Supporting Information

Setny et al. 10.1073/pnas.1221231110

SI Static Friction from Positional Fluctuations Under Harmonic Constraints

An alternative route to the static, position-dependent friction constant $\tilde{\xi}(z)$ is provided by the analysis of the positional fluctuations of the ligand in a harmonically restrained potential at position z_0. Derived from a fully non-Markovian ansatz, Hummer showed in ref. 1 that the diffusion constant is exactly given by

$$\tilde{D}(z_0) = \left\langle (\delta z(z_0))^2 \right\rangle / \tau(z_0), \qquad \textbf{[S1]}$$

where $\langle (\delta z(z_0))^2 \rangle$ is the variance with $\delta z = z_0 - z$, and

$$\tau(z_0) = \int_0^\infty C_{\delta z \delta z}(t)\mathrm{d}t \qquad \textbf{[S2]}$$

is the characteristic time scale of the normalized position autocorrelation function (acf) $C_{\delta z \delta z}(t)$. The position acf is shown for selected z_0 in Fig. 5. We find that variances only increase moderately from roughly 0.28 Å^2 at $z_0 = 10$ Å to 0.35 Å^2 at $z_0 = 3.5$ Å, whereas time scales defined by Eq. **S2** decrease more drastically from roughly 1 to 5 ps, respectively.

From Eq. **S1** and the Einstein relation $\tilde{\xi}(z) = k_B T/\tilde{D}(z)$, we obtain the local friction constant at mean position $z \equiv \langle z \rangle_{z_0}$ as plotted in Fig. S1, shown together with the profiles derived by the Smoluchowski method in Eq. **2** and from the random force acf defined as in Eq. **5**. Far away from the pocket the bulk friction constant is essentially reproduced by Eq. **S1**. More importantly, the profile $\tilde{\xi}(z)$ from Eq. **S1** agrees with and corroborates the observation of a spatial shift of the friction maximum with respect to $\xi(z)$, as exhibited by the force-acf–derived $\tilde{\xi}(z)$. The exact heights of the friction peaks from position acf and force acf do not match exactly, which we believe is the consequence of worse statistical sampling of the decay behavior in the case of the position acf: for $2 < z < 5$ Å the integral of position acf (compare with Eq. **S2**) is still not well converged for the available 100-ps decay range of the acf.

1. Hummer G (2005) Position-dependent diffusion coefficients and free energies from Bayesian analysis of equilibrium and replica molecular dynamics simulations. *New J Phys* 7:1–14.

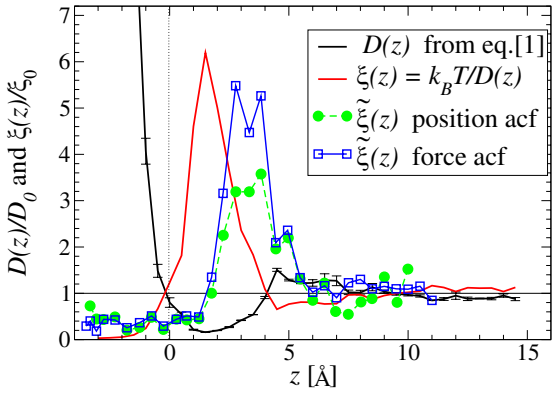

Fig. S1. Diffusivity profile $D(z)$ from the inversion of the Smoluchowski approach Eq. **2** (black line) and its corresponding friction profile $\xi(z) = k_B T/D(z)$ (red line). Also shown are the friction profiles $\tilde{\xi}(z)$ calculated from the force acf as defined in Eq. **5** (blue squares) and the ligand-position acf (green full circles) as defined in Eqs. **S1** and **S2**.