Feedback control scenario

Feedback localization of diffusing nano-particles has been discussed in control-theoretic terms by several groups in the engineering community [14, 34, 5]. Our previous work in this area has focused on the use of linear stochastic control to elucidate fundamental limits to the achievable steady-state tracking variance, associated with actuator response [14] and photon shot noise [17, 18, 7]. In this section we summarize our modeling framework to provide a concrete setting for the proposed new work that follows.

We consider a linear state-space model with configuration coordinates x_p, the position of the tracked particle, and x_s, the position of the centroid of the active imaging volume. The experiment operates in three spatial dimensions, but as these separate at least approximately, we will work here with scalar coordinates for simplicity. The plant model is given by

$$\begin{aligned} d\begin{pmatrix} x_p \\ x_s \end{pmatrix} &= \left[\begin{pmatrix} 0 & 0 \\ 0 & -\gamma_s \end{pmatrix}\begin{pmatrix} x_p \\ x_s \end{pmatrix} + \begin{pmatrix} 0 \\ \gamma_s \end{pmatrix} u\right] dt + \begin{pmatrix} \sqrt{2D} \\ 0 \end{pmatrix} dW_t, \\ dy &= \begin{pmatrix} -\alpha & \alpha \end{pmatrix}\begin{pmatrix} x_p \\ x_s \end{pmatrix} dt + \eta\, dV_t, \end{aligned} \tag{1}$$

and the control objective is to maintain $x_s \approx x_p$. In previous work we have focused on the steady-state tracking variance as a quantitative figure of merit, but below we will propose and motivate rather different criteria. Note that the free particle motion (of x_p with $u \to 0$) would correspond to a Brownian motion with diffusion coefficient D, and that the direct (non-inertial) driving of x_s by u is an approximation that hides an additional high-bandwidth control loop (of the piezo-stage drive electronics).

An elementary tracking controller design can be accomplished by parameterizing

$$C(s) = \frac{\gamma_c}{s}, \tag{2}$$

corresponding to an ideal integrator. With

$$P(s) = \begin{pmatrix} -\alpha & \alpha \end{pmatrix}\begin{pmatrix} s & 0 \\ 0 & s+\gamma_s \end{pmatrix}^{-1}\begin{pmatrix} 0 \\ \gamma_s \end{pmatrix} = \frac{\alpha\gamma_s}{s+\gamma_s} \tag{3}$$

from Eq. (1), the resulting loop transfer function is

$$L(s) = C(s)P(s) = \frac{\alpha\gamma_c\gamma_s}{s\,(s+\gamma_s)}. \tag{4}$$

Here α and γ_s are considered to be parameters of the model, to be identified from the laboratory apparatus, while γ_c is the design degree of freedom. By inspection we see that in the absence of noises $(D, \eta \to 0)$, γ_s would be a reasonable design upper-limit on the unity gain frequency as this would leave us with 45 degree phase-margin. This then provides the guideline

$$\gamma_c \lesssim \frac{\sqrt{2}\gamma_s}{\alpha}, \tag{5}$$

although more conservative controller gains may be called for if the measurement signal-to-noise ratio $\sim \alpha/\eta$ is sufficiently low.

Writing a state-space realization of the corresponding controller with an internal variable x_c, we can write the closed-loop model

$$d\begin{pmatrix} x_p \\ x_s \\ x_c \end{pmatrix} = \begin{pmatrix} 0 & 0 & 0 \\ 0 & -\gamma_s & \gamma_c\gamma_s \\ \alpha & -\alpha & 0 \end{pmatrix}\begin{pmatrix} x_p \\ x_s \\ x_c \end{pmatrix} dt + \begin{pmatrix} \sqrt{2D} & 0 \\ 0 & 0 \\ 0 & \eta \end{pmatrix}\begin{pmatrix} dW_t \\ dV_t \end{pmatrix}, \tag{6}$$

or with a little foresight

$$d\begin{pmatrix} x_p - x_s \\ \gamma_c x_c - x_s \end{pmatrix} = \begin{pmatrix} 0 & -\gamma_s \\ \alpha\,\gamma_c & -\gamma_s \end{pmatrix}\begin{pmatrix} x_p - x_s \\ \gamma_c x_c - x_s \end{pmatrix} dt + \begin{pmatrix} \sqrt{2D} & 0 \\ 0 & -\gamma_c\eta \end{pmatrix}\begin{pmatrix} dW_t \\ dV_t \end{pmatrix}. \tag{7}$$

Introducing an obvious shorthand notation for the above,

$$dx = Axdt + BdW, \tag{8}$$

we note that in general

$$\begin{aligned} d(xx^T) &= (dx)x^T + x(dx^T) + (dx)(dx^T) \\ &= (Axx^T + xx^T A^T)dt + BdWx^T + xdW^T B^T + BdWdW^T B^T. \end{aligned} \tag{9}$$

Hence defining $X \equiv \langle xx^T \rangle$ as the covariance matrix, where $\langle\cdot\rangle$ represents expectation with respect to the stochastic processes,

$$\dot{X} = AX + XA^T + BB^T, \tag{10}$$

and if a steady-state solution X_{ss} exists it satisfies the matrix Lyapunov equation

$$AX_{ss} + X_{ss}A^T + BB^T = 0. \tag{11}$$

We note (from direct computation of eigenvalues) that our above A-matrix is guaranteed to be stable as long as $\alpha, \gamma_c, \gamma_s$ are positive, thus we can indeed use the Lyapunov equation to evaluate the steady-state tracking variance as a function of γ_c.

To illustrate this we first choose representative values for our tracking system [7], $\alpha = 1$ and $\gamma_s = 270$ s^{-1}, and consider noise parameters for both a polystyrene bead ($D = 5$ μm^2/s, $\eta = 0.01$ μm/$\sqrt{\mathrm{Hz}}$) and a 'worst-case' scenario (assuming very high optical background level) for a dye-labeled protein ($D = 20$ μm^2/s, $\eta = 1$ μm/$\sqrt{\mathrm{Hz}}$). Using Matlab's `lyap` routine we obtain the results in Fig. 7, which shows the steady-state value of $\langle (x_p - x_s)^2 \rangle$ as a function of γ_c in the range of $100 - 1000$ s^{-1}. In both cases we see that an optimal range exists for the controller gain γ_c. We note that the simple phase-margin guideline mentioned above would suggest $\gamma_c = \sqrt{2}\gamma_s/\alpha \approx 380$ for both cases.

We can in fact account for the optimum values analytically. Solving the simple 2×2 matrix Lyapunov equation by hand we obtain

$$\langle (x_p - x_s)^2 \rangle_{ss} = \frac{D(\gamma_s + \alpha\gamma_c)}{\alpha\gamma_c\gamma_s} + \frac{\eta^2\gamma_c}{2\alpha}. \tag{12}$$

The optimal value of γ_c is then

$$\gamma_c^* = \frac{\sqrt{2D}}{\eta}, \tag{13}$$

and the corresponding minimum steady-state tracking variance is

$$\langle (x_p - x_s)^2 \rangle_{ss}^* = \frac{\eta\sqrt{2D}}{\alpha} + \frac{D}{\gamma_s}. \tag{14}$$

Looking at this expression we note that the diffusion coefficient D is an intrinsic property of the molecule of interest, the measurement signal-to-noise ratio α/η is bounded from below by a combination of photo-bleaching and optical noise considerations, and only γ_s remains as an