

# 1 Introduction:

## 1.1 A method to establish posterior identifiability of metabolic network models:

This document details a method to establish the practical (posterior) identifiability of metabolic network models using the algebraic relationship between fluxes. Every flux,  $v$ , in a kinetic model of a metabolic network can be expressed as a nonlinear algebraic equation (Equation 1). The fluxes are expressed as a function of the metabolite concentrations  $x$  and the kinetic parameters  $\theta$  in Equation (1).

$$v = f(\mathbf{x}, \theta) \tag{1}$$

Given the nonlinear nature of this model, the function  $f$  in Equation (1) can be expressed, without loss of generality as,

$$v = \frac{N(\mathbf{x}, \theta)}{D(\mathbf{x}, \theta)} \tag{2}$$

where  $N(\mathbf{x}, \theta)$  is the numerator of  $f$ , and  $D(\mathbf{x}, \theta)$  is the denominator of  $f$ .

If  $\theta \in \mathbb{R}^p$ , given a set of experimental measurements for the metabolite concentrations  $\mathbf{x}$  and the reaction fluxes  $\mathbf{v}$ , theoretically, it is possible to choose  $p$  sets of data from these measurements to solve for the  $p$  parameters in  $\theta$ . However, if any of these datasets do not satisfy the condition that  $D(\mathbf{x}, \theta) \neq 0$ , then the number of experiments required to estimate the  $p$  parameters in  $\theta$  can be established to be greater than  $p$ .

This analysis can be performed for each flux in a metabolic network independent of all the other fluxes. This enables this method to be scalable to even genome-scale models.