

Estimating free parameters in stochastic oscillatory models using a weighted cost function

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In this study, we estimate parameter values in stochastic oscillatory systems by developing a cost function. Our cost function incorporates power spectral density, analytic signal, and position crossings, each weighted to capture distinct characteristics of the oscillatory system such as amplitude, frequency, and shape. By minimizing this cost function, we estimate parameter values in a stochastic biophysical model for auditory mechanics. Furthermore, we develop a procedure to align the phases of two time series, allowing us to compare stochastic phase evolution of two time series. As a broader application of our procedure, we establish a framework for fitting stochastic oscillatory systems and comparing stochastic time series in other systems.

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I. INTRODUCTION

Scientific models aim to describe natural phenomena with the goal of predicting future outcomes. Achieving accurate predictions hinges on selecting suitable parameter values, which poses significant challenges for models containing many free parameters, such as those encountered in reaction kinetics [1,2] and climatology [3]. This difficulty further intensifies when models incorporate inherent randomness, as stochastic models must handle not only unavoidable measurement uncertainty but also intrinsic physical noise.

Biological processes naturally exhibit random fluctuations, which typically arise from operating in warm fluid environments. Examples of biological noise sources include thermal fluctuations within organic tissue, shot noise of ion-channel gating, and mechanical clatter of molecular motors. Thus, measurements of noisy biological systems render direct fits of theoretical models to experimental data computationally impractical, especially when the underlying dynamics exhibit chaos [4–7].

To model noisy biological processes, researchers incorporate stochastic differential equations (SDEs) and Markov processes [8]. These theoretical frameworks have successfully described diverse stochastic phenomena, including smartphone acceleration [9], heartbeats and respiratory cycles [10], pancreatic β cells [4,11], and Brownian motion [12,13]. These stochastic approaches provide powerful means to model complex systems with underlying random processes.

For SDEs, common parameter-estimation methods incorporate Bayesian statistics. For example, linear noise approximation yields estimates for parameter values [14,15]. This

technique, though yielding reliable fits for fast-computing systems, remains computationally intensive and often impractical for slow simulations. As another example, Markov chain Monte Carlo approximates distributions for maximum-likelihood parameters given a dataset, but the corresponding maximum-likelihood models [16] may undervalue the desired features in the measured system. Hence, these common methods struggle with large stochastic systems because they require either (1) numerically precise likelihood probabilities, which compute too slowly or (2) analytically intractable likelihood functions, which prove too difficult to derive [17].

As a concrete application for SDEs, we examine theoretical models for the auditory system. Vertebrates rely on hair cells of the inner ear to hear and balance. These sensory cells convert sound waves into neuronal signals with stochastic fluctuations arising from active, nonlinear processes [18]. For hair cells, there exist two broad categories of models, namely, biophysical and phenomenological. Biophysical models incorporate detailed descriptions of experiments performed on biological preparations [19–22]. In contrast, phenomenological models apply nonlinear dynamics and bifurcation theory to describe biophysical phenomena [23–26].

Biophysical models generally incorporate numerous free parameters. These parameters account for many cellular processes, capturing the intricate dynamics of auditory hair cells. The free parameter values vary across experiments, depending on type of hair cell [27], type of end organ [28], and species of host animal (e.g., chick [29], turtle [30], frog [19]).

Although some free parameters can be constrained by experiments, many remain experimentally inaccessible. When measuring these parameter values directly, we encounter various experimental obstacles, such as requiring long recording times, dissecting fragile biological tissue, and observing elusive internal processes. To bypass these obstacles, we instead estimate free parameter values numerically to model experimentally observable behaviors of specific cells. However, simulating stochastic time series involves intensive computations.

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To address this challenge, we need robust, fast techniques to estimate free parameters. Prior studies have applied simulation-based inference [17] to lower-dimensional phenomenological models for hair cells, such as the Duffing equation [31], the van der Pol oscillator [32], a hybrid of these two [33], and a generalized Ornstein-Uhlenbeck process [34]. In this study, we focus on biophysical hair-cell models, which contain high-dimensional systems of coupled SDEs and numerous free parameters. These high-dimensional biophysical models generally require more computing power than their low-dimensional phenomenological counterparts. Furthermore, they benefit from fits to longer datasets, which further increases the required computing power.

To avoid directly fitting time series, modelers can define cost functions. The cost function takes a specific instance of free parameters as input. As its output, it returns a cost—a scalar value that quantifies the deviation between the simulation and the measured dataset. By minimizing this cost, modelers can optimize the free parameters to match their desired features of the data, such as amplitude or frequency of an oscillation. However, crafting an effective cost function can prove nontrivial and usually requires system-specific tailoring, especially for stochastic systems.

In this study, we devise a fast numerical procedure to optimize parameter values in high-dimensional stochastic oscillatory models. We apply this procedure to estimate parameter values for a biophysical model of active hair-bundle oscillations. Our procedure leverages a cost function to evaluate the mismatch between the simulated and measured traces of noisy bundle motion. Finally, we compare the theoretical and experimental time series to demonstrate the fruitfulness of this approach to modeling biological data.

We organize this paper as follows. In Sec. II, we describe the experimental procedure used to prepare and record hair cells of the inner ear. In Sec. III, we describe the biophysical system of SDEs used to simulate traces of motion in hair cells. In Sec. IV, we develop a procedure to phase-align and compare two stochastic time series, which we use to compare the phases of measured and simulated traces of hair-bundle motion. In Sec. V, we define the three components of our cost function and how to combine them into a single cost. We validate the cost function by recovering known parameter values for a collection of simulated triangle waves. In Sec. VI, we describe the procedure used to minimize the cost function and rescale simulated traces. In Sec. VII, we discuss how to interpret the cost function and extend it to other systems, and we summarize the findings obtained from the biophysical model.

II. METHODS

As our biological system, we used the North American bullfrog (*Rana catesbeiana*). Its sacculus is a hearing end organ responsible for detecting vestibular movement and low-frequency sounds. The frog sacculus has been widely used in hearing experiments, due to its robust structure, optical accessibility, and the physiological similarity of its hair cells to those of other auditory systems [18,35]. After each dissection, we ensured that the sacculus maintained sufficient physiological integrity.

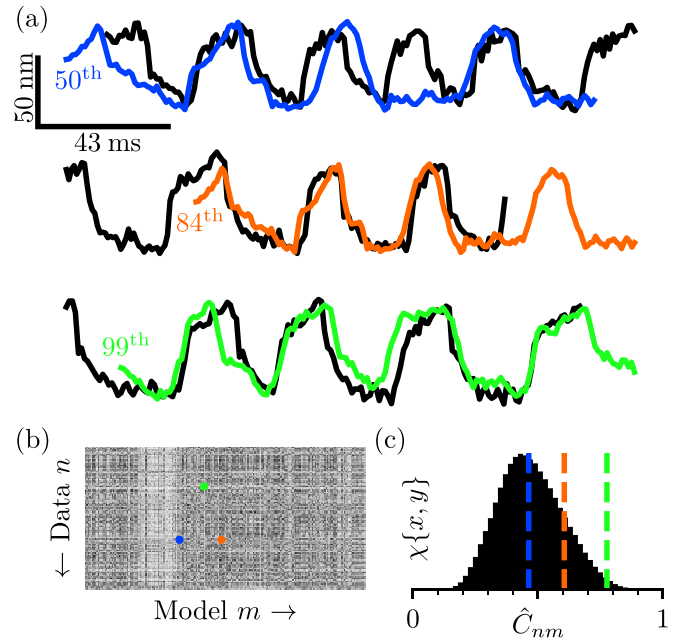


FIG. 1. An illustration of the matrix of cross-correlations described in Sec. IV B. The three colors correspond to different percentiles of $\chi\{x, y\}$: 50th in blue; 84th, orange; 99th, green. (a) The lines display measured traces x (black) and simulated traces y (colored). (b) The heatmap displays elements in the cross-correlation matrix $\mathbf{C}_{\max}$. The heatmap ranges linearly from $\hat{C} = 0$ (white) to $\hat{C} = 1$ (black). The y axis indicates the index n for the measured segment, increasing in time downward. The x axis indicates the index m for the simulated segment, increasing in time rightward. The colored dots indicate the segment indices corresponding to their respective percentiles. (c) The histogram displays PDF $\chi\{x, y\}$. The colored dashed lines indicate cross-correlation $\hat{C}_{n,m}$ corresponding to their respective percentiles.

The dissected sacculi were mounted in specialized chambers, allowing us to image the active motility of their hair cells *ex vivo*. We used optical microscopy techniques to track the position of hair bundles—organelles comprised of roughly 50 stereocilia protruding from the apical surface of the cell body [36]. These measurements yielded time-dependent traces of active hair-bundle motion (illustrated in Figs. 1 and 4). We selected nine recordings of spontaneously oscillating bundles to validate numerical simulations against experimental observations.

To assess the generality of our fitting procedure, we compared parameter values extracted from recordings of hair cells obtained from two different end organs, the sacculus and the amphibian papilla (AP). The AP is a hearing end organ responsible for detecting high-frequency sounds and exhibiting sharper tuning than the sacculus. While hair bundles of the AP exhibit active spontaneous oscillations, similar to those in the sacculus, they appear morphologically distinct to those in the sacculus [28]. Thus, the AP provides an ideal candidate for contrasting the parameter fits obtained for different populations of hair cells. We dissected AP tissue following previously established procedures [37] and recorded bundle oscillations following the same imaging techniques used on

TABLE I. Variables and functions in the stochastic nondimensional model for hair-bundle mechanics. This model consists of eight deterministic parameters, two noise strengths, and three rescaling degrees of freedom. For each quantity, the “Significance” column indicates its physical significance, and the “Equation” column shows its defining equation. The “Type” column indicates whether the quantity represents a variable or a function. The dot derivative indicates a derivative with respect to nondimensional time $\tilde{t}$.

Quantity	Significance	Equation
Variables		
$\tilde{x}_{\text{hb}}$	Hair-bundle position	$\tilde{t}_{\text{hb}}\tilde{x}_{\text{hb}} = -(\tilde{F}_{\text{gs}} + \tilde{x}_{\text{hb}}) + \tilde{\eta}_{\text{hb}}\tilde{B}_{\tilde{t},a}$
$\tilde{x}_a$	Myosin-motor position	$\tilde{x}_a = \tilde{S}_{\text{max}}\tilde{S}(\tilde{F}_{\text{gs}} - \tilde{x}_a) - (1 - \tilde{S}_{\text{max}}) + \tilde{\eta}_a\tilde{B}_{\tilde{t},\text{hb}}$
p_m	Ca^{2+} -binding probability for myosin motor	$\tilde{t}_m\dot{p}_m = p_T(1 - p_m) - p_m$
p_{gs}	Ca^{2+} -binding probability for gating spring	$\dot{p}_{\text{gs}} = \tilde{C}_{\text{gs}}p_T(1 - p_{\text{gs}}) - p_{\text{gs}}$
Functions		
$\tilde{k}_{\text{gs}}$	Dynamic stiffness for gating spring	$\tilde{k}_{\text{gs}} = 1 - p_{\text{gs}}(1 - \tilde{k}_{\text{gs},\text{min}})$
$\tilde{F}_{\text{gs}}$	Effective force (gating/extent springs, pivot)	$\tilde{F}_{\text{gs}} = \tilde{k}_{\text{gs}}(\tilde{x}_{\text{hb}} - \tilde{x}_a - p_T)$
$\tilde{S}$	Slipping rate for myosin motor	$\tilde{S} = -p_m(1 - \tilde{S}_{\text{min}})$
p_T	Open probability for transduction channel	$p_T = [1 + \exp(\tilde{U}_{\text{gs},\text{max}}(\Delta\tilde{E}^\varnothing - \tilde{k}_{\text{gs}}(\tilde{x}_{\text{gs}} - \frac{1}{2})))]^{-1}$

the sacculus. We selected ten recordings of spontaneous bundle oscillations to validate the numerical simulations. For more details on our biological preparation and optical recordings, refer to Appendix A.

III. DEFINING THE THEORETICAL MODEL OF SPONTANEOUS HAIR-BUNDLE MOTILITY

To model the spontaneous oscillations observed in inner-ear hair cells, we derived a system of SDEs, shown in Table I. These oscillations, driven by various cellular processes, manifest as active movements of the stereocilia—a bundle of strandlike sensory organelles atop each hair cell. Stereocilia contain mechano-sensitive ion channels and associated molecular machinery, both essential for translating sound waves into neuronal signals. They oscillate spontaneously, according to previous experiments conducted *in vitro* and *ex vivo* [18,38].

These oscillations originate from three key molecular processes, namely, mechano-electrical transduction (MET; [29,39,40]), myosin-mediated adaptation [41–45], and tip-link tension [46–48]. Together with the ion-channel dynamics that modulate them, these processes form the foundation of the proposed biophysical model [19].

In our previous study, we explored a deterministic model of hair-bundle mechanics, gleaned key experimental insights from prior literature on hair cells [22]. We first systematically reduced this comprehensive biophysical model to a 15-parameter nondimensional model, optimizing it for fitting without loss of generality. We subsequently fixed the least influential parameters sequentially, identifying a five-parameter deterministic model that maximizes predictive power when fitting an individual cycle. We hence concluded that this five-parameter model optimally described the key features of regular hair-bundle oscillations.

Deterministic models, however, fail to fully capture the measured variation in hair-bundle movement. Most recordings display substantial fluctuations in frequency, amplitude, and shape of oscillations, necessitating a stochastic approach. To emulate this noise, we adopted a stochastic model capable of

fitting multiple cycles simultaneously, rather than a deterministic model capable of fitting single cycles individually.

Our stochastic model employs an eight-parameter system of SDEs, with three degrees of freedom for rescaling, adapting our previous five-parameter deterministic system of ordinary differential equations [22]. This model further incorporates two noise terms $\tilde{\eta}_{\text{hb}}$ and $\tilde{\eta}_a$, which represent fluctuations in hair-bundle position $\tilde{x}_{\text{hb}}$ and adaptation-motor position $\tilde{x}_a$, respectively. Throughout this paper, we indicate nondimensional quantities with tilde ($\tilde{\cdot}$) accents. The full system used to simulate hair-bundle motion is summarized in Table I, with analytic derivations and computational methods detailed in Appendix B.

IV. QUANTIFYING AND COMPARING THE SIMILARITY BETWEEN TWO TIME SERIES

To gauge the similarity between a theoretical model and experimental recording, we compared the simulated and measured traces of hair-bundle motion. As two stochastic traces generally remain out of phase with each other over long timescales, we cannot directly compare the traces point by point in time. However, traces sometimes remain in-phase over short timescales, so we can compare short segments from each trace. To assess the overall agreement, we developed a systematic procedure to phase-align and compare two stochastic traces. Specifically, we compared many phase-aligned pairs of short segments, each pair containing a segment from each of the two traces. We then applied this procedure to our system to compare measured hair-bundle traces to their corresponding best-fit simulated traces, as shown in Fig. 1. This procedure provides a distribution of “similarities” between the measured and simulated traces.

A. Defining our mathematical notation

Collections of mathematical objects are often described using tuples, so we define our notation for tuples. We denote the n th element of a tuple S as $(S)_n$, dropping the parentheses implicitly as S_n when appropriate. We denote the tuple

$(S)_{\mathfrak{N}} := (S_n | n \in \mathfrak{N})$ given a set $\mathfrak{N}$ of indices, similarly dropping the parentheses as $S_{\mathfrak{N}}$ when appropriate.

To distinguish between the two types of normalization performed in this paper, we motivate our notation from Lebesgue spaces L^n [49]. We L^1 -normalize a function $F(x)$ by taking $F(x) \mapsto F(x) / \int |F(x)| dx$. We L^∞ -normalize a function by taking $F(x) \mapsto F(x) / \max_x |F(x)|$, and we deem a function that ranges between 0 and 1, inclusively, as L^∞ -normalized. We note that L^∞ -normalized functions, in general, range between -1 and 1 , inclusively; however, we L^∞ -normalize only non-negative functions in this paper, thus leading to a range between 0 and 1, inclusively.

B. Distribution of cross-correlations

To quantify the similarity between two traces, we developed a method to compare their traces. Here, we consider two traces $x(t)$ and $y(t)$, possibly with two identical traces $x(t) \equiv y(t)$.

First, we partitioned x and y into unordered tuples of equal-duration segments $x_{\mathbb{N}}$ and $y_{\mathbb{N}}$, respectively, each of duration T . By comparing these segments, we captured not only the expected match between traces but also their plausible range of agreement.

Next, we considered each pair of segments in $\zeta_T\{x, y\} := x_{\mathbb{N}} \times y_{\mathbb{N}}$, i.e., one segment each from x and y . For each pair $(x_n, y_m) \in \zeta_T\{x, y\}$, we calculated their cross-correlation $\hat{C}_{n,m}(\Delta t) \propto \langle x_n(t) y_m(t + \Delta t) \rangle$ over a time lag Δt . Here, angle brackets $\langle \cdot \rangle$ represent the expected value. We then L^∞ -normalized this cross-correlation to ensure reliable comparisons across different pairs of traces.

Finally, we defined the cross-correlation matrix as $\mathbf{C}_{\max}\{x, y\}$, in which the (n, m) th element equals $\max_{\Delta t} \hat{C}_{n,m}(\Delta t)$ for all $n, m \in \mathbb{N}$. Conceptually, each element represents the maximum cross-correlation between x_n and y_m over all time lags. We further defined the probability density function (PDF) for the flattened matrix $\mathbf{C}_{\max}$ as $\chi\{x, y\}(\hat{C})$, where $\hat{C}$ denotes cross-correlation values. This distribution quantifies the overall correlation between traces x and y , as illustrated in Fig. 1(b).

C. Reduction to Jensen-Shannon divergence

To quantify the dissimilarity between two cross-correlation distributions, we incorporated the Jensen-Shannon divergence, an information-theoretic measure of L^∞ -normalized distance between two probability distributions [50]. Specifically, we calculated the Jensen-Shannon divergence $D_{JS}(\chi\{x, x\}, \chi\{x, y\})$ between the cross-correlation distributions of traces $x(t)$ and $y(t)$, following procedures described in Appendix C 2.

Conceptually, the Jensen-Shannon divergence measures information loss when two distributions try to approximate each other. We prefer the Jensen-Shannon divergence over the related Kullback-Leibler divergence, because the latter remains unbounded, rendering a comparison of divergences across different datasets difficult. For comparisons to other information-theoretic measures, refer to Appendix C.

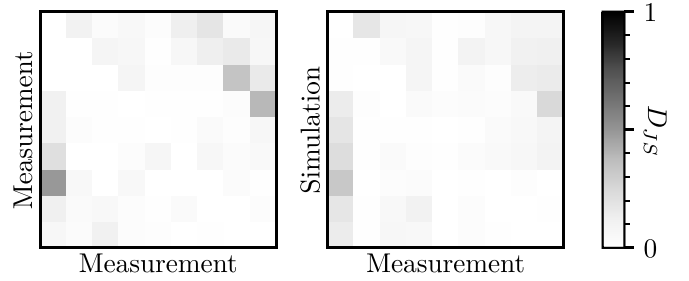


FIG. 2. Two Jensen-Shannon divergence matrices, as described in Sec. IV D, for nine saccular bundles. The colorbar indicates values of Jensen-Shannon divergences between reference and comparison bundles. Left: The heatmap displays a measured-measured divergence matrix comparing nine saccular bundles. The x axis indicates index of measured reference bundle, and the y axis indicates index of measured comparison bundle. Right: The heatmap displays a measured-simulated divergence matrix. The x axis indicates index of measured reference bundle, and the y axis indicates index of simulated comparison bundle.

D. Matrix of Jensen-Shannon divergences

We computed a matrix of Jensen-Shannon divergences to compare a set of reference traces to a set of comparison traces. We refer to this matrix as a “divergence matrix.” Typically, our reference traces were the measured traces, which consisted of experimental recordings of hair-bundle position, and our comparison traces were simulated traces, which were obtained from numerical simulations of bundle positions.

We calculated two versions of the divergence matrices. First, we calculated the divergence matrix for measured traces (reference set) and measured traces (comparison set). Second, we calculated the divergence matrix for measured traces (reference set) and simulated traces (comparison set), illustrated in Fig. 6. We refer to these two divergence matrices as the “measured-measured” and “measured-simulated” divergence matrices, respectively, both displayed in Figs. 2 and 7. Conceptually, a measured-measured matrix reflects the inherent degree of variation among the measured traces, while a measured-simulated matrix reflects the level of disagreement between the measured and simulated traces.

V. DEFINING A WEIGHTED COST FUNCTION TO COMPARE TWO STOCHASTIC OSCILLATORY TRACES

To compare the oscillatory behavior of two traces, we defined a cost function with three components: power spectral density (PSD), analytic signal, and position crossings (see Fig. 3). Examples of these three components are illustrated next to their corresponding traces in Figs. 4 and 8. Each component provides information about a different aspect characterizing the oscillatory behavior of a stochastic trace, and hence, we used all three of these components for a full comparison between the two stochastic traces.

For each of the three components, we defined an individual cost. To keep the three component costs of comparable magnitude, we formulated each cost as an L^∞ -normalized quantity. Because the costs remained comparable, we were then able to combine them into a single overall cost by taking their

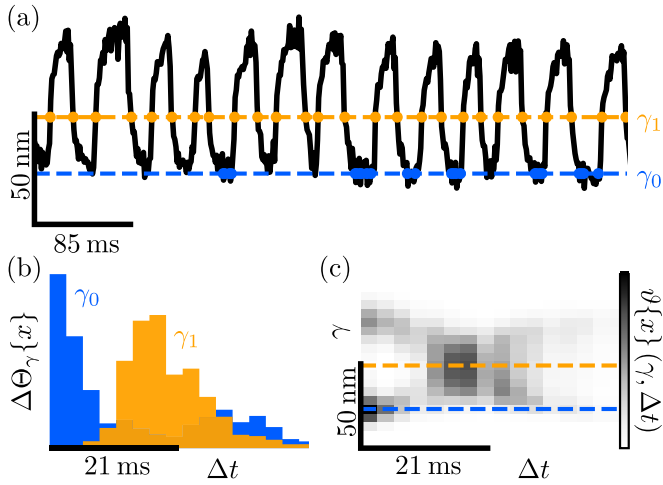


FIG. 3. An illustration of the distribution of position crossings, as described in Sec. V C. Blue and orange colors correspond to γ crossings at $\gamma = \gamma_0$ and $\gamma = \gamma_1$, respectively. (a) The solid line displays position x over time t for a measured hair bundle. The two dashed lines indicate where $x = \gamma_0$ (blue) or γ_1 (orange), and markers correspond to times of γ -crossing events. The scale bar displays one amplitude (50 nm; half peak to peak) and two periods (85 ms) of oscillation. (b) The two histograms show PDF $\Delta\Theta_\gamma\{x\}$ over time difference Δt for $\gamma = \gamma_0$ (blue) or γ_1 (orange). The scale bar displays half-period (21 ms). (c) The heatmap indicates PDF $\vartheta x(\gamma, \Delta t)$ over crossing position γ and time difference, ranging from zero (white) to maximum (black). The two dashed lines indicate where $\gamma = \gamma_0$ (blue) or γ_1 (orange). The scale bar displays amplitude and half-period (21 ms).

weighted average. We used the overall cost to quantify the dissimilarity between the two stochastic oscillatory traces.

To quantify each component cost between the two stochastic traces, we employed the total variation distance (TVD). The TVD is an information-theoretic measure of L^∞ -normalized distance [51] between PDFs. To calculate the TVD, we computed

$$d_{TV}(\rho_1, \rho_2) = \frac{1}{2} \int |\rho_1(x) - \rho_2(x)| dx, \quad (1)$$

where ρ_1 and ρ_2 represent two PDFs. Conceptually, a larger TVD indicates a greater dissimilarity between distributions. Throughout this work, we use TVD to quantify the dissimilarity between L^1 -normalized functions, such as PDFs.

A. Incorporating the shape of the power spectral density into the cost function

To quantify the discrepancy between the power spectral densities from the measured and simulated traces, we computed the TVD between the power spectral densities. The power spectral density characterizes the frequency distribution of a trace, offering insight into the spectral composition of the trace.

We computed the cost between measured and simulated power spectral densities as

$$C_{\text{PSD}} = d_{TV}(\tilde{S}_{xx}^{\text{meas}}, \tilde{S}_{xx}^{\text{sim}}), \quad (2)$$

where $\tilde{S}_{xx}^{\text{meas}}(f)$ and $\tilde{S}_{xx}^{\text{sim}}(f)$ represent the L^1 -normalized power spectral densities of the measured and simulated traces, respectively, over frequency f . We used the cost C_{PSD} as a component cost in our overall cost function. Here, a larger TVD indicates a greater difference in the spectral content between the two traces. For computational details on this power spectral density, refer to Appendix D 2 a.

B. Incorporating the distribution of the analytic signal into the cost function

To quantify the discrepancy between analytic signals from the measured and simulated traces, we computed the TVD between probability distributions of the two analytic signals. The analytic signal encodes information about the amplitude and phase distributions of an oscillation [52–54], and it characterizes the noise statistics for a given trace.

To compute the cost between two analytic signals, we first generated a distribution for the measured and simulated analytic signals. We let $S_a\{x\}(t) = x(t) + i\mathcal{H}\{x\}(t)$ represent the analytic signal of position $x(t)$, where $\mathcal{H}$ denotes the Hilbert transform. To represent the distribution of the analytic signal [55,56], we used the two-dimensional (2D) joint PDF

$$\rho_a(x, \mathcal{H}\{x\}) \propto N[\tilde{S}_a\{x\} = \tilde{s}_a] \quad (3)$$

of the L^1 -normalized analytic signal $\tilde{S}_a\{x\}$, where $N[\cdot]$ represents the number of occurrences for an event. We then computed the cost between the measured and simulated analytic signals as

$$C_{\text{DAS}} = d_{TV}(\rho_a^{\text{meas}}, \rho_a^{\text{sim}}), \quad (4)$$

where ρ_a^{meas} and ρ_a^{sim} represent the distributions of analytic signals for the measured and simulated traces, respectively. We used the cost C_{DAS} as a component cost in our overall cost function. Here, a larger TVD indicates a greater dissimilarity in amplitude, phase, or noise between the two traces. For computational details on this distribution of the analytic signal, refer to Appendix D 2 b.

C. Incorporating the distribution of the position crossings into the cost function

To quantify the discrepancy between position crossings from the measured and simulated traces, we computed the TVD between the respective distributions of position crossings. The position crossings encode information primarily about the frequency and shape distributions for an oscillation. Zero crossings, in particular, have been used to characterize frequencies [57–60].

We first define our notation for the position crossings. We let $\Theta_0\{x\}$ represent the ordered tuple of zero-crossing times from position $x(t)$, sorted in ascending order of time. For a general crossing level $\gamma \in \mathbb{R}$, we defined the ordered tuple of γ -crossing times as $\Theta_\gamma\{x\} := \Theta_0\{x - \gamma\}$. To characterize the interval between consecutive γ -crossing times in $\Theta_\gamma\{x\}$, we defined the unordered tuple $\Delta\Theta_\gamma\{x\}$ by

$$(\Delta\Theta_\gamma\{x\})_{n+1} := (\Theta_\gamma\{x\})_{n+1} - (\Theta_\gamma\{x\})_n \quad (5)$$

for $n \in \mathbb{N}$. Conceptually, the tuple $\Delta\Theta_\gamma\{x\}$ resembles half-periods of an oscillation.

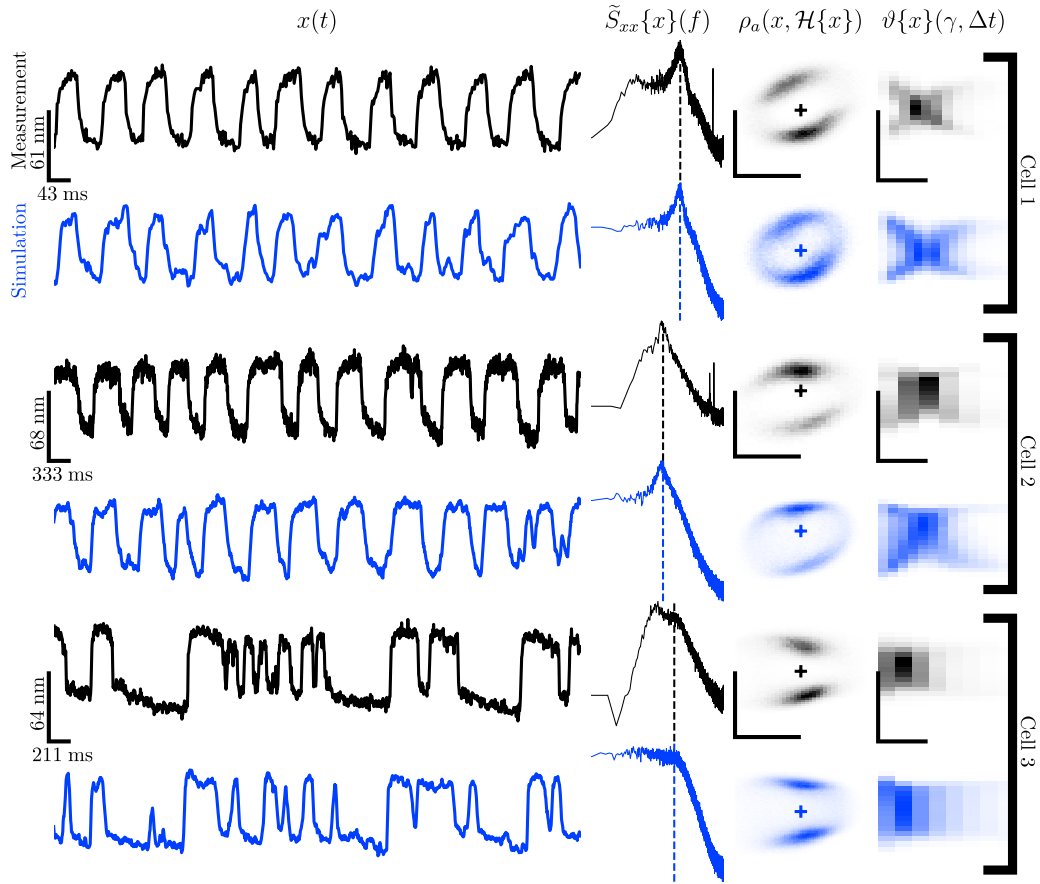


FIG. 4. The three cost-function components, described in Sec. V, for three saccular bundle pairs. Black and blue colors indicate measured and simulated hair bundles, respectively. Each pair of rows corresponds to a measured bundle (black) and its concomitant simulation (blue). Column 1: The solid lines display position x over time t for measured and simulated hair bundles, each with zero mean position. The scale bars display amplitudes of $2\langle|\tilde{S}_a(x)|\rangle$ along the y axis and timescales of half-period along the x axis, shared between each pair of measured and simulated traces. Column 2: In a log-log scale, the solid lines display power spectral density $\tilde{S}_{xx}$ over frequency f , and the dashed lines indicate their median frequency. Column 3: The heatmaps display PDF $\rho_a(x, \mathcal{H}\{x\})$ over position x along the y axis and Hilbert transform $\mathcal{H}\{x\}$ along the x axis. The plus signs indicate the origin of $(x, \mathcal{H}\{x\})$. The scale bars display amplitude along both axes. Column 4: The heatmaps display PDF $\vartheta\{x\}(\gamma, \Delta t)$ over crossing position γ along the y axis and time difference Δt along the x axis. The scale bars display one amplitude along the y axis and half period along the x axis.

To compute the cost between two collections of position crossings, we first generated a distribution for position crossings of the measured and simulated traces. To represent the distribution of position crossings (DPC), we used the 2D joint PDF

$$\vartheta\{x\}(\gamma, \Delta t) \propto N[x = \gamma \wedge \Delta\Theta_\gamma\{x\} = \Delta t], \quad (6)$$

where N denotes the number of γ crossings with half-periods Δt . We then computed the cost between measured and simulated position crossings as

$$C_{\text{DPC}} = d_{\text{TV}}(\vartheta^{\text{meas}}, \vartheta^{\text{sim}}), \quad (7)$$

where ϑ^{meas} and ϑ^{sim} represent distributions of position crossings for the measured and simulated traces, respectively. We used the cost C_{DPC} as a component cost in our cost function. A larger TVD indicates a greater dissimilarity in frequency or shape between the two traces. For computational details on this distribution of position crossings, refer to Appendixes D 2 c and Fig. 3.

D. Weighting the three components to obtain an overall cost function

To obtain one quantity that represents the dissimilarity between two stochastic traces, we combined the three components described above into one overall cost. Specifically, we combined the costs by finding their weighted average. After defining an L^1 -normalized weight vector $\mathbf{w} = (0.1, 0.5, 0.4)$, we asserted $C_{\text{tot}} = \mathbf{w} \cdot \mathbf{C}$ as the overall cost function, where $\mathbf{C} := (C_{\text{PSD}}, C_{\text{DAS}}, C_{\text{DPC}})$ represents a tuple of costs, one from each of the three components. After expanding the terms in the cost function, we have

$$\begin{aligned} C_{\text{tot}} = & 0.1 \int |\tilde{S}_{xx}^{\text{meas}}(f) - \tilde{S}_{xx}^{\text{sim}}(f)| df \\ & + 0.5 \iint |\rho_a^{\text{meas}}(x, x_{\mathcal{H}}) - \rho_a^{\text{sim}}(x, x_{\mathcal{H}})| dx dx_{\mathcal{H}} \\ & + 0.4 \iint |\vartheta^{\text{meas}}(\gamma, \Delta t) - \vartheta^{\text{sim}}(\gamma, \Delta t)| d\gamma d\Delta t. \end{aligned} \quad (8)$$

Similar to its constituent costs, the weighted overall cost remains L^∞ -normalized. By adopting a *weighted* cost function, we were able to emphasize desired features of the numerical fits relative to the measured datasets. Weighted cost functions have proven effective across diverse fields, including healthcare [61,62], economics [63–65], and mathematics [7,66–68]. For more details on the definition and computation of this cost function, refer to Appendix D.

VI. MATCHING THE SIMULATED AND MEASURED TRACES BY MINIMIZING THE COST FUNCTION

To match the simulated and measured traces of hair-bundle motion, we minimized the cost function, applying differential evolution to search for the best-fit parameter values in the model. Nondimensional units of the simulations were rescaled to match the dimensional units of the measurements.

A. Optimizing the cost function using differential evolution

We minimized the cost function numerically using differential evolution [69,70], an algorithm that has received wide usage in a variety of fields, including biology [71,72] and physics [73–75]. Applying differential evolution, we optimized parameter values for each individual hair bundle. During each fit, we performed 2000 iterations within 12 h using an Intel i9-13900K (24 cores and 32 threads). For more details on differential evolution, refer to Appendix D 1.

B. Rescaling the nondimensional simulation to match the dimensional measurements

In an earlier study, we showed that nondimensionalizing a deterministic model for hair-bundle mechanics naturally reduced its number of free parameters [22]. After optimizing parameter values, this noiseless model reproduced individual measured oscillations of hair-bundle motion. Extending this approach, we assimilated a stochastic version of this model to fit multiple oscillation cycles simultaneously. By including stochastic terms, we captured variations in instantaneous frequency and amplitude as well as oscillation shape, observed experimentally.

To compare simulations with measurements, we rescaled from the simulated nondimensional units into the measured dimensional units. Specifically, we fit three rescaling factors $\hat{x}_{\text{hb}}$, $\check{x}_{\text{hb}}$, and $\hat{\tau}$ defined by

$$X_{\text{hb}}(t) = \hat{x}_{\text{hb}}(\tilde{x}_{\text{hb}}(\tilde{t}) - \check{x}_{\text{hb}}), \quad \tilde{t} = \frac{t}{\hat{\tau}}, \quad (9)$$

where $\hat{x}_{\text{hb}}$ and $\check{x}_{\text{hb}}$ represent multiplicative scaling and constant offset, respectively, of nondimensional bundle position $\tilde{x}_{\text{hb}}$, and $\hat{\tau}$ represents multiplicative scaling for nondimensional time $\tilde{t}$. To reduce computing time, we independently rescaled each component of the cost function instead of directly rescaling the position, as described in Appendix D.

C. Validating the efficacy of the cost function by recovering triangle waves

To validate our cost function, we tested it on a controlled dataset of triangle waves. We generated triangle waves with

the form

$$\Delta(t, w) = A\tilde{\Delta}(2\pi ft, w) + x_0 + \mathcal{N}(0, \sigma_\Delta^2), \quad (10)$$

where $\mathcal{N}(0, \sigma^2)$ represents a normal random variable with zero mean and variance σ^2 . Here, the five parameters represent amplitude A , frequency f , offset x_0 , width w , and noise strength σ_Δ .

We simulated and recovered 600 triangle waves. For each simulation, we varied all five parameters simultaneously within a predefined range, ensuring a diversity of waveforms. By applying differential evolution to minimize the cost function, we recovered all 600 sets of known parameters. These results demonstrate that the cost function can successfully recover optimal parameter sets, as shown in Fig. 9, even in the presence of noise. For more details on the computational methods and parameter ranges, refer to Appendix D 3.

For the triangle wave, the fitted parameters comprise the triangle width, noise strength, and three rescaling variables, giving five fitting parameters in total. For the hair bundle, the fitted parameters comprise the eight deterministic and two noise-strength parameters shown in Table I, as well as the three rescaling variables defined in Sec. VI B, which gives 13 fitted parameters in total.

VII. DISCUSSION

A. Comparison of the stochastic time series

One approach to modeling stochastic time traces involves fitting ensemble averages between the motion of the measured and simulated traces. However, because hair bundles (both measured and simulated) exhibit chaotic dynamics [7,24], the averaged motion traces do not retain key features of the biological oscillations. For example, one feature of hair-bundle motion includes bursting behavior, which consists of intertwined intervals of quiescent and oscillatory behavior, as shown in the bottom trace of Fig. 4. As bursts occur at irregular intervals, bursting behavior vanishes in ensemble averages of bundle motion.

We note that the cross-correlation distribution derived in Sec. IV and the cost function developed in Sec. V may be applied independently to a dynamical system. For example, a nonoscillatory system may benefit from the cross-correlation distributions to compare the overall behavior of its nonoscillatory traces, but this system likely will not benefit from the cost function to fit the traces. Overall, the cross-correlation distribution and the cost function serve two different purposes. First, one can apply the cross-correlation distribution to quantify the similarity between two stochastic traces, including a step to account for out-of-phase alignment. Second, one can incorporate the cost function to estimate best-fit parameters that match stochastic traces in oscillatory systems.

B. Interpretation of the divergence matrix

1. Distribution of cross-correlations

The cross-correlation distribution, defined in Sec. IV B, compares *every* pair of segments from two traces, including noncoincident pairs. This approach assumes that the biophysical system exhibits Markovian dynamics, implying that it lacks an absolute time reference. Consequently, we can

justifiably compare noncoincident pairs of segments. We emphasize that the median cross-correlation (shown in Fig. 1) reflects the expected agreement when selecting *any* random pair of segments, one from each trace.

The cross-correlation distribution requires significantly longer traces for non-Markovian than Markovian systems. Non-Markovian systems yield at most $\Theta(N)$ cross-correlations for this distribution. In contrast, Markovian systems generate up to $\Theta(N^2)$ cross-correlations, offering greater sample sizes and higher numerical precision for estimating the distribution.

Using the cross-correlation distribution, we analyzed intracellular variation within a measured trace. For a given trace $x(t)$, the distribution $\chi\{x, x\}$ captures this variation, which arises in hair bundles due to various stochastic processes, as described in Appendix B. To quantify variation in position within a single trace, we used $\langle\chi\{x, x\}\rangle$. We note that a large $\langle\chi\{x, x\}\rangle$ indicates regular oscillations (i.e., with high quality-factor), whereas a small value indicates irregular movement. This value varies with segment duration T , so its nominal value communicates little information. However, comparing $\langle\chi\{x, x\}\rangle$ across different traces elucidates which bundles exhibit more regular oscillations relative to others.

2. Divergence of cross-correlations

We evaluated the agreement between measured and simulated traces. The simulated traces qualitatively reproduced the measured traces, as shown in Figs. 1 and 4. From Fig. 2, we observed a small $\langle D_{JS} \rangle$ between the measured bundle traces and their corresponding simulations, indicating little information loss. This suggests that the model effectively captures both local and global features of the measurements, maintaining strong predictive power for a stochastic system.

3. Matrix of divergences

We examined intercellular variation among the measured traces, using the divergence matrix described in Sec. IV D. For a given set of traces, the divergence matrix reveals this variation. To quantify this variation, we calculated the mean $\langle D_{JS} \rangle_{i \neq j}$ across the matrix, excluding diagonal elements. Conceptually, this mean represents the variation in motion across different traces. We note that a small $\langle D_{JS} \rangle$ indicates similar motion, whereas a large value reflects dissimilar motion. The measured-measured divergence matrix yielded a small $\langle D_{JS} \rangle_{i \neq j} = 0.064 \pm 0.088$, highlighting low intercellular variation compared to arbitrary functions.

The measured-measured divergence matrix may distinguish between different modalities of bundle movement such as regular [19], bursting [76–78], and spiking [79,80] dynamics. Well-defined clusters within this matrix may correspond to discrete mechanical modes driven by distinct biophysical processes. Conversely, the absence of clusters fails to rule out the existence of distinguishable modes. For example, spiking may represent a neighboring state to bursting, where bursts continuously shorten until they resemble spikes. Thus, hair bundles may exhibit a continuum of mechanical behaviors, transitioning smoothly between the three proposed modes.

C. Benefits of the cost function

We developed a cost function to fit parameters in oscillatory system of SDEs, prioritizing speed, interpretability, and adaptability.

1. Computational speed

The cost function computes efficiently. The rate-limiting steps in our fitting procedure involve (1) propagating the SDEs forward in time and (2) computing the cost-function components. When rescaling a trace directly using Eq. (9), we must repeatedly recalculate the cost function, which requires extensive computational time. Thus, we instead rescaled the cost-function components directly, detailed in Appendix D, providing a quicker rescaling option.

2. Scientific interpretability

The cost function retains scientific interpretability. It remains transparent throughout the fitting procedure, allowing users to conceptualize why particular costs yield certain fit qualities. Specifically, it contains three components, each capturing key aspects of active oscillations. Given a trace $x(t)$, the power spectral density $\tilde{S}_{xx}\{x\}$ and distribution $\vartheta\{x\}(\gamma, \Delta t)$ hold frequency and shape information, while the distribution $\rho_a\{x\}$ encodes amplitude and phase information. The two distributions had heavier weights because they contained the most relevant details for the hair-bundle oscillations. We still included the power spectral density because it converts timescales economically from nondimensional to dimensional units, discussed in more detail in Appendix D 2 a.

3. General adaptability

Beyond remaining interpretable, the cost function generally fits versatile types of oscillatory dynamics. For instance, we used the cost function to fit two types of distinct oscillatory behavior, as discussed in Sec. VII D. Researchers can tailor it to their applications, for example, by adjusting component weights, assimilating additional components, or deriving system-specific models.

The cost function accommodates adaptable weights for its components. Researchers can adjust these weights to align with their scientific systems and objectives. To further customize these weights, they can update them dynamically during differential evolution [61,65,68].

In addition to offering adjustable weights, the cost function can assimilate additional components. For example, we explored incorporating the distribution of velocities from the analytic signal in Appendix D 2 d. We excluded this fourth component due to its sensitivity to noise, but it may benefit systems with higher signal-to-noise ratios.

After including extra components, the cost function may extend to other chaotic systems. Prior studies have leveraged concepts from topological data analysis, such as persistence homologies [81], CROCKER plots [82–84], and Takens's embeddings [24,85–87]. These approaches could replace the distribution of the analytic signal described in Sec. V B, acting as robust metrics for fitting chaotic systems.

While we estimated parameters in a model for hair-bundle mechanics, our methodology extends to various oscillatory

TABLE II. The best-fit parameter sets for the sacculus and amphibian papilla. We fit nine sacculi and ten amphibian papillae. The header row indicates the parameter names corresponding to Table I. These best-fit parameters correspond to those shown in Fig. 10.

$\tilde{C}_{gs}$	$\tilde{\tau}_{hb}$	$\tilde{S}_{max}$	$\tilde{U}_{gs,max}$	$\tilde{\chi}_a$	$\tilde{k}_{gs,min}$	$\tilde{\tau}_m$	$\Delta\tilde{E}^\varnothing$	$\tilde{\eta}_{hb}$	$\tilde{\eta}_a$
Sacculus									
4.48	1.62	0.371	24.3	1.9	0.699	26.7	2.35	0.0237	0.0845
50.5	2.47	0.443	11.2	0.741	0.866	28.1	0.648	0.0149	0.108
83.9	0.166	0.467	23.2	2.04	0.555	9.63	1.15	0.013	0.172
35.4	0.155	0.758	9.87	4.6	0.699	3.23	0.912	0.0261	0.0582
7.31	23.6	0.0603	6.12	4.65	0.566	20.3	2.24	0.0691	0.108
91.0	11.7	0.851	15.2	6.91	0.217	17.6	1.95	0.00728	0.103
57.0	0.315	0.570	27.3	1.54	0.664	30.6	1.07	0.00607	0.171
36.7	0.196	0.562	15.1	3.78	0.618	10.8	1.43	0.00201	0.0951
40.2	2.13	0.409	17.9	0.813	0.676	17.1	0.884	0.0214	0.219
Amphibian papilla									
98.7	1.55	0.467	26.3	7.3	0.275	19.3	1.50	0.0165	0.183
88.3	1.55	0.630	24.3	1.57	0.319	18.7	0.704	0.00244	0.0327
98.7	7.83	0.217	0.228	1.99	0.96	6.62	0.656	0.0469	0.0964
90.8	1.52	0.529	4.44	3.64	0.698	7.67	2.97	0.0127	0.143
44.1	2.76	0.455	20.1	6.52	0.574	9.29	2.46	0.0098	0.225
39.2	1.94	0.600	19.4	2.94	0.53	24.7	1.51	0.0101	0.0961
21.5	0.589	0.631	11.3	0.872	0.557	26.7	2.32	0.0717	0.0849
94.2	1.01	0.447	22.4	1.33	0.447	24.2	1.32	0.0155	0.154
24.2	6.99	0.906	21.5	7.97	0.461	26.8	3.05	0.0491	0.222
85.2	2.80	0.634	12	9.68	0.983	10.3	1.29	0.0363	0.275

systems. In the current study, we modeled hair-bundle motion in two hearing end organs, the sacculus and AP [37]. To model other inner-ear end organs (e.g., utricle or basilar papilla [28]), researchers can incorporate additional terms into the model or extend parameter ranges before evaluating the cost function. For general oscillatory systems, they must develop suitable models, and they can continue to implement our cost-function approach to characterize and optimize the match between their measured and simulated datasets.

D. Evaluation of the hair-bundle parameters

We compared best-fit parameter sets for saccular and AP hair bundles, measuring nine bundles from the sacculus and ten from the AP. We focused our analysis primarily on clusters formed by joint distributions of two parameters, shown in Fig. 10. These clusters displayed comparable centers and shapes across the two end organs. However, the parameter sets for AP bundles appear more dispersed than those for saccular bundles. For the best-fit parameters of each cell, see Table II.

Parameters for the AP reveal wider visual spread than those for the sacculus. Potentially, this spread occurs because the AP exhibits richer oscillatory dynamics and poses greater recording challenges. As we reported previously, AP bundles exhibit a broader range of dynamical behaviors, including spiking and bursting oscillations, unlike the typically regular oscillations observed in saccular bundles [37]. Additionally, AP bundles tend to oscillate faster, so individual cycles consist of fewer sample points than the sacculus, which increases fitting error. Moreover, the AP appears more opaque, decreasing its signal-to-noise ratio and further compromising the parameter fit.

We examined the best-fit noise strengths acting on the hair bundle and myosin motors. To model these noisy processes, we added Brownian motions to the differential equations for both components, as detailed in Appendix B. The fits typically yielded stronger noise for the motors than for the bundle, suggesting that thermal fluctuations disproportionately affect the motors. These fitted strengths provide recommended parameter ranges, constraining the corresponding physical observables described in Eq. (B3).

After adding these noise terms, we toggled them in the model to understand their effects on bundle dynamics. For most bundles, the best-fit simulation oscillated independently of both noise strengths, remaining perpetually either oscillatory or quiescent. Using the best-fit parameters from the stochastic model, we simulated nine nonoscillating bundles in the deterministic model (i.e., with $\tilde{\eta}_{hb} = \tilde{\eta}_a = 0$). When introducing bundle noise alone to these bundles (i.e., $\tilde{\eta}_{hb} > 0$), we failed to induce an oscillation ($n = 9$). However, when adding motor noise (i.e., $\tilde{\eta}_a > 0$), we sometimes induced oscillations ($n \leq 5$), regardless of noise strength for the bundle. Hence, motor noise partially determines the dynamic state of the hair bundle.

Motor noise appears essential for observing bursting behavior in hair bundles. Simulations for two bursting bundles, based on their best-fit parameters, required motor noise independent of bundle noise. These simulations also revealed a low $\tilde{\tau}_{hb} \approx 0.03$ and a high $\tilde{\eta}_{hb} \approx 0.08$ relative to the general distribution. By fitting and simulating additional bursting bundles, future studies can identify their underlying biophysical mechanisms.

By examining how simulated parameters shape model behavior, we can explore which internal processes drive bundle

dynamics, such as bursting. While many internal cellular processes remain experimentally inaccessible, we can fit their associated parameters to infer how they influence over hair-bundle oscillations. Using our fitting methodology, we can elucidate the underlying dynamics of biophysical systems such as hair bundles.

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DATA AVAILABILITY

The data and code that support the findings of this article are openly available at [88].

APPENDIX A: SYSTEM-SPECIFIC DETAILS FOR EXPERIMENTAL METHODS

1. Biological preparation

North American bullfrogs (*Rana catesbeiana*) of either gender were anesthetized (pentobarbital: 150 ml kg⁻¹), double pithed, and decapitated following protocols approved by the University of California, Los Angeles Chancellor's Animal Research Committee. We extracted sacculi from the inner ears of the frogs and placed them in oxygenated, artificial-perilymph solution [in mM as follows: 110 Na⁺, 2 K⁺, 1.5 Ca²⁺, 113 Cl⁻, 3 D-(+)-glucose, 1 Na⁺ pyruvate, 1 creatine, 5 HEPES]. To mimic the *in vivo* physiological conditions of the surrounding fluid, we mounted the epithelium in a two-compartment chamber. We bathed the apical surfaces in artificial endolymph [in mM as follows: 2 Na⁺, 118 K⁺, 0.25 Ca²⁺, 118 Cl⁻, 3 D-(+)-glucose, 5 HEPES] and basolateral membranes in perilymph [19]. To access individual hair bundles, we removed the otolithic membrane after dissociating it with 15 g ml⁻¹ of collagenase IV (Sigma-Aldrich) for 8 min.

Using a similar procedure, we extracted the amphibian papilla—the main auditory organ of the frog—from the dissected inner ears [37]. We mounted the epithelium in a one-compartment chamber, submerging it in an artificial-perilymph solution with lowered calcium (0.25 mM). Analogous to the saccular dissection, we removed the tectorial membrane after dissociating it in collagenase IV for 9 min.

2. Optical recordings

We collected recordings using an upright optical microscope (Olympus BX51WI) with a water-immersion objective lens (Olympus LUMPlanFL N 60X, NA:1.00), mounted on an optical table (Technical Manufacturing). The microscope was placed inside an acoustically isolated chamber (Industrial Acoustics), minimizing mechanical disturbances to the sensitive hair cells. We recorded innate hair-bundle movement, obtaining 16-bit images at a resolution of

108.3 ± 0.8 nm px⁻¹, with a high-speed camera (ORCA-Flash4.0 CMOS) at either 500 or 1000 frames per second. Throughout experiments, the hair bundles sustainably oscillated.

To maximize resolution, we collected differential interference contrast images of the oscillating bundles. Each image accounted for 1 or 2 ms of exposure time, depending on frame rate. To analyze these images, we used custom matlab scripts. Specifically, for each frame, we determined the centroid of the bundle weighted by pixel intensity.

To track hair-bundle motion, we calculated position for each video frame. Typical traces yielded noise floors around 3–5 nm, manifesting primarily as thermal [89,90] and ionic [20,91,92] fluctuations. When recording, the hair cell gradually relaxes, slowly drifting the apparent bundle positions. To remove this drift, we subtracted a wide-size, Hann moving average from its corresponding trace.

APPENDIX B: ANALYTIC DERIVATION OF STOCHASTIC TERMS

To derive the stochastic terms for our model of hair-bundle mechanics, we adapted the dimensional system of ODEs presented in Ref. [22]. We denote differentials of Brownian motion as $dB_t \sim \mathcal{N}(0, dt)$, where $\mathcal{N}(\mu, \sigma^2)$ represents a normal distribution with mean μ and variance σ^2 .

We added stochastic terms to the differentials governing hair-bundle and adaptation-motor positions. We introduced thermal noise to Eq. (S21), following prior literature on stochastic systems [20,93] to obtain

$$\begin{aligned} \lambda_{hb} dX_{hb} = & -[\gamma N f_{gs} + k_{sp}(X_{hb} - X_{sp})]dt \\ & + \sqrt{2k_B T \lambda_{hb}} dB_{t,hb}, \\ dx_a = & [S(f_{gs} - k_{es}(x_a + x_{es})) - C]dt \\ & + \sqrt{\frac{2k_B T}{\lambda_a}} dB_{t,a}, \end{aligned} \quad (B1)$$

where $B_{t,hb}$ and $B_{t,a}$ represent independent Brownian motions, such that $dB_t \sim \mathcal{N}(0, dt)$, for bundle and motor positions, respectively. Consistent with frog saccular hair bundles [91,94], we treat the transduction open-channel probability as deterministic, ignoring channel noise [95].

After nondimensionalizing, the equations take the form

$$\begin{aligned} \tilde{\tau}_{hb} d\tilde{x}_{hb} = & -(\tilde{F}_{gs} - \tilde{x}_{hb})d\tilde{t} + \tilde{\eta}_{hb} d\tilde{B}_{\tilde{t},hb}, \\ \tilde{\tau}_a d\tilde{x}_a = & [\tilde{S}_{max} \tilde{S}(\tilde{F}_{gs} - \tilde{x}_a) - \tilde{C}_{max} \tilde{C}]d\tilde{t} + \tilde{\eta}_a d\tilde{B}_{\tilde{t},a}, \end{aligned} \quad (B2)$$

where $\tilde{B}_{\tilde{t},hb}$ and $\tilde{B}_{\tilde{t},a}$ represent nondimensional Brownian motions, such that $d\tilde{B}_{\tilde{t}} \sim \mathcal{N}(0, d\tilde{t})$. The nondimensional noise strengths $\tilde{\eta}_{hb}$ and $\tilde{\eta}_a$ for bundle and motor noise, respectively, relate to their dimensional counterparts by

$$\begin{aligned} \tilde{\eta}_{hb} &:= \frac{\hat{\eta}_{hb}}{\sqrt{\tilde{\tau}}}, & \hat{\eta}_{hb} &:= \frac{\sqrt{2k_B T \lambda_{hb}}}{\gamma N d k_{gs,max}}, \\ \tilde{\eta}_a &:= \frac{\hat{\eta}_a}{\sqrt{\tilde{\tau}}}, & \hat{\eta}_a &:= \frac{\sqrt{2k_B T / \lambda_a}}{C_{max} + S_{max} k_{gs,max} d}, \end{aligned} \quad (B3)$$

where $\hat{\eta}_{hb}$ and $\hat{\eta}_a$ represent characteristic noise strengths for bundle and motor noise, respectively.

To solve these SDEs numerically, we employed the Euler-Maruyama algorithm [96,97], adapted from `sdeint.integrate.itoEuler`. We simulated the system up to nondimensional time $\tilde{t} = 500$ using time steps of $\Delta\tilde{t} = 2 \times 10^{-3}$.

APPENDIX C: INFORMATION-THEORETIC MEASURES FOR COMPARING TRACES

We compared three information-theoretic measures of “distance” between two probability distributions [98,99], namely, total variation distance, Hellinger distance d_H , and Jensen-Shannon divergence (JSD). We chose these three measures specifically because all three remain L^∞ -normalized, rendering comparison across datasets feasible.

1. Total Variation Distance

We derived an efficient computational method to calculate TVD. Let $\rho_1(x, y)$ and $\rho_2(x, y)$ represent two joint PDFs. We denote the minimum and maximum x such that $\rho_i(x, y) > 0$ as $x_{i,L}$ and $x_{i,R}$, respectively. Similarly, we denote the minimum and maximum y such that $\rho_i(x, y) > 0$ as $y_{i,B}$ and $y_{i,T}$, respectively. These bounds yield eight total quantities: minima and maxima x and y for each $\rho_1(x, y)$ and $\rho_2(x, y)$.

To determine the minimal axis-aligned bounding box [100] for the intersection between $\rho_1(x, y)$ and $\rho_2(x, y)$, we found

$$\begin{aligned} x_L &= \max\{x_{1L}, x_{2L}\}, \\ x_R &= \min\{x_{1R}, x_{2R}\}, \\ y_B &= \max\{y_{1B}, y_{2B}\}, \\ y_T &= \min\{y_{1T}, y_{2T}\}. \end{aligned} \quad (C1)$$

This bounding box defines the smallest axis-aligned rectangle for all crossing arrangements of $\rho_1(x, y)$ and $\rho_2(x, y)$, before accounting for topological symmetries (i.e., rotation and stretching) and distribution swapping, as visualized in Fig. 5 excluding touching [101].

To determine the nonintersecting regions of ρ_i toward TVD, we found

$$\begin{aligned} 2d_{i,\text{TV}} &= 1 - F_i(x_R, y_T) + F_i(x_R, y_B) + F_i(x_L, y_T) \\ &\quad - F_i(x_L, y_B), \end{aligned} \quad (C2)$$

where $|\cdot|$ represents the absolute value or complex modulus and $F_i(x, y)$ represents the cumulative distribution function for $\rho_i(x, y)$.

Finally, we calculated the TVD between $\rho_1(x, y)$ and $\rho_2(x, y)$. For crossing arrangements, we calculated TVD as

$$\begin{aligned} d_{\text{TV}}(\rho_1, \rho_2) &= d_{1,\text{TV}} + d_{2,\text{TV}} \\ &\quad + \frac{1}{2} \int_{y_B}^{y_T} \int_{x_L}^{x_R} |\rho_2(x, y) - \rho_1(x, y)| dx dy. \end{aligned} \quad (C3)$$

Conceptually, the terms $d_{1,\text{TV}}$ and $d_{2,\text{TV}}$, respectively, account for the nonintersecting regions of ρ_1 and ρ_2 , whereas the integral accounts for the intersecting region. For disjoint arrangements, we immediately returned $d_{\text{TV}} = 1$ instead of computing from the previous equation. Overall, this hybrid

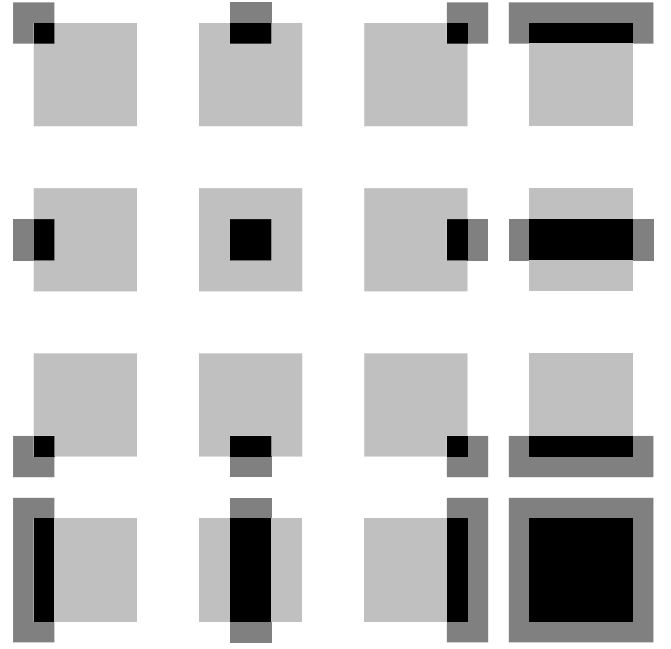


FIG. 5. Sixteen possible crossing arrangements for a pair of 2D probability distributions. The (light and dark) gray regions show minimal axis-aligned bounding boxes for the disjoint domains of the two distributions. The black regions show minimal axis-aligned bounding boxes for the intersecting domain of the two distributions.

formulation improved computational speed and numerical precision.

2. Hellinger distance and Jensen-Shannon divergence

We calculated d_H and JSD by expressing them as their respective f divergences [102,103], using

$$D_f(P||Q) = \int p(x) f\left(\frac{q(x)}{p(x)}\right) dx, \quad (C4)$$

where f_D represents the f divergence for divergence D , and $p(x)$ and $q(x)$ represent actual and guessed probability distributions, respectively. Across all measures of dissimilarity, we used continuous PDFs rather than discrete distributions to ensure the divergences remained L^1 -normalized.

To calculate JSD, we used

$$\begin{aligned} D_{\text{JS}}(P, Q) &= D_f(P||Q), \\ f(x) &= x \log_2(x) - (x + 1) \log_2\left(\frac{x + 1}{2}\right). \end{aligned} \quad (C5)$$

To calculate d_H , we used

$$d_H(P, Q) = 1 - D_f(P||Q), \quad f(x) = \sqrt{x}. \quad (C6)$$

For d_H , we computed only within the overlapping region between ρ_1 and ρ_2 , as nonoverlapping regions leave d_H unchanged.

3. Cross-correlation of trace segments

We compared three versions of divergence matrices, using total variation distance, Hellinger distance, and JSD, all shown in Fig. 7. From these three, we selected JSD for further

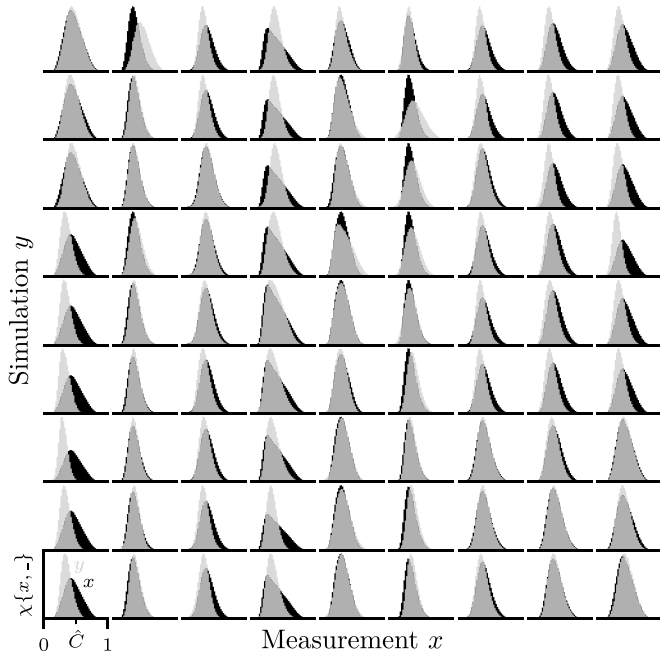


FIG. 6. A comparison between measured and simulated distributions of cross-correlations for nine saccular bundles. Columns (large x axis) correspond to measured bundle traces $x(t)$, and rows (large y axis) correspond to simulated bundle traces $y(t)$. The small x axis displays cross-correlation $\hat{C}$. The small y axis displays PDF $\chi(\hat{C})$, ranging up to the maximum probability density per plot. Black histograms show PDF $\chi\{x, x\}(\hat{C})$, which correlates a measured bundle to itself. Gray histograms show PDF $\chi\{x, y\}(\hat{C})$, which correlates a measured bundle to a simulated bundle.

analysis, for the following reasons. First, we eliminated total variation distance, as it was less clear in indicating similarity between the measured and simulated traces, compared to Hellinger distance or JSD. Second, we chose JSD over Hellinger distance, because JSD more directly quantifies information loss between a pair of distributions, compared to Hellinger distance.

Segment duration affects the divergence matrices described in Sec. IV D, so we calculated these matrices for $T = 4, 8, 12, 16, 20$ cycles. Ultimately, we chose segment duration T equal to four periods of reference trace $x(t)$, calculating periods as the reciprocal median frequency in $S_{xx}\{x\}$. Relative to larger durations, this choice widened the cross-correlation distributions, yielding a median around 0.5 as shown in Fig. 6.

We ranked values in the measured-simulated divergence matrices. We then performed Page’s trend test ($p < 0.001$; [104]), which indicated consistent rankings in the divergence matrices across different durations. Furthermore, we performed linear regression pairwise on these divergence matrices, resulting in $r^2 = 0.977 \pm 0.026$, indicating that JSD increased by a roughly constant factor with changing T . When performing the same test on the other divergence matrices (e.g., measured-measured, simulated-simulated), these rankings retained low p value and high r^2 value.

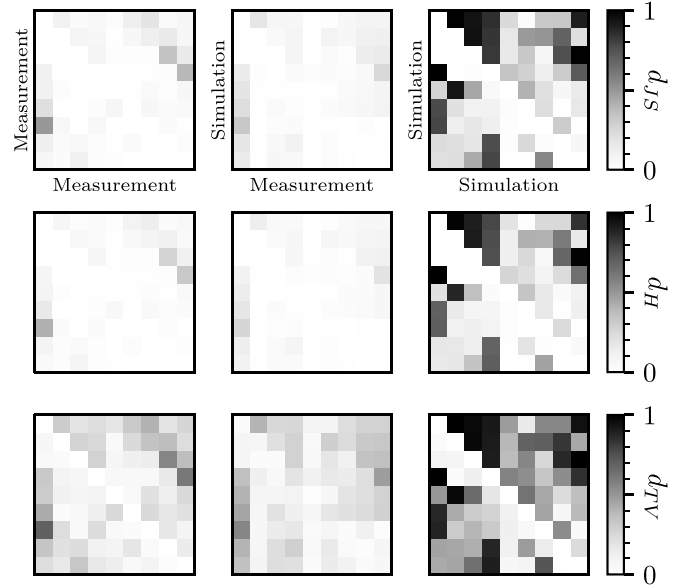


FIG. 7. A comparison between alternative divergence matrices, as described in Sec. IV D, for nine saccular bundles. Each row indicates a different L^1 -normalized information-theoretic measure for dissimilarity, corresponding to Jensen-Shannon divergence (top), Hellinger distance (center), and total variation distance (bottom). Each column indicates a different version of divergence matrix, corresponding to measured-measured (left), measured-simulated (center), and simulated-simulated (right).

We performed linear regression to recover the divergence matrices at different cycle lengths. Letting $D_{JS}(\chi\{x_T, x_T\}, \chi\{x_T, y_T\})$ represent divergence from the matrix corresponding to segment duration T cycles, we fit the curve

$$\frac{D_{JS}(\chi\{x_T, x_T\}, \chi\{x_T, y_T\})}{D_{JS}(\chi\{x_4, x_4\}, \chi\{x_4, y_4\})} = a(1 + bT), \quad (C7)$$

where $a, b \in \mathbb{R}$, a form justified by the high r^2 between $D_{JS}(\chi\{x_4, x_4\}, \chi\{x_4, y_4\})$ and $D_{JS}(\chi\{x_T, x_T\}, \chi\{x_T, y_T\})$ for $T = 4, 8, 12, 16, 20$. Using least-squares regression, we found $a = 0.815 \pm 0.035$ and $b = 0.035 \pm 0.006$. These values for a, b can be used to approximate $D_{JS}(\chi\{x_T, x_T\}, \chi\{x_T, y_T\})$ at different segment durations. This linear regression fails for large T because $D_{JS}(\chi\{x_T, x_T\}, \chi\{x_T, y_T\})$ asymptotically approaches a constant value as $T \rightarrow \infty$. However, this regression remains accurate for T between 4 and 20 cycles.

APPENDIX D: DETAILS FOR FITTING PROCEDURE

1. Application of differential evolution

We used `scipy.optimize.differential_evolution` to perform differential evolution [69,70]. For our differential evolution hyperparameters, we set population size to 64 [105], initial guesses to Sobol sampling [106], strategy to “randlexp” [107], recombination to 0.7, and mutation to dynamically between 0.5 and 1. Notably, we changed the initial guesses, population size, and strategy from the defaults in `scipy.optimize.differential_evolution`.

During differential evolution, we declared the same noise seed before each simulation and across iterations. As a result, we asserted the same noise instances independently for $d\tilde{B}_{i,\text{hb}}$ and $d\tilde{B}_{i,a}$, only multiplying them by their respective noise strengths $\tilde{\eta}_{\text{hb}}$ and $\tilde{\eta}_a$.

2. Components of cost function

As components of the cost function, we evaluated the PSD, the distribution of analytic signal (DAS), and the DPC to characterize oscillations. For each of these representative functions, we used TVD as a measure of dissimilarity. While statisticians traditionally apply TVD to compare two probability distributions, we applied it more broadly to L^1 -normalized functions.

a. Shape of power spectral density

The PSD contributed 10% to the total weight of our cost function, capturing primarily the shape and timescale of a trace. We denote the PSD of position x as $S_{xx}\{x\}(f)$. To effectively smooth power spectral density, we used the Bartlett method [108,109] to segment the trace into eight nonoverlapping parts.

We L^1 -normalized this PSD as $\tilde{S}_{xx}\{x\}(f)$. This normalized version resembles a PDF with unit area. Thus, we quantified the dissimilarity between measured and simulated PSDs by evaluating their TVD.

To convert from simulated into measured position, we directly rescaled

$$\tilde{S}_{xx} \mapsto \hat{\tau} \tilde{S}_{xx}, \quad f \mapsto \frac{f}{\hat{\tau}}. \quad (\text{D1})$$

This rescaling relies solely on $\hat{\tau}$, remaining independent of $\hat{x}_{\text{hb}}$ and $\check{x}_{\text{hb}}$, which implies that the normalized PSD efficiently rescales time in particular.

b. Distribution of analytic signal

The DAS contributed 50% to the total weight of our cost function, capturing both the shape and amplitude of a trace. We denote the joint PDF of the analytic signal over position x and its Hilbert transform $\mathcal{H}\{x\}$ as $\rho_a(x, \mathcal{H}\{x\})$. To quantify the dissimilarity between measured and simulated DASs, we evaluated their TVD.

To convert from simulated into measured position, we rescaled

$$\rho_a \mapsto \frac{\rho_a}{\hat{x}_{\text{hb}}^2}, \quad x \mapsto \hat{x}_{\text{hb}}(x - \check{x}_{\text{hb}}), \quad \mathcal{H}\{x\} \mapsto \check{x}_{\text{hb}} \mathcal{H}\{x\}, \quad (\text{D2})$$

leveraging the identity $\mathcal{H}\{ax + b\} = a\mathcal{H}\{x\}$ with constants a, b [110]. This rescaling depends exclusively on $\hat{x}_{\text{hb}}$ and $\check{x}_{\text{hb}}$, not on $\hat{\tau}$, which suggests that the nondimensional DAS methodically rescales position.

We determined the number of bins for each axis of the analytic signal dynamically. Let N_x denote the number of points in the computational array for trace $x(t)$. We set the number of bins for x and $\mathcal{H}\{x\}$ individually to $\lfloor \sqrt[3]{N_x} \rfloor$, where $\lfloor \cdot \rfloor$ represents the rounding function (to the nearest integer). This cube-root heuristic balances the number of bins along each x and $\mathcal{H}\{x\}$ as well as points per bin.

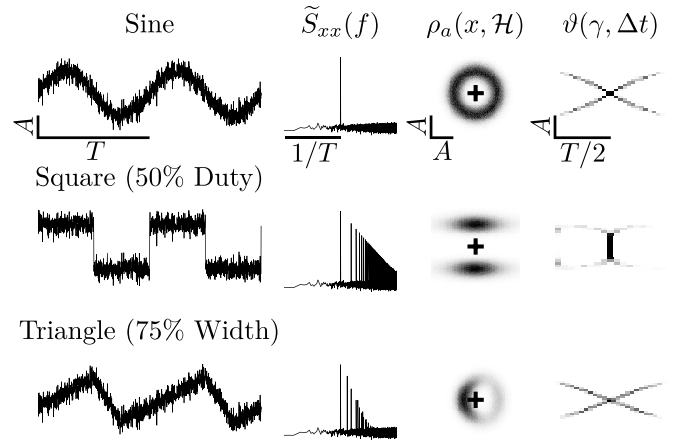


FIG. 8. The three cost-function components, described in Sec. V, for three common waveforms. Rows correspond to waveforms of sine (top), square (50% duty, center), and triangle (75% width, bottom). Column 1: The solid lines display position x over time t , each with zero mean position. The scale bar displays amplitude A along the y axis and period T along the x axis. Column 2: In a log-log scale, the solid lines display power spectral density $\tilde{S}_{xx}$ over frequency f , and the dashed lines indicate their median frequency. The scale bar displays frequency $1/T$ along the x axis. Column 3: The heatmaps display PDF $\rho_a(x, \mathcal{H})$ over position x along the y axis and Hilbert transform $\mathcal{H}\{x\}$ along the x axis. The plus signs indicate the origin of $(x, \mathcal{H}\{x\})$. The scale bar displays amplitude along both axes. Column 4: The heatmaps display PDF $\vartheta\{x\}(\gamma, \Delta t)$ over crossing position γ along the y axis and time difference Δt along the x axis. The scale bar displays amplitude along the y axis and half-period along the x axis.

c. Distribution of position crossings

The DPC contributed 40% of the total weight to our cost function, capturing the shape, timescale, and amplitude of a trace. We denote the joint PDF of position crossings over crossing position γ and half-period Δt as $\vartheta(\gamma, \Delta t)$. Before calculating this distribution, we denoised traces using wavelets [111]. Computationally, we chose the “VisuShrink” method [112] with the “soft” mode and “sym4” wavelet [113] via `skimage.restoration.denoise_wavelet`. To quantify the dissimilarity between measured and simulated DPCs, we evaluated their TVD.

To convert from simulated into measured position, we rescaled

$$\vartheta \mapsto \frac{\vartheta}{\hat{\tau} \hat{x}_{\text{hb}}}, \quad \gamma \mapsto \hat{x}_{\text{hb}}(\gamma - \check{x}_{\text{hb}}), \quad \Delta t \mapsto \hat{\tau} \Delta t. \quad (\text{D3})$$

This rescaling depends on all three variables (i.e., $\hat{x}_{\text{hb}}$, $\check{x}_{\text{hb}}$, $\hat{\tau}$), meaning the nondimensional DPC versatily rescales the simulated traces in full.

We included only robust crossing events, ignoring extraneous events due to noise. A trace x can register multiple crossings during a single crossing event, by fluctuating stochastically through a position multiple times in quick succession. To mitigate unwanted crossings from noise, we used bins surrounding γ rather than individual values.

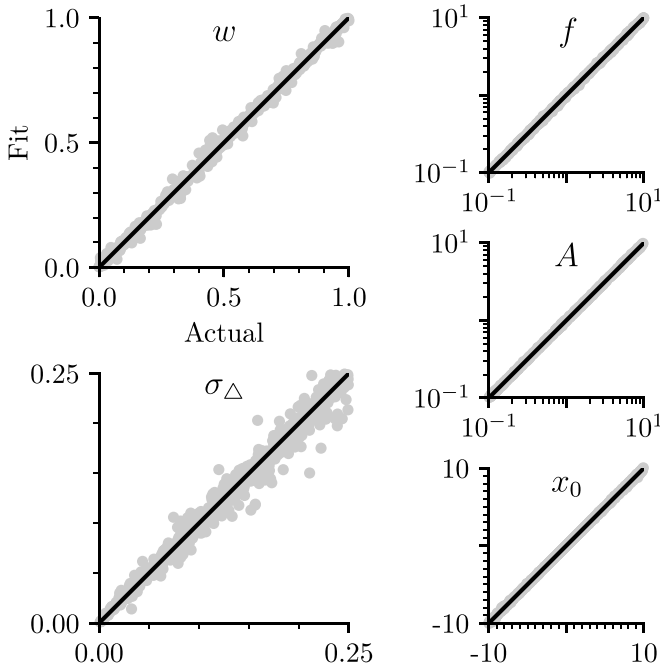


FIG. 9. A comparison between fit and actual parameters for simulated triangle waves. The plot titles indicate the parameter for the triangle wave in Eq. (10): width w , noise strength η_Δ , frequency f , amplitude A , and offset x_0 . The y axis shows fit parameter values, and the x axis shows actual parameter values. The markers show pairs of fit and actual parameter values for simulated triangle waves. The lines indicate where fit and actual values equal each other.

We assigned a single representative time to each γ -crossing event. Initially, we characterized each event computationally with multiple crossing times as the trace passed through the two boundaries of a bin. These degenerate crossing times occurred because the trace crossed through both boundaries, potentially multiple times on either one. To consolidate these into a single crossing time, we calculated the midpoint between the final two crossing times, one through each boundary of the bin.

To generate the tuple $\Theta_\gamma\{x\}$ of γ -crossing times, we analyzed the denoised position $x(t)$. We denote the ordered tuples of upward- and downward-crossing times as $\Theta_{\gamma\uparrow}\{x\}$ and $\Theta_{\gamma\downarrow}\{x\}$, respectively, both sorted in ascending order of time. Furthermore, we represent the number of crossings in these tuples as $N_{\gamma\uparrow} := |\Theta_{\gamma\uparrow}\{x\}|$ and $N_{\gamma\downarrow} := |\Theta_{\gamma\downarrow}\{x\}|$, respectively.

We counted a γ crossing only when x crossed fully through a bin around γ . For a small neighborhood size $\delta x > 0$, we separately counted upward and downward crossings. We counted an upward crossing in $\Theta_{\gamma\uparrow}\{x\}$, incrementing $N_{\gamma\uparrow}$, when x crossed consecutively through $\gamma - \delta x$ followed by $\gamma + \delta x$. Similarly, we counted a downward crossing in $\Theta_{\gamma\downarrow}\{x\}$, incrementing $N_{\gamma\downarrow}$, when x crossed consecutively through $\gamma + \delta x$ followed by $\gamma - \delta x$.

We determined a number N_γ of equidistant bin edges for crossing position γ manually. In general, the optimal number for N_γ depends on the signal-to-noise ratio of the position [114], which varies across biophysical systems. Smaller values for N_γ provide greater precision for $\vartheta(\gamma, \Delta t)$, whereas

larger values yield greater precision for γ . To balance these trade-offs, we chose $N_\gamma = 21$ arbitrarily after analyzing several hair-bundle traces, achieving sufficient precision in both $\vartheta(\gamma, \Delta t)$ with γ . We selected the minimum and maximum values for γ to span those in x .

After discretizing bin edges for γ , we determined a number $N_{\Delta t}$ of equidistant bin edges for half-period Δt dynamically. Specifically, we calculated

$$N_{\Delta t} = \lfloor \sqrt[6]{N_\uparrow N_\downarrow} \rfloor$$

$$N_{(\uparrow\downarrow)} := \sum_\gamma N_{\gamma(\uparrow\downarrow)} \quad (\text{D4})$$

where $N_\uparrow$ and $N_\downarrow$ represent the total number of upward- and downward-crossing times, respectively. Conceptually, this formula computes the cube root of the geometric mean of $N_\uparrow$ and $N_\downarrow$. Similar to the heuristic in Appendix D 2 b, we included this cube root to balance the number of bins along each γ and Δt with points per bin.

Finally, we selected the minimum $\Delta t_{\min}$ and maximum $\Delta t_{\max}$ bin-edge values for Δt to balance coverage and accuracy. Let $\Theta\{x\} := \bigcup_\gamma \Theta_\gamma\{x\}$ represent the ordered tuple containing all crossing times in $\Theta_\gamma\{x\}$ across all N_γ values of γ , sorted in ascending order of time. We chose

$$\Delta t_{\min} = \min \Theta\{x\}, \quad \Delta t_{\max} = \sqrt{N_\gamma} \max \Theta\{x\}. \quad (\text{D5})$$

By incorporating the extent of $\Theta\{x\}$, we covered a broad range over Δt . By including the scaling factor $\sqrt{N_\gamma}$, we compensated for the shorter crossing times in $\Theta\{x\}$ compared to those in individual $\Theta_\gamma\{x\}$ tuples.

d. Velocity field of analytic signal

As an alternative cost-function component, we examined the 2D velocity field $\tilde{S}_a\{x\}$ of trace $x(t)$. Using `scipy.stats.binned_statistic_2d`, we binned this field along $(x, \mathcal{H}\{x\})$ to generate a 2D joint PDF, analogous to $\rho_a\{x\}$ in Eq. (3). To quantify the discrepancy between velocity fields of the measured and simulated traces, we computed their TVD, taking the complex modulus in Eq. (C3). Ultimately, we excluded this component as part of the cost function because this PDF remained too sensitive to transient noise in the traces.

3. Validation on triangle waves

To validate the cost function, we recovered parameter values for 600 simulated triangle waves using Eq. (10). For each wave, we generated five parameters using `numpy.random.uniform` as follows:

$$w \in U[0, 1),$$

$$\sigma_\Delta \in U[0, 0.25),$$

$$f, A \in 10^{U[-1, 1]},$$

$$x_0 \in U[-10, 10), \quad (\text{D6})$$

where $U[a, b)$ represents a uniform random variable spanning the interval $[a, b)$.

Computationally, we first calculated the deterministic triangle wave. During each simulation, we covered a time

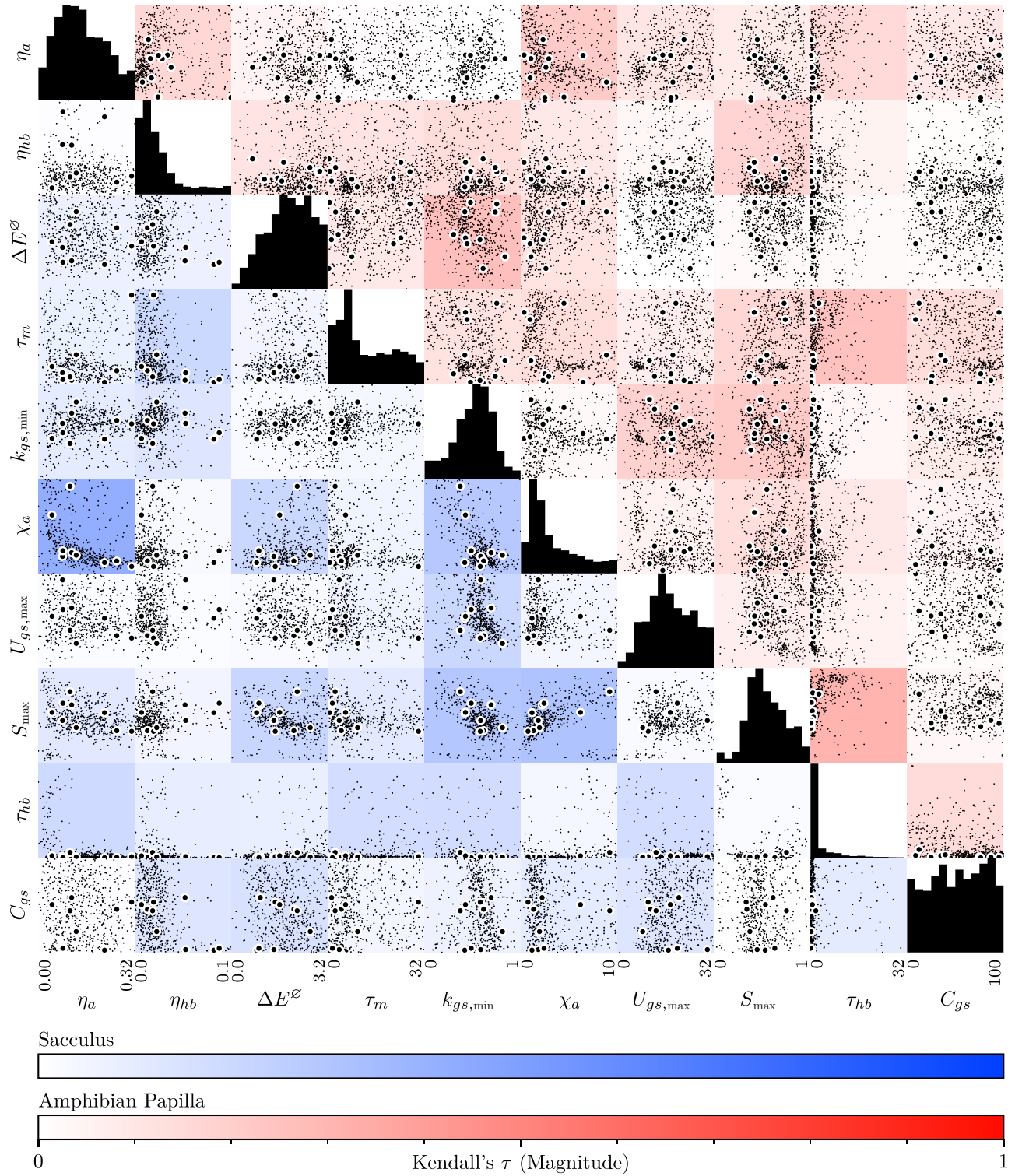


FIG. 10. The pairwise distributions of best-fit parameters for sacculi and amphibian papillae. On-diagonal: The histograms show PDFs of all parameters during the final iteration of differential evolution, combining saccular and papillar bundles. Off-diagonal: Blue (bottom left) and red (top right) backgrounds correspond to saccular and AP bundles, respectively. The x and y axes range from minimum to maximum parameter bounds used when fitting. Large markers display best-fit parameters during the final iteration, nine for the sacculus and ten for the papilla. Small markers display all parameters during the final iteration (population size 64), with $9 \times 64 = 576$ for the sacculus and $10 \times 64 = 640$ for the papilla. The colorbars indicate magnitude of Kendall's τ , displayed as saturation of background color, for each pair of parameters (entire population), distinguishing between the sacculus (blue) and papilla (red).

interval $t \in [0, 20]$ with a fixed time step of $\Delta t = 2 \times 10^{-3}$, generating an array with 20 000 points. We then added noise independently to each point, sampling from $\mathcal{N}(0, 1)$ and scaling by noise strength. In Fig. 8, we exemplified a triangle wave with $w = 0.75$ and $\sigma_{\Delta} = 0.25$.

For each simulated triangle wave, we fit parameters using the cost function described in Sec. V. During differential evolution, we reused a single instance of noise, scaling by the

guessed noise strength in each parameter set. By fixing the noise seed, we mitigated the risk of anchoring prematurely to an unstable minimum, caused by noise realizations with unusually low cost.

APPENDIX E: PYTHON PACKAGES

numpy [115], scipy [116], sdeint [117], skimage [118], matplotlib [119], pandas [120].

- [1] R. D. Mortlock, S. K. Georgia, and S. D. Finley, Dynamic regulation of jak-stat signaling through the prolactin receptor predicted by computational modeling, *Cell. Mol. Bioeng.* **14**, 15 (2021).
- [2] N. J. Linden, B. Kramer, and P. Rangamani, Bayesian parameter estimation for dynamical models in systems biology, *PLoS Comput. Biol.* **18**, e1010651 (2022).
- [3] C. G. Knight, S. H. E. Knight, N. Massey, T. Aina, C. Christensen, D. J. Frame, J. A. Kettleborough, A. Martin, S. Pascoe, B. Sanderson, D. A. Stainforth, and M. R. Allen, Association of parameter, software, and hardware variation with large-scale behavior across 57,000 climate models, *Proc. Natl. Acad. Sci. USA* **104**, 12259 (2007).
- [4] G. L. Baker and J. P. Gollub, *Chaotic Dynamics: An Introduction* (Cambridge University Press, Cambridge, 2002), 2nd ed.
- [5] J. C. Sprott, *Chaos and Time-Series Analysis* (Oxford University Press, Oxford, 2006), 2nd ed.
- [6] J. Faber and D. Bozovic, Noise-induced chaos and signal detection by the nonisochronous Hopf oscillator, *Chaos* **29**, 043132 (2019).
- [7] J. Faber and D. Bozovic, Criticality and chaos in auditory and vestibular sensing, *Sci. Rep.* **14**, 13073 (2024).
- [8] C. W. Gardiner, *Handbook of Stochastic Methods for Physics, Chemistry, and the Natural Sciences*, Springer Series in Synergetics (Springer, Berlin, 2004), 3rd ed.
- [9] S. Särkkä, V. Tolvanen, J. Kannala, and E. Rahtu, Adaptive Kalman filtering and smoothing for gravitation tracking in mobile systems, in *2015 International Conference on Indoor Positioning and Indoor Navigation (IPIN)* (IEEE, Banff, AB, Canada, 2015), pp. 1–7.
- [10] S. Särkkä, A. Solin, A. Nummenmaa, A. Vehtari, T. Auranen, S. Vanni, and F.-H. Lin, Dynamic retrospective filtering of physiological noise in BOLD fMRI: DRIFTER, *NeuroImage* **60**, 1517 (2012).
- [11] D. L. Cook, L. S. Satin, and W. F. Hopkins, Pancreatic B cells are bursting, but how? *Trends Neurosci.* **14**, 411 (1991).
- [12] N. N. Taleb, *Dynamic Hedging: Managing Vanilla and Exotic Options*, Series in Financial Engineering (Wiley, New York, 1997).
- [13] T. Li, S. Kheifets, D. Medellin, and M. G. Raizen, Measurement of the instantaneous velocity of a brownian particle, *Science* **328**, 1673 (2010).
- [14] C. Zimmer and S. Sahle, Deterministic inference for stochastic systems using multiple shooting and a linear noise approximation for the transition probabilities, *IET Syst. Biol.* **9**, 181 (2015).
- [15] C. Zimmer, Reconstructing the hidden states in time course data of stochastic models, *Math. Biosci.* **269**, 117 (2015).
- [16] G. I. Webb, Naïve bayes, in *Encyclopedia of Machine Learning and Data Mining*, edited by C. Sammut and G. I. Webb (Springer US, Boston, MA, 2017), pp. 895–896.
- [17] K. Cranmer, J. Brehmer, and G. Louppe, The frontier of simulation-based inference, *Proc. Natl. Acad. Sci. USA* **117**, 30055 (2020).
- [18] A. J. Hudspeth, Making an effort to listen: Mechanical amplification in the ear, *Neuron* **59**, 530 (2008).
- [19] P. Martin, D. Bozovic, Y. Choe, and A. J. Hudspeth, Spontaneous oscillation by hair bundles of the bullfrog's sacculus, *J. Neurosci.* **23**, 4533 (2003).
- [20] B. Nadrowski, P. Martin, and F. Jülicher, Active hair-bundle motility harnesses noise to operate near an optimum of mechanosensitivity, *Proc. Natl. Acad. Sci. USA* **101**, 12195 (2004).
- [21] D. Ó Maoiléidigh, E. M. Nicola, and A. J. Hudspeth, The diverse effects of mechanical loading on active hair bundles, *Proc. Natl. Acad. Sci. USA* **109**, 1943 (2012).
- [22] J. M. Marcinik, M. A. Toderi, and D. Bozovic, Comparing parameter-reduction methods on a biophysical model of an auditory hair cell, *Phys. Rev. Res.* **6**, 033121 (2024).
- [23] A. J. Hudspeth, F. Jülicher, and P. Martin, A Critique of the Critical Cochlea: Hopf—a Bifurcation—Is Better Than None, *J. Neurophysiol.* **104**, 1219 (2010).
- [24] J. Faber and D. Bozovic, Chaotic dynamics enhance the sensitivity of inner ear hair cells, *Sci. Rep.* **9**, 18394 (2019).
- [25] A. J. Hudspeth and P. Martin, The critical thing about the ear's sensory hair cells, *J. Neurosci.* **44**, e1583242024 (2024).
- [26] C. Metzler-Winslow, M. A. Toderi, and D. Bozovic, Neural control and innate self-tuning of the hair cell's active process, *Biophys. J.* **123**, 3550 (2024).
- [27] W. Marcotti and S. Masetto, Hair cells, in *eLS* (John Wiley & Sons, Ltd, Chichester, UK, 2010).
- [28] M. S. Smotherman and P. M. Narins, Hair cells, hearing, and hopping: A field guide to hair cell physiology in the frog, *J. Exp. Biol.* **203**, 2237 (2000).
- [29] H. Ohmori, Mechano-electrical transduction currents in isolated vestibular hair cells of the chick, *J. Physiol.* **359**, 189 (1985).
- [30] A. C. Crawford and R. Fettiplace, The mechanical properties of ciliary bundles of turtle cochlear hair cells., *J. Physiol.* **364**, 359 (1985).
- [31] R. Belousov, F. Berger, and A. J. Hudspeth, Volterra-series approach to stochastic nonlinear dynamics: The Duffing oscillator driven by white noise, *Phys. Rev. E* **99**, 042204 (2019).
- [32] R. Belousov, F. Berger, and A. J. Hudspeth, Volterra-series approach to stochastic nonlinear dynamics: Linear response of

- the Van der Pol oscillator driven by white noise, *Phys. Rev. E* **102**, 032209 (2020).
- [33] Y. Thipmaungprom, L. Saliekh, R. Alonso, É. Roldán, F. Berger, and R. Belousov, Active energy harvesting and work transduction by hair-cell bundles in bullfrog's inner ear, [arXiv:2502.14485](#).
- [34] G. Tucci, É. Roldán, A. Gambassi, R. Belousov, F. Berger, R. G. Alonso, and A. J. Hudspeth, Modeling active non-markovian oscillations, *Phys. Rev. Lett.* **129**, 030603 (2022).
- [35] J. Howard and A. J. Hudspeth, Mechanical relaxation of the hair bundle mediates adaptation in mechano-electrical transduction by the bullfrog's saccular hair cell, *Proc. Natl. Acad. Sci. USA* **84**, 3064 (1987).
- [36] M. E. Benser, R. E. Marquis, and A. J. Hudspeth, Rapid, active hair bundle movements in hair cells from the bullfrog's sacculus, *J. Neurosci.* **16**, 5629 (1996).
- [37] D. Vaido, M. A. Toderi, and D. Bozovic, On spontaneous oscillations of hair bundles in the amphibian papilla, *Hear. Res.* **460**, 109238 (2025).
- [38] A. J. Hudspeth, Integrating the active process of hair cells with cochlear function, *Nat. Rev. Neurosci.* **15**, 600 (2014).
- [39] R. A. Eatock, D. P. Corey, and A. J. Hudspeth, Adaptation of mechano-electrical transduction in hair cells of the bullfrog's sacculus, *J. Neurosci.* **7**, 2821 (1987).
- [40] J. Howard, W. M. Roberts, and A. J. Hudspeth, Mechano-electrical transduction by hair cells, *Annu. Rev. Biophys. Biophys. Chem.* **17**, 99 (1988).
- [41] R. G. Walker, A. J. Hudspeth, and P. G. Gillespie, Calmodulin and calmodulin-binding proteins in hair bundles, *Proc. Natl. Acad. Sci. USA* **90**, 2807 (1993).
- [42] R. G. Walker and A. J. Hudspeth, Calmodulin controls adaptation of mechano-electrical transduction by hair cells of the bullfrog's sacculus, *Proc. Natl. Acad. Sci. USA* **93**, 2203 (1996).
- [43] J. L. Cyr, R. A. Dumont, and P. G. Gillespie, Myosin-1c Interacts with Hair-Cell Receptors through Its Calmodulin-Binding IQ domains, *J. Neurosci.* **22**, 2487 (2002).
- [44] J. R. Holt, S. K. H. Gillespie, D. William, K. Shah, K. M. Shokat, D. P. Corey, J. A. Mercer, and P. G. Gillespie, A chemical-genetic strategy implicates myosin-1c in adaptation by hair cells, *Cell* **108**, 371 (2002).
- [45] P. G. Gillespie and J. L. Cyr, Myosin-1c, the hair cell's adaptation motor, *Annu. Rev. Physiol.* **66**, 521 (2004).
- [46] N. Hacohen, J. A. Assad, W. J. Smith, and D. P. Corey, Regulation of tension on hair-cell transduction channels: Displacement and calcium dependence, *J. Neurosci.* **9**, 3988 (1989).
- [47] J. A. Assad, G. M. Shepherd, and D. P. Corey, Tip-link integrity and mechanical transduction in vertebrate hair cells, *Neuron* **7**, 985 (1991).
- [48] P. Martin, A. D. Mehta, and A. J. Hudspeth, Negative hair-bundle stiffness betrays a mechanism for mechanical amplification by the hair cell, *Proc. Natl. Acad. Sci. USA* **97**, 12026 (2000).
- [49] T. Gowers, *The Princeton companion to mathematics*, in *Mathematical Concepts*, edited by J. Barrow-Green and I. Leader (Princeton University Press, Princeton, 2010), pp. 157–314.
- [50] Y. Polyanskiy and Y. Wu, *Information Theory: From Coding to Learning* (Cambridge University Press, Cambridge, 2022), 1st ed.
- [51] A. B. Tsybakov and V. Zaiats, *Introduction to Nonparametric Estimation*, Springer Series in Statistics (Springer, New York, 2009), English ed.
- [52] D. E. Vakman and L. A. Vaĩnshteĩn, Amplitude, phase, frequency—Fundamental concepts of oscillation theory, *Sov. Phys. Usp.* **20**, 1002 (1977).
- [53] J. Justice, Analytic signal processing in music computation, *IEEE Trans. Acoust., Speech, Signal Process.* **27**, 670 (1979).
- [54] D. Vakman, On the analytic signal, the Teager-Kaiser energy algorithm, and other methods for defining amplitude and frequency, *IEEE Trans. Signal Process.* **44**, 791 (1996).
- [55] M. Feldman, Hilbert transform in vibration analysis, *Mech. Syst. Sig. Process.* **25**, 735 (2011).
- [56] J. D. Salvi, D. Ó Maoiléidigh, and A. J. Hudspeth, Identification of Bifurcations from Observations of Noisy Biological Oscillators, *Biophys. J.* **111**, 798 (2016).
- [57] S. Kay and R. Sudhaker, A zero crossing-based spectrum analyzer, *IEEE Trans. Acoust., Speech, Signal Process.* **34**, 96 (1986).
- [58] S.-Z. Hsue and S. S. Soliman, Automatic modulation classification using zero crossing, *IEE Proc. F Radar Signal Process.* **UK 137**, 459 (1990).
- [59] S. C. Sekhar and T. V. Sreenivas, Adaptive Window Zero-Crossing-Based Instantaneous Frequency Estimation, *EURASIP J. Adv. Signal Process.* **2004**, 249858 (2004).
- [60] D. Ramunno-Johnson, C. E. Strimbu, L. Fredrickson, K. Arisaka, and D. Bozovic, Distribution of frequencies of spontaneous oscillations in hair cells of the bullfrog sacculus, *Biophys. J.* **96**, 1159 (2009).
- [61] D. Parr and J. M. Thompson, Solving the multi-objective nurse scheduling problem with a weighted cost function, *Ann. Oper. Res.* **155**, 279 (2007).
- [62] K. Veerkamp, N. F. J. Waterval, T. Geijtenbeek, C. P. Carty, D. G. Lloyd, J. Harlaar, and M. M. van der Krogt, Evaluating cost function criteria in predicting healthy gait, *J. Biomech.* **123**, 110530 (2021).
- [63] M. D. Adler, Benefit–Cost Analysis and Distributional Weights: An Overview, *Rev. Environ. Econ. Policy* **10**, 264 (2016).
- [64] J. Miettinen, M. Ollikainen, M. Nieminen, and L. Valsta, Cost function approach to water protection in forestry, *Water Resour. Econ.* **31**, 100150 (2020).
- [65] U.-E.-H. Alvi, W. Ahmed, K.-S. Hong, M. Rehan, and S. Ahmed, Optimality condition and distributed optimization for economic dispatch using a novel weighted incremental cost consensus approach, *Front. Energy Res.* **10**, 722256 (2022).
- [66] Z. Wu and Y. Tian, Weighted-loss-function control charts, *Int. J. Adv. Manuf. Technol.* **31**, 107 (2006).
- [67] Y. Ho and S. Wookey, The real-world-weight cross-entropy loss function: Modeling the costs of mislabeling, *IEEE Access* **8**, 4806 (2020).
- [68] K. Báńdy and P. Stumpf, Dynamic weighting factor assignment method for the predictive control of electrical drives, *IET Power Electron.* **17**, 2083 (2024).
- [69] R. Storn and K. Price, Differential evolution—A simple and efficient heuristic for global optimization over continuous spaces, *J. Global Optim.* **11**, 341 (1997).

- [70] K. V. Price, R. M. Storn, and J. A. Lampinen, *Differential Evolution*, Natural Computing Series (Springer, Berlin, 2005).
- [71] C. Oguz, T. Laomettachit, K. C. Chen, L. T. Watson, W. T. Baumann, and J. J. Tyson, Optimization and model reduction in the high dimensional parameter space of a budding yeast cell cycle model, *BMC Syst. Biol.* **7**, 53 (2013).
- [72] I. De Falco, A. Della Cioppa, U. Scafuri, and E. Tarantino, Differential evolution to estimate the parameters of a SEIAR model with dynamic social distancing: The case of COVID-19 in Italy, in *Data Science for COVID-19*, edited by U. Kose, D. Gupta, V. H. C. de Albuquerque, and A. Khanna (Academic Press, London, UK, 2021), Chap. 5, pp. 75–90.
- [73] R. Heller, N. Klingner, N. Claessens, C. Merckling, and J. Meersschaut, Differential evolution optimization of Rutherford backscattering spectra, *J. Appl. Phys.* **132**, 165302 (2022).
- [74] S. Yuan, Y. Ji, Y. Chen, X. Liu, and W. Zhang, An Improved Differential Evolution for Parameter Identification of Photovoltaic Models, *Sustainability* **15**, 13916 (2023).
- [75] M. Aljaidi, S. P. Agrawal, P. Jangir, S. B. Pandya, A. Parmar, Arpita, A. F. Alkoradees, B. I. Trivedi, and M. Khishe, A two stage differential evolution algorithm for parameter estimation of proton exchange membrane fuel cell, *Sci. Rep.* **15**, 5354 (2025).
- [76] Y. Roongthumskul, L. Fredrickson-Hemsing, A. Kao, and D. Bozovic, Multiple-timescale dynamics underlying spontaneous oscillations of saccular hair bundles, *Biophys. J.* **101**, 603 (2011).
- [77] R. Shlomovitz, L. Fredrickson-Hemsing, A. Kao, S. W. Meenderink, R. Bruinsma, and D. Bozovic, Low frequency entrainment of oscillatory bursts in hair cells, *Biophys. J.* **104**, 1661 (2013).
- [78] S. W. Meenderink, P. M. Quiñones, and D. Bozovic, Voltage-mediated control of spontaneous bundle oscillations in saccular hair cells, *J. Neurosci.* **35**, 14457 (2015).
- [79] M. A. Rutherford and W. M. Roberts, Spikes and membrane potential oscillations in hair cells generate periodic afferent activity in the frog sacculus, *J. Neurosci.* **29**, 10025 (2009).
- [80] R. Shlomovitz, Y. Roongthumskul, S. Ji, D. Bozovic, and R. Bruinsma, Phase-locked spiking of inner ear hair cells and the driven noisy Adler equation, *Interface Focus* **4**, 20140022 (2014).
- [81] S. Tymochko, E. Munch, J. Dunion, K. Corbosiero, and R. Torn, Using persistent homology to quantify a diurnal cycle in hurricanes, *Pattern Recognit. Lett.* **133**, 137 (2020).
- [82] C. M. Topaz, L. Ziegelmeier, and T. Halverson, Topological data analysis of biological aggregation models, *PLoS One* **10**, e0126383 (2015).
- [83] M. Ulmer, L. Ziegelmeier, and C. M. Topaz, A topological approach to selecting models of biological experiments, *PLoS One* **14**, e0213679 (2019).
- [84] İ. Güzel, E. Munch, and F. A. Khasawneh, Detecting bifurcations in dynamical systems with CROCKER plots, *Chaos* **32**, 093111 (2022).
- [85] F. Takens, Detecting strange attractors in turbulence, in *Dynamical Systems and Turbulence, Warwick 1980*, edited by D. Rand and L.-S. Young (Springer, Berlin, 1981), pp. 366–381.
- [86] J. P. Eckmann and D. Ruelle, Ergodic theory of chaos and strange attractors, *Rev. Mod. Phys.* **57**, 617 (1985).
- [87] A. D. Myers, M. M. Chumley, and F. A. Khasawneh, Delay parameter selection in permutation entropy using topological data analysis, *La Matematica* **3**, 1103 (2024).
- [88] <https://github.com/jmarcinik3/Stochastic-Oscillation-Fitter>.
- [89] T. Holton and A. J. Hudspeth, The transduction channel of hair cells from the bull-frog characterized by noise analysis, *J. Physiol.* **375**, 195 (1986).
- [90] S. Ji, D. Bozovic, and R. Bruinsma, Amphibian sacculus and the forced Kuramoto model with intrinsic noise and frequency dispersion, *Phys. Rev. E* **97**, 042411 (2018).
- [91] W. Denk and W. W. Webb, Forward and reverse transduction at the limit of sensitivity studied by correlating electrical and mechanical fluctuations in frog saccular hair cells, *Hear. Res.* **60**, 89 (1992).
- [92] J. Barral, F. Jülicher, and P. Martin, Friction from transduction channels' gating affects spontaneous hair-bundle oscillations, *Biophys. J.* **114**, 425 (2018).
- [93] V. Balakrishnan, *Elements of Nonequilibrium Statistical Mechanics* (Springer International Publishing, Cham, 2021).
- [94] S. M. van Netten, T. Dinklo, W. Marcotti, and C. J. Kros, Channel gating forces govern accuracy of mechano-electrical transduction in hair cells, *Proc. Natl. Acad. Sci. USA* **100**, 15510 (2003).
- [95] L. Han and A. B. Neiman, Spontaneous oscillations, signal amplification, and synchronization in a model of active hair bundle mechanics, *Phys. Rev. E* **81**, 041913 (2010).
- [96] G. Maruyama, Continuous Markov processes and stochastic equations, *Rend. Circ. Mat. Palermo* **4**, 48 (1955).
- [97] S. Särkkä and A. Solin, *Applied Stochastic Differential Equations* (Cambridge University Press, Cambridge, 2019), 1st ed.
- [98] S.-H. Cha, Comprehensive Survey on Distance/Similarity Measures between Probability Density Functions International J. Mathe. Models Methods Appl. Sci. **1**, 300 (2007).
- [99] I. Sason and S. Verdú, F-divergence inequalities, *IEEE Trans. Inf. Theory* **62**, 5973 (2016).
- [100] C. Ericson, Axis-aligned Bounding Boxes (AABBs), in *Real-Time Collision Detection* (CRC Press, Boca Raton, FL, 2004), pp. 75–124.
- [101] Y. Fu, M. Li, X. Zhang, S. Zhang, C. Wei, W. Guo, H. Cai, L. Sun, P. Wang, and F. Zha, Spatial topological relation analysis for cluttered scenes, *Sensors (Basel)* **20**, 7181 (2020).
- [102] Y. Qiao and N. Minematsu, F-divergence is a generalized invariant measure between distributions, in *Interspeech 2008* (ISCA, Brisbane, Australia, 2008), pp. 1349–1352.
- [103] F. Nielsen, On the jensen–shannon symmetrization of distances relying on abstract means, *Entropy* **21**, 485 (2019).
- [104] E. B. Page, Ordered hypotheses for multiple treatments: A significance test for linear ranks, *J. Am. Stat. Assoc.* **58**, 216 (1963).
- [105] A. P. Piotrowski, Review of differential evolution population size, *Swarm Evol. Comput.* **32**, 1 (2017).
- [106] M. Renardy, L. R. Joslyn, J. A. Millar, and D. E. Kirschner, To Sobol or not to Sobol? The effects of sampling schemes in systems biology applications, *Math. Biosci.* **337**, 108593 (2021).

- [107] J. Qiang and C. Mitchell, A unified differential evolution algorithm for global optimization, *IEEE Trans. Evol. Comput.* (2014), <https://www.osti.gov/biblio/1163659>
- [108] M. S. Bartlett, Periodogram analysis and continuous spectra, *Biometrika* **37**, 1 (1950).
- [109] P. Welch, The use of fast Fourier transform for the estimation of power spectra: A method based on time averaging over short, modified periodograms, *IEEE Trans. Audio Electroacoust.* **15**, 70 (1967).
- [110] S. L. Hahn and K. M. Snopek, *Complex and Hypercomplex Analytic Signals: Theory and Applications*, Artech House Signal Processing Library (Artech House, Boston, MA; London, UK, 2017).
- [111] S. Chang, B. Yu, and M. Vetterli, Adaptive wavelet thresholding for image denoising and compression, *IEEE Trans. Image Process.* **9**, 1532 (2000).
- [112] D. L. Donoho and I. M. Johnstone, Ideal spatial adaptation by wavelet shrinkage, *Biometrika* **81**, 425 (1994).
- [113] S. Arfaoui, A. B. Mabrouk, and C. Cattani, *Wavelet Analysis: Basic Concepts and Applications* (CRC Press, Boca Raton, FL, 2021), 1st ed.
- [114] S. Tanweer, F. A. Khasawneh, and E. Munch, Robust crossings detection in noisy signals using topological signal processing, *FoDS* **6**, 154 (2024).
- [115] C. R. Harris, *et al.*, Array programming with NumPy, *Nature (London)* **585**, 357 (2020).
- [116] P. Virtanen, *et al.*, SciPy 1.0: Fundamental algorithms for scientific computing in Python, *Nat. Methods* **17**, 261 (2020).
- [117] M. J. Aburn, Critical fluctuations and coupling of stochastic neural mass models, Ph.D. thesis, The University of Queensland, 2017.
- [118] S. van der Walt, J. L. Schönberger, J. Nunez-Iglesias, F. Boulogne, J. D. Warner, N. Yager, E. Gouillart, and T. Yu, Scikit-image: Image processing in Python, *PeerJ* **2**, e453 (2014).
- [119] J. D. Hunter, Matplotlib: A 2D Graphics Environment, *Comput. Sci. Eng.* **9**, 90 (2007).
- [120] W. McKinney, Data structures for statistical computing in python, in *Proceedings of the 9th Python in Science Conference*, edited by S. van der Walt and J. Millman (SciPy, Austin, 2010), Vol. 445, pp. 56–61.