GPSIM with a driving input (DISIM)

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1 GPSIM

The ODE underlying the linear GPSIM model is

$$\frac{dx_j}{dt} = B_j + S_j f(t) - D_j x_j(t). \tag{1}$$

Its solution is

$$x_j(t) = \frac{B_j}{D_j} + S_j \exp(-D_j t) \int_0^t f(u) \exp(D_j u) du. \tag{2}$$

In linear GPSIM model, the kernel of the genes is

$$k_{x_j x_k}(t, t') = S_j S_k \exp(-D_j t - D_k t') \int_0^t \exp(D_j u) \int_0^{t'} \exp(D_k u') k_{ff}(u, u') du' du. \tag{3}$$

For the squared exponential kernel

$$k_{ff}(t, t') = \exp\left(-\frac{(t-t')^2}{l^2} \right), \tag{4}$$

this can be evaluated to yield

$$k_{x_j x_k}(t, t') = \frac{S_j S_k \sqrt{\pi} l}{2(D_j + D_k)} \exp(-D_j t - D_k t')[h_{kj}(t', t) + h_{jk}(t, t')], \tag{5}$$

where

$$\begin{aligned} h_{kj}(t', t) = \exp(\gamma_k^2) \Bigg\{ & \exp[(D_j + D_k)t] \left[\operatorname{erf}\left(\gamma_k + \frac{t}{l} \right) - \operatorname{erf}\left(\gamma_k + \frac{t-t'}{l} \right) \right] \\ & + \left[\operatorname{erf}\left(\gamma_k - \frac{t'}{l} \right) - \operatorname{erf}\left(\gamma_k \right) \right] \Bigg\}. \end{aligned} \tag{6}$$

2 GPSIM with a driving input (DISIM)

Assume now that the profile $f(t)$ is driven by the corresponding mRNA profile $y(t)$ through

$$\frac{df}{dt} = \sigma y(t) - \delta f(t). \tag{7}$$

The solution of this equation is

$$f(t) = \sigma \exp(-\delta t) \int_0^t y(v) \exp(\delta v) dv. \tag{8}$$

The corresponding solution for $x_i(t)$ is now

$$x_j(t) = \frac{B_j}{D_j} + S_j \exp(-D_j t) \int_0^t \exp(D_j u) \sigma \exp(-\delta u) \int_0^u y(v) \exp(\delta v) dv du. \tag{9}$$

For this model, the kernel between the genes is

$$\begin{aligned} k_{x_j x_k}(t, t') = \sigma^2 S_j S_k \exp(-D_j t - D_k t') \int_0^t \exp((D_j - \delta)u) \int_0^{t'} \exp((D_k - \delta)u') \\ \int_0^u \exp(\delta v) \int_0^{u'} \exp(\delta v') k_{yy}(v, v') \, dv' \, dv \, du' \, du. \end{aligned} \tag{10}$$

Assuming k_{yy} is a squared exponential of the from (4), the quadruple integral can be evaluated to yield

$$\begin{aligned} &\int_0^t \exp((D_j - \delta)u) \int_0^{t'} \exp((D_k - \delta)u') \\ &\qquad \int_0^u \exp(\delta v) \int_0^{u'} \exp(\delta v') k_{yy}(v, v') \, dv' \, dv \, du' \, du \\ &\qquad = \int_0^t \exp((D_j - \delta)u) \int_0^{t'} \exp((D_k - \delta)u') \\ &\qquad \int_0^u \exp(\delta v) \int_0^{u'} \exp(\delta v') \exp\left(-\frac{(v - v')^2}{l^2}\right) dv' \, dv \, du' \, du \\ &= \frac{\sqrt{\pi} l}{2} \exp\left(\left(\frac{\delta l}{2}\right)^2\right) \int_0^t \exp((D_j - \delta)u) \int_0^{t'} \exp((D_k - \delta)u') \\ &\int_0^u \exp(2\delta v)(\mathrm{erf}(\delta l/2 + v/l) - \mathrm{erf}(\delta l/2 + (v - u')/l)) \, dv \, du' \, du \\ &= \frac{\sqrt{\pi} l}{4\delta} \exp\left(\left(\frac{\delta l}{2}\right)^2\right) \int_0^t \exp((D_j - \delta)u) \int_0^{t'} \exp((D_k - \delta)u') \\ &\Big(\mathrm{erf}(\delta l/2 - u/l) - \mathrm{erf}(\delta l/2) + \mathrm{erf}(\delta l/2 - u'/l) - \mathrm{erf}(\delta l/2) \\ &\quad + \exp(2\delta u)(\mathrm{erf}(\delta l/2 + u/l) - \mathrm{erf}(\delta l/2 + (u - u')/l)) \\ &\quad + \exp(2\delta u')(\mathrm{erf}(\delta l/2 + u'/l) - \mathrm{erf}(\delta l/2 + (u' - u)/l)) \Big) \, du' \, du \end{aligned} \tag{11}$$

After some more straightforward integration using the identity

$$\begin{aligned} \int_0^t \exp(Du) \, \mathrm{erf}(u/l + E) \, du = \frac{1}{D} \Big(\exp(Dt) \, \mathrm{erf}(E + t/l) - \mathrm{erf}(E) \\ + \exp\left(\left(\frac{Dl}{2}\right)^2 - EDl\right) [\mathrm{erf}(E - Dl/2) - \mathrm{erf}(E - Dl/2 + t/l)] \Big), \end{aligned} \tag{12}$$

we get

$$
\begin{aligned}
k_{x_j x_k}(t,t') = \sigma^2 S_j S_k \exp(-D_j t - D_k t') \int_0^t \exp((D_j-\delta)u) \int_0^{t'} \exp((D_k-\delta)u') \\
\int_0^u \exp(\delta v) \int_0^{u'} \exp(\delta v') k_{yy}(v,v')\, dv'\, dv\, du'\, du \\
= \frac{\sqrt{\pi} l \sigma^2 S_j S_k}{2} \Big(h_{kj}(t,t') + h_{jk}(t',t) + h'_{kj}(t,t') + h'_{jk}(t',t) \Big) \quad (13)
\end{aligned}
$$

where

$$
\begin{aligned}
h_{kj}(t,t') = \frac{1}{2\delta} \exp\left(\left(\frac{\delta l}{2} \right)^2 \right) \frac{\exp(-D_k t' - \delta t)}{(D_j - \delta)} \Bigg\{ \\
\frac{(D_k+\delta)\exp((D_k-\delta)t') - 2\delta}{(D_k^2 - \delta^2)} [\operatorname{erf}(\delta l/2 - t/l) - \operatorname{erf}(\delta l/2)] \\
+ \frac{\exp((D_k+\delta)t')}{D_k+\delta} [\operatorname{erf}(\delta l/2 + t'/l) - \operatorname{erf}(\delta l/2 - (t-t')/l)] \Bigg\} \\
(14)
\end{aligned}
$$

$$
\begin{aligned}
h'_{kj}(t,t') = \frac{\exp(-D_j t - D_k t')}{D_j + D_k} \frac{1}{(\delta^2 - D_k^2)} \exp\left(\left(\frac{D_k l}{2} \right)^2 \right) \\
\Bigg\{ \frac{D_k + \delta - (D_j + D_k)\exp((D_j - \delta)t)}{\delta - D_j} [\operatorname{erf}(D_k l/2 - t'/l) - \operatorname{erf}(D_k l/2)] \\
+ \exp((D_j + D_k)t) [\operatorname{erf}(D_k l/2 + t/l) - \operatorname{erf}(D_k l/2 + (t-t')/l)] \Bigg\} \quad (15)
\end{aligned}
$$

2.1 Other kernels

In addition to $k_{x_j x_k}$, kernels $k_{f x_k}$ and $k_{y x_k}$ are also needed for learning and inference. The integrals needed to evaluate these are

$$
\begin{aligned}
&\frac{k_{f x_k}(t,t')}{\sigma^2 S_k \exp(-\delta t - D_k t')} = \\
&\quad \int_0^{t'} \exp((D_k-\delta)u') \int_0^t \exp(\delta v) \int_0^{u'} \exp(\delta v') k_{yy}(v,v')\, dv'\, dv\, du' \\
&\qquad = \frac{\sqrt{\pi} l}{4\delta} \exp\left(\left(\frac{\delta l}{2}\right)^2\right) \int_0^{t'} \exp((D_k-\delta)u') \\
&\qquad \Bigg(\operatorname{erf}(\delta l/2 - t/l) + \operatorname{erf}(\delta l/2 - u'/l) - 2\operatorname{erf}(\delta l/2) \\
&\qquad + \exp(2\delta t)(\operatorname{erf}(\delta l/2 + t/l) - \operatorname{erf}(\delta l/2 + (t-u')/l)) \\
&\qquad + \exp(2\delta u')(\operatorname{erf}(\delta l/2 + u'/l) - \operatorname{erf}(\delta l/2 + (u'-t)/l))\Bigg)\, du' \\
&\qquad = \frac{\sqrt{\pi} l}{4\delta} \exp\left(\left(\frac{\delta l}{2}\right)^2\right) \Bigg(\frac{2\delta}{\delta^2 - D_k^2}[\operatorname{erf}(\delta l/2 - t/l) - \operatorname{erf}(\delta l/2)] \\
&\qquad + \frac{\exp((D_k-\delta)t')}{\delta - D_k}[2\operatorname{erf}(\delta l/2) - \operatorname{erf}(\delta l/2 - t'/l) - \operatorname{erf}(\delta l/2 - t/l)] \\
&\qquad + \frac{\exp((D_k+\delta)t')}{\delta + D_k}[\operatorname{erf}(\delta l/2 + t'/l) - \operatorname{erf}(\delta l/2 - (t-t')/l)] \\
&\qquad + \frac{\exp(2\delta t + (D_k-\delta)t')}{\delta - D_k}[\operatorname{erf}(\delta l/2 + (t-t')/l) - \operatorname{erf}(\delta l/2 + t/l)]\Bigg) \\
&\qquad + \frac{\sqrt{\pi} l}{2(\delta^2 - D_k^2)} \exp\left(\left(\frac{D_k l}{2}\right)^2\right) \Bigg(\operatorname{erf}(D_k l/2 - t'/l) - \operatorname{erf}(D_k l/2) \\
&\qquad + \exp((D_k+\delta)t)[\operatorname{erf}(D_k l/2 + t/l) - \operatorname{erf}(D_k l/2 + (t-t')/l)]\Bigg)
\end{aligned} \tag{16}
$$

and

$$
\begin{aligned}
k_{y x_k}(t,t') &= \sigma S_k \exp(-D_k t') \int_0^{t'} \exp((D_k-\delta)u) \int_0^u \exp(\delta v) k_{yy}(t,v)\, dv\, du \\
&= \sigma S_k \frac{\sqrt{\pi} l}{2(\delta - D_k)} \exp(-(D_k+\delta)t')) \\
&\Bigg(\exp\left(\left(\frac{\delta l}{2}\right)^2 + \delta t + D_k t'\right)[\operatorname{erf}(\delta l/2 + t/l) - \operatorname{erf}(\delta l/2 + (t-t')/l)] \\
&+ \exp\left(\left(\frac{D_k l}{2}\right)^2 + D_k t + \delta t'\right)[\operatorname{erf}(D_k l/2 + t/l) - \operatorname{erf}(D_k l/2 + (t-t')/l)]\Bigg)
\end{aligned} \tag{17}
$$