Applying parameter selection and verification techniques to an HIV model

March 31 2016

Physical and biological models often have hundreds of inputs, many of which may have a negligible effect on a model's response. Establishing parameters that can be fixed at nominal values without significantly affecting model outputs is often challenging; sometimes these parameters cannot be simply discerned by the outputs. Thus, verifying that a parameter is noninfluential is both computationally challenging and quite expensive.

In a paper publishing this week in the *SIAM Journal on Uncertainty Quantification*, authors Mami Wentworth, Ralph Smith, and H.T. Banks apply robust parameter selection and verification techniques to a dynamic HIV model. "Biological and physical models, such as the HIV model, often have a large number of parameters and initial conditions that cannot be measured directly, and instead must be inferred through statistical analysis," says Smith. "For this to be successfully accomplished, measured responses must adequately reflect changes in these inputs."

The authors implement global sensitivity analysis to identify input subsets, fix noninfluential inputs, and pinpoint those with the most potential to affect model response. "The role of global sensitivity analysis is to isolate those parameters that are influential and that can and must be inferred through a fit to data," says Smith. "Noninfluential parameters are fixed at nominal values for subsequent analysis." Discerning influential parameters from noninfluential ones enables the authors to reduce the parameter dimensions and look more closely at the

portions of the model that affect HIV treatment plans.

Using data from patients who were part of a clinical study, the authors verify the HIV model's predictive capability. A system of ordinary differential equations (ODEs) describes HIV in the model, including uninfected and infected cells that are both activated and resting. The selection and verification techniques enhance the model's reliability, and are more effective than the local sensitivity-based method originally performed on the HIV model, which is used as a point of comparison. "Models of this type [those analyzed by local sensitivity-based methods] exhibit highly nonlinear dependencies between parameters and responses, which limits the applicability of local sensitivity analysis," says Smith. Ultimately, more reliable models facilitate the development of enhanced treatment methods that increase T-cell counts in patients with HIV.

Determining their model's influential factors allow Wentworth et al. to fix the noninfluential parameters and minimize the parameter dimensions for future uncertainty quantification. Their selection techniques are essential in regulating better control for drug therapy. Ultimately, the authors seek to better comprehend HIV dynamics and eventually establish optimal treatment strategies. They chose to employ an HIV model because of Banks' familiarity with the model type. "He developed it and has substantial experience employing it to characterize HIV dynamics and develop potential treatment regimes," says Smith.

The authors' parameter selection and verification techniques are applicable to multiple types of physical and biological models, including those of behavior patterns and other diseases. "The techniques illustrated here are general in nature and can be applied to a wide range of biological and physical applications modeled by systems of ordinary differential equations or partial differential equations," says Smith.