Additional File 1

Hooman Sedghamiz

December 6, 2017

Discrete Mathematical Equations Governing HPA axis

According to Chaouiya et al. [1], the image function might be written as;

$$y_i = \sum_{I \subseteq q(i)} K_{i.I} \left[\prod_{j \in I} S^{u_{ij}}(x_j, w_{ij}) \prod_{j \in q(i) \setminus I} \left(1 - S^{u_{ij}}(x_j, w_{ij})\right) \right]. \quad (1)$$

The image function simply states that when there is no active interaction modulating x_i, the image is equal to its basal value $K_{i\varnothing} = D(k_{i\varnothing})$ and when more than one interaction is applied concurrently, the image is equal to their joint logical parameter (e.g. $K_{1.12} = D(k_{11} + k_{12})$ when both variable 1 and 2 are modulating variable 1). According to Eq. 1, the corresponding ODE model of the HPA axis can be expressed in a generalized discrete form as follows,

$$\begin{aligned} y_2 = &\left[K_{2\varnothing}\left(1 - S^{\alpha_{21}}(x_1, \theta_{21})\right)\left(1 - S^{\alpha_{24}}(x_4, \theta_{24})\right) \right] \\ &+ \left[K_{21}\left(S^{\alpha_{21}}(x_1, \theta_{21})\right)\left(1 - S^{\alpha_{24}}(x_4, \theta_{24})\right) \right] \\ &+ \left[K_{24}\left(1 - S^{\alpha_{21}}(x_1, \theta_{21})\right)\left(S^{\alpha_{24}}(x_4, \theta_{24})\right) \right] \\ &+ \left[K_{2.14}\left(S^{\alpha_{21}}(x_1, \theta_{21})\right)\left(S^{\alpha_{24}}(x_4, \theta_{24})\right) \right] \end{aligned} \quad (2)$$

$$\begin{aligned} y_3 = &\left[K_{30}\left(1 - S^{\alpha_{32}}(x_2, \theta_{32})\right)\left(1 - S^{\alpha_{35}}(x_5, \theta_{35})\right) \right] \\ &+ \left[K_{32}\left(S^{\alpha_{32}}(x_2, \theta_{32})\right)\left(1 - S^{\alpha_{35}}(x_5, \theta_{35})\right) \right] \\ &+ \left[K_{35}\left(1 - S^{\alpha_{32}}(x_2, \theta_{32})\right)\left(S^{\alpha_{35}}(x_5, \theta_{35})\right) \right] \\ &+ \left[K_{3.25}\left(S^{\alpha_{32}}(x_2, \theta_{32})\right)\left(S^{\alpha_{35}}(x_5, \theta_{35})\right) \right] \end{aligned} \quad (3)$$

$$y_4 = \left[K_{40}\Big(1 - S^{\alpha_{43}}(x_3, \theta_{43})\Big)\right] + \left[K_{43}\Big(S^{\alpha_{43}}(x_3, \theta_{43})\Big)\right] \tag{4}$$

$$\begin{aligned} y_5 = &\left[K_{50}\Big(1 - S^{\alpha_{54}}(x_4, \theta_{54})\Big)\Big(1 - S^{\alpha_{55}}(x_5, \theta_{55})\Big)\right] \\ &+ \left[K_{55}\Big(S^{\alpha_{55}}(x_5, \theta_{55})\Big)\Big(1 - S^{\alpha_{54}}(x_4, \theta_{54})\Big)\right] \\ &+ \left[K_{54}\Big(1 - S^{\alpha_{55}}(X_5, \theta_{55})\Big)\Big(S^{\alpha_{54}}(x_4, \theta_{54})\Big)\right] \\ &+ \left[K_{5.54}\Big(S^{\alpha_{55}}(X_5, \theta_{55})\Big)\Big(S^{\alpha_{54}}(x_4, \theta_{54})\Big)\right] \end{aligned} \tag{5}$$

Where the indices 1 - 5 correspond to the state variables Stress, CRH, ACTH, CORT and the receptor R respectively.

References

[1] C. Chaouiya, E. Remy, B. Moss, and D. Thieffry. Qualitative Analysis of Regulatory Graphs : A Computational Tool Based on a Discrete Formal Framework. *Positive Systems*, pages 119–126, 2003.