Data Assimilation for Systems and Mathematical Biology

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Abstract

Mathematical models are increasingly used as a tool to deal with the tremendous complexity of biological systems. Data Assimilation, defined as the process of combining models with experimental observations, is a key step in order to better align the model outputs with reality. Despite new and improved experimental techniques, it is usually impossible to directly observe all the states of a biological system. This renders Data Assimilation an inverse problem requiring sophisticated mathematical and statistical techniques and the systematic integration of prior knowledge or assumptions.

1 Introduction

2 The Data Assimilation problem

3 Outlook

$$
\begin{aligned}
x_1 &: \mathrm{EpoR}\\
x_2 &: \mathrm{Epo}\\
x_3 &: \mathrm{Epo\text{-}EpoR}\\
x_4 &: \mathrm{Epo\text{-}EpoR}_i\\
x_5 &: \mathrm{dEpo}_i\\
x_6 &: \mathrm{dEpo}_e
\end{aligned}
$$

$$
\dot{\boldsymbol{x}} = \underbrace{\begin{pmatrix} k_t B_{max} - k_t x_1 - k_{on} x_1 x_2 + k_{off} x_3 + k_{ex} x_4 \\ -k_{on} x_1 x_2 + k_{off} x_3 + k_{ex} x_4 \\ k_{on} x_1 x_2 - k_{off} x_3 - k_e x_3 \\ k_e x_3 - k_{ex} x_4 - k_{di} x_4 - k_{de} x_4 \\ k_{di} x_4 \\ k_{de} x_4 \end{pmatrix}}_{\boldsymbol{f}(\boldsymbol{x})}
$$

$$
\begin{aligned}
y_1 &: \mathrm{Epo} + \mathrm{dEpo}_i\\
y_2 &: \mathrm{Epo\text{-}EpoR}\\
y_3 &: \mathrm{Epo\text{-}EpoR}_i + \mathrm{dEpo}_i
\end{aligned}
$$

$$
\boldsymbol{y} = \underbrace{\begin{pmatrix} \kappa_1 (x_2 + 2x_6) \\ \kappa_2 (x_3) \\ \kappa_3 (x_4 + x_5) \end{pmatrix}}_{\boldsymbol{h}(\boldsymbol{x})}
$$

x_1	x_2	x_3	x_4	x_5	x_6
EpoR	Epo	Epo-EpoR	Epo-EpoR$_i$	dEpo$_i$	dEpo$_e$

y_1	y_2	y_3
Epo + dEpo$_i$	Epo-EpoR	Epo-EpoR$_i$ + dEpo$_i$

To illustrate different aspects of DA we will use a model for the information processing at the erythropoietin (Epo) receptor (EpoR) as a running example [**?**]. The state $\boldsymbol{x} = (x_1, \ldots, x_6)^T$ of this model is given by the concentrations of the Epo receptor (x_1) on the cell surface which can bind to Epo (x_2) and build the ligand-receptor complex (x_3). This complex is able to activate subsequent signaling cascades, e.g. the JAK-STAT signaling pathway. In addition the ligand-receptor complex can be internalized (x_4) and dissociate from Epo which then is degraded (x_5) and transported to the extracellular space (x_5).

$$
\begin{aligned}
\dot{x}_1 &= k_t B_{max} - k_t x_1 - k_{on} x_1 x_2 + k_{off} x_3 + k_{ex} x_4 \\
\dot{x}_2 &= -k_{on} x_1 x_2 + k_{off} x_3 + k_{ex} x_4 \\
\dot{x}_3 &= k_{on} x_1 x_2 - k_{off} x_3 - k_e x_3 \\
\dot{x}_4 &= k_e x_3 - k_{ex} x_4 - k_{di} x_4 - k_{de} x_4 \\
\dot{x}_5 &= k_{di} x_4 \\
\dot{x}_6 &= k_{de} x_4 \\
y_2 &= \kappa_1 \left(x_2 + 2x_6 \right) \\
y_1 &= \kappa_2 \left(x_3 \right) \\
y_3 &= \kappa_3 \left(x_4 + x_5 \right),
\end{aligned}
$$

The complex regulation of this receptor is characterized by receptor mobilization, turnover and recycling. The rate constants correspond to (i) receptor turnover (k_t), (ii) ligand-receptor binding (k_{on}) or dissociation (k_{off}), (iii) ligand-induced endocytosis (k_e), (iv) recycling (k_{ex}) and (v) internal (k_{di}) or external (k_{de}) degradation of Epo. Only the the Epo concentration in medium (y_1), on surface (y_2) and in cells (y_3) can be measured up to some scaling paramters κ_j, $j \in \{1, 2, 3\}$.

$$
\dot{\boldsymbol{x}} = \begin{array}{cl} \underbrace{\begin{pmatrix} k_t B_{max} - k_t x_1 - k_{on} x_1 x_2 + k_{off} x_3 + k_{ex} x_4 \\ -k_{on} x_1 x_2 + k_{off} x_3 + k_{ex} x_4 \\ k_{on} x_1 x_2 - k_{off} x_3 - k_e x_3 \\ k_e x_3 - k_{ex} x_4 - k_{di} x_4 - k_{de} x_4 \\ k_{di} x_4 \\ k_{de} x_4 \end{pmatrix}}_{\boldsymbol{f}(\boldsymbol{x},\boldsymbol{u})} & \begin{array}{l} \text{EpoR} \\ \text{Epo} \\ \text{Epo-EpoR} \\ \text{Epo-EpoR}_i \\ \text{dEpo}_i \\ \text{dEpo}_e \end{array} \end{array}
$$

$$
\boldsymbol{y} = \begin{array}{cl} \underbrace{\begin{pmatrix} \kappa_1 \left(x_2 + 2 x_6 \right) \\ \kappa_2 \left(x_3 \right) \\ \kappa_3 \left(x_4 + x_5 \right) \end{pmatrix}}_{\boldsymbol{h}(\boldsymbol{x})} & \begin{array}{l} \text{Epo + dEpo}_i \\ \text{Epo-EpoR} \\ \text{Epo-EpoR}_i + \text{dEpo}_i \end{array} \end{array}
$$

A Appendix name