**Biophysical Journal, Volume *116***

## Supplemental Information

# Quantifying Dynamic Regulation in Metabolic Pathways with Nonparametric Flux Inference

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# SUPPLEMENTARY MATERIAL

1. Supplementary Information

## 1.1. MULTI-OUTPUT GAUSSIAN PROCESS

The $K_{*o}^{M}$ , $K_{o*}^{M}$ and $K_{**}^{M}$ in (18) are defined as:

$$K_{*o}^{M}=\begin{bmatrix} C_{ij}\left(t_{1,1}^{*}-t_{1,1}\right)\cdots C_{ij}\left(t_{1,1}^{*}-t_{1,R_1}\right) & \cdots & C_{ij}\left(t_{1,1}^{*}-t_{N,1}\right)\cdots C_{ij}\left(t_{1,1}^{*}-t_{N,R_N}\right) \\ \vdots & \ddots & \vdots \\ C_{ij}\left(t_{N,R_N^t}^{*}-t_{1,1}\right)\cdots C_{ij}\left(t_{N,R_N^t}^{*}-t_{1,R_1}\right) & \cdots & C_{ij}\left(t_{N,R_N^t}^{*}-t_{N,1}\right)\cdots C_{ij}\left(t_{N,R_N^t}^{*}-t_{N,R_N}\right) \end{bmatrix}_{[R_t\times R]}$$

$$K_{**}^{M}=\begin{bmatrix} C_{ij}\left(t_{1,1}^{*}-t_{1,1}^{*}\right)\cdots C_{ij}\left(t_{1,1}^{*}-t_{1,R_1^t}^{*}\right) & \cdots & C_{ij}\left(t_{1,1}^{*}-t_{N,1}^{*}\right)\cdots C_{ij}\left(t_{1,1}^{*}-t_{N,R_N^t}^{*}\right) \\ \vdots & \ddots & \vdots \\ C_{ij}\left(t_{N,R_N^t}^{*}-t_{1,1}^{*}\right)\cdots C_{ij}\left(t_{N,R^t}^{*}-t_{1,R_1^t}^{*}\right) & \cdots & C_{ij}\left(t_{N,R_N^t}^{*}-t_{N,1}^{*}\right)\cdots C_{ij}\left(t_{N,R_N^t}^{*}-t_{N,R_N^t}^{*}\right) \end{bmatrix}_{[R_t\times R_t]}$$

and $K_{o*}^{M}=\left(K_{*o}^{M}\right)^{T}$

## 1.2. PROBABLITY DENSITY OF THE RATIO BETWEEN TWO DEPENDENT GAUSSIAN VARIABLES

The probability density of the ratio between two dependent Gaussian variables (i.e. $z=x/y$ , $x\sim\mathcal{N}\left(\mu_x,\sigma_x^2\right)$ and $y\sim\mathcal{N}\left(\mu_y,\sigma_y^2\right)$) can be calculated from the means, standard deviations and correlation coefficient of the two Gaussian variables:

$$p_z\left(z;\mu_x,\mu_y;\sigma_x,\sigma_y;r\right)=K\frac{2\left(1-r^2\sigma_x^2\sigma_y^2\right)}{\sigma_y^2Z^2-2r\sigma_x\sigma_y z+\sigma_x^2}\cdot F\left(1;\frac{1}{2};\theta_2\left(z\right)\right) \quad (28)$$

where

$$\theta_2\left(z\right)=\frac{\left(-\sigma_y^2\mu_x z+r\sigma_x\sigma_y\left(\mu_y z+\mu_x\right)-\mu_y\sigma_x^2\right)^2}{2\sigma_x^2\sigma_y^2\left(1-r^2\right)\left(\sigma_y^2z^2-2r\sigma_x\sigma_y z+\sigma_x^2\right)}$$

$$K=\frac{1}{2\pi\sigma_x\sigma_y\sqrt{1-r^2}}\cdot exp\left(-\frac{\sigma_y^2\mu_x^2-2r\sigma_x\sigma_y\mu_x\mu_y+\mu_y^2\sigma_x^2}{2\left(1-r^2\right)\sigma_x^2\sigma_y^2}\right)$$

$$F\left(\alpha;\gamma;\beta\right)=\sum_{k=0}^{\infty}\frac{\left(\alpha,k\right)}{\left(\gamma,k\right)}\cdot\frac{\beta^k}{k!},\quad \gamma\neq 0,-1,-2,\ldots$$

where the Pochhammer symbol $\left(\alpha,k\right)$ is defined by $\left(\alpha,k\right)=\alpha\left(\alpha+1\right)\cdots\left(\alpha+k-1\right)=\Gamma\left(\alpha+k\right)/\Gamma\left(\alpha\right)$ with $\Gamma$ the Gamma function. *r* is the correlation coefficient between the two Gaussian variables.