Arrow of Time in Active Fluctuations

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We introduce lower bounds for the rate of entropy production of an active stochastic process by quantifying the irreversibility of stochastic traces obtained from mesoscopic degrees of freedom. Our measures of irreversibility reveal signatures of time’s arrow and provide bounds for entropy production even in the case of active fluctuations that have no drift. We apply these irreversibility measures to experimental spontaneous hair-bundle oscillations from the ear of the bullfrog.

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Active systems are maintained out of equilibrium by processes that consume resources of energy and produce entropy. This is the case of living cells, where energy is provided in the form of biochemical fuel such as adenosine triphosphate that drives active mesoscopic cellular processes. A well studied example of active cellular fluctuations are spontaneous oscillations of mechanosensory hair bundles of auditory hair cells [1, 2]. These oscillations have been proposed to amplify sound stimuli in the ear of many vertebrates, providing exquisite sensitivity and sharp frequency selectivity [3].

Active mesoscopic processes do not obey the fluctuation-dissipation theorem: measuring both the linear response of the system to weak external stimuli and spontaneous fluctuations provides a means to quantify deviations from thermal equilibrium [4–9]. A related important question is how entropy production can be estimated in active mesoscopic systems. In cases where active systems generate movement with drift, such as molecular motors moving along filaments [10–12], the rate of entropy production can be estimated from measurements of drift velocities and viscous forces [10, 13]. However, for active fluctuations without drift, such as spontaneous oscillations, it is unclear how entropy production can be characterized. Time irreversibility is a signature of the nonequilibrium nature of a system [14]. This suggests that quantification of irreversibility of fluctuations provides information about entropy production.

In this Letter, we introduce a hierarchy of bounds for the steady-state rate of entropy production based on measures of irreversibility of sets of mesoscopic observables. We show that quantifying irreversibility can reveal whether a noisy signal is produced by an active process or by a passive system. We apply the theory to experimental recordings of spontaneous mechanical oscillations of mechanosensory hair bundles in an excised preparation from the ear of the bullfrog (Rana catesbeiana) [15]. Our measures of irreversibility provide lower bounds for entropy production of active processes, as we demonstrate using a biophysical model for hair-bundle oscillations and experimental data.

We first discuss the relation between entropy production and irreversibility for generic nonequilibrium stationary processes. Consider a physical system described by a set of variables labeled as \( X_\alpha \), with \( \alpha = 1, 2, \ldots \). In a stationary nonequilibrium process of time duration \( t \), the physical system traces a trajectory in the phase space described by the stochastic processes \( X_\alpha(t) \). We denote by \( \Gamma_{[0,t]} = \{(x_1(s), x_2(s), \ldots)\}_{s=0}^t \) a given trajectory described by the system variables and its corresponding time-reversed trajectory as \( \tilde{\Gamma}_{[0,t]} = \{(\theta_1 x_1(t-s), \theta_2 x_2(t-s), \ldots)\}_{s=0}^t \), where \( \theta_\alpha = \pm 1 \) is the time-reversal signature of the \( \alpha \)-th variable. Assume now that \( X_\alpha \) are the variables that may be out of equilibrium, i.e. we do not include in \( \Gamma_{[0,t]} \) those variables corresponding to thermal reservoirs, chemostats, etc. In that case, the steady-state rate of entropy production \( \sigma_{tot} \) is given by

\[
\sigma_{tot} = k_B \lim_{t \to \infty} \frac{1}{t} D \left[ P(\Gamma_{[0,t]}^0) \right] \left|\left| P(\tilde{\Gamma}_{[0,t]}^0) \right|\right], \tag{1}
\]

where \( k_B \) is the Boltzmann constant and \( P \) denotes the steady-state path probability [16–19]. Here \( D[Q||R] \geq 0 \) is the Kullback-Leibler (KL) divergence between the probability measures \( Q \) and \( R \), which quantifies the distinguishability between these two distributions. For measures of a single random variable \( x \) the KL divergence is given by \( D[Q(x)||R(x)] \equiv \int dx \ln[Q(x)/R(x)] \). Note that for isothermal systems \( \sigma_{tot}T \) equals to the rate of heat dissipated to the environment at temperature \( T \).

Often in experiments only one or several of the nonequilibrium variables can be tracked in time. Consider the case where only \( X_1, \ldots X_k \) are known. We define the \( k \)-variable rate of entropy production in terms of path probabilities of \( k \) mesoscopic variables

\[
\sigma_k = k_B \lim_{t \to \infty} \frac{1}{t} D \left[ P(\Gamma_{[0,t]}^{(k)}) \right] \left|\left| P(\tilde{\Gamma}_{[0,t]}^{(k)}) \right|\right], \tag{2}
\]
production increases with the number of tracked degrees of freedom $0 \leq \sigma_1 \leq \cdots \leq \sigma_k \leq \sigma_{k+1} \leq \cdots \leq \sigma_{tot}$. It can also be shown that the estimator $\sigma_k$ equals the physical entropy production $\sigma_{tot}$ if the missing variables, $X_\ell$ with $\ell > k$, are at thermal equilibrium [20–22]. When the missing variables are not at thermal equilibrium, which is often the case in active systems, the estimator $\sigma_k \leq \sigma_{tot}$ yields only a lower bound for the entropy production rate.

We now discuss irreversibility and entropy production in active mechanosensory hair cells from the bullfrog’s ear. Hair cells work as cellular microphones that transduce mechanical vibrations evoked by sound into electrical signals [23]. They are endowed with a tuft of cylindrical protrusions—the hair bundle (Fig. 1A)—that serves both as sensory antenna and as active oscillator that amplifies sound [3]. In experimental recordings of spontaneous hair-bundle oscillations, only the position of the bundle’s tip $X_1$ is measured (Fig. 1B). Measuring $X_1$, we can only estimate $\sigma_1$, which provides a lower bound to the total steady-state entropy production rate $\sigma_{tot}$.

Spontaneous hair-bundle oscillations are thought to result from an interplay between opening and closing of mechanosensitive ion channels, activity of molecular motors that pull on the channels, and fast calcium feedback. This interplay can be described by two coupled stochastic differential equations for the position of the bundle $X_1$ and of the motors $X_2$ [2, 15, 24]:

$$\begin{align*}
\lambda_1 \dot{X}_1 &= -\frac{\partial V}{\partial X_1} + \sqrt{2k_B T \lambda_1} \xi_1 \\
\lambda_2 \dot{X}_2 &= -\frac{\partial V}{\partial X_2} - F_{act} + \sqrt{2k_B T_{eff} \lambda_2} \xi_2 ,
\end{align*}$$

where $\lambda_1$ and $\lambda_2$ are friction coefficients and $\xi_1$ and $\xi_2$ in (3-4) are two independent Gaussian white noises with zero mean ($\langle \xi_i(t) \rangle = 0$ $(i = 1, 2)$ and correlation $\langle \xi_i(t) \xi_j(t') \rangle = \delta_{ij} \delta(t-t')$, with $i, j = 1, 2$ and $\delta_{ij}$ the Kronecker’s delta. $T$ is the temperature of the environment, whereas the parameter $T_{eff} > T$ is an effective temperature that characterizes fluctuations of the motors. The conservative forces derive from the potential associated with elastic elements and mechano-sensitive ion channels

$$
V(X_1, X_2) = \frac{k_{gs} \Delta X^2 + k_{ap} X_1^2}{2} + Nk_B T \ln \left[ \exp \left( \frac{k_{gs} D \Delta X}{Nk_B T} \right) + A \right] ,
$$

where $\Delta X = X_1 - X_2$: $k_{gs}$ and $k_{ap}$ are stiffness coefficients; $D$ is the gating swing of a transduction channel; and $A = \exp[(\Delta G + (k_{gs} D^2)/2N)/(k_B T)]$, $\Delta G$ being the energy difference between open and closed states of the channels and $N$ the number of transduction elements. The force $F_{act}(X_1, X_2) = F_{max}(1 - SP_o(X_1, X_2))$ is an active nonconservative force exerted by the molecular motors with a maximum value $F_{max}$. The parameter $S$ quantifies calcium-mediated feedback on the motor force [25] and $P_o(X_1, X_2) = 1/[1 + A \exp(-k_{gs} D \Delta X / N k_B T)]$ is the open probability of the transduction channels. With this model, we can capture key features of noisy spontaneous oscillations of hair-bundle position $X_1$ that have been observed experimentally (Fig. 1C and D). The oscillation of the motors’ position (Fig. 1D) is known in the model but hidden in experiments. Trajectories of only $X_1(t)$ or $X_2(t)$ do not reveal obvious signs of a net current, which here would correspond to a drift. However, trajectories in the $(X_1, X_2)$ plane show a net current which is a signature of entropy production (Fig. 1E). In the following, we will use this stochastic model to compare the irreversibility measure $\sigma_1$ to the total entropy production $\sigma_{tot}$.

In the stochastic model of hair-bundle oscillations given by Eqs. (3-4) we deal with only two variables, therefore $\sigma_{tot} = \sigma_2$. From the analytical expression of $\sigma_2$, we find that the steady-state entropy production rate can be written as [26, 27]

$$\sigma_{tot} = -\langle \dot{Q}_1 \rangle \left( \frac{1}{T} - \frac{1}{T_{eff}} \right) + \frac{\langle W_{act} \rangle}{T_{eff}} ,$$

where $\langle \cdot \rangle$ denotes time average.

FIG. 1: (A) Electron micrograph of a hair-cell bundle extracted from the bullfrog’s inner ear. The distance from top to bottom is $\sim 7 \mu$m. (B) Experimental recording of the position of the tip of an active mechanosensory hair bundle. (C, D) Trajectories of the reduced variables $X_1$ (C) and $X_2$ (D) as a function of time obtained from a simulation of the stochastic model given by Eqs. (3-4). (E) Representation of a 2-s trace of the simulations in (C, D) in the $(X_1(t), X_2(t))$ plane. The black arrows illustrate the value of the instantaneous velocity and the base of the arrow the position. Parameters of the simulations: $\lambda_1 = 0.9 \text{pNms/} \mu \text{m}, \lambda_2 = 5 \text{pNms/} \mu \text{m}, k_{gs} = 0.55 \text{pN/} \mu \text{m}, k_{ap} = 0.3 \text{pN/} \mu \text{m}, D = 72 \text{nm}, S = 0.73, F_{max} = 45.76 \text{pN}, N = 50, \Delta G = 10 k_B T, k_B T = 4.143 \text{pNms}$ and $T_{eff}/T = 1.5$. The trajectories of the bundle in the $\{X_1(t), X_2(t)\}$ plane show a net current which is a signature of entropy production.
where $\langle \dot{Q} \rangle = -\langle \partial V / \partial X_i \circ \dot{X}_i \rangle$ is the steady-state average heat dissipated to the thermal bath at temperature $T$ and $(W_{\text{act}}) = -\langle F_{\text{act}} \circ \dot{X}_2 \rangle$ is the power exerted by the active force on the motors. Here $\langle \cdot \rangle$ denote steady state averages and $\circ$ the Stratonovich product [28, 29]. Equation (6) reveals two sources of nonequilibrium in the model: the difference of effective product $[28, 29]$. Equation (6) reveals two sources of nonequilibrium in the model: the difference of effective product $[28, 29].

We now introduce a new method to estimate the irreversibility measure $\sigma_1$ for any nonequilibrium steady state from a single stationary time series $x_i = X(i \Delta t)$ with $i = 1, \ldots, n$. We describe the technique for a single variable, but it can be generalized to several variables $X_n(t)$. In discrete processes, the KL divergence in $\sigma_1$ can be accurately measured from the statistics of sequences [30, 31]. In continuous processes however, estimating $\sigma_1$ is a herculean task due to the difficulties in sampling the whole phase space of paths [32–34].

The key idea of our method is to exploit the invariance of the KL divergence under one-to-one transformations. Suppose that there exists a one-to-one map $\xi_i(x_1, \ldots, x_n)$, that transforms the original time series and its time reversal into two new time series $\xi^F_i = \xi_i(x_1, \ldots, x_n)$ and $\xi^R_i = \xi_i(x_n, \ldots, x_1)$ that are independent and identically distributed (i.i.d.) processes. Such a procedure is often called a whitening filter [35, 36]. Because the new series are i.i.d., the KL divergence is now simple to calculate: it is given by the KL divergence between two univariate distributions $p(\xi)$ and $q(\xi)$, corresponding to the stationary probability distribution of $\xi^F_i$ and $\xi^R_i$, respectively [34]. In general, it is not possible to find a one-to-one map that fully eliminates the correlations of both the forward ($x_1, \ldots, x_n$) and the backward ($x_n, \ldots, x_1$) time series. In that case, the removal of the correlations in the backward series is enough to provide a lower bound for $\sigma_1$:

$$\sigma_1 \geq k_B f_s D[p(\xi)||q(\xi)] = \tilde{\sigma}_1,$$

where $f_s = (\Delta t)^{-1}$ is the sampling frequency and $D[p(\xi)||q(\xi)] = \int d\xi p(\xi) \ln [p(\xi)/q(\xi)]$ is the KL divergence between the univariate distributions $p(\xi)$ and $q(\xi)$. The proof of this inequality and further details of the method are found in the Supplemental Material [29].

In the following, we make use of autoregressive (AR) models for the whitening transformation. More precisely, we obtain the transformed time series $\xi^F_i$ ($\xi^R_i$) as the difference between the observed values of the forward (backward) time series and the forecast of that value based on an AR model of order $m = 10$. Parameters of the model are determined from fits of the AR-model to the time-reversal series of positions. Note that the estimation of the KL divergence and the validity of the bound (7) do not rely on the ability of the AR model to reproduce the underlying dynamics of the time series or to predict its behavior.

Figure 2 illustrates our estimate of $\sigma_1$ applied to one experimental time series of hair-bundle oscillations, plotted in panel A (top left). The residual time series $\xi^F_i$ and $\xi^R_i$ (Fig. 2A, bottom) obtained from the whitening transformation barely have any time correlation (Fig. 2B) and are therefore i.i.d. processes in good approximation. Although the time series and its time reversed (Fig. 2A, top right) do not look different by eye, the residual distributions $p(\xi)$ and $q(\xi)$ are different with statistical power of 94% (Fig. 2C). Quantifying their difference by means of the KL divergence yields, using Eq. (7), a measure of irreversibility of $\tilde{\sigma}_1 = (4.3 \pm 0.5)k_B / s$ for this example. Since $\sigma_{\text{tot}}$ is not determined by $\tilde{\sigma}_1$, Eq. (7) implies that our irreversibility measure $\tilde{\sigma}_1$ provides for this case the bound $\sigma_{\text{tot}} \geq (4.3 \pm 0.5)k_B / s$ for the rate of entropy production. This bound corresponds to an entropy production rate of at least $(0.19 \pm 0.2)k_B$ per oscillation cycle [29]. Interestingly, this value corresponds to a rate of heat dissipation that is below, here by two orders of magnitude, the estimated mean power output per hair cell $\sim 10k_B T /$ cycle found for spontaneous emissions of sound by the ears of lizards [37].
We apply our method to quantify irreversibility in active oscillatory hair bundles (Fig. 3A, top), in quiescent hair bundles exposed to a drug (gentamicin) that blocks the transduction channels (Fig. 3A, magenta and green) and for noisy signals produced by the recording apparatus when there is no hair bundle under the objective of the microscope (Fig. 3A, black). The finite-size scaling of the irreversibility measure $\hat{\sigma}_1$ with respect to the duration of the recording allows to discriminate between active and passive oscillations (Fig. 3B): At sufficiently long times, $\hat{\sigma}_1$ saturates to a positive value for active oscillations whereas it goes to zero for cells exposed to gentamicin and for experimental noise (Fig. 3B inset). Using a population of 182 hair cells that showed spontaneous hairbundle oscillations [15], we obtained a probability density of $\hat{\sigma}_1$ that was well described by an exponential distribution with mean $3 \text{k}_B/\text{s}$ (Fig. 3C). Notably, we find that for 83 cells (46%) of the oscillatory hair bundles, the distributions $p(\xi)$ and $q(\xi)$ are distinguishable with statistical power of at least 80%, with the average irreversibility of this subpopulation of cells being $(6.0 \pm 0.4) \text{k}_B/\text{s}$ [29]. This result depends on the sampling frequency $f_s$; we find an optimum range $f_s \sim (200 - 500) \text{Hz}$ at which nearly 80% of the oscillations are found to be time irreversible by our method and show a higher mean value of $\hat{\sigma}_1$ than at $f_s = 2.5 \text{kHz}$. This variation may provide additional information about timescales of the underlying active process [29].

Finally, we relate these estimates of entropy production to results obtained for a stochastic model of hairbundle oscillations. We performed numerical simulations of Eqs. (3-4) for different values of the control parameters $F_{\text{max}}$ and $S$ (Fig. 4) to explore entropy production throughout the state diagram of the system. The quality factor of the oscillation $Q$—given by the ratio between the oscillation frequency and the bandwidth at half the maximal height of the power spectrum—and the average open probability $\langle P_o \rangle$ at steady state are displayed in Fig. 4A-B in the state diagram. The irreversibility measure $\hat{\sigma}_1$ for trajectories $X_i(t)$ of spontaneous oscillations is shown in Fig. 4C. This measure can be com-

FIG. 3: (A) Examples of experimental traces for the tip position of different mechanosensory hair bundles as a function of time. Top: active hair bundles. Bottom: passive hair bundles when the channel blocker gentamicin is present (magenta, green) and experimental noise trace (black). (B) Irreversibility measure $\hat{\sigma}_1$ (symbols) as a function of the observation time obtained from the experimental traces partially shown in A). The solid lines are fits to $A + B \exp(-t/\tau)$ and the inset shows the plot in semilogarithmic scale. (C) Histogram of the irreversibility measure $\hat{\sigma}_1$ obtained from 182 experimental recordings of spontaneous active oscillations of the hair bundle of duration $t_{\text{exp}} = 30 \text{s}$. The experimental average value of the irreversibility measure $\bar{\hat{\sigma}}_1$ is $\sim 3 \text{k}_B/\text{s}$. Inset: Empirical cumulative distribution function (CDF) of irreversibility (black circles). The red line is a fit to an exponential distribution with mean value $(2.82 \pm 0.02) \text{k}_B/\text{s}$ and $R^2 = 0.9990$.

FIG. 4: Dynamical and thermodynamic features of hairbundle spontaneous oscillations as a function the Calcium feedback strength $S$ and maximal motor force $F_{\text{max}}$ obtained from numerical simulations of the model given by Eqs. (3-4): (A) Quality factor $Q$; (B) Steady-state average of the open channel probability $\langle P_o \rangle$; (C) Irreversibility measure $\hat{\sigma}_1$; (D) Steady-state entropy production rate $\sigma_{\text{tot}}$. In (B,C,D) we indicate the parameter values for which $\langle P_o \rangle = 0.1, 0.5$ and 0.9 (white dashed lines). The results are obtained from numerical simulations of Eqs. (3-4) of total duration $t_{\text{sim}} = 300 \text{s}$, sampling frequency $f_s = 1 \text{kHz}$ and parameter values $\lambda_1 = 2.8 \text{pNms}/\text{nm}$, $\lambda_2 = 10 \text{pNms}/\text{nm}$, $k_{sp} = 0.75 \text{pN}/\text{nm}$, $k_{sp} = 0.6 \text{pN}/\text{nm}$, $D = 61 \text{nm}$, $N = 50$, $\Delta G = 10 \text{k}_B T$, $k_B T = 4 \text{pNms}$ and $T_{\text{eff}}/T = 1.5$. 

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pared to the quantification of total entropy production \( \sigma_{\text{tot}} \) of the model, given by Eq. (6), which is shown in Fig. 4D. Irreversibility of trajectories and total entropy production correlate strongly. However, as expected, \( \hat{\sigma}_1 \) provides a lower bound: irreversibility is here typically three orders of magnitude smaller than entropy production. Clearly, measuring other degrees of freedom additional to the hair-bundle position would be required to obtain tighter bounds to the rate of entropy production with our method or other estimation techniques [38–42].

In summary, we have shown that fluctuations of active systems can reveal the arrow of time even in the absence of net drifts or currents. The hierarchy of measures of time irreversibility introduced here provides lower bounds for the entropy production of an active process. These irreversibility measures are applicable to quantify contributions to entropy production in active matter, including living systems, from fluctuations of only a few mesoscopic degrees of freedom.

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SUPPLEMENTAL MATERIAL

Here we present additional details of the methods and results discussed in the Main Text. In Secs. S1 and S2, we provide a derivation of the bound used in Eq. (7) in the Main Text, and describe the whitening transformation that we use to estimate irreversibility of stochastic time traces. In Sec. S3, we provide further details on the experimental results and error analysis for the data shown in Fig. 2 in the Main Text. In Sec. S4, we provide further details on the experimental results reported in Fig. 3 in the Main Text. In Sec. S5, we analyze how our irreversibility measure depends on the data sampling rate of the experimental recordings of hair-bundle spontaneous fluctuations. In Sec. S6, we discuss how entropy production is estimated in numerical simulations of the hair-bundle biophysical model. Section S7 provides details on the calculation of the quality factor of spontaneous oscillations shown in Fig. 4A in the Main Text. In Sec. S8, we discuss the biophysical model of hair-bundle oscillations and the experimental techniques.

S1. BOUNDS ON THE MULTIVARIATE KULLBACK-LEIBLER DIVERGENCE

Here we prove a general lower bound for the Kullback-Leibler (KL) divergence between two multivariate probability densities $P_X(x_1,\ldots,x_n)$ and $Q_X(x_1,\ldots,x_n)$ that fulfill the following: there exits a one-to-one map $\xi_i = \xi_i(x_1,\ldots,x_n)$ with $i = 1,\ldots,n$, such that

1. the transformed variables $\xi_i$ are identically distributed under both $P$ and $Q$, that is, the distributions $P_\Xi(\xi_1,\ldots,\xi_n)$ and $Q_\Xi(\xi_1,\ldots,\xi_n)$ have, respectively, identical marginal distributions $p(\xi)$ and $q(\xi)$ for any $\xi_i$ ($i = 1,\ldots,n$);

2. the transformed variables $\xi_i$ are independent and identically distributed (i.i.d.) under the distribution $Q$, that is, $Q_\Xi(\xi_1,\ldots,\xi_n) = \Pi_i q(\xi_i)$.

The first step in the derivation is a simple application of the invariance of the KL distance under a one-to-one map:

$$D [P_X(x_1,\ldots,x_n)||Q_X(x_1,\ldots,x_n)] = D [P_\Xi(\xi_1,\ldots,\xi_n)||Q_\Xi(\xi_1,\ldots,\xi_n)] .$$  \hspace{1cm} (S8)

Second, we can rewrite the relative entropy as

$$D [P_\Xi(\xi_1,\ldots,\xi_n)||Q_\Xi(\xi_1,\ldots,\xi_n)] = \int d\xi_1 \cdots \int d\xi_n \frac{P_\Xi(\xi_1,\ldots,\xi_n) \ln \frac{P_\Xi(\xi_1,\ldots,\xi_n)}{\Pi_i q(\xi_i)}}{P_\Xi(\xi_1,\ldots,\xi_n)} = \int d\xi_1 \cdots \int d\xi_n \left[ P_\Xi(\xi_1,\ldots,\xi_n) \ln \frac{\Pi_i p(\xi_i)}{\Pi_i q(\xi_i)} + P_\Xi(\xi_1,\ldots,\xi_n) \ln \frac{P_\Xi(\xi_1,\ldots,\xi_n)}{\Pi_i p(\xi_i)} \right] = nD[p(\xi)||q(\xi)] + D [P_\Xi(\xi_1,\ldots,\xi_n)||\Pi_i p(\xi_i)] .$$  \hspace{1cm} (S9)

Because the KL divergence between two distributions is always positive, Eqs. (S8) and (S9) yield the bound

$$D [P_X(x_1,\ldots,x_n)||Q_X(x_1,\ldots,x_n)] \geq nD[p(\xi)||q(\xi)] ,$$  \hspace{1cm} (S10)

and the inequality saturates if the transformed variables $\xi_i$ ($i = 1 \ldots n$) are also i.i.d. under $P_\Xi(\xi_1,\ldots,\xi_n)$, i.e. when $P_\Xi(\xi_1,\ldots,\xi_n) = \Pi_i p(\xi_i)$. If one can find a one-to-one that transforms the original random variables into i.i.d. variables under both distributions $P$ and $Q$, then (S10) becomes an equality and the exact KL divergence between the two multivariate distributions $P_X$ and $Q_X$ can be reduced to the KL divergence between single variable distributions $p(\xi)$ and $q(\xi)$, which is much easier to evaluate from real data. This is the key idea of our method to estimate the irreversibility of experimental time series.

S2. IRREVERSIBILITY IN CONTINUOUS TIME SERIES: THE WHITENING TRANSFORMATION

The estimation of the KL divergence rate from single stationary trajectories of both discrete and continuous random variables have been previously discussed [34]. For continuous random variables, the most common strategy is to make a symbolization or discretization of the time series [32]. Then, the KL divergence is estimated from the statistics of substrings of increasing length [30, 31]. The main limitation of this method is that one easily reaches lack of statistics even for short substrings. If the observed time series is non-Markovian, this limitation could yield inaccurate
bounds for the entropy production. For instance, the KL divergence between two data substrings can be zero in non-equilibrium stationary states without observable currents [30, 31, 34].

Here we introduce a new method to estimate the KL divergence rate

$$\frac{\sigma_1}{k_B} \equiv \lim_{t \to \infty} \frac{1}{t} D \left[ |P \{ (x(s))_{s=0}^t \} || P \{ (x(t-s))_{s=0}^t \} \right] ,$$

(S11)

that is valid for continuous and possibly non-Markovian stochastic processes $X(t)$. First, in practice one has access to discrete-time observations of the process $x_i \equiv X(i \Delta t)$, $i = 1, \ldots, n$, i.e., a time series containing $n = t/\Delta t$ consecutive samples of the process with sampling rate $f_s = 1/\Delta t$. The time discretization implies a loss of information yielding a lower bound to the KL divergence rate:

$$\frac{\sigma_1}{k_B} \geq f_s \lim_{n \to \infty} \frac{1}{n} D[|P_X(x_1, \ldots, x_n)||Q_X(x_1, \ldots, x_n)] ,$$

(S12)

where $Q_X(x_1, \ldots, x_n) = P_X(x_n, \ldots, x_1)$ is the probability to observe the reverse trajectory $(x_n, \ldots, x_1)$.

We can now apply the inequality (S10) to the right-hand side in Eq. (S12) To do that, it is necessary to find a one-to-one map $\xi_i = \xi_i(x_1, \ldots, x_n)$ that transforms the reverse time series $(x_n, \ldots, x_1)$ into a sequence of $n$ i.i.d. random variables, that is, into a white noise. Such a transformation is usually termed whitening transformation.

An example of whitening transformation is the time series formed by the residuals of an autoregressive model, which is the transformation that we will use along this paper. A discrete-time stochastic process $Y_i$ is called autoregressive of order $m$, AR($m$), when its value at a given time is given by a linear combination of its previous values plus a noise term. Such process is univocally determined by $m \geq 1$ real coefficients, $a_1, a_2, \ldots, a_m$, a discrete-time white noise $\eta_i$ and a set of initial values $Y_1, Y_2, \ldots, Y_m$. The values of $Y_i$ for $i > m$ are given by the linear recursion

$$Y_i = \sum_{j=1}^{m} a_j Y_{i-j} + \eta_i .$$

(S13)

Inspired by the AR($m$) process, we introduce the following one-to-one map

$$\xi_i = \begin{cases} x_i & \text{if } i \leq m \\ x_i - \sum_{j=1}^{m} a_j x_{i-j} & \text{if } i > m \end{cases} ,$$

(S14)

which is a linear transformation defined by a unitriangular matrix with Jacobian equal to one. With an appropriate choice of the coefficients $a_j$, one can get a new process $(\xi_1, \ldots, \xi_n)$ which is approximately i.i.d. A good choice is given by a maximum likelihood fit of the process to the AR($m$) model. In that case, the elements $\xi_i$ in this new time series for $i > m$ are usually called residuals of the original time series $(x_1, \ldots, x_n)$ with respect to the AR($m$) model. Notice also that, if $(x_1, \ldots, x_n)$ is indeed a realization of the stochastic process (S13), then the residuals are i.i.d. random variables and the process $(\xi_{m+1}, \ldots, \xi_n)$ has correlations $\langle \xi_i \xi_j \rangle = \delta_{ij}$ for all $i, j > m$.

We now apply the bound (S10) to the KL divergence in the right hand side of Eq. (S12), using the transformation defined by Eq. (S14). Since the contribution of the first, possibly correlated, $m$ values of the time series $\xi_i$, vanishes in the limit $n \to \infty$, we obtain the following lower bound to the KL divergence rate [Eq. (7) in the Main Text]:

$$\frac{\sigma_1}{k_B} \geq f_s D[p(\xi)||q(\xi)] .$$

(S15)

We can obtain empirical estimates of $p(\xi)$ and $q(\xi)$ from a single stationary time series $(x_1, \ldots, x_n)$ as follows. We apply the transformation (S14) to both the original time series $(x_1, \ldots, x_n)$ and to its time reversal $(x_n, \ldots, x_1)$ obtaining, respectively, two new time series $(\xi_1^R, \ldots, \xi_n^R)$ and $(\xi_1^L, \ldots, \xi_n^L)$, which are stationary at least for $i > m$. The empirical PDFs obtained from the data of each series are estimations of, respectively, $p(\xi)$ and $q(\xi)$. Note that the same transformation (S14) must be applied to both the original time series $(x_1, \ldots, x_n)$ and its time reverse $(x_n, \ldots, x_1)$, but the inequality (S10) only requires uncorrelated residuals in the reverse series. For this purpose, we calculate the coefficients $a_1, \ldots, a_m$ by fitting the reverse time series $(x_n, \ldots, x_1)$ to the AR($m$) model in Eq. (S13).

As indicated in the previous section, the inequality (S15) is tighter when the residuals are uncorrelated in the forward series as well. This is the case of the experimental series that we have analyzed (see, for instance, Fig. 2B in the Main Text) although, in principle, it is not guaranteed by this procedure. We remark that the inequality (S15) is a rigorous result if the transformation (S14) applied to the reverse time series yields an uncorrelated series.
(ξ₁ⁿ, ..., ξᵣⁿ). In that case, \( k_B f_s D[p(ξ)||q(ξ)] \) is an estimate of \( σ_1 \) with only two possible sources of error: i) the discrete sampling of the process \( X(t) \) and ii) the remnant correlation time in the residuals (\( ξ₁ⁿ, ..., ξᵣⁿ \)) obtained from the forward time series.

To summarize, our theory provides an estimate \( \hat{σ}_1 \) for the KL divergence rate \( σ_1 \) which can be evaluated as follows:

1. Estimate the coefficients, \( a_1, ..., a_m \), by fitting the time-reversed series \( (x_n, ..., x_1) \) to an autoregressive AR(\( m \)) model of order \( m > 1 \). A reasonable choice is \( m = 10 \), but it should be tuned to minimize the correlation time in the residuals (\( ξ₁ⁿ, ..., ξᵣⁿ \)).

2. Apply the whitening transformation \( (S14) \) to the original series \( (x_n, ..., x_1) \) and to its time reversal \( (x_n, ..., x_1) \) to obtain, respectively, new time series \( (ξ₁ⁿ, ..., ξᵣⁿ) \) and \( (ξ₁ⁿ, ..., ξᵣⁿ) \). Note that the new processes are not each other’s time reversal.

3. Obtain the empirical distributions \( p(ξ) \) and \( q(ξ) \) from the time series \( (ξ₁ⁿ, ..., ξᵣⁿ) \) and \( (ξ₁ⁿ, ..., ξᵣⁿ) \), respectively.

4. Calculate the KL divergence between \( p(ξ) \) and \( q(ξ) \)

\[
D[p(ξ)||q(ξ)] = \int dξ \frac{p(ξ) \ln p(ξ)}{q(ξ)} ,
\]

(S16)

which can be estimated from numerical integration of the right hand side in (S16) using the empirical normalized histograms \( p(ξ) \) and \( q(ξ) \). We call this estimate \( \hat{D} \), which is given by

\[
\hat{D} = \sum_i \frac{n_i^{F}}{\left(\sum_i n_i^{F}\right)} \ln \frac{n_i^{F}}{n_i^{R}} ,
\]

(S17)

where \( n_i^{F} \) and \( n_i^{R} \) are respectively the number of counts of \( (ξ₁ⁿ, ..., ξᵣⁿ) \) and \( (ξ₁ⁿ, ..., ξᵣⁿ) \) in the \( i \)-th bin. The sum in (S17) runs over all bins for which \( n_i^{F} > 0 \) and \( n_i^{R} > 0 \). For simplicity, we used 100 bins of equal spacing ranging from the minimum to the maximum values of the residual time series \( (ξ₁ⁿ, ..., ξᵣⁿ) \).

5. The value of the estimate \( \hat{D} \) of the KL divergence (S16) is then weighted by the "irreversibility statistical power" \( γ \) defined in terms of the probability to reject the null hypothesis \( p(ξ) = q(ξ) \). We use this procedure to correct the statistical bias in the estimation of the KL divergence that appears when two stochastic processes have similar statistics [31, 43]. For this purpose, we measure the Kolmogorov–Smirnov statistic under the null hypothesis \( H_0 : p(ξ) = q(ξ) \) which yields a significance \( p_{KS} \) for the two distributions to be equal. Here, small \( p_{KS} \) means that there is stronger statistical evidence in favour of the alternative hypothesis \( p(ξ) \neq q(ξ) \), thus \( γ = 1 - p_{KS} \) serves as a weight of irreversibility: \( γ \approx 0 \) when it is hard to reject \( H_0 \) (reversibility) and \( γ \approx 1 \) when it is easy to reject \( H_0 \). Finally, our estimate of \( σ_1 \) is thus given by:

\[
\hat{σ}_1 = k_B f_s γ \hat{D} .
\]

(S18)
S3. DETAILS OF THE EXPERIMENTAL RESULTS IN FIG. 2

In this section, we describe the procedure used to estimate the bound \( \sigma_{\text{tot}} \geq (4.3 \pm 0.5) k_B / s \) for the experimental data shown in Fig. 2 in the Main Text. For different values of the observation time \( t \) ranging from 1.5s to 30s, we slice the time series \( x_1, \ldots, x_n \) into \( N \geq 1 \) non-overlapping time series. We then evaluate the estimate \( \hat{\sigma}_1 \) given by Eq. (S18) for each of the slices following the procedure described in Sec. S2. The value of the irreversibility measure at each time \( t \) shown in Fig. S6 is the average of the estimate \( \hat{\sigma}_1 \) evaluated over the different slices. We estimate the expected value and the error of the irreversibility measure from the errors in the fitting parameter \( A \) (with 95% confidence bounds) obtained from the fit of the data to a time-decreasing function \( \hat{\sigma}_1(t) = A + B \exp(-t/\tau) \), see Fig. S5.

![Graph showing the values of the irreversibility measure \( \hat{\sigma}_1 \) for different time traces of \( t \leq t_{\text{exp}} \) with \( t_{\text{exp}} = 30 \) s, obtained for the experimental recording shown in Fig. 2 and Fig. 3A (red) in the Main Text. The solid line is a fit of the data to a function \( \hat{\sigma}_1(t) = A + B \exp(-t/\tau) \). Parameters of the fit (with 95% confidence bounds): \( A = (4.3 \pm 0.5) k_B / s \), \( B = (16 \pm 7) k_B / s \), \( \tau = (2 \pm 1) s \). Goodness of fit \( R^2 = 0.87 \).]

S4. DETAILS OF THE EXPERIMENTAL RESULTS IN FIG. 3

In this section, we provide further details of the experimental results shown in Fig. 3 in the Main Text and additional information on the error and statistical significance analysis of these results.

The results in Fig. 3B of the Main text were obtained as follows. For different values of \( t \) ranging from \( t_{\text{exp}}/2 = 15s \) to \( t_{\text{exp}}/2 = 15s \) (with \( t_{\text{exp}} = 30s \) the total time of the recording), we analyse \( N_t \) non-overlapping time series obtained by slicing the experimental time series \( (x_1, \ldots, x_n) \), with \( n \Delta t = t_{\text{exp}} \). Here, \( N_t \) equals to \( t_{\text{exp}}/t \) rounded to the lowest integer. For each value of \( t \), we obtain \( N_t \) estimates of \( \hat{\sigma}_1 \) as described by Eq. (S18). The data points plotted in Fig. 3B in the Main Text are given by the average of the \( N_t \) values of \( \hat{\sigma}_1 \), and the error bars are the standard deviation of the \( N_t \) values of \( \hat{\sigma}_1 \).

The results in Fig. 3C of the Main text were obtained as follows. For each of the 182 experimental recordings of hair bundle oscillations at sampling frequency \( f_s = 2.5 \) kHz, we estimate \( \hat{\sigma}_1 \) from the residual time series of duration \( t_{\text{exp}} = 30s \) and following the procedure described in Sec. S2.

In Fig. S6A we show the values of the estimate \( \hat{\sigma}_1 \) given by the parameter \( A \) in the fit of \( \hat{\sigma}_1 \) vs \( t \) in Fig. 3B to the function \( A + B \exp(-t/\tau) \). The error bars correspond to the error in the fitting parameter with 95% confidence bounds. For this set of data, we can distinguish different levels of irreversibility among the active spontaneous oscillations. Fig. S6B shows the value of the irreversibility statistical power obtained for these 30s experimental recordings. We remind that here, \( p_{\text{KS}} \) is the Kolmogorov–Smirnov (KS) statistic under the null hypothesis \( H_0 : p = q \) to be true, i.e. \( 1 - p_{\text{KS}} \) is an estimate of the significance for the time series to not be time reversible. This analysis reveals that recordings obtained from this set of active oscillations are not time reversal invariant with a significance of \( \sim 80\% \) (dashed line in Fig. S6B). In Fig. S6C we show the distribution of the irreversibility statistical power \( \gamma \) for the full ensemble of experimental recordings analyzed in this work. We find that in 46% of the experimental recordings, the statistical power for the distributions \( p(\xi) \) and \( q(\xi) \) to be different is at least 80% (blue shaded area Fig. S6D).
FIG. S6: (A) Long-time estimate of the irreversibility measure given by the value of the parameter $A$ in the fit of $\hat{\sigma}_1$ vs $t$ to the function $A + Be^{-t/\tau}$ for the oscillations depicted in Fig. 3A of the Main Text. The error bars are given by the error in the fitting parameter with 95% confidence interval. (B) Value of the statistical power $1 - p_{KS}$ for the same oscillations, with $p_{KS}$ the p-value of the Kolmogorov-Smirnov statistic for the distributions of the residuals $\xi^F$ and $\xi^R$ to be the identical. (C) Histogram of statistical power for irreversibility given by one minus the p-value of the Kolmogorov-Smirnov statistic with the null hypothesis that the residual distributions are identical. The data shown here was obtained from 30s time series of 182 experimental recordings of hair bundle oscillations. As indicated on the figure by the vertical dashed line, time-irreversibility of hair-bundle oscillations was ascertained with a statistical power of at least 80% for 46% of the recordings. The sampling frequency of the oscillation is $f_s = 2.5$ kHz.

FIG. S7: Histograms of the irreversibility measure $\hat{\sigma}_1$ in units of $k_B/s$ (A) and in units of $k_B$ per oscillation cycle (B). The histograms were obtained from the full ensemble of 182 oscillatory hair cells (yellow bars) and from the sub-ensemble of 66 cells that display irreversibility with statistical power $> 80\%$ (blue bars). The sampling frequency of the oscillation is $f_s = 2.5$ kHz.

The irreversibility measure $\hat{\sigma}_1$ for this sub-ensemble of irreversible oscillations, consisting of 66 recordings, displays a distribution with mean equal to twice the mean of the full ensemble (Fig. S7A). We also compare the irreversibility measure in units of $k_B$ per oscillation cycle, i.e. $\hat{\sigma}_1/f_o$, where $f_o$ is determined from a fit of the power-spectrum density (see Sec. S7), and show that the irreversibility of our experimental recordings is on average of the order of $0.2 k_B/cycle$ ($0.4 k_B/cycle$) for the full (sub-) ensemble of the cells analyzed (Fig. S7B).

Our quantification of irreversibility thus predicts that hair bundles produce entropy at an average rate of at least...
0.2kB per oscillation cycle. Investigating the tightness of the bound $\sigma_{\text{tot}} \geq \hat{\sigma}_1$ is a challenging experimental task since no direct measurements of heat dissipation in spontaneous hair-bundle oscillations have yet been reported. Reference [37] reports experimental estimates of the sound power in spontaneous oto-acoustic emissions by the iguanoid lizard Anolis sagrei. Spontaneous oto-acoustic emissions are weak sounds that are emitted spontaneously by the ears of the animal; these sounds are though to be produced by spontaneous hair-bundle oscillations in the auditory organ of the inner ear. From these measurements, the mean power output of individual hair bundles is estimated to be on average of 141 aW = $1.41 \times 10^{-16}$ J/s = $3.37 \times 10^4$ kB T/s, where $k_B T = 4.18 \times 10^{-21} J$ for $T = 30^\circ C$. The oscillation frequency of lizards’ hair bundles used in [37] was in the range $1 \sim 8$ kHz. Using an average oscillation frequency $f_o = 3.5$ kHz, we estimate the mean power output to be on the order of $3.37 \times 10^4$ kB T/s/(3.5 $\times 10^3$ cycle/s) $\approx 10$kB T/cycle, i.e. 50 times larger than the average value of our measure of irreversibility (Fig. S7B).

**S5. Dependency of the Irreversibility Measure with the Sampling Frequency**

In this section, we analyse the dependency of our irreversibility measure on the sampling frequency $f_s$. For this purpose, we evaluate $\hat{\sigma}_1$ defined in Eq. (S18) for 30s recordings of the 182 cells that showed spontaneous oscillations at different sampling frequencies, ranging from 125Hz to 2500Hz (the latter corresponding to the data shown in Fig. 3C in the Main text). Figure S8 shows that the distribution of the irreversibility measure depends strongly on the sampling frequency of the data. Notably, the distributions shift towards higher irreversibility when the sampling frequency is reduced, until there is too much filtering $f_s < 250$Hz such that oscillations cannot be distinguished clearly.

![Figure S8](image-url)  
**Figure S8:** Histograms of the irreversibility measure $\hat{\sigma}_1/k_B$ for different values of the sampling frequency $f_s$ indicated above each panel of the figure. All the histograms were obtained from the same ensemble of 182 oscillatory hair cells that displayed active oscillations.

From these distributions, we quantify the average statistical power and the irreversibility measure $\hat{\sigma}_1$ ($\pm$ standard deviation) across the population of active cells. Fig. S9A shows that the mean statistical power of irreversibility depends on the sampling frequency of the trajectories $X(t)$; we find an optimum range in the interval $f_s \in [250, 625]$Hz where the mean power is $\sim$ 80%, i.e. 20% larger than for the highest frequency 2.5kHz. Fig. S9B shows that the mean value of the distributions of the irreversibility measure in Fig. S8 also attains a maximum value also in the range $f_s \in [250, 625]$Hz, with a peak value at $f_s = 633$ Hz of $\hat{\sigma}_1 = (4.3 \pm 0.4)$kB/s, which is $\sim 1kB/s$ larger than the value at $f_s = 2.5$ kHz reported in the Main Text. This result reveals that the timescale at which the active process is more noticeable using our irreversibility measure is on the order of milliseconds.
In this Section, we provide numerical results for the stochastic model of the ear hair bundle given by Eqs. (3-5) in the Main Text. The steady-state entropy production rate of the model is given by
\[
\sigma_{\text{tot}} = \frac{1}{T} \left( F_1 \circ \frac{dX_1}{dt} \right) + \frac{1}{T_{\text{eff}}} \left( F_2 \circ \frac{dX_2}{dt} \right), \tag{S19}
\]
where \( F_1 = F_1(X_1, X_2) \), \( F_2 = F_2(X_1, X_2) \) and \( \circ \) denotes the Stratonovich product. Using the definitions of the forces in Eq. (S19) one obtains after some algebra Eq. (6) in the Main Text. In all our numerical simulations, we estimate the steady-state averages of the type
\[
\left\langle F \circ \frac{dX}{dt} \right\rangle = \lim_{t \to \infty} \frac{1}{t} \int_{0}^{t} F(t') \circ dX(t') \tag{S20},
\]
for a generic force \( F(t) = F(X(t), Y(t)) \) from a single stationary trajectory of total duration \( t_{\text{sim}} = 300 \, \text{s} \) and sampling time \( \Delta t = 1 \, \text{ms} \) as follows:
\[
\left\langle F \circ \frac{dX}{dt} \right\rangle \approx \frac{1}{t_{\text{sim}}} \sum_{i=1}^{n} \left( F(t_i) + F(t_{i-1}) \right) \left( X(t_i) - X(t_{i-1}) \right), \tag{S21}
\]
where \( t_i = i \Delta t \) and \( n = t_{\text{sim}}/\Delta t \).

### S7. ESTIMATION OF THE QUALITY FACTOR OF STOCHASTIC OSCILLATIONS

We estimate the quality factor \( Q \) of spontaneous hair-bundle oscillations from numerical simulations of the hair-bundle stochastic model given by Eqs. (3-4) in the Main Text. For this purpose, we generate a single numerical simulation of duration \( t_{\text{sim}} = 300 \, \text{s} \). We then partition the simulation into 10 consecutive traces of duration \( T = t_{\text{sim}}/10 = 30 \, \text{s} \). For each of these traces \( \{X_\alpha(t)\} \ (\alpha = 1, \ldots, 10) \) we compute the power spectral density as \( C_\alpha(f) = (1/T) \left| \int_{0}^{T} X_\alpha(s) e^{2\pi ifs} \, ds \right|^2 \). We then calculate the average of the power spectral density over the 10 different traces \( \tilde{C}(f) = (1/10) \sum_{\alpha=1}^{10} C_\alpha(f) \) and fit the estimate \( \tilde{C}(f) \) as a function of \( f \) to the sum of two Lorentzian functions [4, 15, 44]
\[
\tilde{C}(f) = \frac{A}{(f_0/2Q)^2 + (f - f_0)^2} + \frac{A}{(f_0/2Q)^2 + (f + f_0)^2}, \tag{S22}
\]
where \( Q \) is the quality factor, \( f_0 \) is the oscillation frequency and \( A > 0 \) is an amplitude parameter. Figure S10 shows examples of numerical simulations for which we apply this procedure to determine the value of the quality factor by extracting the value \( Q \) from the fit of the data to Eq. (S22). Notably, Eq. (S22) reproduces power spectra of hair-bundle simulations for oscillations with values \( Q \) that are in a wide range of orders of magnitude (Fig. S10C).
FIG. S10: Estimation of the quality factor $Q$ from numerical simulations of the hair bundle. (A) Values of the quality factor $Q$ calculated from numerical simulations of duration $t_{sim} = 300$ s for the same parameter values as in Fig. 4 in the Main Text. (B) Examples of 0.5-second traces of $X_1$ as a function of time for the parameter values indicated in A: B.1) [1 in (A)]; B.2) [2 in (A)]; B.3) [3 in (A)]; B.4) [4 in (A)]. (C) Power spectral density (black line) of the numerical simulations with parameter values indicated with black open circles in (A). The quality factor is estimated from a fit of the power spectra to Eq. (S22) (red line). The values of $Q$ and $f_o$ extracted from the fits are: $Q = 0.5$, $f_o = 7.3$ Hz (C.1), $Q = 7$, $f_o = 25$ Hz (C.2), $Q = 0.45$, $f_o = 10.6$ Hz (C.3), $Q = 3.8$, $f_o = 41.3$ Hz (C.4).

S8. BIOPHYSICS OF MECHANOSENSORY HAIR BUNDLES

Details of the experimental procedure have been published elsewhere [2]. In short, an excised preparation of the bullfrog’s (*Rana catesbeiana*) sacculus was mounted on a two-compartment chamber to reproduce the ionic environment of the inner ear. This organ is devoted to sensitive detection of low-frequency vibrations (5−150 Hz) of the animal’s head in a vertical plane; it contains about 3000 sensory hair cells that are arranged in a planar epithelium. The basal bodies of hair cells were bathed in a standard saline solution and the hair bundles projected in an artificial endolymph. The preparation was viewed through a ×60 water-immersion objective of an upright microscope. Under these conditions, spontaneous hair-bundle oscillations were routinely observed. The oscillations could be recorded by imaging, at a magnification of ×1000, the top of the longest stereociliary row onto a displacement monitor that included a dual photodiode. Calibration was performed by measuring the output voltages of this photometric system in response to a series of offset displacements. Here, we analyzed 182 spontaneously oscillating hair bundles from data previously published [15].

Spontaneous hair-bundle oscillations were described by a published model of active hair-bundle motility [2] that rest on a necessary condition of negative hair-bundle stiffness, on the presence of molecular motors that actively pull on the tip links, and on feedback by the calcium component of the transduction current. Hair-bundle deflections affect tension in tip links that interconnect neighbouring stereocilia of the bundle. Changes in tip-link tension in turn modulate the open probability of mechanosensitive ion channels connected to these links. Importantly, the relation between channel gating and tip-link tension is reciprocal: gating of the transduction channels affects tip-link tension. Consequently, channel gating effectively reduces the stiffness of a hair bundle, a phenomenon appropriately termed "gating compliance", which can result in negative stiffness if channel-gating forces are strong enough. Active hair-bundle movements result from the activity of the adaptation motors. By controlling tip-link tension, adaptation motors regulate the open probability of the mechanosensitive channels. The force produced by the motors is in turn
regulated by the Ca$^{2+}$ component of the transduction current which thus provides negative feedback on the motor force [2]. When the fixed point of this dynamical system corresponds to an unstable position of negative stiffness, the system oscillates spontaneously. The maximal force exerted by the motors $F_{\text{max}}$ and the calcium feedback strength $S$ are control parameters of the system and fully determine its dynamics (oscillatory, quiescent, bi-stable) [25].