Detecting active processes from spontaneous oscillations of ear hair bundles

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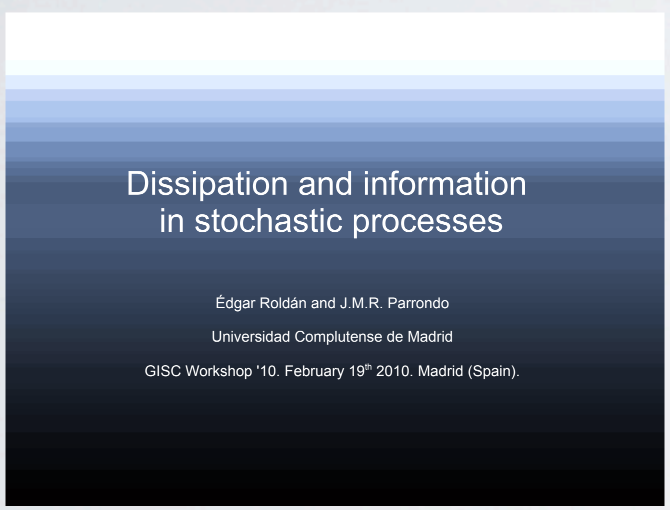
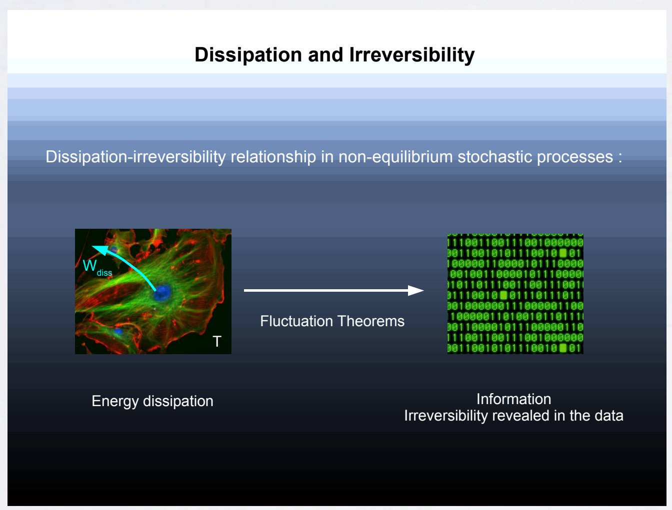
X GISC Workshop (UC3M, Madrid, 8th Feb 2013)

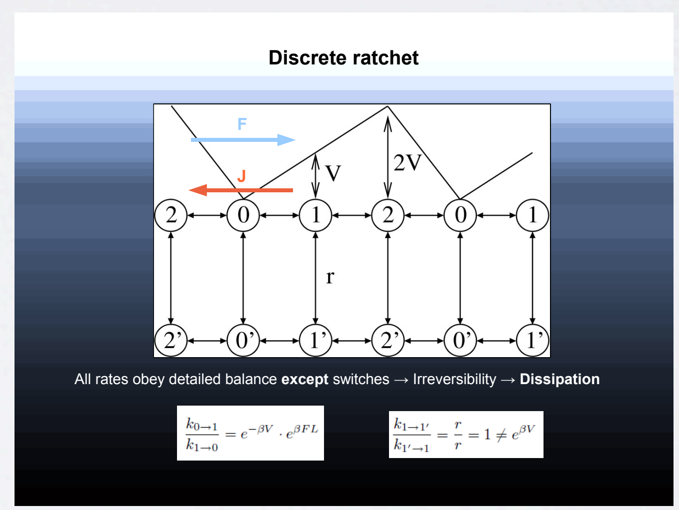
Detecting active processes from spontaneous oscillations of Ear Hair bundles

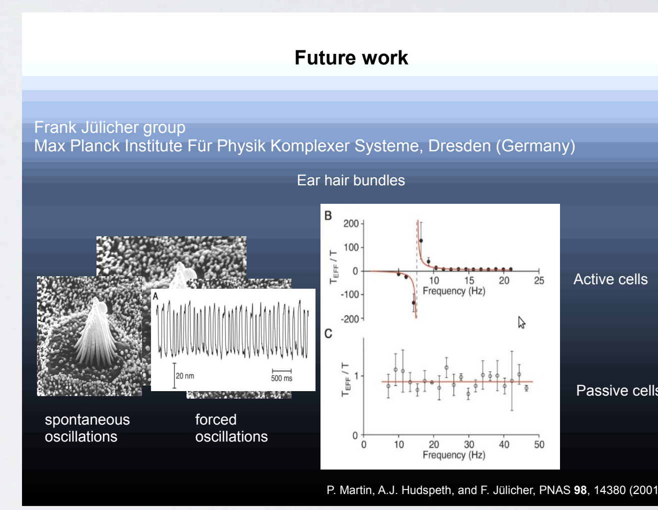
GISC Workshop 2010 :

"Dissipation and information in stochastic processes"









Detecting active processes from spontaneous oscillations of Ear Hair bundles

1. Biophysics of the hair-bundle: motivation

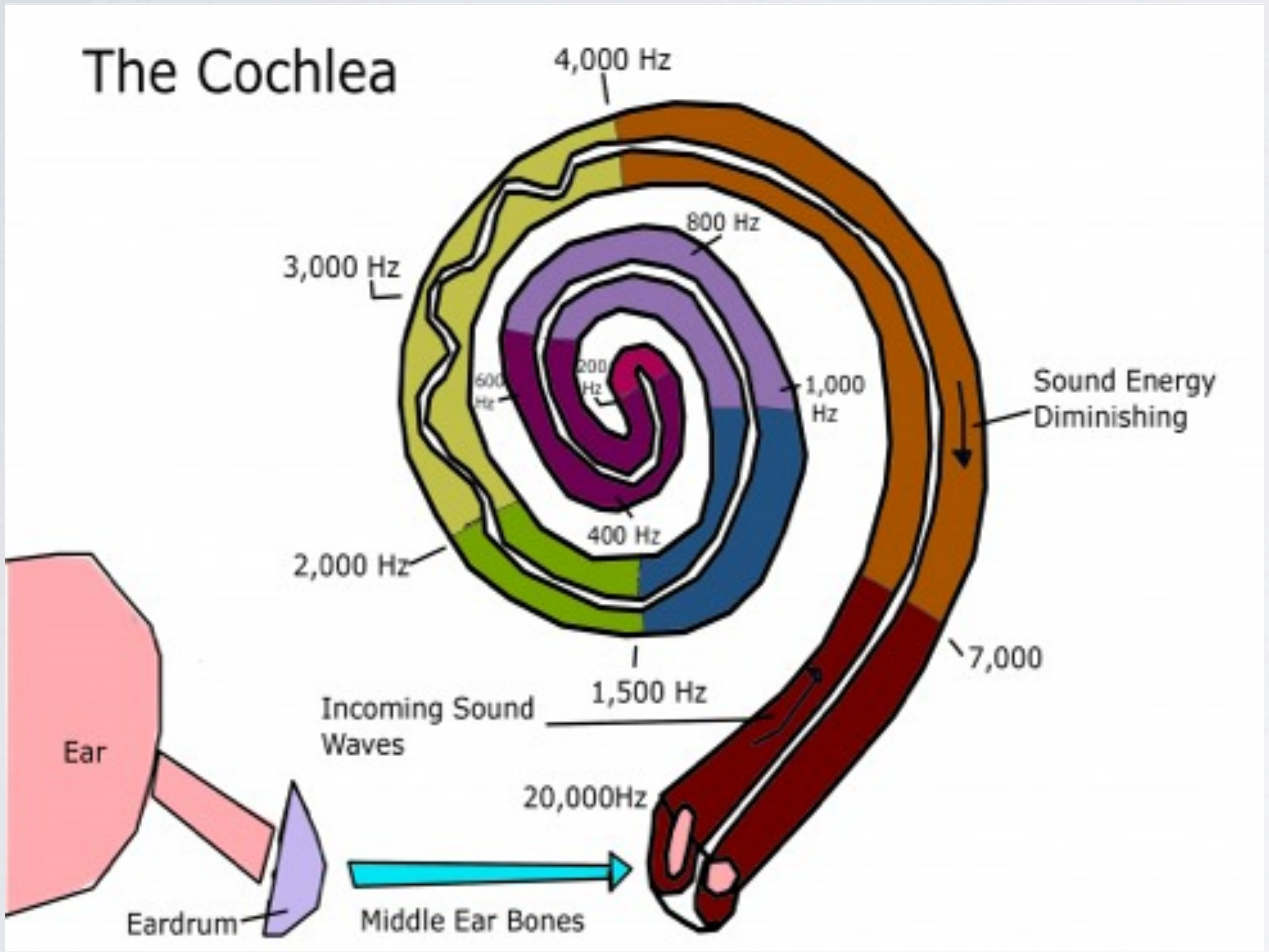
2. Estimating time irreversibility

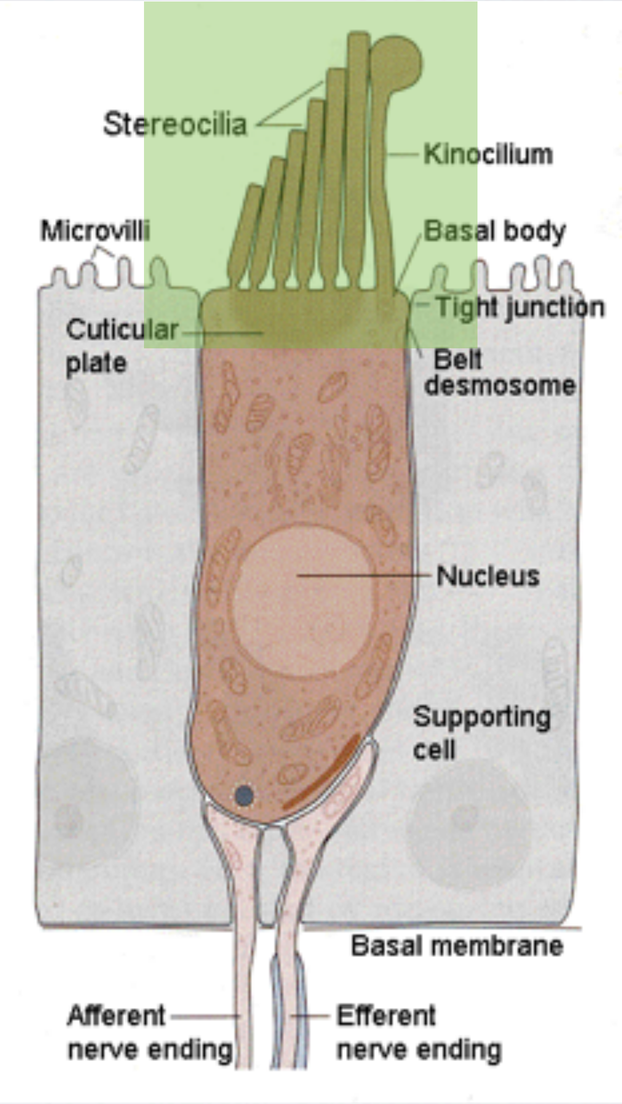
3. Results : simulations

4. Results : experiments

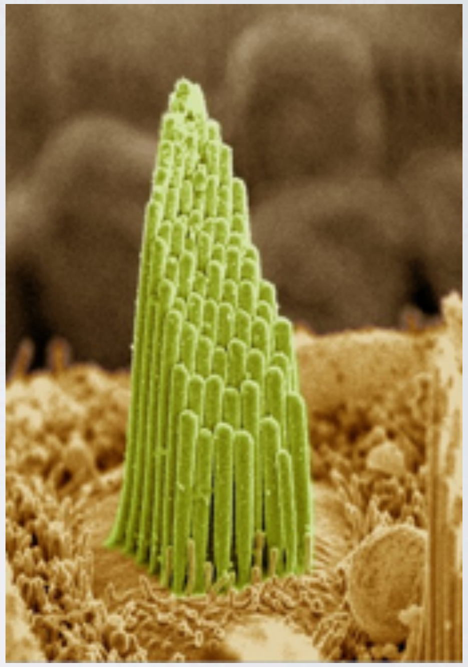
5. Conclusion

Biophysics of the ear hair bundle: motivation





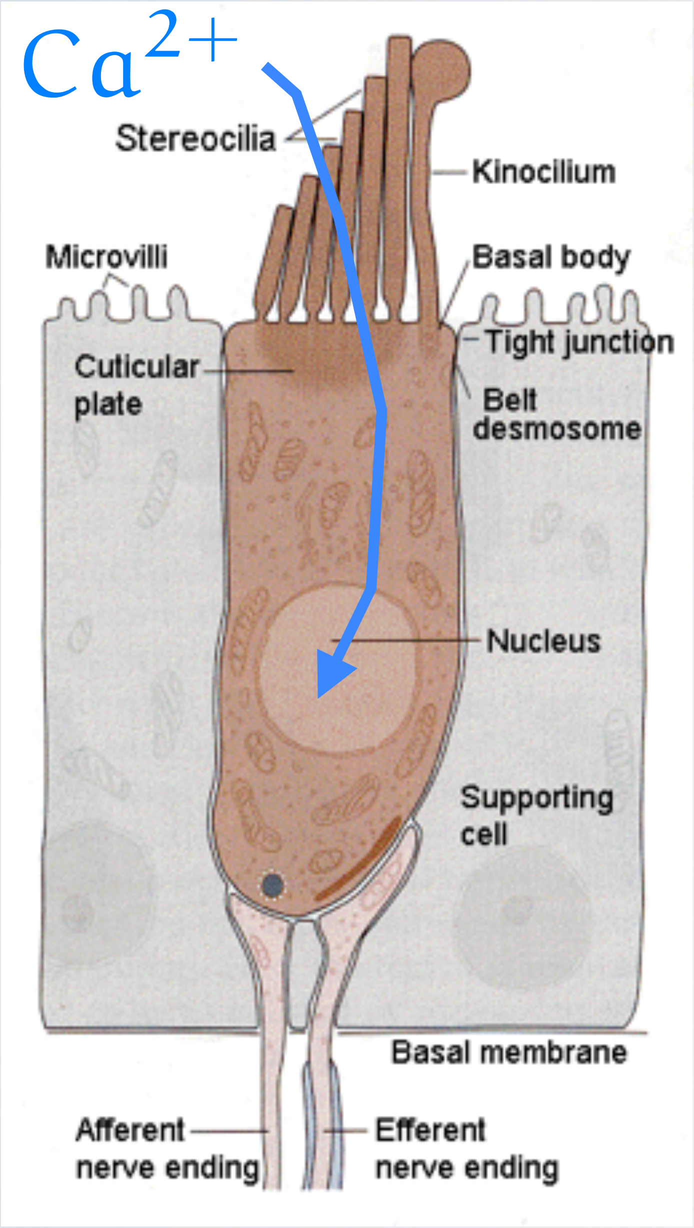
Ear hair cell

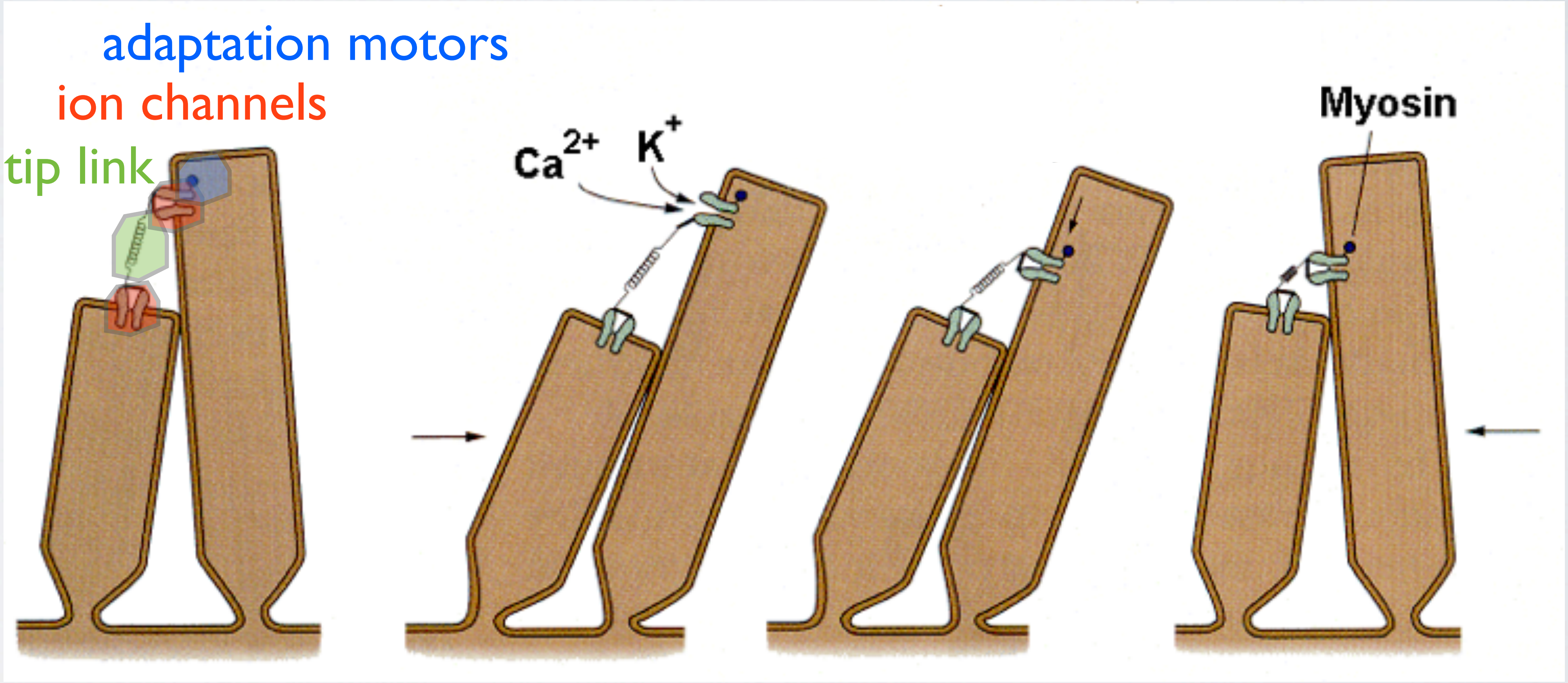


Ear hair bundle

Biophysics of the hair bundle: motivation

Transduction ⟶ Calcium ions

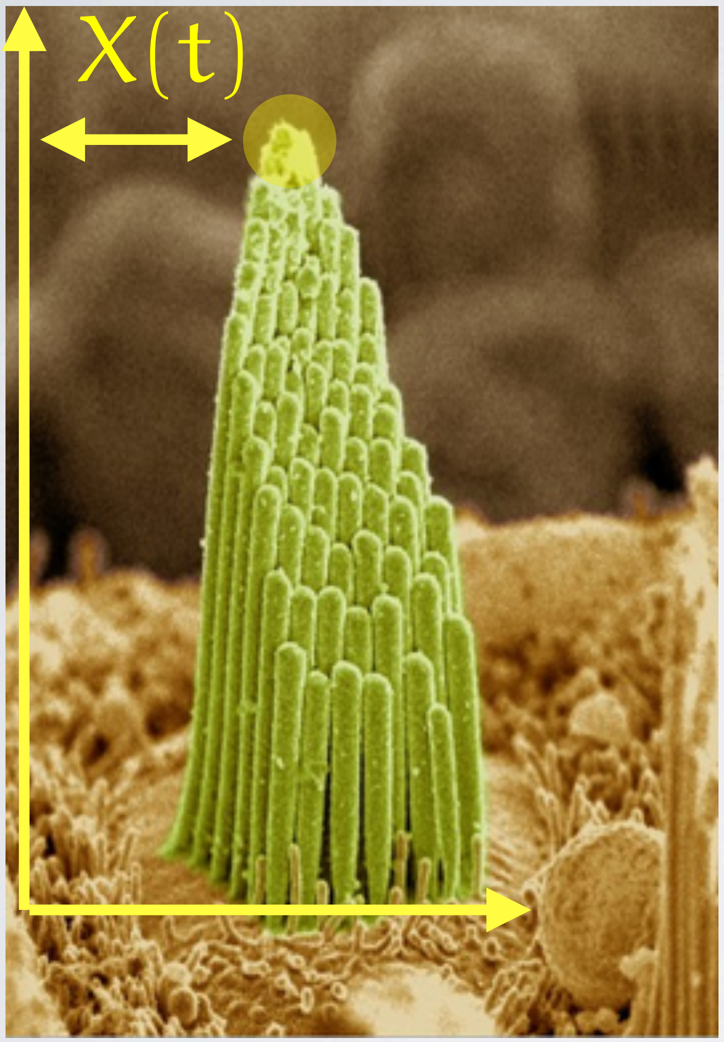


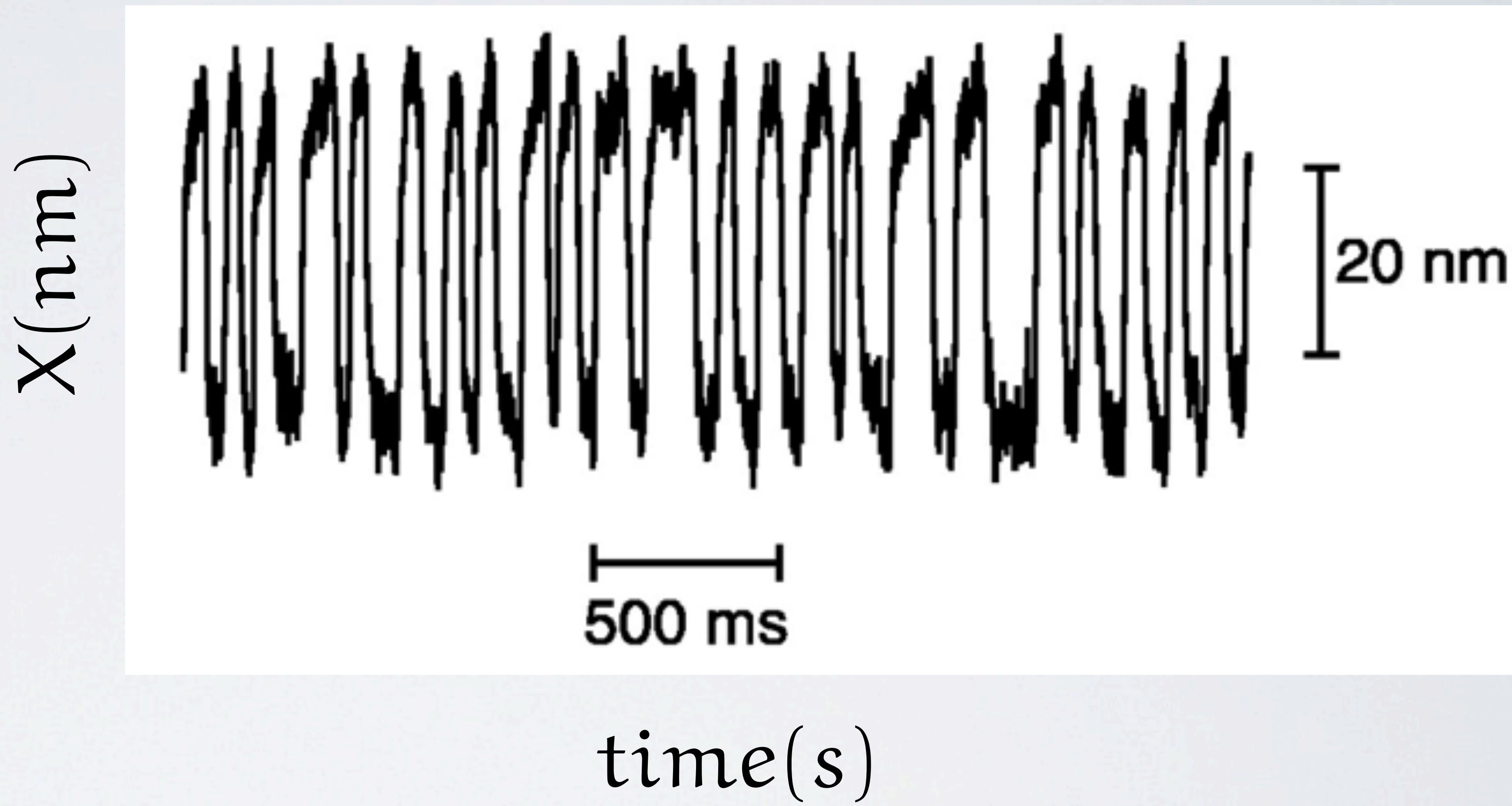


Gating-spring model

G. A. Manley and R. R. Fay, *Active Processes and Otoacoustic Emissions in Hearing*, **30** (2008).

Biophysics of the hair bundle: motivation

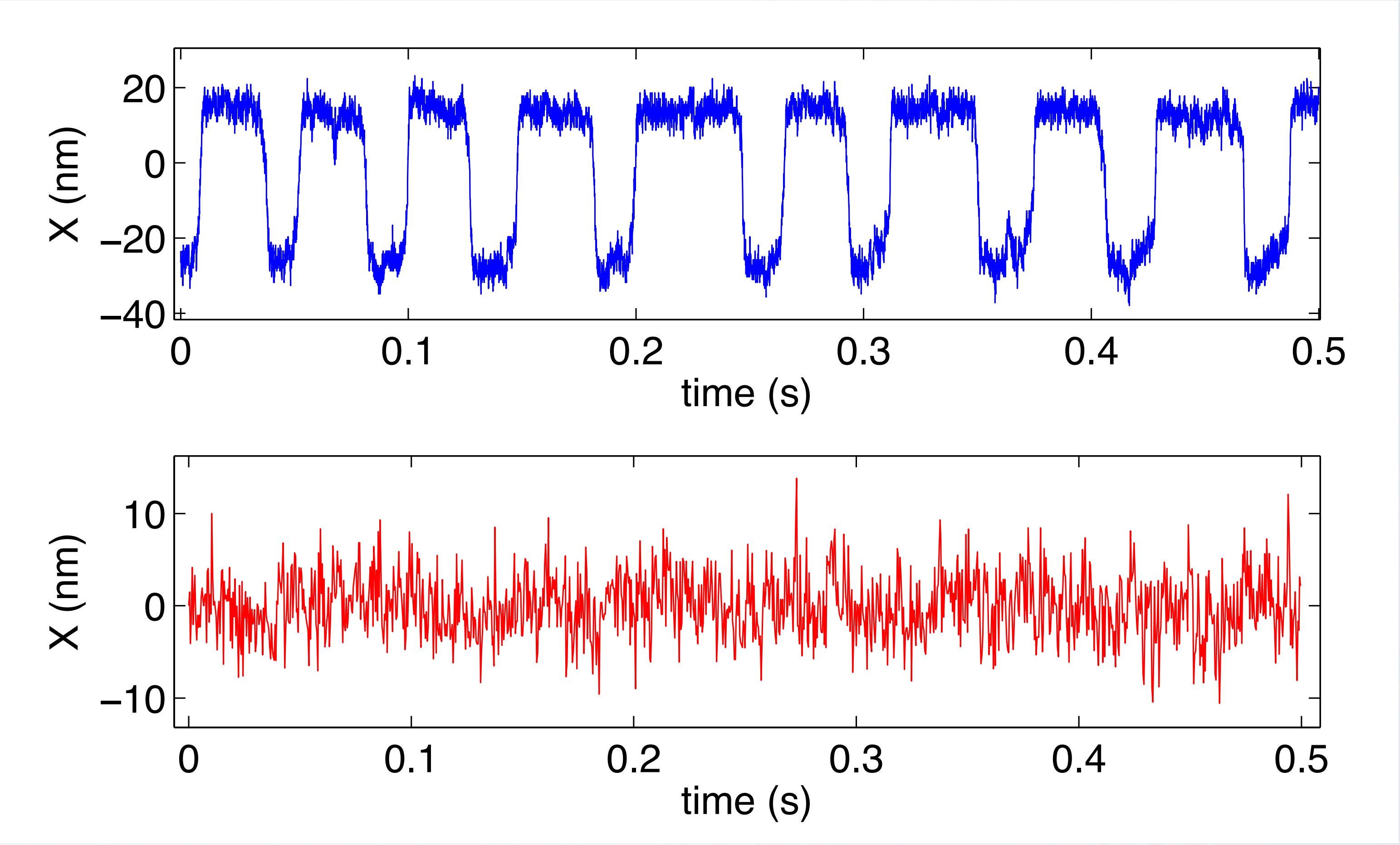




Spontaneous oscillations of the hair bundle
in the absence of external forces

Biophysics of the hair bundle: motivation

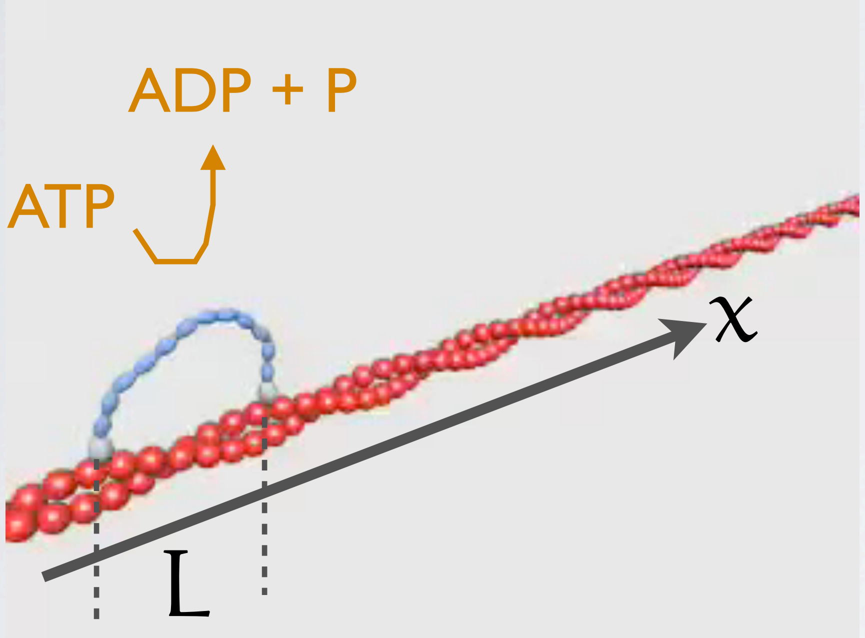
Motivation: From spontaneous oscillations



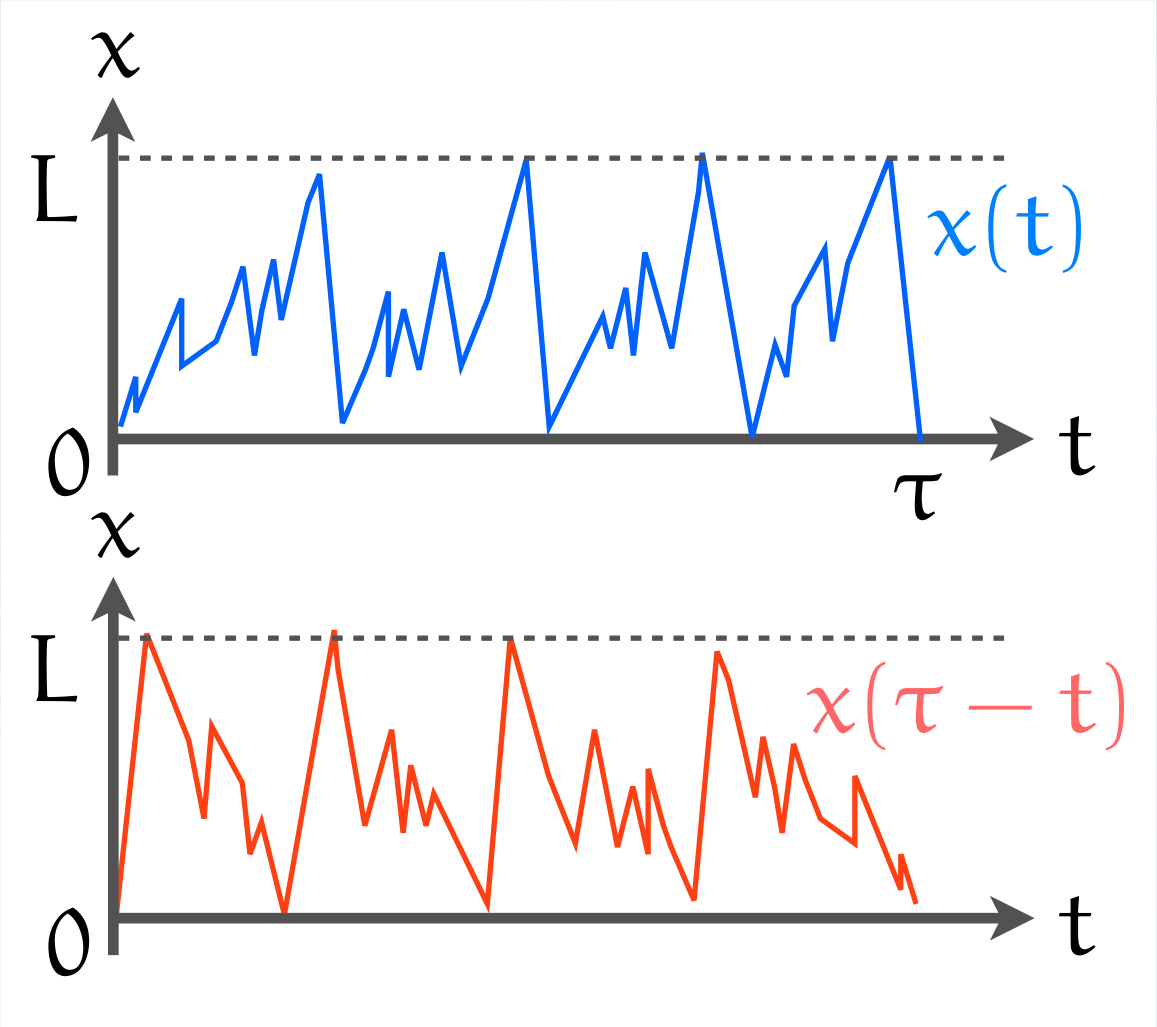
1. Distinguish between active and passive cells
2. Estimate energy dissipation

Estimating time irreversibility

Microscopic systems in the nonequilibrium stationary state



$$W_{diss} = W - \Delta F$$



$$\frac{\langle \dot{W}_{diss} \rangle}{k_B T} = \lim_{\tau \to \infty} \frac{1}{\tau} D \left[\mathcal{P}\left(\{z(t)\}_{t=0}^{\tau}\right) \middle|\middle| \mathcal{P}\left(\{\tilde{z}(\tau - t)\}_{t=0}^{\tau}\right) \right]$$

É. Roldan, J.M.R. Parrondo, *Phys. Rev. E.* **85** 031129 (2012)

Estimating time irreversibility

$$\frac{\langle \dot{W}_{\mathrm{diss}} \rangle}{k_B T} = \lim_{\tau \to \infty} \frac{1}{\tau} D\left[\mathcal{P}\left(\{z(t)\}_{t=0}^{\tau} \right) \middle| \middle| \mathcal{P}\left(\{\tilde{z}(\tau - t)\}_{t=0}^{\tau} \right) \right]$$

Dissipation

Irreversibility

Kullback-Leibler Divergence (KLD)

$$D[\mathcal{P}\{z(t)\} || \mathcal{P}\{z(\tau - t)\}] = \int dz \, \mathcal{P}\{z(t)\} \ln \frac{\mathcal{P}\{z(t)\}}{\mathcal{P}\{z(\tau - t)\}}$$

KLD with partial information

$$\frac{\langle \dot{W}_{\mathrm{diss}} \rangle}{k_B T} \geq \lim_{\tau \to \infty} \frac{1}{\tau} D\left[\mathcal{P}\left(\{x(t)\}_{t=0}^{\tau} \right) \middle| \middle| \mathcal{P}\left(\{\tilde{x}(\tau - t)\}_{t=0}^{\tau} \right) \right] \geq 0$$

Estimating time irreversibility

$$\frac{\langle \dot{W}_{diss} \rangle}{k_B T} \geq \lim_{\tau\to\infty} \boxed{\frac{1}{\tau} D\left[\mathcal{P}\left(\{x(t)\}_{t=0}^{\tau}\right) \middle|\middle| \mathcal{P}\left(\{\tilde{x}(\tau - t)\}_{t=0}^{\tau}\right)\right]} \geq 0$$

$\dot{d}_x$ **(KLD rate)**

How to estimate the KLD rate of a continuous system

$$\dot{d}_x = \frac{1}{\tau} D\left[\mathcal{P}\left(\{x(t)\}_{t=0}^{\tau}\right) \middle|\middle| \mathcal{P}\left(\{\tilde{x}(\tau - t)\}_{t=0}^{\tau}\right)\right]$$

from a single stationary trajectory?

$$x_1^n = x_1, x_2, \cdots, x_n \qquad n \gg 1$$

Δt

Estimating time irreversibility

Estimating $\dot{d}_x$

String counting (finite time statistics)

$$\dot{d}_{x,1} = \frac{1}{\Delta t} D[p_X(x)||p_{\tilde{X}}(x)] = 0$$

$$\dot{d}_{x,2} = \frac{1}{2\Delta t} D[p_X(x_1, x_2)||p_{\tilde{X}}(x_1, x_2)]$$

$$\dot{d}_x = \lim_{m\to\infty} \dot{d}_{x,m}$$

Unfeasible in continuous (lack of statistics)

É. Roldan, J.M.R. Parrondo, *Phys. Rev. E.* **85** 031129 (2012)

É. Roldan, J.M.R. Parrondo, *Phys. Rev. Lett.* **105** 150607 (2010)

Estimating time irreversibility

A new estimator of $\dot{d}_x$

Transform the original series $X(t)$, $\tilde{X}(t)$ into new series $\epsilon(t)$, $\tilde{\epsilon}(t)$

one-to-one transformation $\Rightarrow \dot{d}_x = \dot{d}_\epsilon$

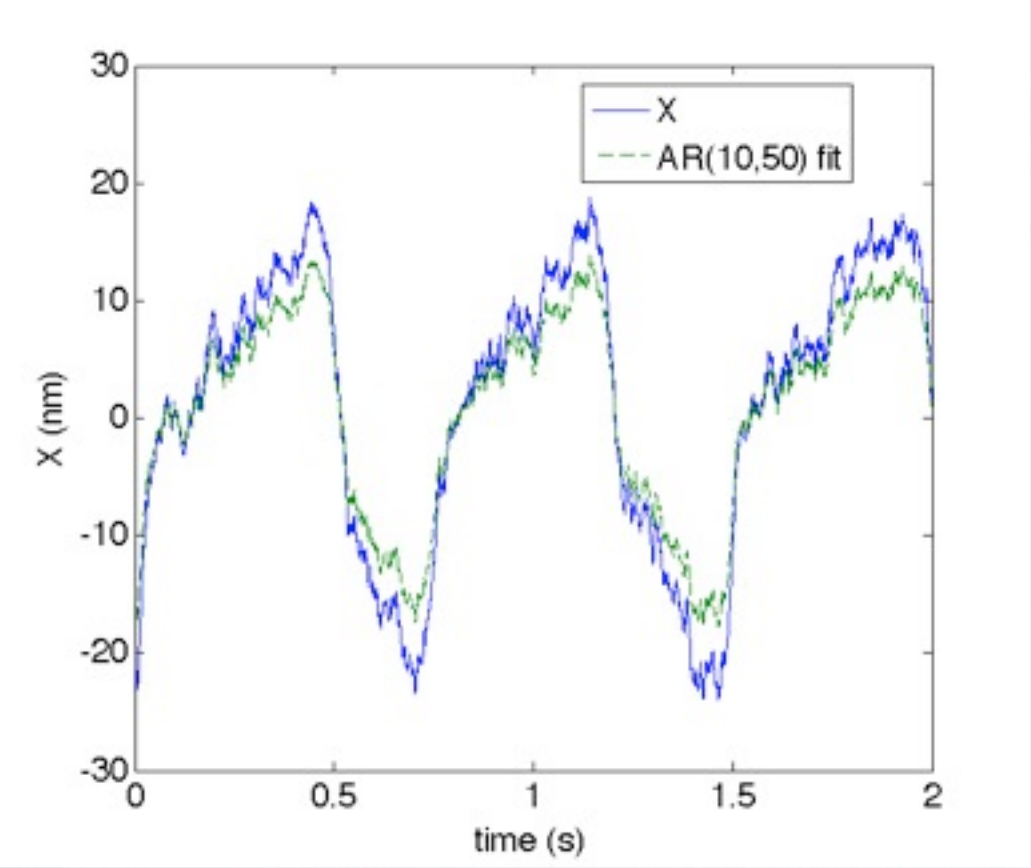
$\epsilon(t)$ $\tilde{\epsilon}(t)$ are almost uncorrelated $\Rightarrow \dot{d}_\epsilon \simeq \dot{d}_{\epsilon,1}$

$\epsilon(t)$ is not the time reversal of $\tilde{\epsilon}(t)$ $\Rightarrow \dot{d}_{\epsilon,1} > 0$

$$\frac{\langle \dot{W}_{\mathrm{diss}} \rangle}{k_B T} \geq \dot{d}_x = \dot{d}_\epsilon \geq \dot{d}_{\epsilon,1} \quad \Rightarrow \quad \frac{\langle \dot{W}_{\mathrm{diss}} \rangle}{k_B T} \geq \dot{d}_{\epsilon,1}$$

Estimating time irreversibility

Choosing the transformation $X(t) \xrightarrow{\epsilon} \epsilon(t)$



$AR(k, \ell)$ model

$$x_{1+kl} = \mathbf{A_1} x_{1+(k-1)l} + \cdots + \mathbf{A_k} x_1$$

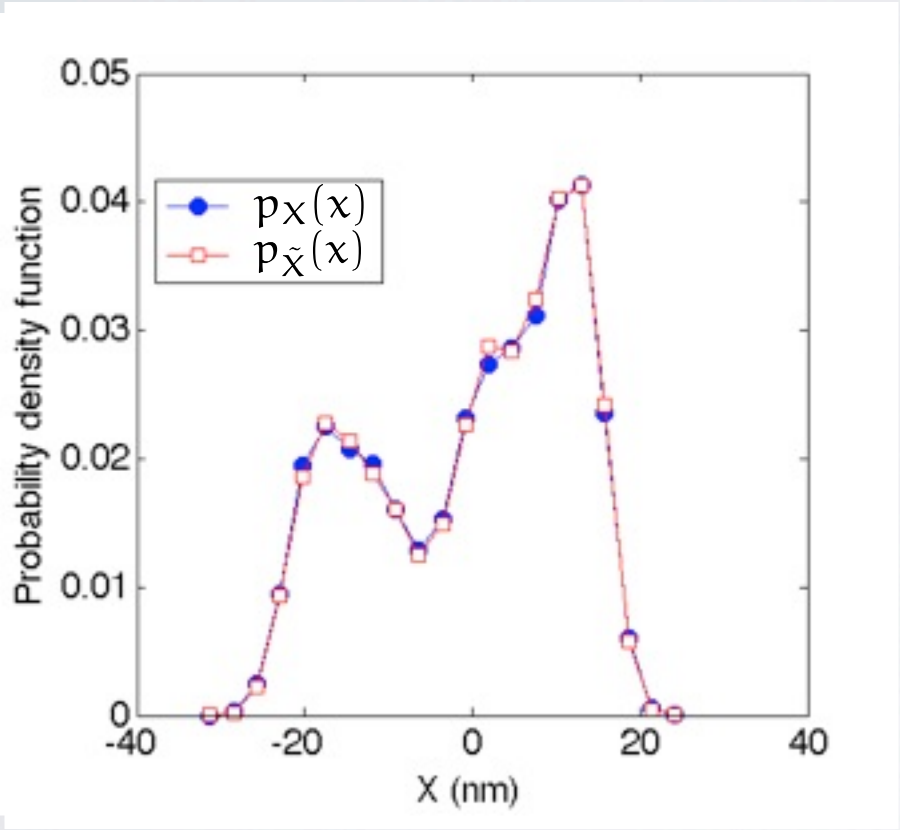
$AR(3,2)$

$$x_6 = \mathbf{A_1} x_5 + \mathbf{A_2} x_3 + \mathbf{A_3} x_1$$

$$x_m \rightarrow \epsilon_m = \epsilon(x_1, \cdots, x_m) = x_m - (\mathbf{A_1} x_{m-\ell} + \mathbf{A_2} x_{m-2\ell} + \cdots + \mathbf{A_k} x_{m-k\ell})$$
$$\tilde{x}_m \rightarrow \epsilon_m = \epsilon(\tilde{x}_1, \cdots, \tilde{x}_m) = \tilde{x}_m - (\mathbf{A_1} \tilde{x}_{m-\ell} + \mathbf{A_2} \tilde{x}_{m-2\ell} + \cdots + \mathbf{A_k} \tilde{x}_{m-k\ell})$$

Residual functional one-to-one ✓ $\epsilon(t), \tilde{\epsilon}(t) \sim$ uncorrelated ✓ $\dot{d}_{\epsilon,1} > 0$ ✓

Estimating time irreversibility



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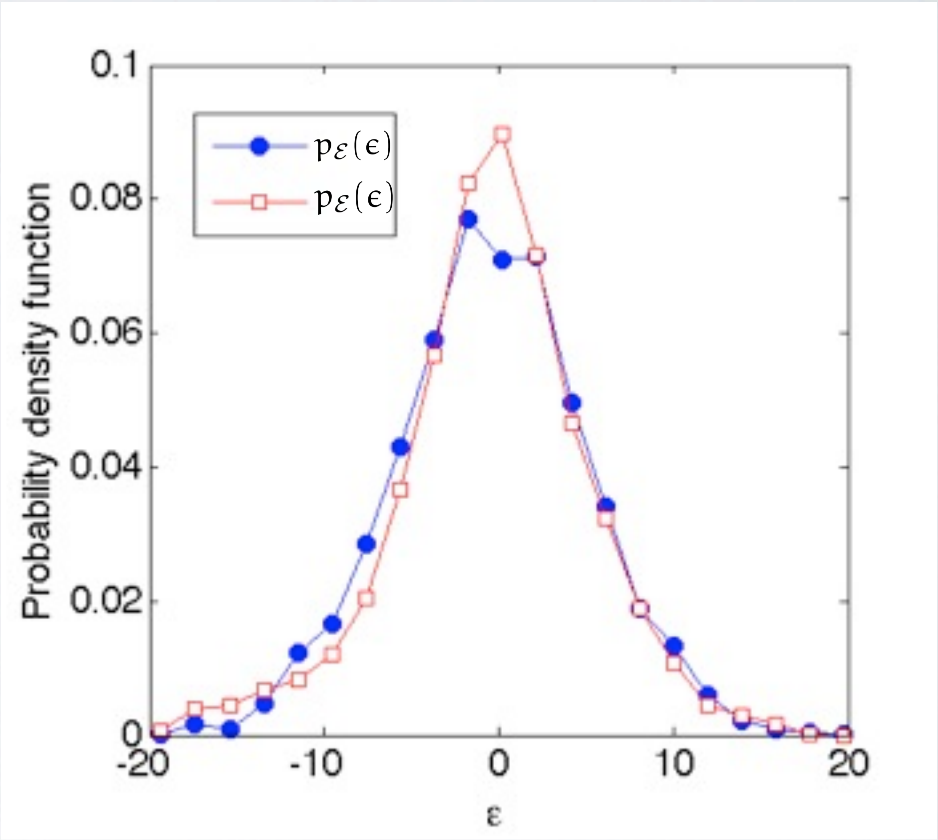


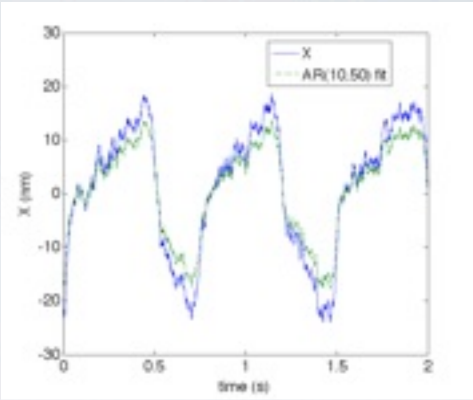
$$\dot{d}_{x,1} = 0$$

$$\dot{d}_{\epsilon,1} > 0$$

$$\frac{\langle \dot{W}_{diss} \rangle}{k_B T} \geq \dot{d}_{\epsilon,1}$$

Estimating time irreversibility

1st Fit $X(t)$ to $AR(k,\ell)$ model



Get $\mathbf{A_1}, \cdots, \mathbf{A_k}$

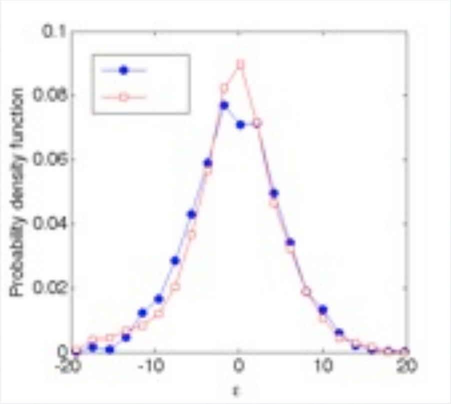
2nd Apply the residual function

$$\epsilon(x_1, \cdots, x_m) = x_m - (\mathbf{A_1} x_{m-\ell} + \mathbf{A_2} x_{m-2\ell} + \cdots + \mathbf{A_k} x_{m-k\ell})$$

$$X(t) \xrightarrow{\epsilon} \epsilon(t)$$

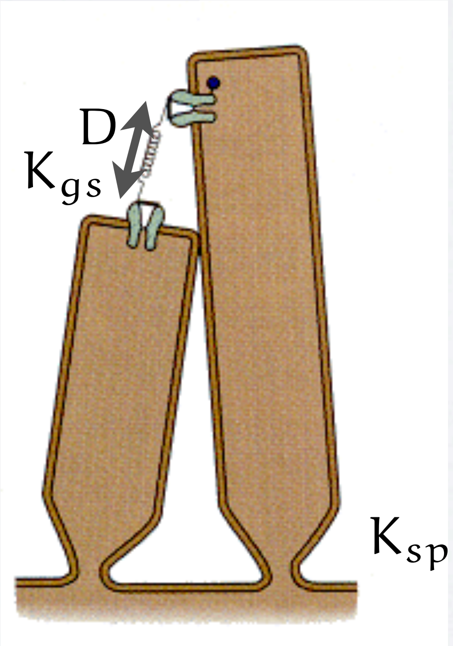
$$\tilde{X}(t) \xrightarrow{\epsilon} \tilde{\epsilon}(t)$$

3rd Compute $\dot{d}_{\epsilon,1}$



Results : simulations

$$\begin{cases} \lambda \dfrac{dX}{dt} = -K_{gs}(X - X_a - DP_o) - K_{sp}X + \eta & \textit{top} \\ \lambda_a \dfrac{dX_a}{dt} = K_{gs}(X - X_a - DP_o) - \gamma N_a f p(C) + \eta_a & \textit{motors} \\ \tau \dfrac{dC}{dt} = -C + C_M P_o + \delta c & \textit{Calcium} \end{cases}$$



$$\begin{bmatrix} X(t) \\ X_a(t) \\ C(t) \end{bmatrix} \longrightarrow X(t)$$

only position

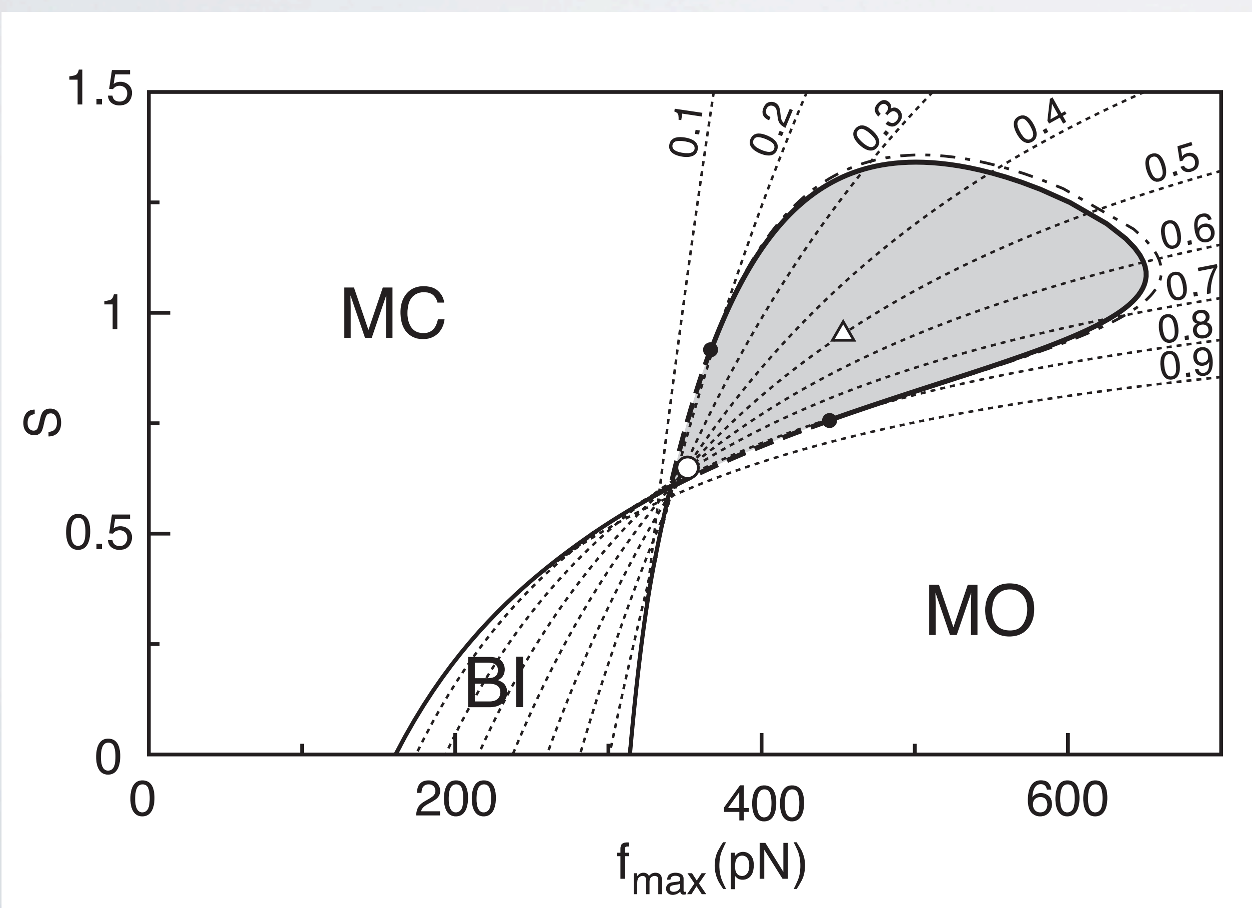
B. Nadrowski, P. Martin, and F. Jülicher., *PNAS* **101**, 12195 (2004)

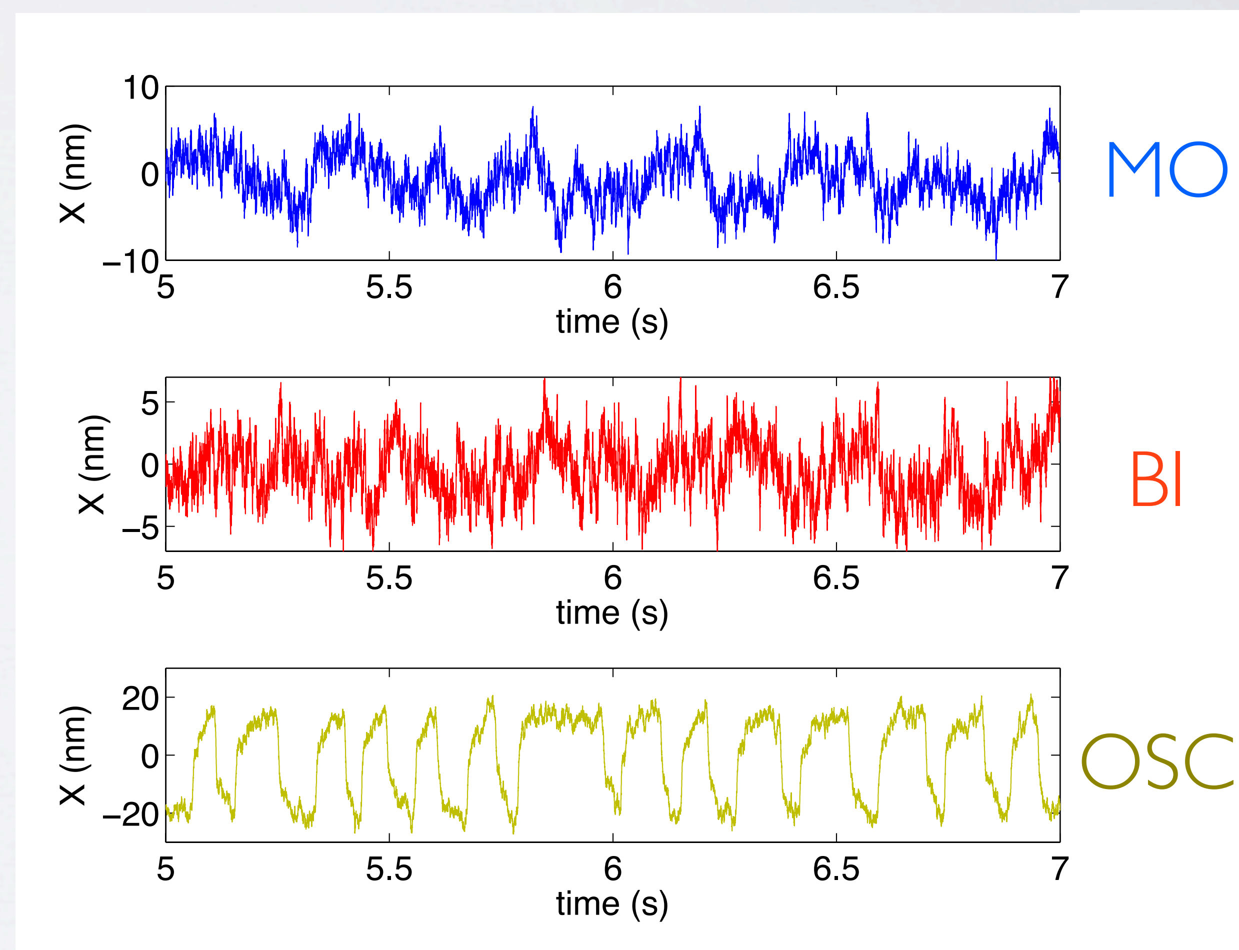
Results : simulations

$$(k_{gs}, D, k_{sp}, \cdots) \rightarrow (f_{max}, S)$$

$f_{max} =$ Maximum force of the motors

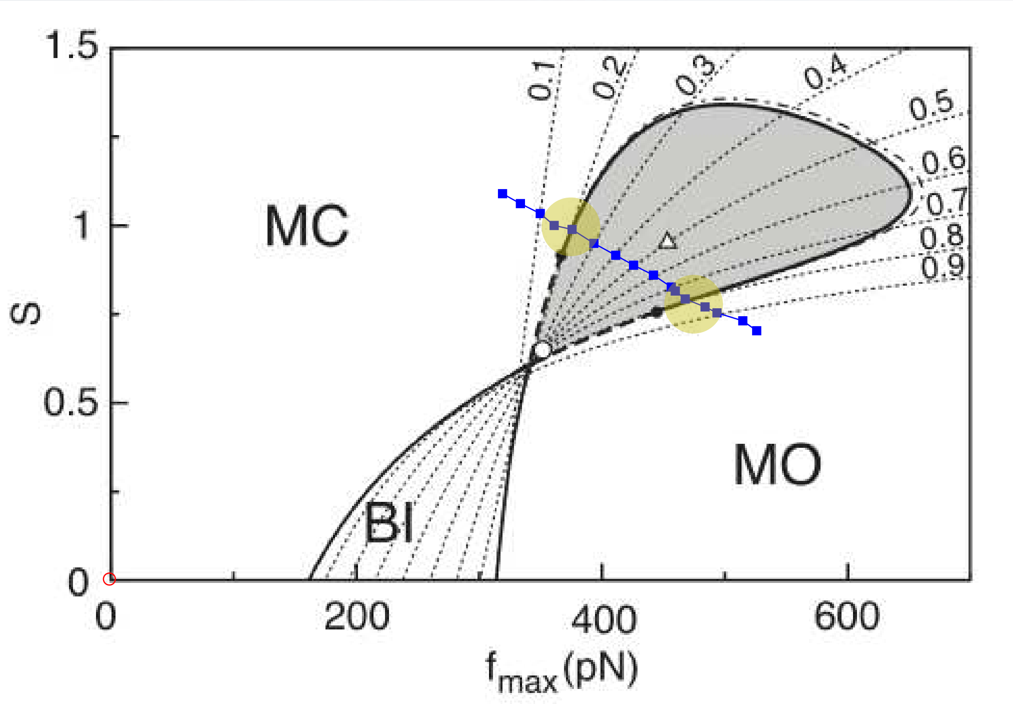
$$S = -\frac{C_M}{f_{max}} \frac{df_a}{dC}$$ Strength of Calcium feedback

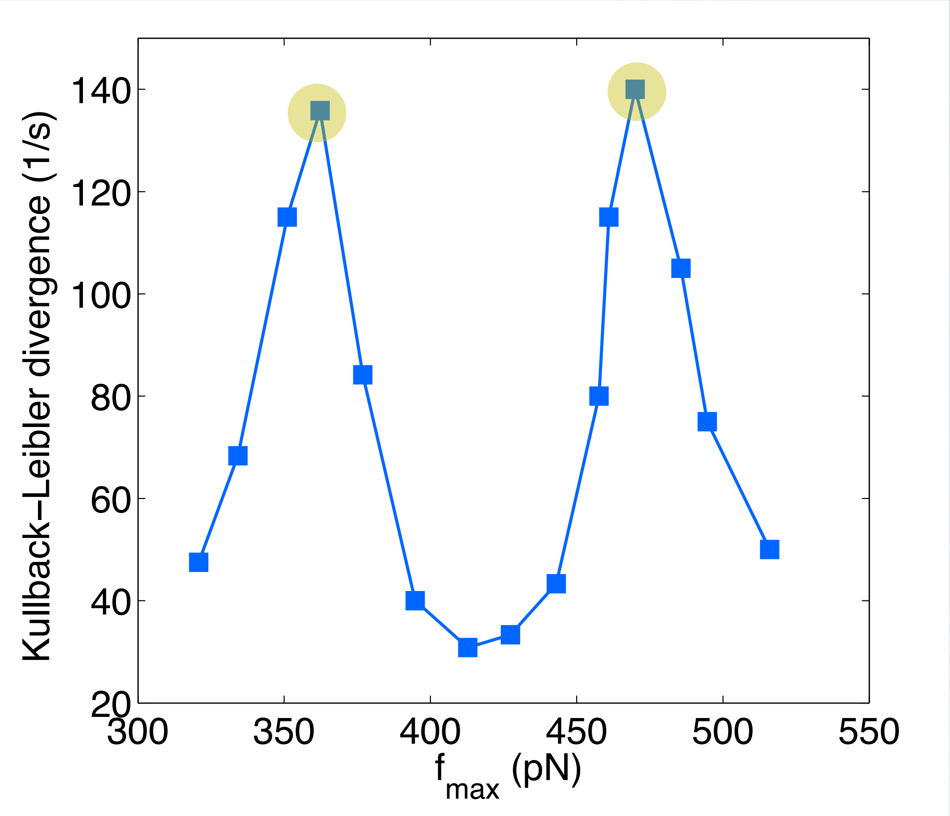




Results : simulations

Hopf bifurcation





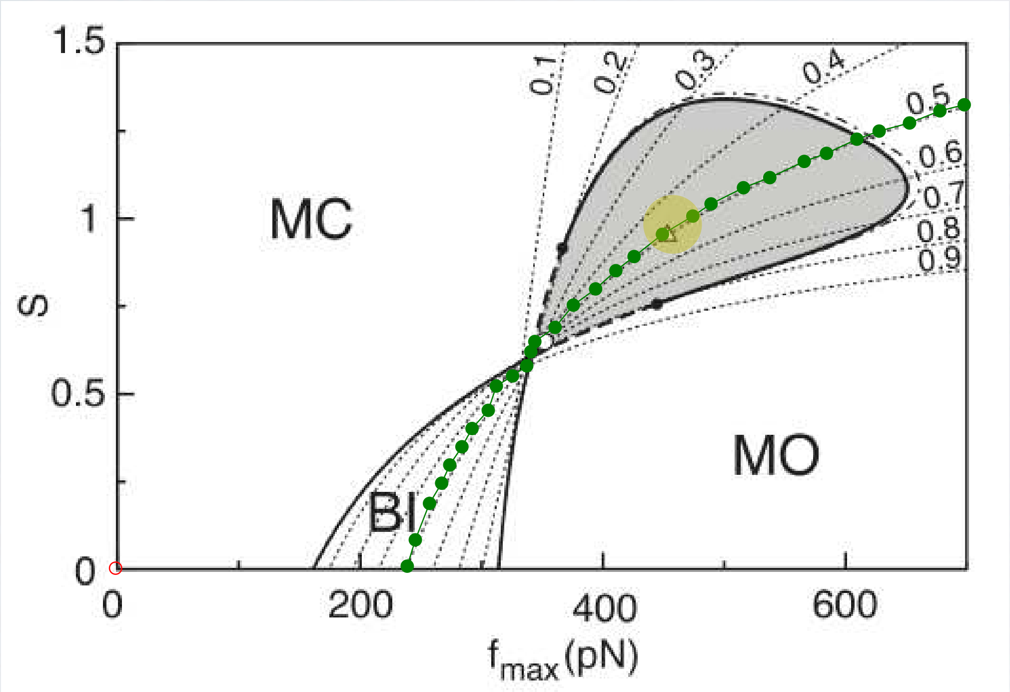
$\tau = 1200s, f_{acq} = 8.3kHz$

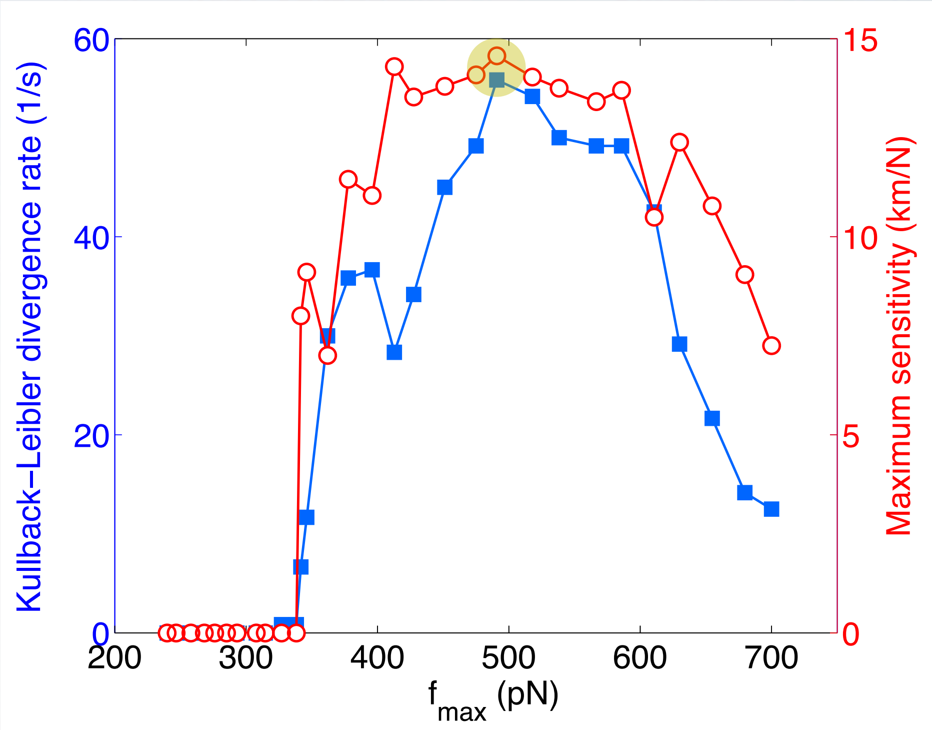
$\dot{d}_{\epsilon,1}, \quad AR(10, 50)$

KLD finds the bifurcation

Results : simulations

Bistable to oscillatory



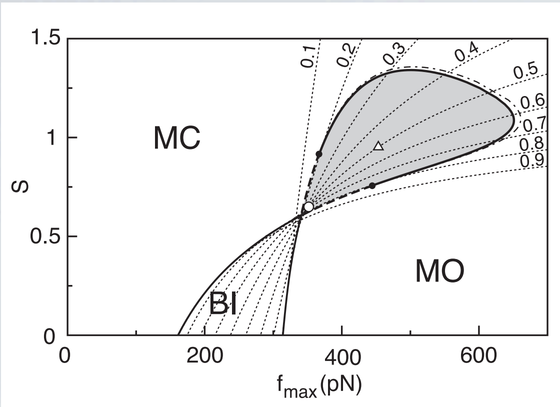


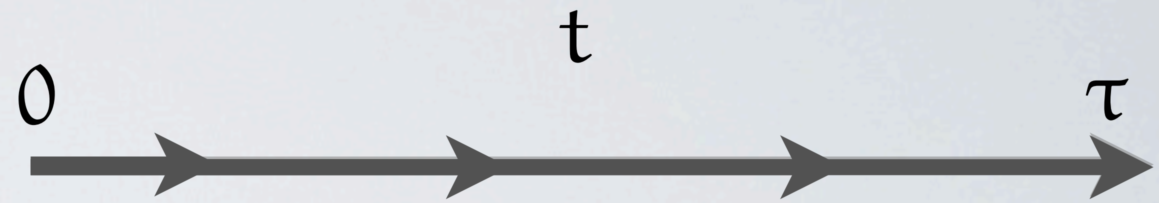
$\tau = 1200\text{s}, f_{acq} = 8.3\text{kHz}$

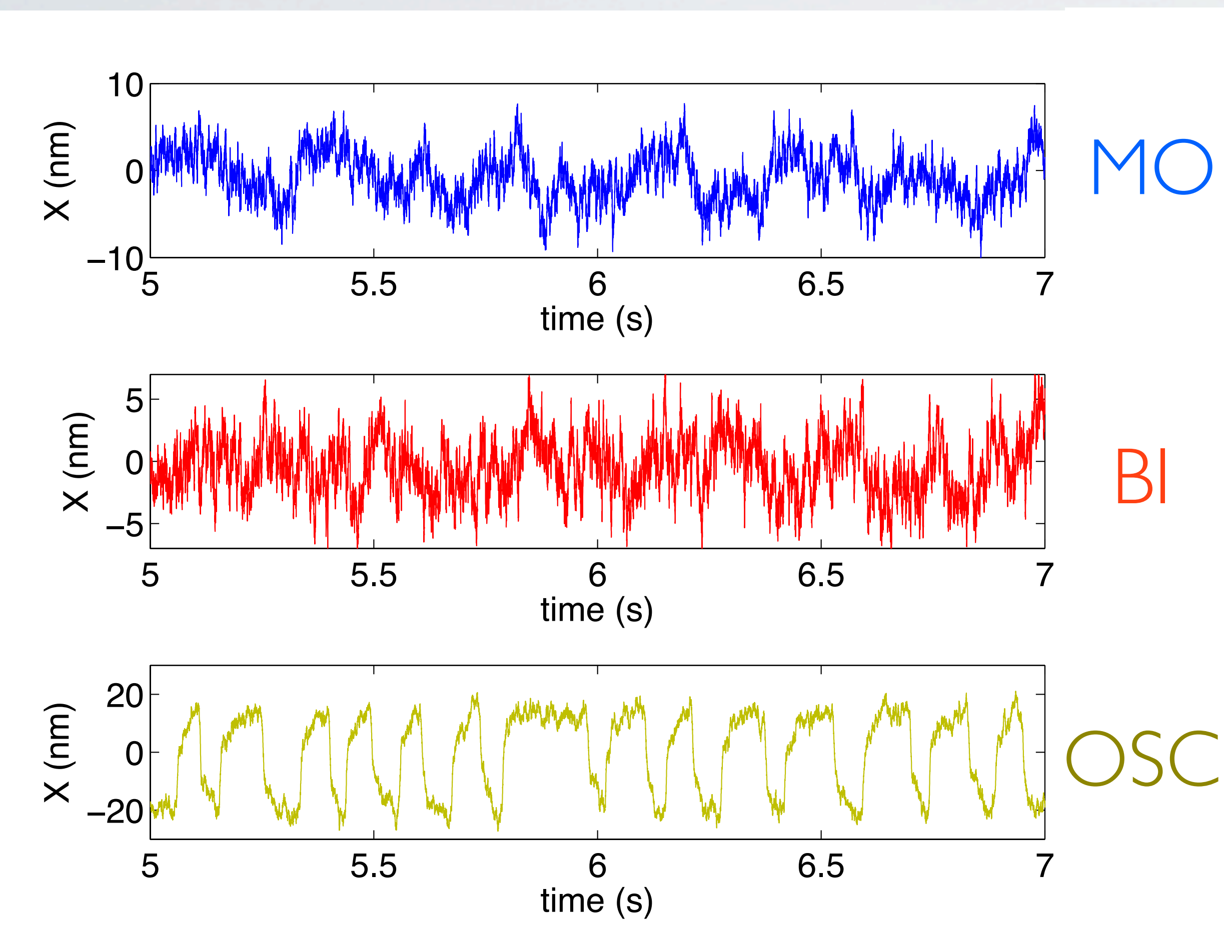
$\dot{d}_{\epsilon,1}, \quad AR(10,50)$

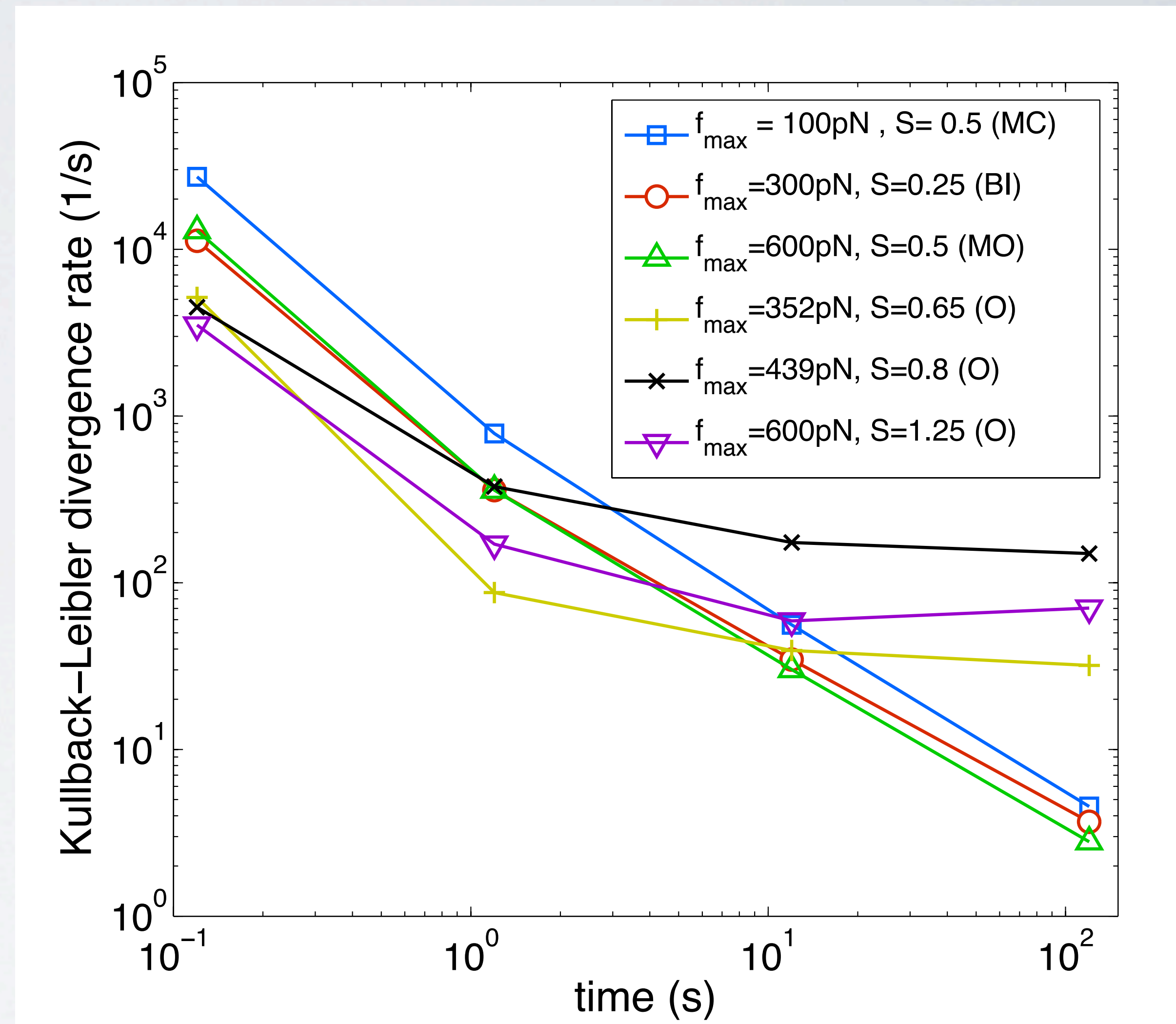
KLD is maximum
at maximum sensitivity

Results : simulations









$$\dot{d}_{\epsilon,1}, \quad AR(10,50)$$

KLD distinguishes active prom passive oscillations

Results : experiments

American bullfrog (Rana catesbeiana)

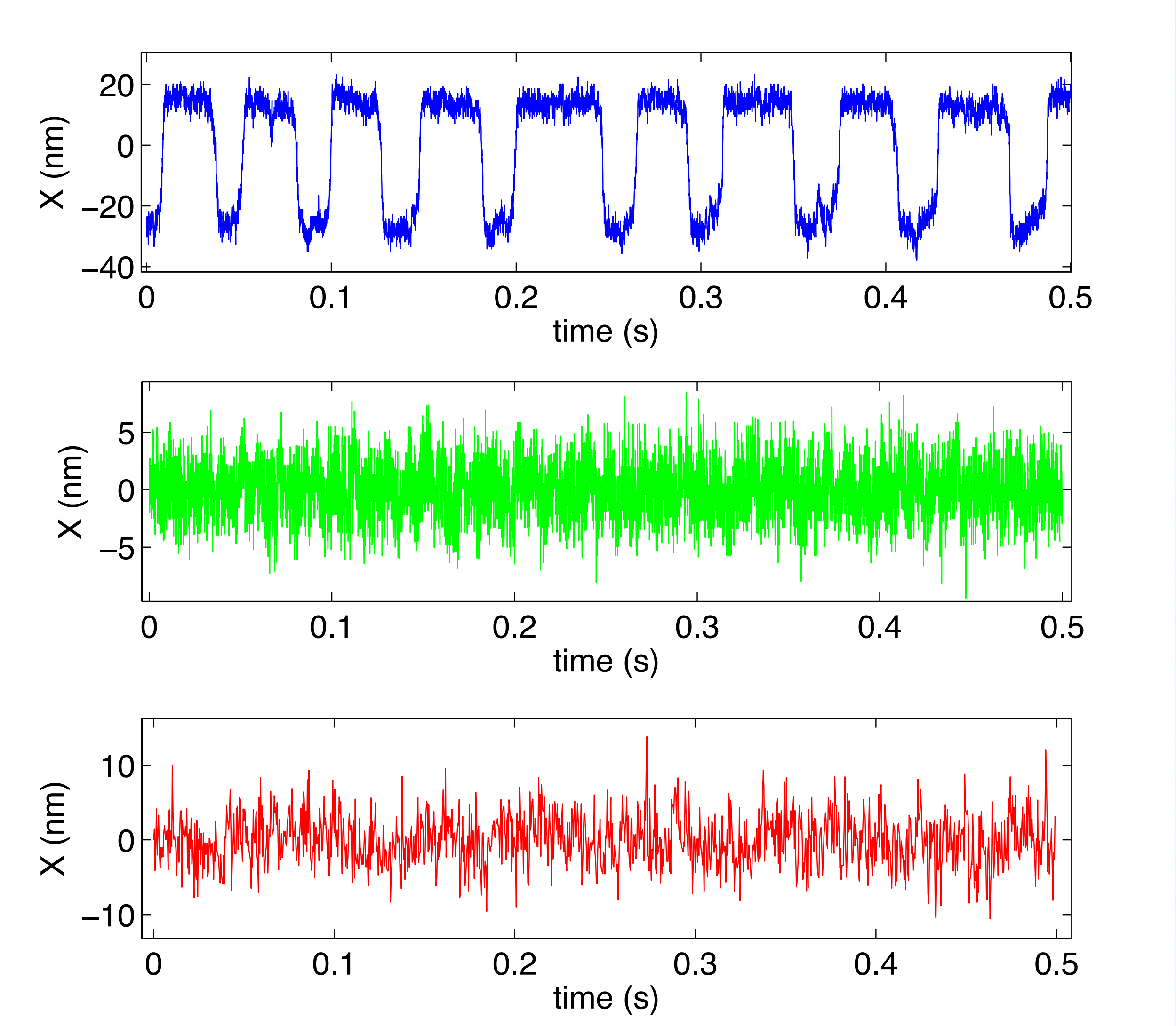
Experiments: P. Martin, J. Barral

Results : experiments

Rana catesbeiana

$\tau \sim 100s$

$f_{osc} = \{8, 15, 20\}$ Hz



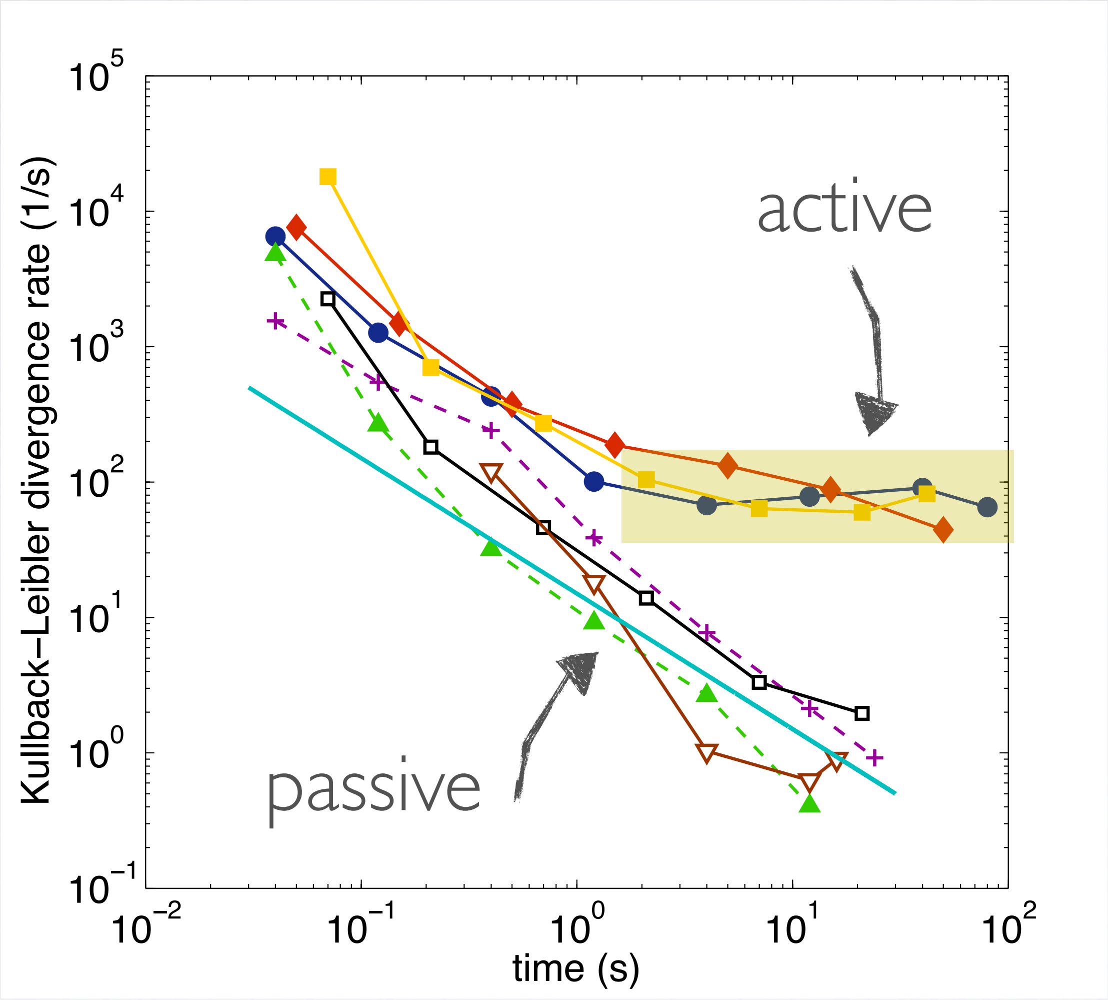
active (alive)

gentamicin (drugged)

passive (dead)

Results : experiments

$0 \quad t \quad \tau$ $\qquad \tau \sim 100s$



$\dot{d}_{\epsilon,1}, \quad AR(10, 50)$

$\dot{d}_{\epsilon,1} \sim 100 s^{-1}$

$\langle W_{diss} \rangle \geq 100 \frac{k_B T}{s}$

Energy dissipation of a single motor

KLD distinguishes active / passive and estimates dissipation

Conclusion

The KLD has potential applications in stationary processes of microscopic **biological** systems:

Detection of bifurcations

Distinction between active and passive oscillations

Estimation of minimum energy dissipation

Thanks for your attention