SUPPLEMENTARY MATERIAL

1. Metabolite network analysis

The network analysis is based on the method of [1]. The following data analysis is performed separately for the fasted group and the fed group. Each set of data contains 48 metabolites measured at a baseline, and 6 sampling times, measured in hours after hemorrhage. The baseline is denoted time $t_0 = 0$, and the other sampling times are $\{t_k\}_{k=1}^6 = \{0.75, 3, 5, 9, 17, 21\}$ as described in Table 1 of the manuscript.

• Let $x_\ell(k)$ be the data for Metabolite $\ell$ at sample time $t_k$.

• Pre-processing:
  – The data is normalized as follows: For all $\ell$, set $\bar{x}_\ell(k) = \frac{x_\ell(k)}{\sqrt{\sum_{k=0}^6 x_\ell^2(k)}}$.
  – The data is shifted so that the baseline measurement is 0 as follows: $\tilde{x}_\ell(k) = \bar{x}_\ell(k) - \bar{x}_\ell(0)$.

• Regression Matrix: The data from all metabolites is placed into a matrix, with each column a different metabolite, and each row a different sampling time, starting after hemorrhage and continuing until the 5th sample.

$$A = \begin{bmatrix}
\tilde{x}_1(1) & \tilde{x}_2(1) & \cdots & \tilde{x}_{48}(1) \\
\tilde{x}_1(2) & \tilde{x}_2(2) & \cdots & \tilde{x}_{48}(2) \\
\vdots & \vdots & \ddots & \vdots \\
\tilde{x}_1(5) & \tilde{x}_2(5) & \cdots & \tilde{x}_{48}(5)
\end{bmatrix}$$

• For $n = 1$ to 48:
  – The metabolite $n$ is chosen as the “controlled node”. The data that is to be predicted is the change in this metabolite from one sample to the next. This is denoted by $\Delta \tilde{x}_n(k)$, where $\Delta \tilde{x}_n(k) = (\tilde{x}_n(k+1) - \tilde{x}_n(k)) / (t_{k+1} - t_k)$. Since there are 6 samples, we can calculate $\Delta \tilde{x}_n(k)$ for $k = 1, \ldots, 5$. Set

$$y = \begin{bmatrix}
\Delta \tilde{x}_n(1) \\
\Delta \tilde{x}_n(2) \\
\vdots \\
\Delta \tilde{x}_n(5)
\end{bmatrix}$$

  – The following re-weighted regularized optimization is used to select regressors and weights that best explain the rate of change of the metabolite concentration of the controlled node. The regularization $\|Wz\|_1$ promotes sparsity in the solution, so that only a few elements of $z$ will be non-zero. Select $t = .95$, $\delta = .001$ and length 48 vector $w$ as $w_i = 1$ for $i = 1, \ldots, 48$. For $j = 1$ to 3, do the following

  * Set $W = \text{diag}(w)$,

    $$\min_{z, \epsilon} \quad t\|Wz\|_1 + (1 - t)\epsilon$$

    subject to $\|y - Ax\|_2 \leq \epsilon$

    where for length $m$ vector $x$, $\|x\|_2 = \sqrt{\sum_{i=1}^m x_i^2}$, and $\|x\|_1 = \sum_{i=1}^m |x_i|$.

  * set

    $$w(i) = \frac{\delta}{\delta + |z(i)|}$$

  – Determine if $\epsilon < \frac{1}{2}(\|y_{i_1}\|_2 + \|y_{i_2}\|_2 + \cdots + \|y_{i_m}\|_2)$. If so, this is noted as a potentially interesting node. Find the indices $i$ for which the weights $|z(i)| > 0.1$ and denote the metabolites $i$ as controlling node $n$. 

1
REFERENCES