

by means of the Gershgorin circle theorem, for example, it is straightforward to get a sufficient condition for $[s\mathbf{I} - \mathbf{A}]$ to be invertible and assuming that $\mathbf{u}(t)g\mathbf{t}\mathbf{0}$ for some t values (before and after mitosis), the system transfer matrix reads:

$$\mathbf{H}(s) = \alpha e^{-\tau s} [s\mathbf{I} - \mathbf{A}]^{-1} \quad (5)$$

In order to write each of the components of the transfer matrix as the ratio of two polynomials the Padé formula is used to approximate the exponential term $e^{-\tau s}$ by a rational function. For the sake of simplicity in the analysis a first order approximation will be used: $e^{-\tau s} = (2 - \tau s)/(2 + \tau s)$.

Exploiting the fact that the matrix $[s\mathbf{I} - \mathbf{A}]$ is tridiagonal and symmetric it is possible to analytically obtain its inverse (see, for example, [2]) and therefore the elements of the transfer matrix result:

$$H_{ij}(s) = \alpha \frac{2 - \tau s}{2 + \tau s} \frac{(-1)^{i+j} D^{j-1} \gamma_{i-1} \beta_{i+1}}{\gamma_n} \quad (6)$$

with:

- $\gamma_0 = 1$; $\gamma_1 = s - a_0$; $\gamma_i = (s - a_1)\gamma_{i-1} - D^2\gamma_{i-2}$, $i \geq 2$
- $\beta_n + 1 = 1$; $\beta_n = s - a_0$; $\beta_i = (s - a_1)\beta_{i+1} - D^2\beta_{i+2}$, $i \leq n - 1$

and $H_{ij} = H_{ji}$ (the transfer matrix is symmetric).

It should be noted that, even though the matrix $[s\mathbf{I} - \mathbf{A}]$ is tridiagonal and symmetric, its inverse will be dense, thus $H_{ij} \neq \mathbf{0}, \forall i, j \leq n$. In addition the complexity of the corresponding elements increases with the size of the model, i.e. with n , due to the recursive nature of the expressions in Eq. 6.

We now limit the analysis to a simplified model with a reduced spatial domain of 3 nuclei. This will not affect general conclusions and simplifies the symbolic manipulation. The canonical form of the transfer matrix results:

$$\begin{aligned} H_{11}(s) &= \frac{-\frac{1}{2}\tau\alpha s^3 - \frac{s^2\alpha(3D\tau^2+2\tau(\tau\lambda-1))}{2\tau} - \frac{s\alpha(2D^2\tau+6D(\tau\lambda-2)+2\lambda(\tau\lambda-4))}{2\tau} - \frac{\alpha(-2D^2\tau-6D\tau\lambda-2\tau\lambda^2)}{2\tau}}{s^4 + \frac{s^3(4D\tau+3\tau\lambda+2)}{\tau} + \frac{s^2(3D^2\tau+8D\tau\lambda+8D+3\tau\lambda^2+6\lambda)}{\tau} + \frac{s(3D^2\tau\lambda+6D^2+4D\tau\lambda^2+16D\lambda+\tau\lambda^3+6\lambda^2)}{\tau} + \frac{6D^2\lambda+8D\lambda^2+2\lambda^3}{\tau}} \\ H_{12}(s) &= \frac{-\frac{sD\alpha+2D\alpha}{\tau}}{s^3 + \frac{s^2(3D\tau+2\tau\lambda+2)}{\tau} + \frac{s(3D\tau\lambda+6D+\tau\lambda^2+4\lambda)}{\tau} + \frac{6D\lambda+2\lambda^2}{\tau}} \\ H_{13}(s) &= \frac{-sD^2\alpha + \frac{2D^2\alpha}{\tau}}{s^4 + \frac{s^3(4D\tau+3\tau\lambda+2)}{\tau} + \frac{s^2(3D^2\tau+8D\tau\lambda+8D+3\tau\lambda^2+6\lambda)}{\tau} + \frac{s(3D^2\tau\lambda+6D^2+4D\tau\lambda^2+16D\lambda+\tau\lambda^3+6\lambda^2)}{\tau} + \frac{6D^2\lambda+8D\lambda^2+2\lambda^3}{\tau}} \\ H_{22}(s) &= \frac{-s^2\alpha + \frac{s2\alpha(-\frac{D\tau}{\tau}-\frac{\tau\lambda}{\tau}+1)}{\tau} + \frac{2\alpha(D+\lambda)}{\tau}}{s^3 + \frac{s^2(3D\tau+2\tau\lambda+2)}{\tau} + \frac{s(3D\tau\lambda+6D+\tau\lambda^2+4\lambda)}{\tau} + \frac{6D\lambda+2\lambda^2}{\tau}} \\ H_{23}(s) &= \frac{-\frac{sD\alpha+2D\alpha}{\tau}}{s^3 + \frac{s^2(3D\tau+2\tau\lambda+2)}{\tau} + \frac{s(3D\tau\lambda+6D+\tau\lambda^2+4\lambda)}{\tau} + \frac{6D\lambda+2\lambda^2}{\tau}} \\ H_{33}(s) &= \frac{-\frac{1}{2}\tau\alpha s^3 - \frac{s^2\alpha(3D\tau^2+2\tau(\tau\lambda-1))}{2\tau} - \frac{s\alpha(2D^2\tau+6D(\tau\lambda-2)+2\lambda(\tau\lambda-4))}{2\tau} - \frac{\alpha(-2D^2\tau-6D\tau\lambda-2\tau\lambda^2)}{2\tau}}{s^4 + \frac{s^3(4D\tau+3\tau\lambda+2)}{\tau} + \frac{s^2(3D^2\tau+8D\tau\lambda+8D+3\tau\lambda^2+6\lambda)}{\tau} + \frac{s(3D^2\tau\lambda+6D^2+4D\tau\lambda^2+16D\lambda+\tau\lambda^3+6\lambda^2)}{\tau} + \frac{6D^2\lambda+8D\lambda^2+2\lambda^3}{\tau}} \end{aligned}$$

Using symbolic manipulation it is possible to asses condition in Eq. 3 is satisfied. Therefore the model is structurally globally identifiable under a general input provided $u_i(t - \tau) \neq 0$, i.e. all parameters may be given unique solutions provided protein are available for time points before or after mitosis (*i. e.* when the production rate is not zero).

References

1. Walter E, Pronzato L (1997) Identification of parametric models from experimental data. Berlin: Springer.
2. da Fonseca C, Petronilho J (2001) Explicit inverses of some tridiagonal matrices. Linear Algebra and its Applications 325: 7 - 21.