The Laplace transform operator is $\mathscr{L}$, defined as $\mathscr{L}[f(t)] = \tilde{f}(s) = \int_0^\infty dt e^{-st} f(t)$. The convolution operator is $\star$, defined as $f \star g(t) = \int_0^t dt' f(t-t')g(t')$. The real part of a complex variable $z = x + iy$ is denoted $\Re(z) = x$.

1. Suppose $f(t) = 1/(t^2+2)$.

   (a) Evaluate $f(2)$.

$$f(2) = \frac{1}{6}$$

   (b) Evaluate $e^{[3\frac{d}{dt}f(t)]}$ at $t = 4$

$$e^{[3\frac{d}{dt}f(t)]}\ |_{t=4} = e^{-\frac{2}{27}}$$

   (c) Evaluate $(e^{3\frac{d}{dt}})f(t)$ at $t = 4$.

$$\begin{aligned} e^{a\frac{d}{dt}} f(t) &= \sum_{n=0}^{\infty} \frac{a^n}{n!}(\frac{d}{dt})^n f(t) \\ &= f(t+a) \\ (e^{3\frac{d}{dt}}) f(t)|_{t=4} &= f(t+3)\ |_{t=4} = f(7) \\ &= \frac{1}{51} \end{aligned}$$

2. Suppose $f(t) = \sin(\omega t)$, with $f(t) = 0$ for $t < 0$. Let $g(t) = f(t-a)$, with $g(t) = 0$ for $t < a$.

   (a) Provide $\mathscr{L}[f(t)]$.

$$\begin{aligned} \mathscr{L}[f(t)] &= \Im(\mathscr{L}[e^{i\omega t}]) \\ &= \Im(\int_0^\infty dt\, e^{-(s-i\omega)t}) \\ &= \frac{\omega}{s^2+\omega^2} \end{aligned}$$

(b) Provide $\mathscr{L}[g(t)]$.

$$\mathscr{L}[g(t)] = e^{-as}\frac{\omega}{s^2+\omega^2}$$

(c) Simplify $(e^{\frac{\pi}{2}\frac{d}{dt}})\sin(\omega t)$.

$$(e^{\frac{\pi}{2}\frac{d}{dt}})\sin(\omega t) = \sin[\omega(t+\frac{\pi}{2})]$$

3. Let $x(t)$ be a time response. Moment $n$ of the response is defined as

$$\langle t^n\rangle = \frac{\int_0^\infty dt\, t^n x(t)}{\int_0^\infty dt\, x(t)}.$$

(a) Prove that $(-d/ds)^2 \ln\tilde{x}(s)|_{s=0} = \langle t^2\rangle - \langle t\rangle^2$.

$$\begin{aligned}
(-\frac{d}{ds})^2 \ln\tilde{x}(s) &= (-1)^2\frac{d}{ds}(\frac{d}{ds}ln\tilde{x}(s)) \\
&= \frac{d}{ds}(\frac{1}{\tilde{x}(s)}\frac{d}{ds}\tilde{x}(s)) \\
&= \frac{1}{\tilde{x}(s)}\frac{d^2}{ds^2}\tilde{x}(s) - \frac{1}{\tilde{x}(s)^2}(\frac{d}{ds}\tilde{x}(s))^2 \\
&= \frac{\int_0^\infty dt\, t^2 e^{-st}X(t)}{\int_0^\infty dt\, e^{-st}X(t)} - \frac{(\int_0^\infty dt\, te^{-st}X(t))^2}{(\int_0^\infty dt\, e^{-st}X(t))^2}
\end{aligned}$$

when $s=0$

$$\begin{aligned}
&= \frac{\int_0^\infty dt\, t^2 X(t)}{\int_0^\infty dt\, X(t)} - \frac{(\int_0^\infty dt\, tX(t))^2}{(\int_0^\infty dt\, X(t))^2} \\
&= \langle t^2\rangle - \langle t\rangle^2
\end{aligned}$$

(b) Provide $(-d/ds)^3 \ln\tilde{x}(s)|_{s=0}$ in terms of the moments.

$$\begin{aligned}
(-\frac{d}{ds})^3 \ln\tilde{x}(s) &= (-1)^3\frac{d}{ds}(\frac{d^2}{ds^2}\ln\tilde{x}(s)) \\
&= (-1)^3\frac{d}{ds}(\frac{1}{\tilde{x}(s)}\frac{d^2}{ds^2}\tilde{x}(s) - \frac{1}{\tilde{x}(s)^2}(\frac{d}{ds}\tilde{x}(s))^2) \\
&= \frac{-2}{\tilde{x}(s)^3}(\frac{d}{ds}\tilde{x}(s))^3 + \frac{3}{\tilde{x}(s)^2}(\frac{d}{ds}\tilde{x}(s))(\frac{d^2}{ds^2}\tilde{x}(s)) - \frac{1}{\tilde{x}(s)}(\frac{d^3}{ds^3}\tilde{x}(s))
\end{aligned}$$

when $s = 0$

$$
\begin{aligned}
&= (-2)\left(-\frac{\int_0^\infty dt\, tX(t)}{\int_0^\infty dt\, X(t)}\right)^3 + 3\left(-\frac{\int_0^\infty dt\, tX(t)}{\int_0^\infty dt\, X(t)}\right)\left(\frac{\int_0^\infty dt\, t^2X(t)}{\int_0^\infty dt\, X(t)}\right) + \frac{\int_0^\infty dt\, t^3X(t)}{\int_0^\infty dt\, X(t)} \\
&= 2\langle t\rangle^3 - 3\langle t\rangle\langle t^2\rangle + \langle t^3\rangle
\end{aligned}
$$

4. The MAPK signaling cascade usually has three levels denoted $k \in \{1,2,3\}$. The activation state of level $k$ at time $t$ is denoted $x_k(t)$. When activation is weak, a linear model may be appropriate:

$$
\begin{aligned}
\dot{x}_1(t) &= b\beta(t) - \alpha x_1(t) \\
\dot{x}_2(t) &= bx_1(t) - \alpha x_2(t) \\
\dot{x}_3(t) &= bx_2(t) - \alpha x_3(t).
\end{aligned}
$$

Consider an exponentially decaying input, $\beta(t) = \beta_0 k e^{-kt}$. For $t < 0$, $\beta(t) = 0$, and $x_k(0) = \dot{x}_k(0) = 0$ for $k \in 1\ldots 3$. Provide all results in terms of model parameters $\{\beta_0, k, \omega, b, \alpha\}$, as well as $s$ or $t$ as appropriate.

(a) Provide $\tilde{\beta}(s)$, $\tilde{x}_1(s)$, $\tilde{x}_2(s)$, and $\tilde{x}_3(s)$.

$$
\begin{aligned}
\tilde{\beta}(s) &= \beta_0 k \frac{1}{s+k} \\
\tilde{x}_1(s) &= \frac{b}{s+\alpha}\frac{\beta_0 k}{s+k} \\
\tilde{x}_2(s) &= \frac{b^2}{(s+\alpha)^2}\frac{\beta_0 k}{s+k} \\
\tilde{x}_3(s) &= \frac{b^3}{(s+\alpha)^3}\frac{\beta_0 k}{s+k}
\end{aligned}
$$

(b) Provide the gain, $\int_0^\infty dt\, x_3(t) / \int_0^\infty dt\, \beta(t)$.

$$
\text{gain} = \frac{b^3}{\alpha^3}
$$

(c) Provide the mean time of the response, $\langle t\rangle = \int_0^\infty dt\, t x_3(t)/\int_0^\infty dt\, x_3(t)$, which will include a contribution from the input $\beta(t)$.

$$\langle t\rangle = \frac{1}{k}+\frac{3}{\alpha}$$

(Contribution from input is $\frac{1}{k}$.)

(d) Provide the square width of the response,

$$\sigma^2 = \frac{\int_0^\infty dt\, t^2 x_3(t)}{\int_0^\infty dt\, x_3(t)} - \left[\frac{\int_0^\infty dt\, t\, x_3(t)}{\int_0^\infty dt\, x_3(t)}\right]^2.$$

$$\sigma^2 = \frac{1}{k^2}+\frac{3}{\alpha^2}$$

5. Now consider a cascade with $n$ steps with the same form as above and with output $x_n(t)$. The input is a $\delta$-function, $\beta(t) = \beta_0\delta(t)$, and the cascade off at time 0.

   (a) Provide $\tilde{x}_n(s)$, the gain, the mean time $\langle t\rangle$, and the square width $\sigma^2$ of the output.

$$\begin{aligned}\tilde{x}_n(s) &= \frac{b^n}{(s+\alpha)^n}\beta_0\\ \text{gain} &= \frac{b^n}{\alpha^n}\\ \langle t\rangle &= \frac{n}{\alpha}\\ \sigma^2 &= \frac{n}{\alpha^2}\end{aligned}$$

   (b) We can think about the sharpness of a response as $\langle t\rangle/\sigma$, where the duration $\sigma$ is $\sqrt{\sigma^2}$. How does the sharpness of the output depend on the number of elements $n$ in the cascade?

$$\frac{\langle t\rangle}{\sigma} = \sqrt{n}$$

Sharpness depends on the square root of the number of elements n