Electronic Supplementary Material (ESI) for Molecular BioSystems

SUPPLEMENTARY MATERIAL IV

Computing the Covariance matrix

The Covariance matrix ***Cov*** is computed from the Hessian (***H***) of the χ^2 minimization function.

$$\boldsymbol{H}(\chi^2) = \frac{\partial^2 \chi^2}{\partial \boldsymbol{vf}_i \partial \boldsymbol{vf}_j} = 2\sum_{k=1}^{p} \frac{1}{\sigma_j^2}\left[\frac{\partial \boldsymbol{I}_k}{\partial \boldsymbol{v}_i}\frac{\partial \boldsymbol{I}_k}{\partial \boldsymbol{v}_j}\right],$$

here k,l are counters that go over all the fluxes and p is the total number of measured isotopomers.

$$\boldsymbol{Cov}(\boldsymbol{vf}, \boldsymbol{I}) = [\boldsymbol{H}(\chi^2)]^{-1}$$

Although reversibilities are also parameters of our metabolic model only net free fluxes were used in computing the sensitivity matrix i.e. derivatives of the isotopomer measurements only with respect to net free fluxes were computed. This is because reversibilities were ill conditioned parameters that rendered the Hessian ill posed and difficult to invert even with singular value decomposition. Elimination of parameters (called subset selection) in computing the Hessian is a commonly used practice in parameter estimation problems[1] and there exist matrix-based methods to identify the ill conditioned parameters[2,3]. From previous literature, we know that the accuracy of estimation of reversibility parameters is lower than that of net fluxes[4]. Therefore we eliminated the reversibility parameters and found that the Hessian was easily inverted by singular value decomposition. Furthermore elimination of the ill-conditioned parameters not only improves the confidence with which the well-conditioned parameters are estimated but also reduces the order of the parameter estimation problem and saves computation time[1].

References

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