Supporting Information

Improving real-time in vivo molecular monitoring: multi-Gaussian with Laplacian voltammogram fitting enhances the precision of electrochemical aptamer-based sensors

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1. Simplification of equation (8)

The solution to the minimization in equation (8) provides the precise value for the maximum likelihood estimate of the parameters. However, as we shall see below, it can be simplified to provide essentially the same estimates more reliably and at lower computational cost (and thus more rapidly).

For any physically meaningful values of the relevant parameters, $\frac{\bar{\sigma}}{m}\|\boldsymbol{y}-\bar{\boldsymbol{y}}-\boldsymbol{\ell}\|_2^2$ dominates over $log\bar{\sigma}$ and $\frac{\bar{b}}{m}\|\boldsymbol{\ell}\|_1$ dominates over $log\bar{b}$. Given this, we can approximate Eq. 8 as:

$$\underset{L,\boldsymbol{c},\boldsymbol{\lambda},\boldsymbol{\mu},\boldsymbol{\ell},\bar{\sigma},\bar{b}}{arg\min}\frac{1}{2}\left(\frac{\bar{\sigma}}{m}\|\boldsymbol{y}-\bar{\boldsymbol{y}}-\boldsymbol{\ell}\|_2^2\right)+\left(\frac{\bar{b}}{m}\|\boldsymbol{\ell}\|_1\right)(9)$$

The parameter values that minimize this function will not change if we multiply the optimization criterion by $\frac{2m}{\bar{\sigma}}$ since this quantity is always positive. In view of this, the exact same estimates can be obtained by solving

$$\underset{L,\boldsymbol{c},\boldsymbol{\lambda},\boldsymbol{\mu},\boldsymbol{\ell},\beta}{arg\min}\|\boldsymbol{y}-\bar{\boldsymbol{y}}-\boldsymbol{\ell}\|_2^2+\beta\|\boldsymbol{\ell}\|_1,\ \ \beta:=\frac{2\bar{b}}{\bar{\sigma}}(10)$$

To reformulate the optimization using the epigraph form only for the $\beta\|\boldsymbol{\ell}\|_1$ term, we introduce another variable, t:

$$\underset{L,\boldsymbol{c},\boldsymbol{\lambda},\boldsymbol{\mu},\boldsymbol{\ell},\beta,\mathrm{t}}{arg\min}\|\boldsymbol{y}-\bar{\boldsymbol{y}}-\boldsymbol{\ell}\|_2^2+\mathrm{t}11)$$

$$s.t.\quad \|\boldsymbol{\ell}\|_1\leq\alpha,\ \ \alpha:=\frac{t}{\beta}$$

Instead of solving this to find the optimal solution of the parameters β and t, we find a suboptimal solution by fixing the value α heuristically. Given this, we can remove the parameter t, which is a constant, from the optimization:

$$\underset{L,\boldsymbol{c},\boldsymbol{\lambda},\boldsymbol{\mu},\boldsymbol{\ell}}{arg\min}\|\boldsymbol{y}-\bar{\boldsymbol{y}}-\boldsymbol{\ell}\|_2^2(12)$$

$$s.t.\quad \|\boldsymbol{\ell}\|_1\leq\alpha$$

The reason we consider this suboptimal solution is that the optimization (Eq. 12) is, at the cost of some suboptimality, much more efficient in terms of speed.

2. Noise plots (Figures 4D, 5D, 6D)

In figures 4D, 5D, 6D, we quantify the noise by calculating the “fraction” of the total variance that falls above each given frequency f. This fraction is given by the ratio:

$$\frac{\int_f^\infty \left|\hat{x}(2\pi\bar{f})\right|^2 d\bar{f}}{\int_0^\infty \left|\hat{x}(2\pi\bar{f})\right|^2 d\bar{f}} \quad (13)$$

where $\hat{x}(2\pi\bar{f})$ denotes the Fourier transform of the estimated concentration $x(t)$ with its frequency-independent component removed. We recall that the denominator is proportional to the “energy” of $x(t)$ by Parseval's theorem, whereas the numerator is proportional to the “energy” of $x(t)$ above the frequency f. In this context, “energy” refers to the mean-square value of $x(t)$, or to be more precise to its L-2 norm (1).

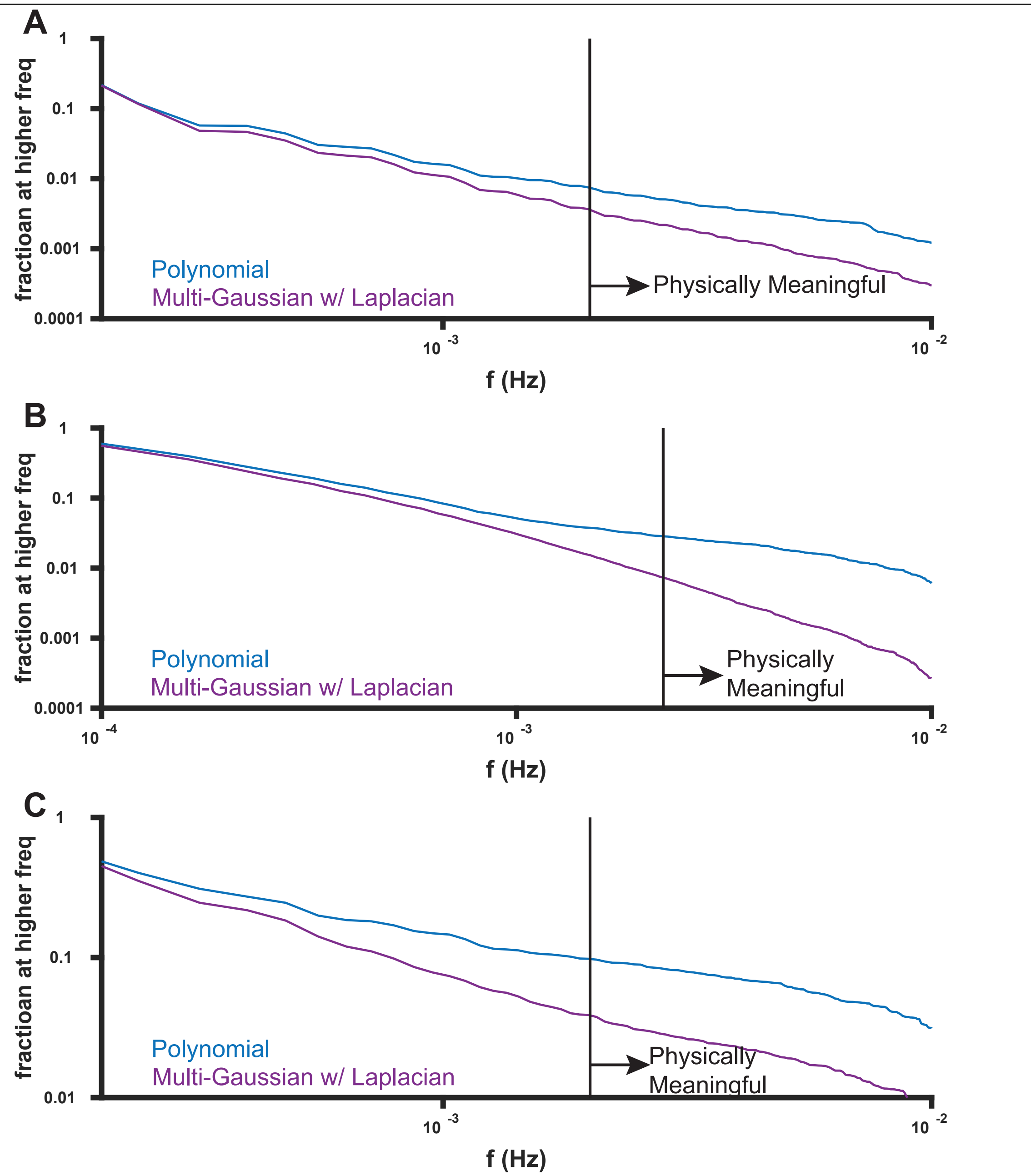

Figure SI1. The fraction of the total variance analysis of the datasets in Figures 8 and 9. The multi-Gaussian with Laplacian method out performs our other fitting approaches for all of our examples.

References

1. Oppenheim, A. V.; Willsky, A. S.; Nawab, S. H. Signals and Systems, 2nd Edition. *Prentice-Hall, Inc.* 1996.