering perturbations to all parameters except  $p_g$ ,  $p_{on}$ , and  $p_{in}$ .