The role of chaos and noise in hair cell sensitivity

KITP Physics of Hearing
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Phenomenology: Specs for the mechanical detector

sensitivity

0.3 nm displacement

robustness

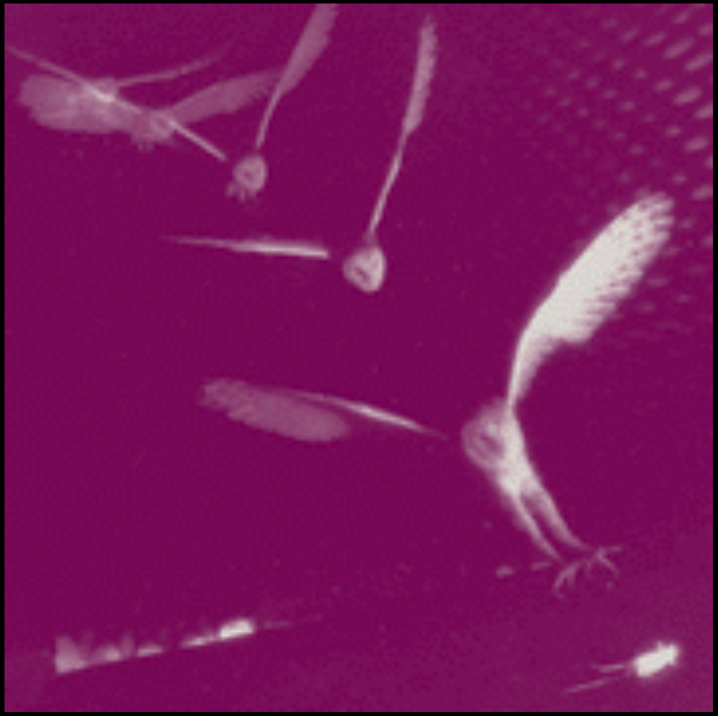
6 orders of magnitude in pressure

temporal resolution

10 μs inter-aural time difference

frequency range

20 Hz – 20 kHz

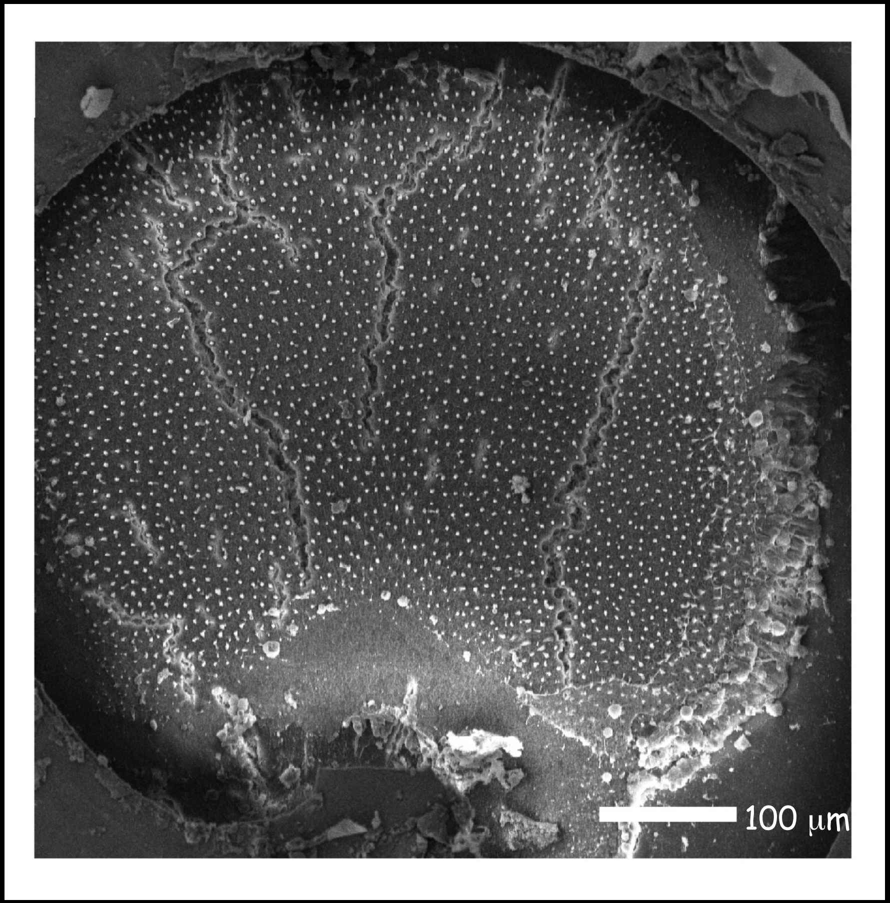


M. Konishi, California Institute of Technology

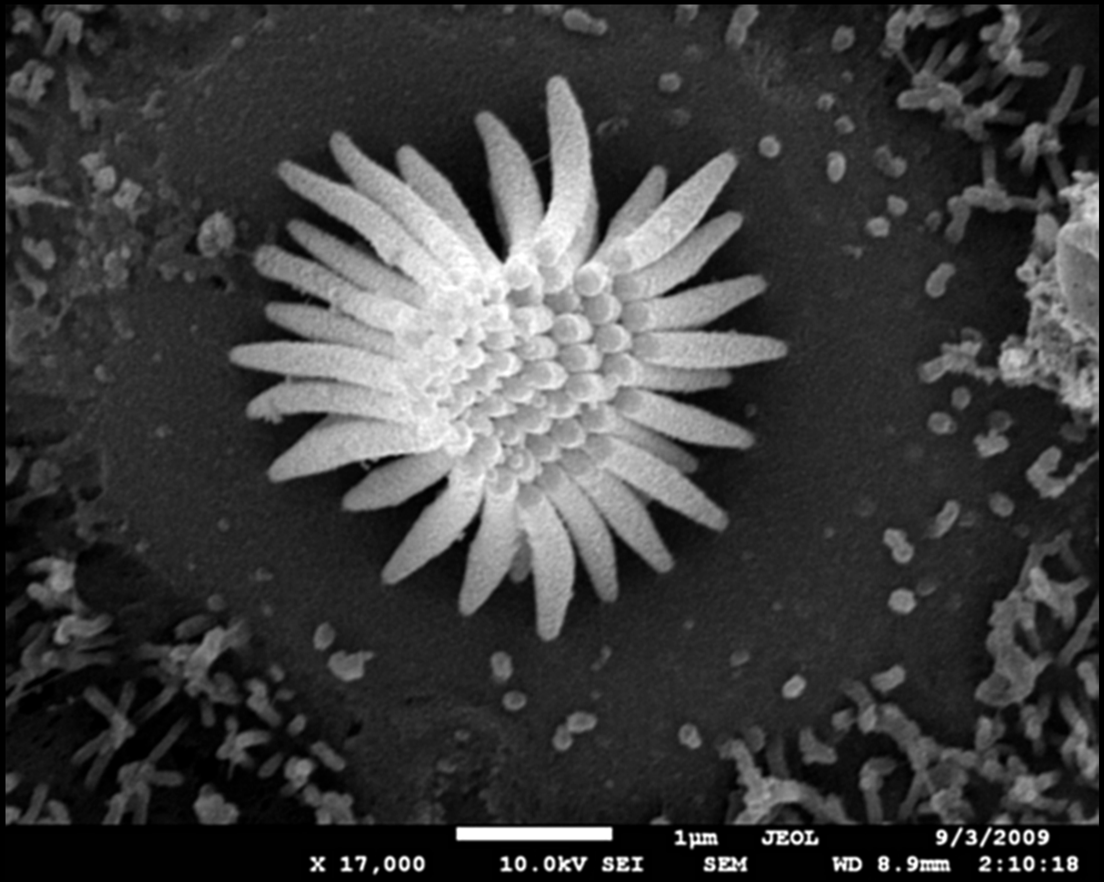
Introduction

North American bullfrog

sacculus, top-down view



hair cell, bullfrog sacculus

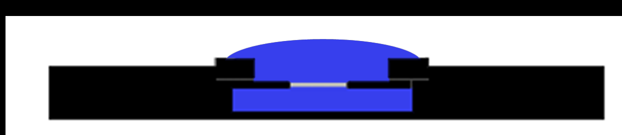


Acoustic isolation booth

Olympus optical microscope

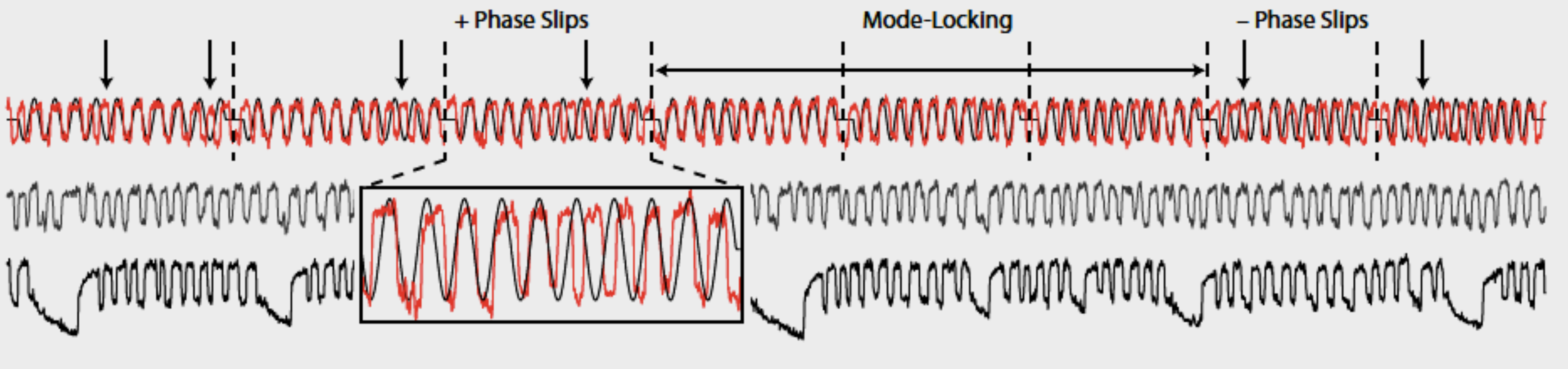
Photron FASTCAM SA1.1

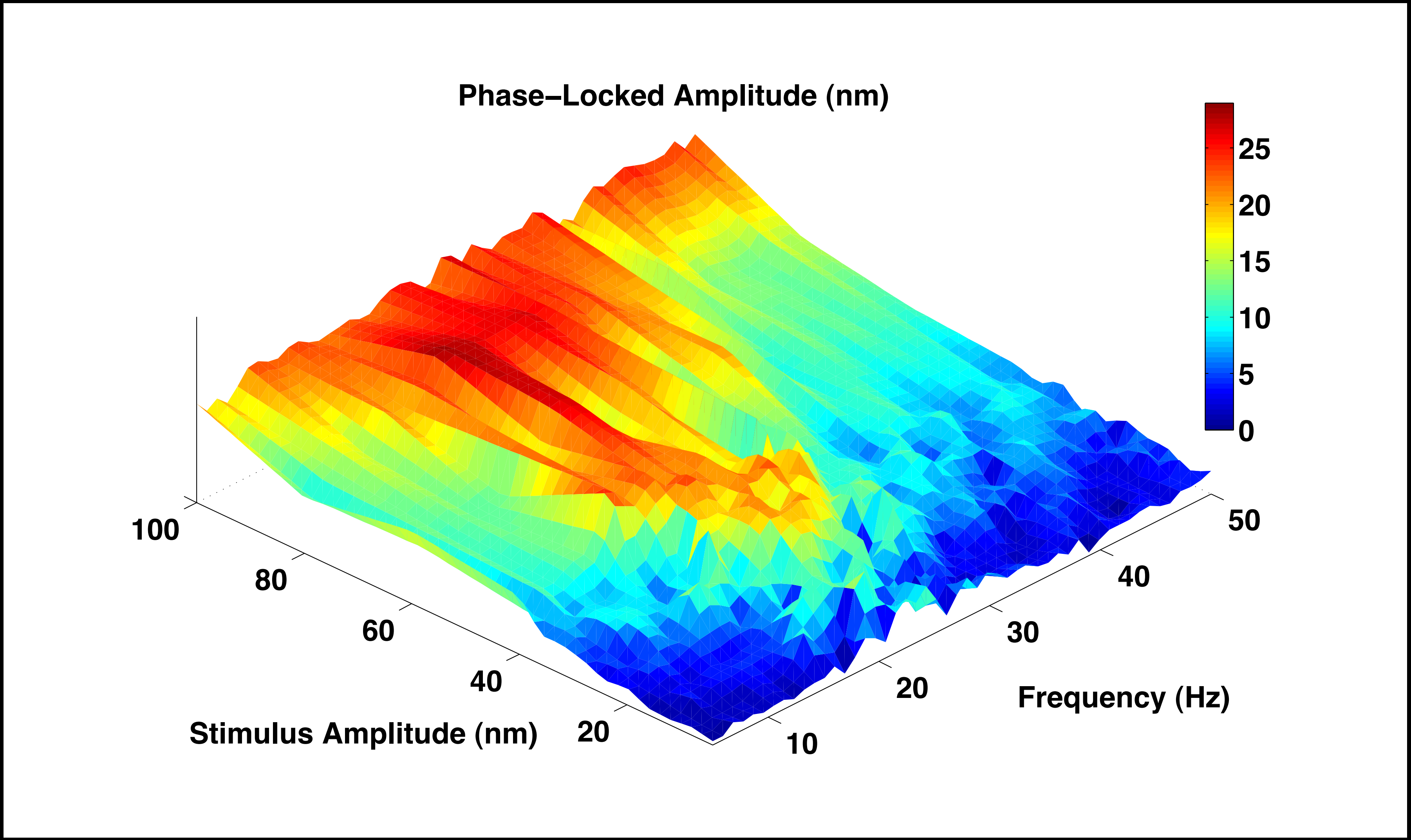
1024 x 1024 pixels
5400 fps



2-compartment chamber
artificial perilymph and endolymph

A small mechanical stimulus can entrain spontaneous oscillations.

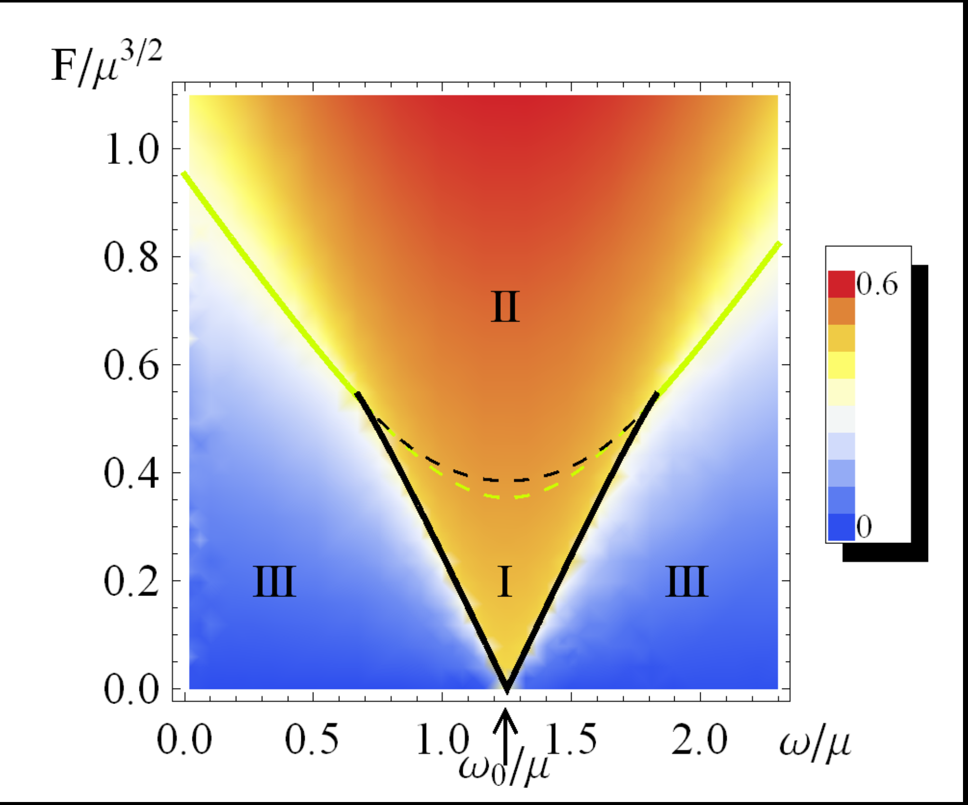




Arnold Tongue (1:1 mode-locking)

$$\dot{z} = (\mu + i\omega_0)z - |z|^2 z + Fe^{i\omega t}$$

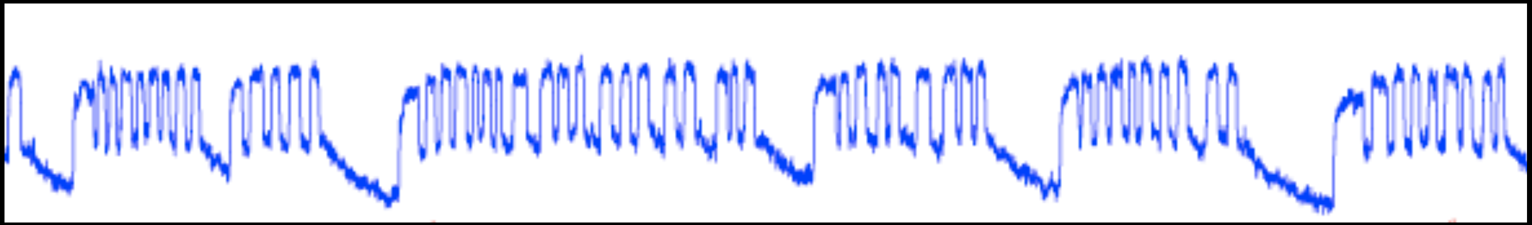
Theoretical phase diagram



The system can support a SNIC (saddle-node on invariant circle), a supercritical Hopf, or a multi-critical (Bogdanov-Takens) bifurcation.

Feedback process

Bursting behavior



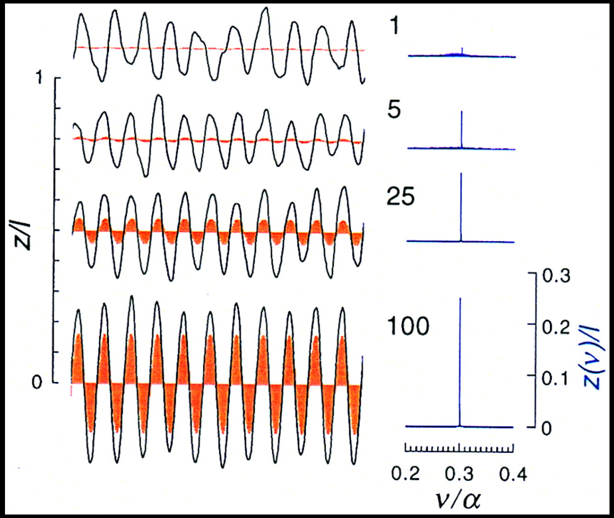
Limit cycle oscillations are interspersed with quiescent intervals. This indicates more complex dynamics than a simple limit cycle.

Camalet et al proposed that the system is self-tuned to the vicinity of the critical point.

Calcium feedback maintains the hair cell near the Hopf bifurcation, on the oscillatory side.

$$\frac{1}{C}\frac{\partial C}{\partial t} = \frac{1}{\tau}\left(\frac{x^2}{\delta^2} - 1\right)$$

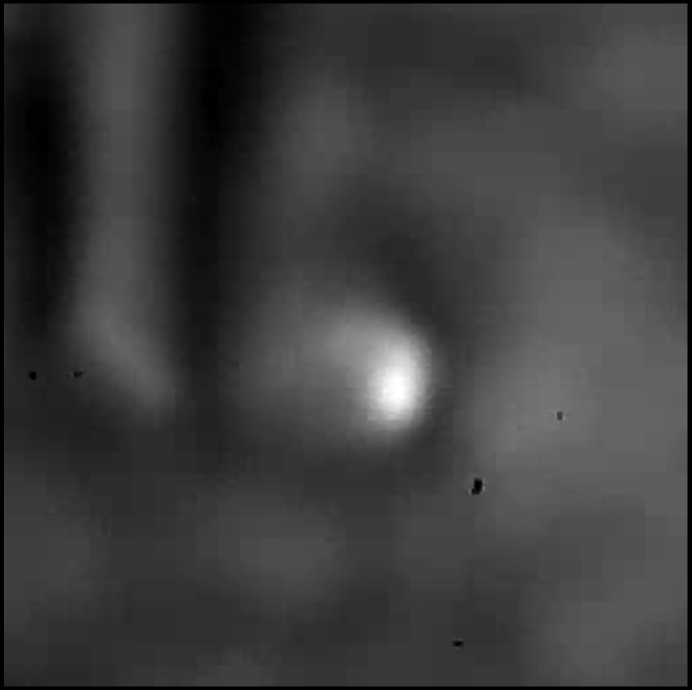
self-tuned critical oscillations



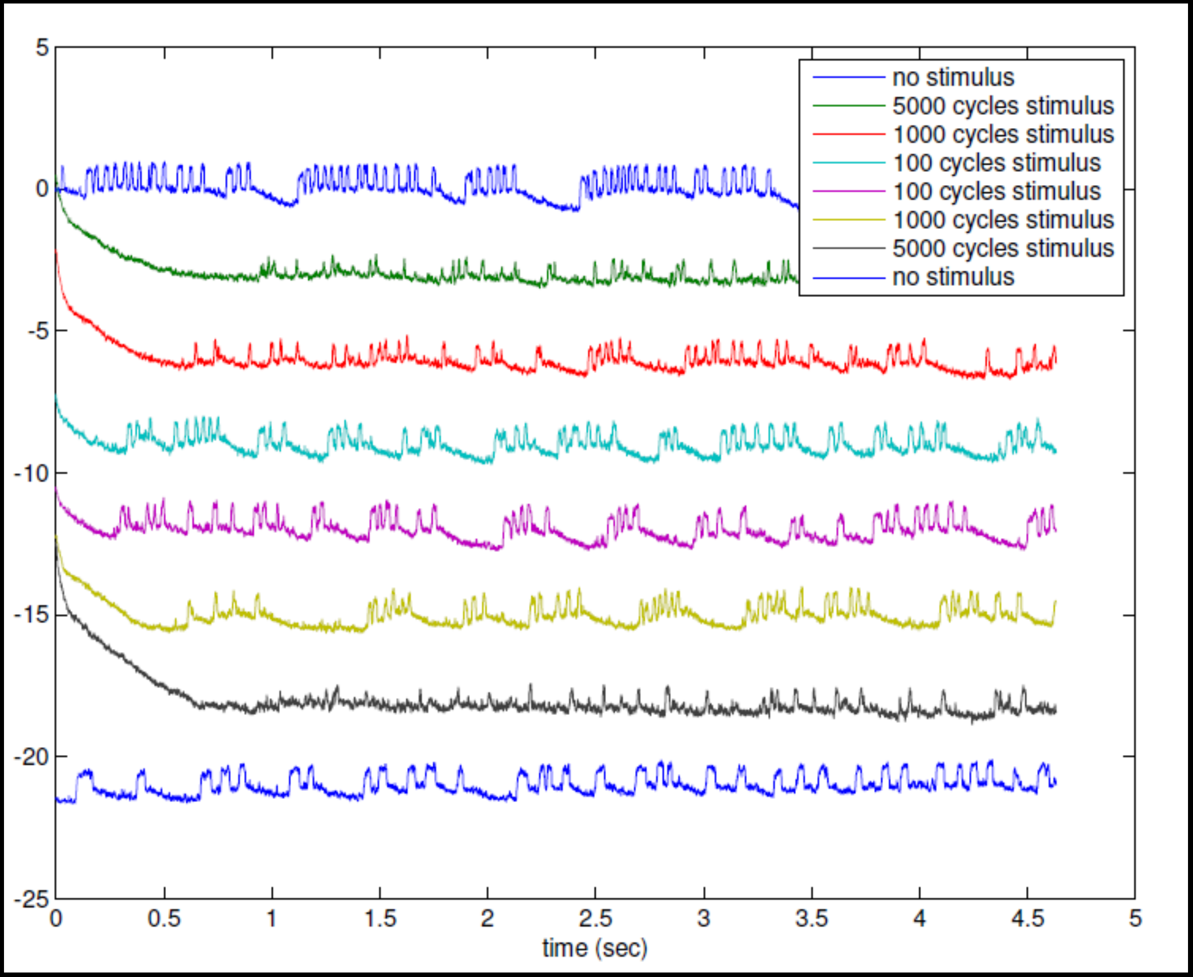
Response of a system with n = 2,000 motors to a sinusoidal force at frequency ν = 0.3α, close to the hair bundle's characteristic frequency.

Camalet, S. et al, Proc. Nat. Acad. Sci. 97, 3185 (2000)

Experiments on dynamic feedback



Over-stimulation leads to transient suppression of the spontaneous oscillation.

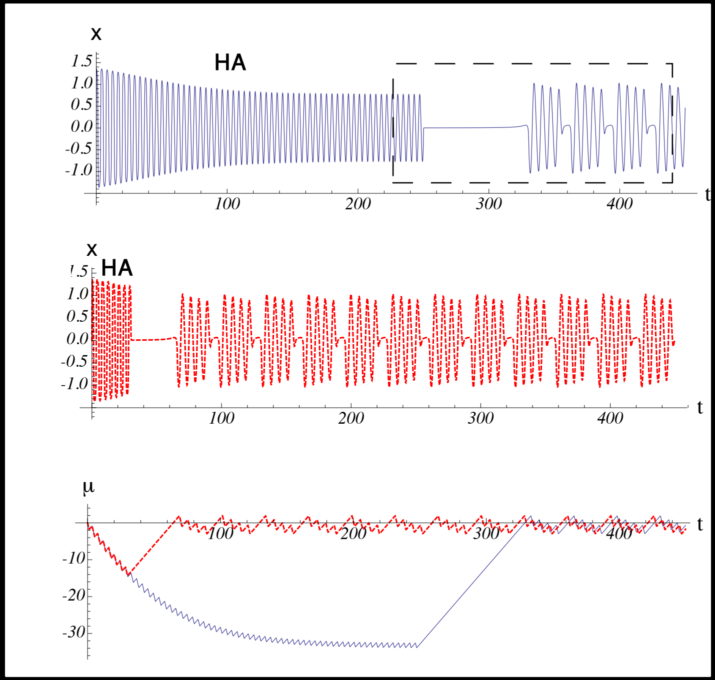


Subcritical Hopf bifurcation with a feedback on the control parameter

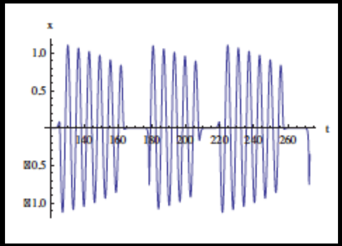
$$\frac{dz}{dt} = z\left(\mu - i\omega_0 + A|z|^2 - B|z|^4\right) + f_D + f_A \cos\left(\omega_f t\right)$$

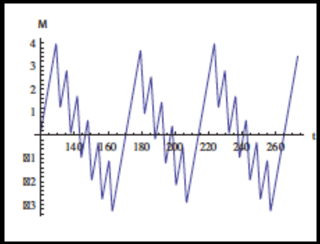
$$\frac{d\mu}{dt} = k_{on} - k_{off}\Theta(x - x_0)$$

recovery from overstimulation



bursting behavior

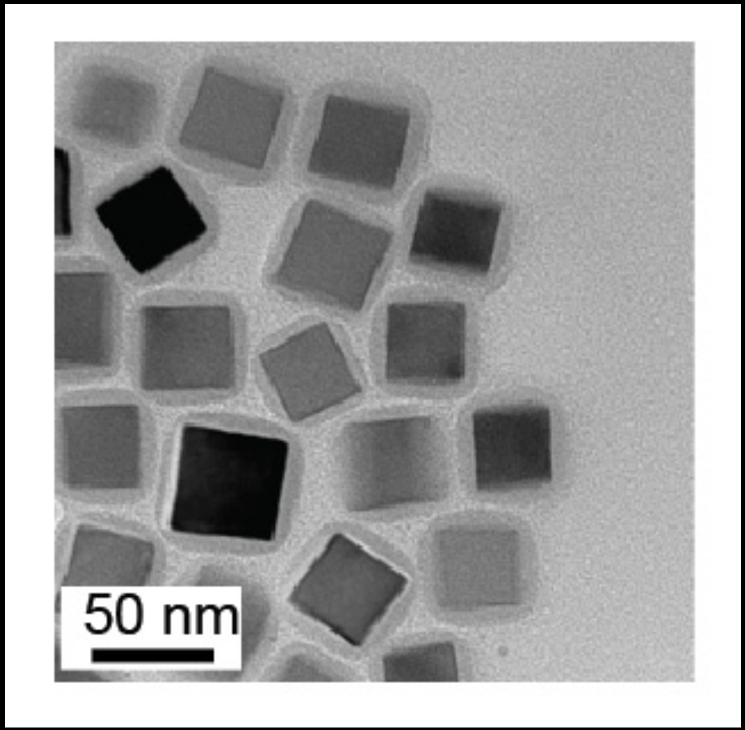


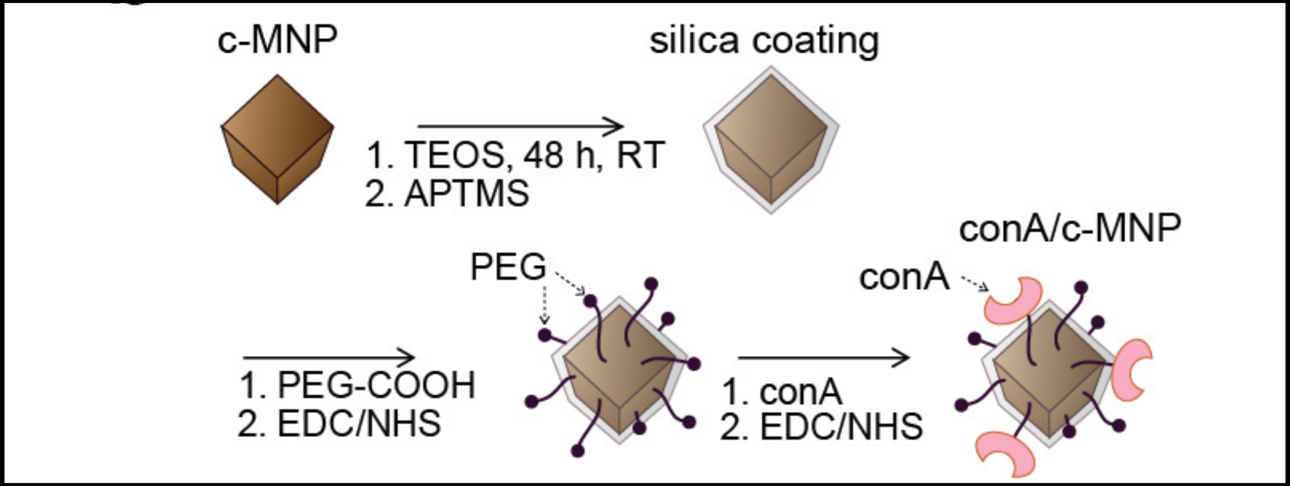


In this regime, feedback tunes the system away from criticality, in the limit cycle regime.

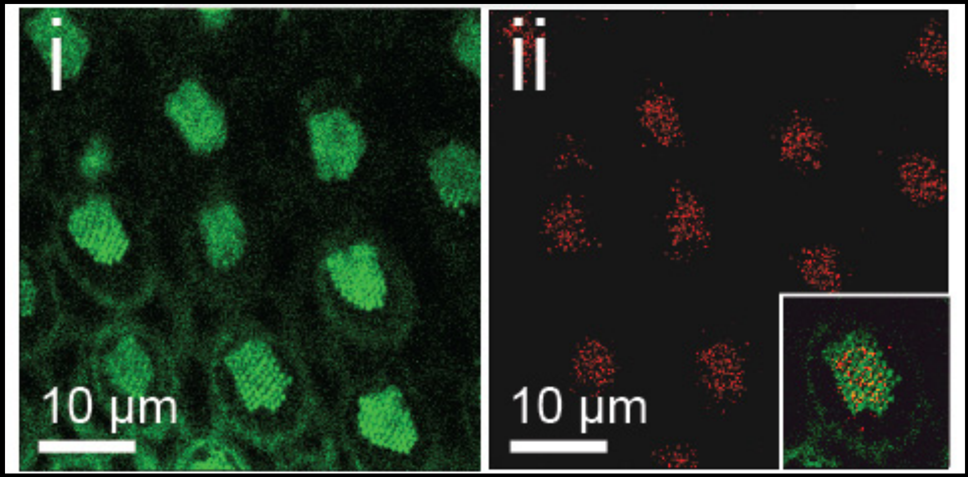
High-order mode-locking

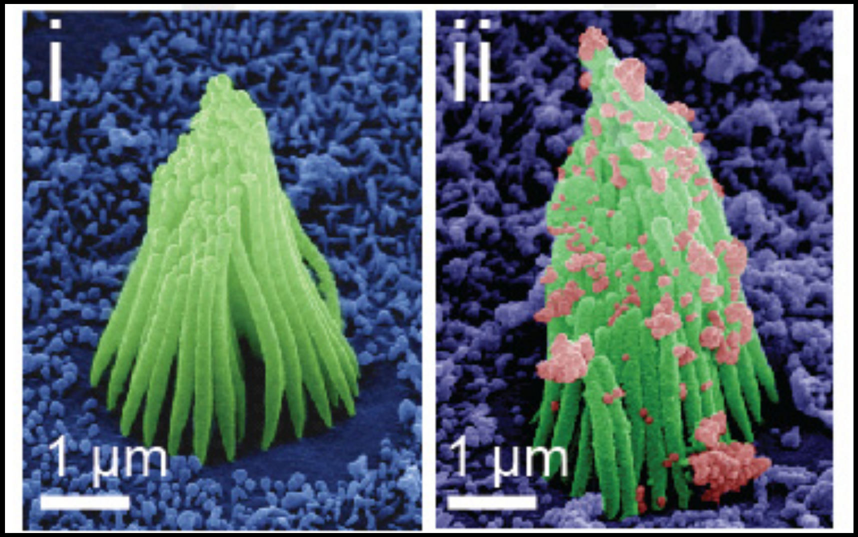
magnetic nanoparticles

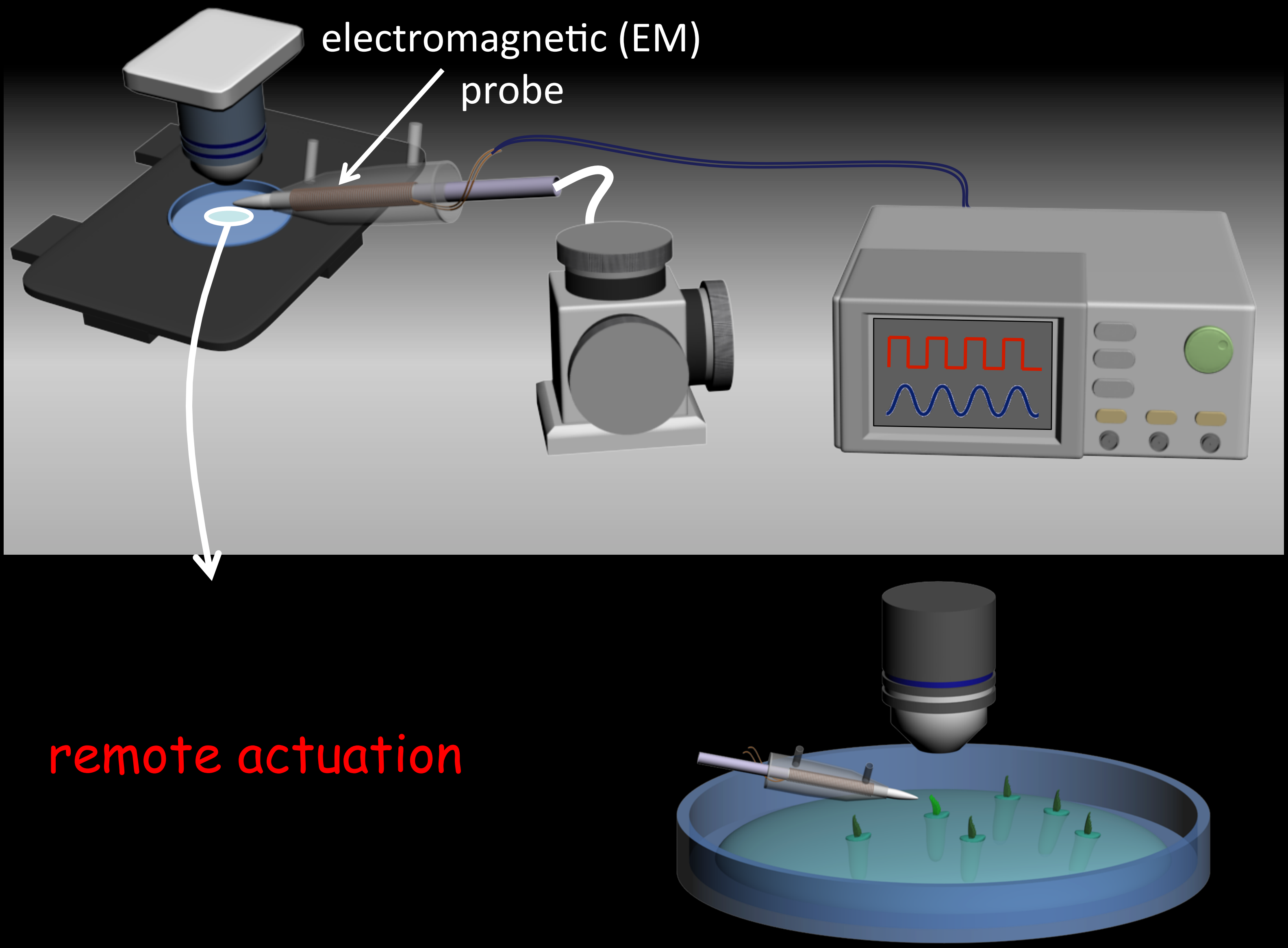




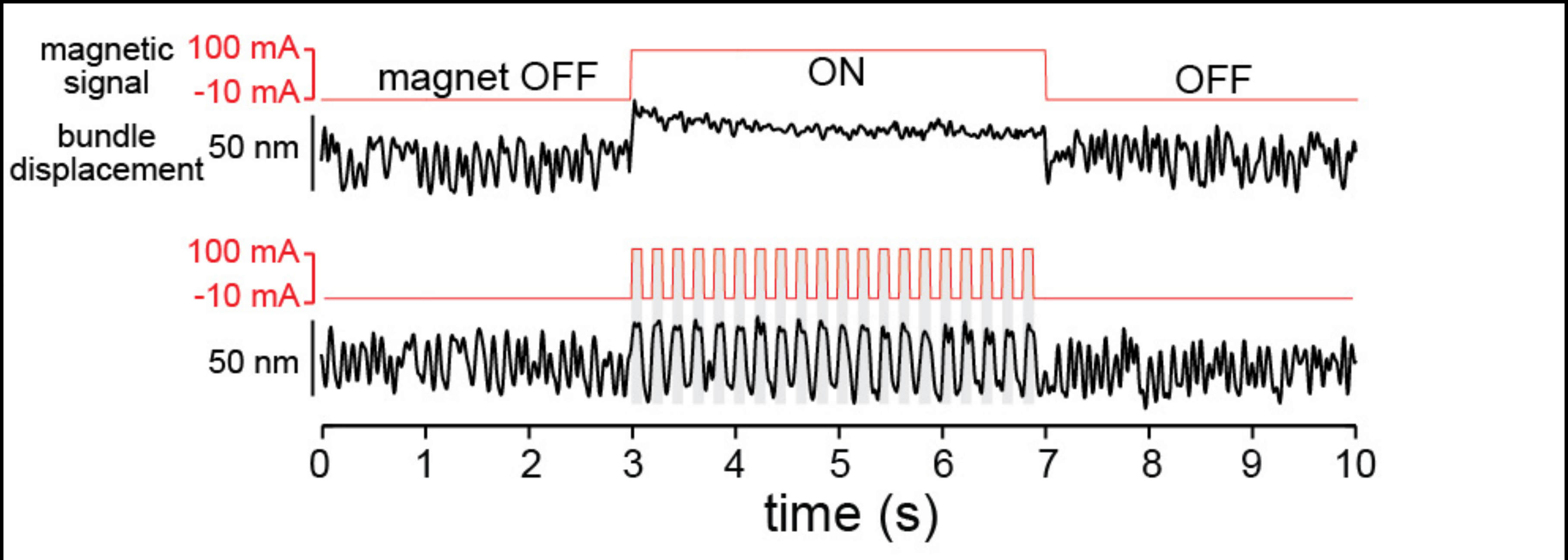
attachment to hair bundles



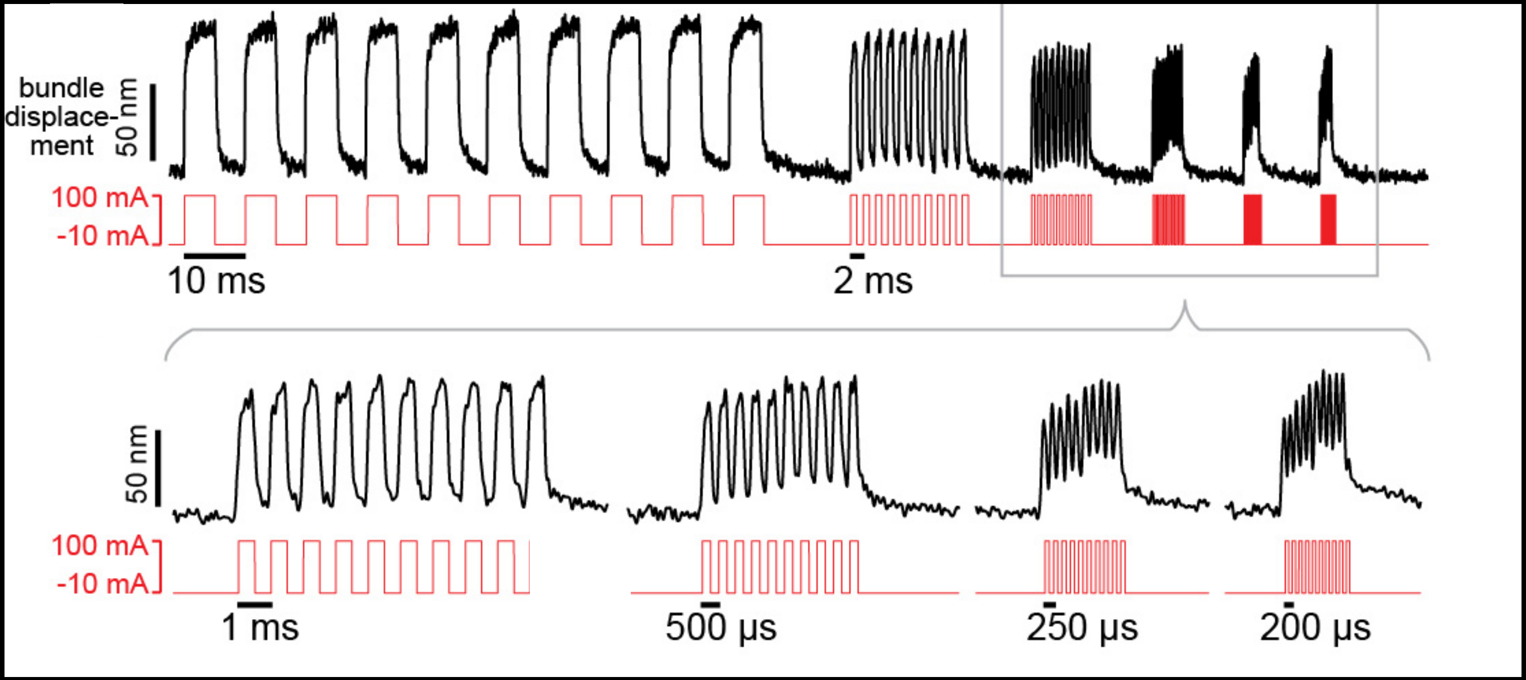



electromagnetic (EM)
probe
remote actuation

bundle response

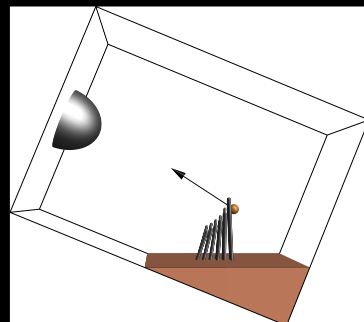


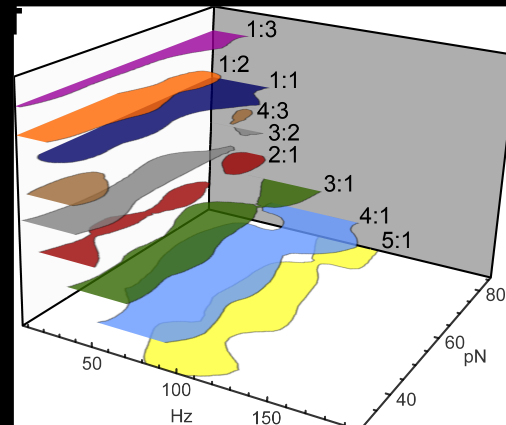
High-frequency stimulus

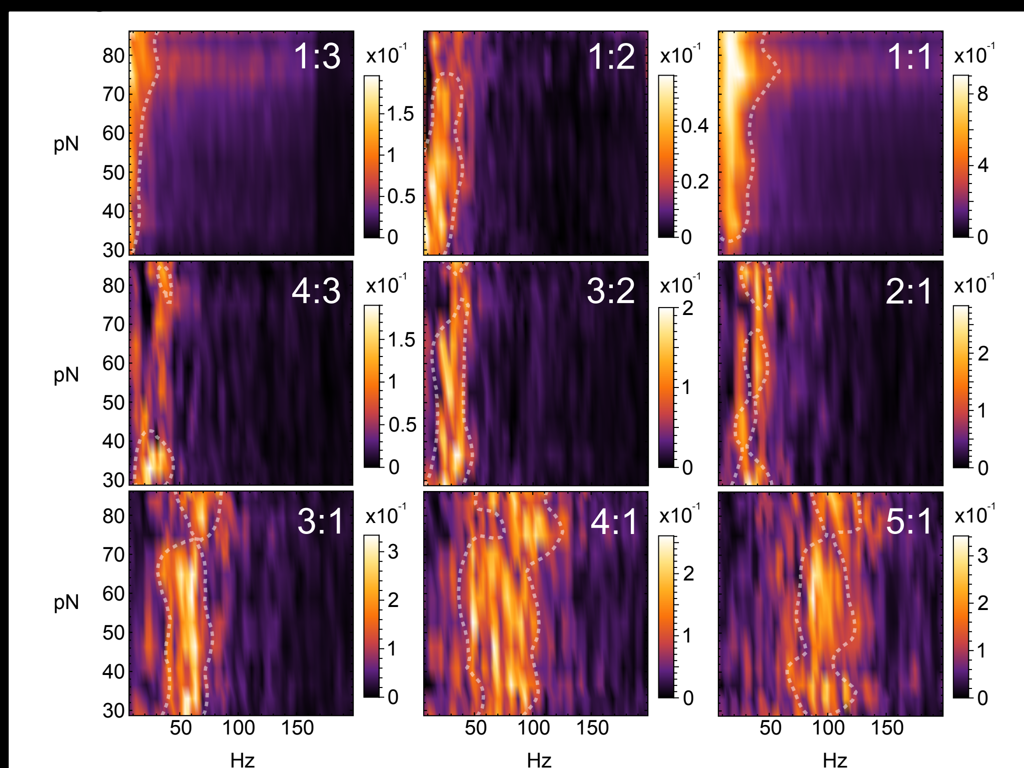


Lee et al, *ACS Nano*, **8**, 6590 (2014)

Phase-locked regimes at n:m frequency ratios form highly overlapping Arnold Tongues.

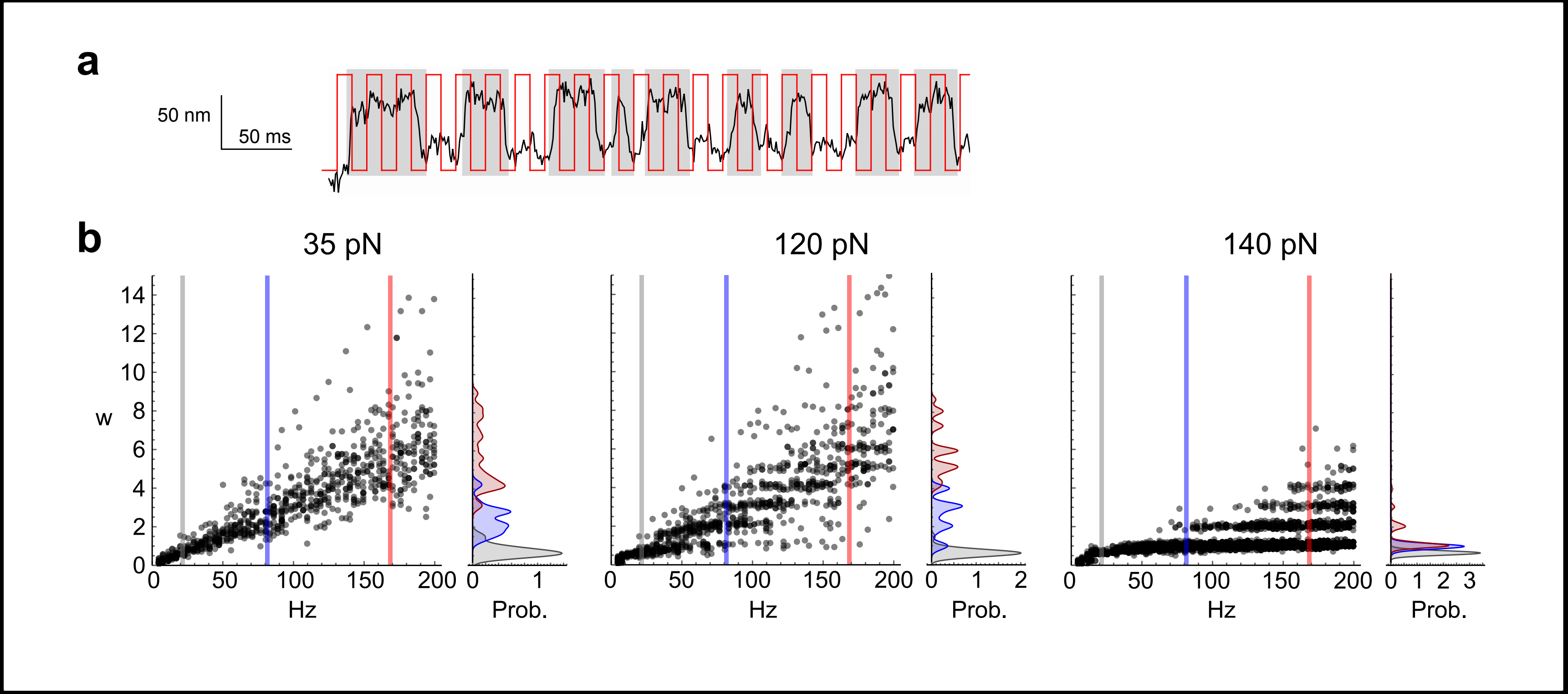






Levy et al, *Sci. Rep.*, **6**, 39116 (2016)

Ensemble response to higher frequency stimuli



The hair bundle synchronizes to the signal at different frequency ratios, flickering between different modes of entrainment.

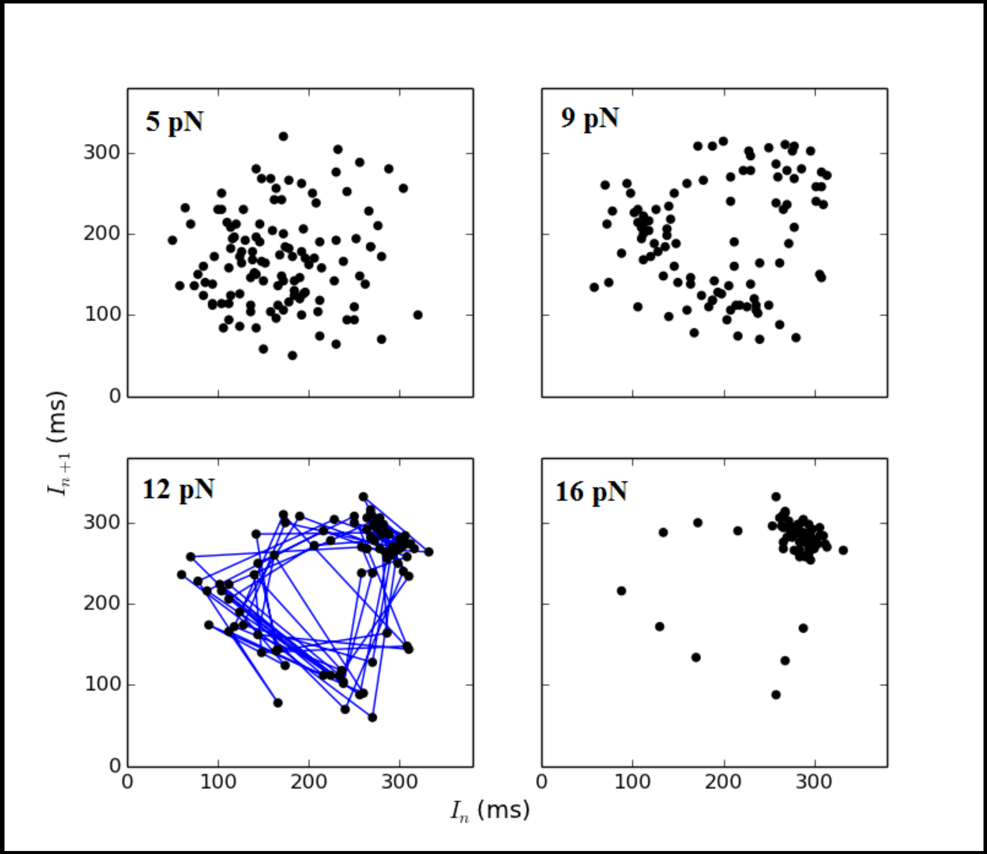
Chaos in bundle dynamics

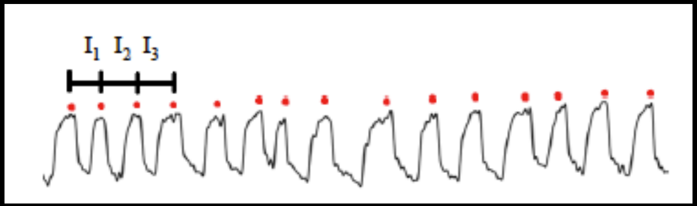
Do hair bundle dynamics exhibit chaos?

If so, how is it affected by external stimuli?

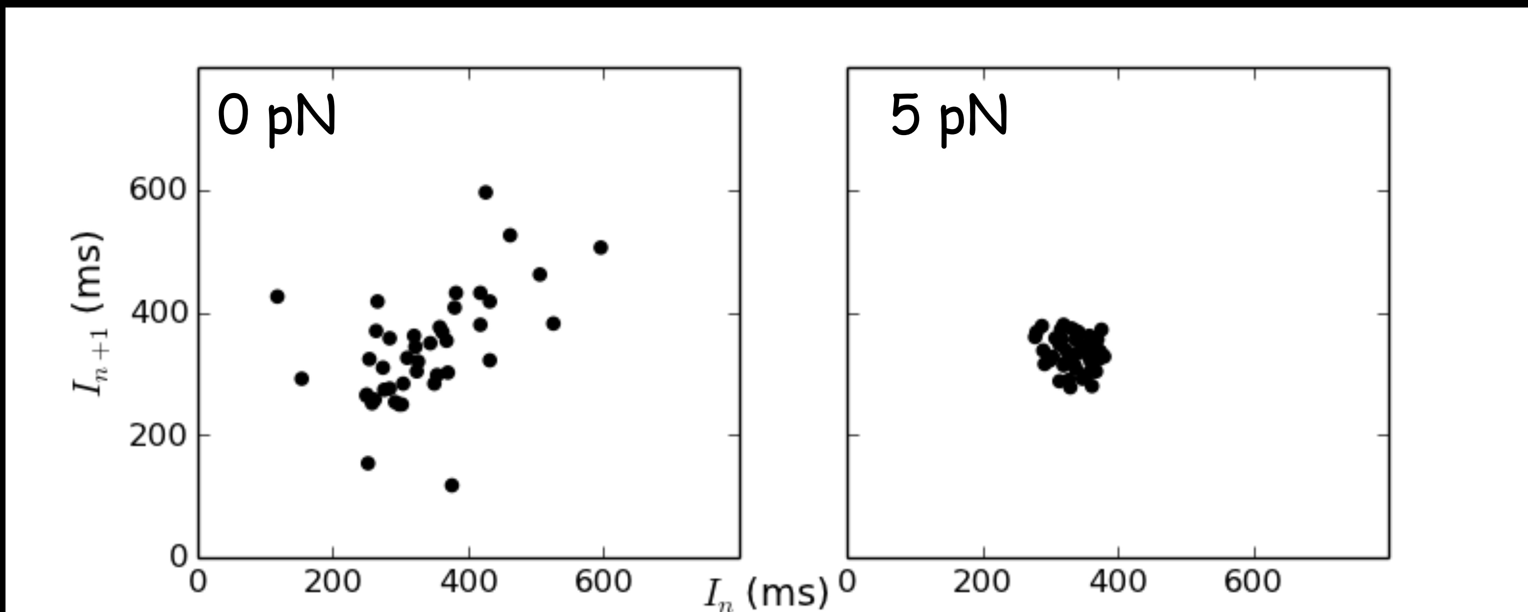
Does it aid in achieving sensitivity of detection?

Poincare maps

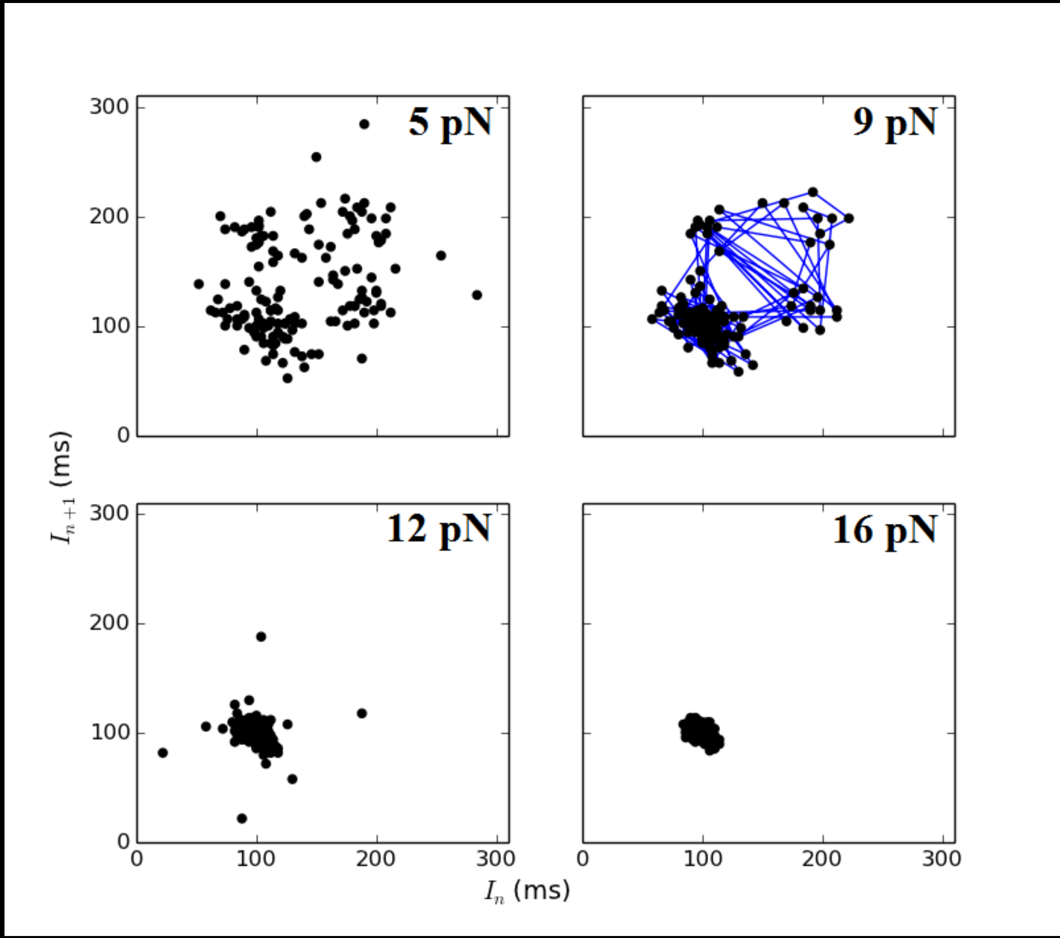




below resonance:
quasiperiodic
transition



on resonance

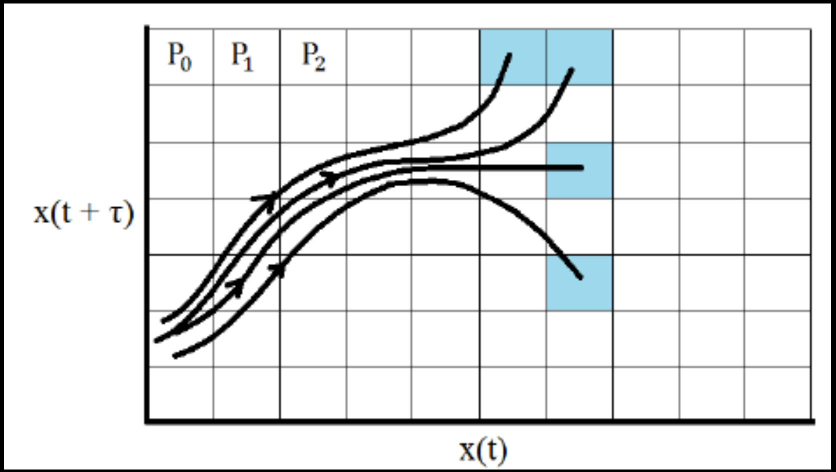


above resonance: multimode locking

Kolmogorov entropy

$$S(t) = -\sum_{n=0}^{all\ boxes} P_n \log(P_n)$$

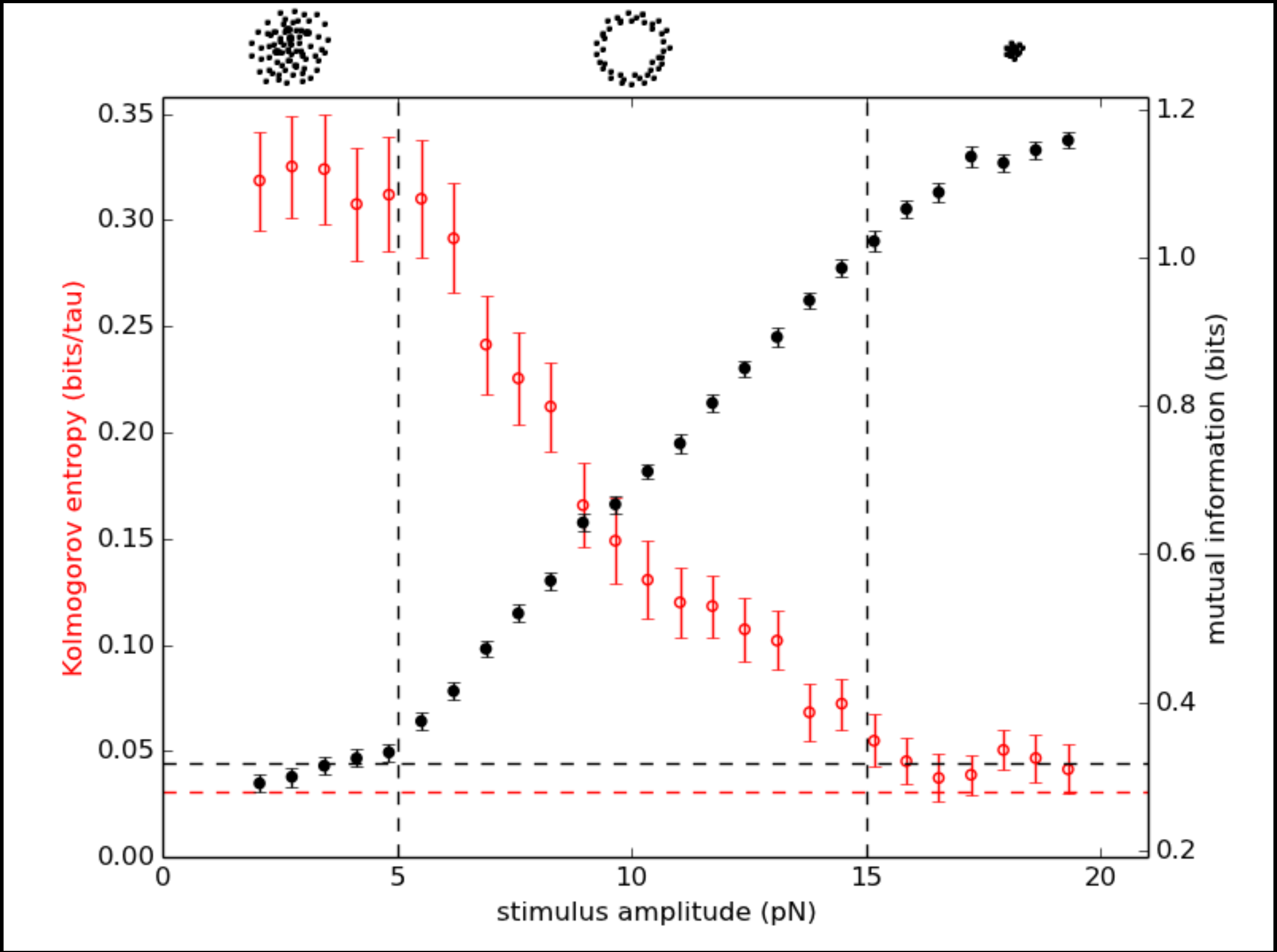
$$K = \langle \frac{dS(t)}{dt} \rangle$$



K- entropy measures the degree of chaos in the system. It corresponds to the sum of positive Lyapunov exponents.

Mutual information between a signal (X) and response (Y)

$$M_{XY} = \sum_{x \in X} \sum_{y \in Y} P(x,y) \log\left(\frac{P(x,y)}{P(x)P(y)}\right)$$



Kolmogorov entropy (bits/tau)
mutual information (bits)
stimulus amplitude (pN)
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0.35
0.2
0.4
0.6
0.8
1.0
1.2
0
5
10
15
20

Experimental findings

Actively oscillating hair bundles exhibit a chaotic attractor.

Chaoticity is reduced by the application of a signal. The steepest reduction of Kolmogorov entropy and steepest gain in mutual information is observed in the transition from chaos to regular limit cycle.

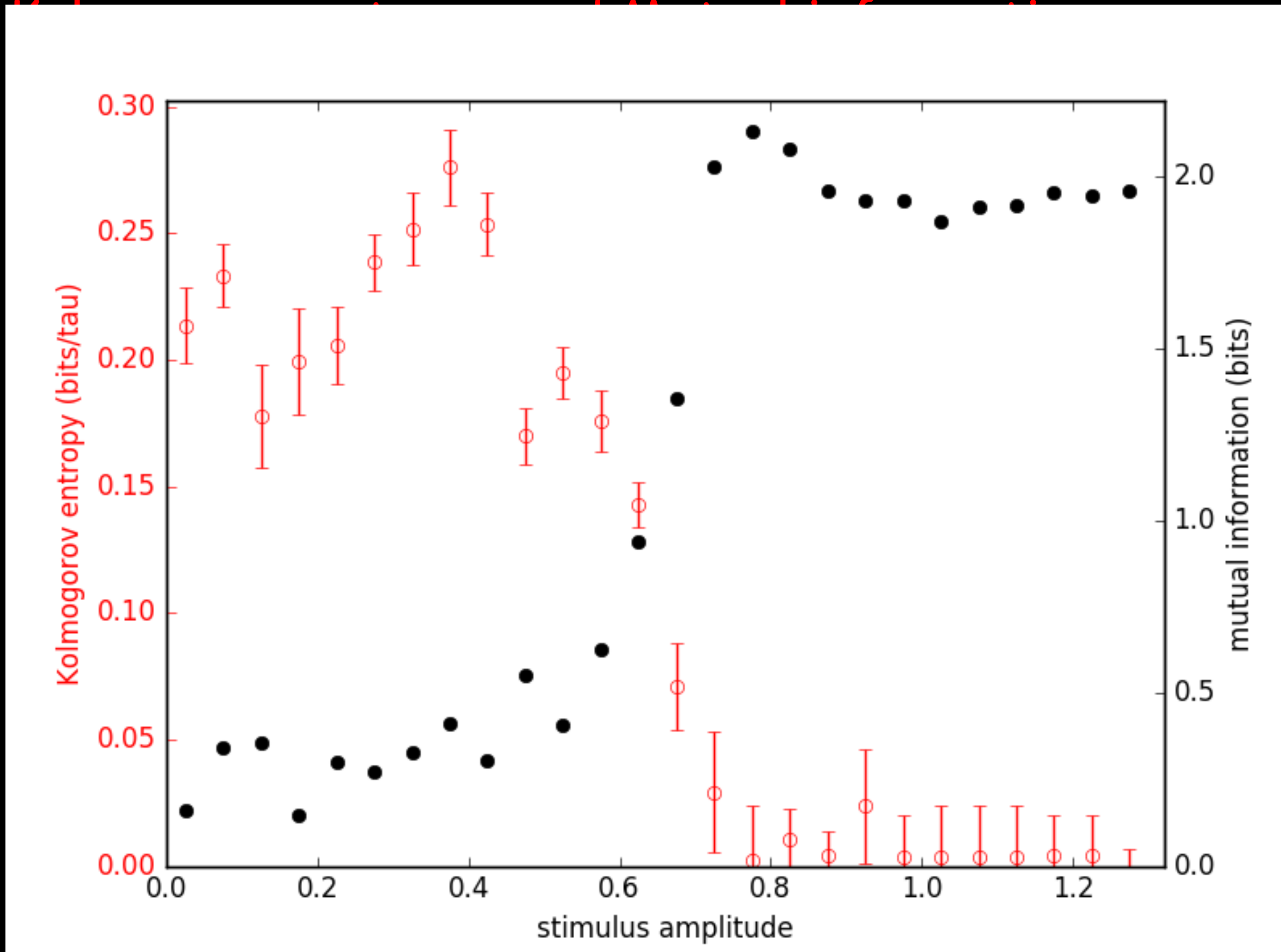
Theoretical model

$$\frac{dz}{dt} = z(\mu - i\omega_0 + A|z|^2 - B|z|^4) + f_A \cos(w_d t)$$

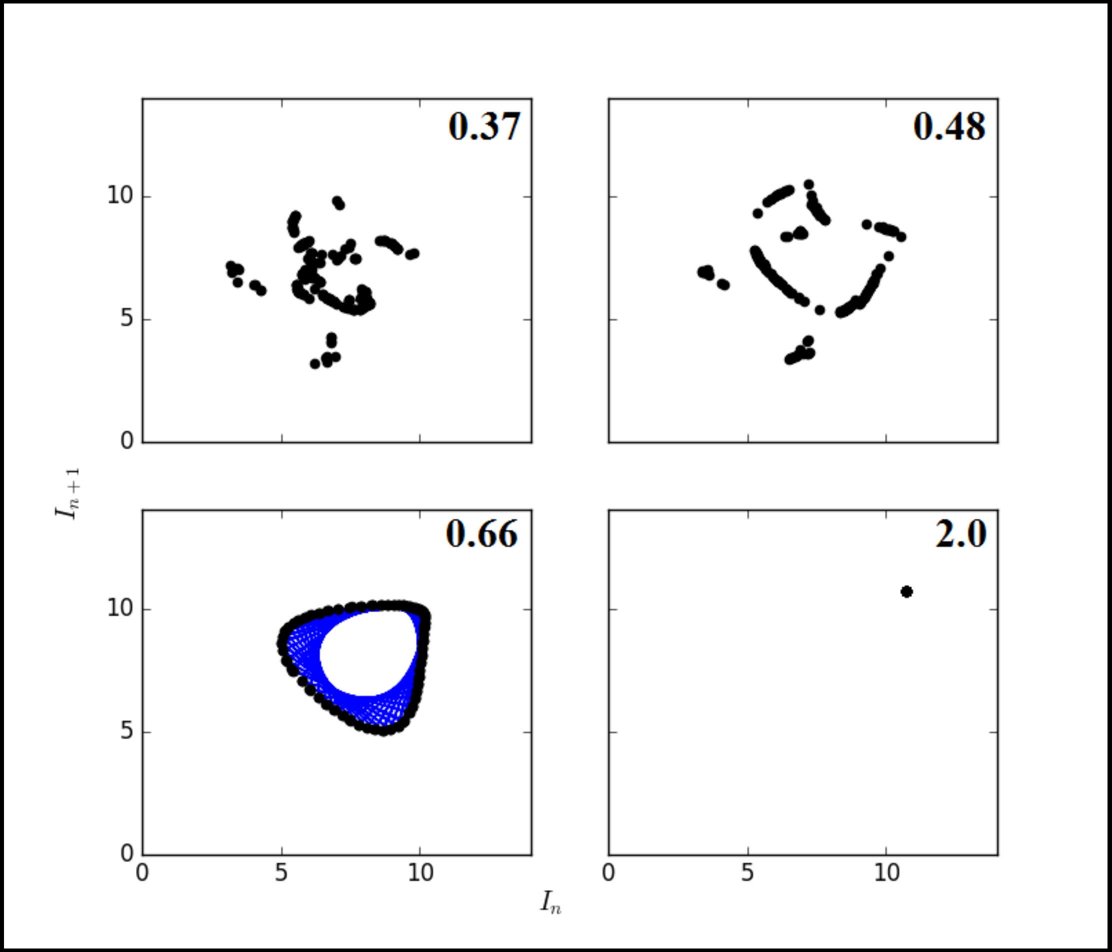
$$\frac{d\mu}{dt} = k_{on} - k_{off}\Theta(x - x_0) + f_A$$

Does this simple model capture the chaotic structure of the measured bundle dynamics?

K-entropy and MI: numerical simulations



Poincare maps: numerical simulations

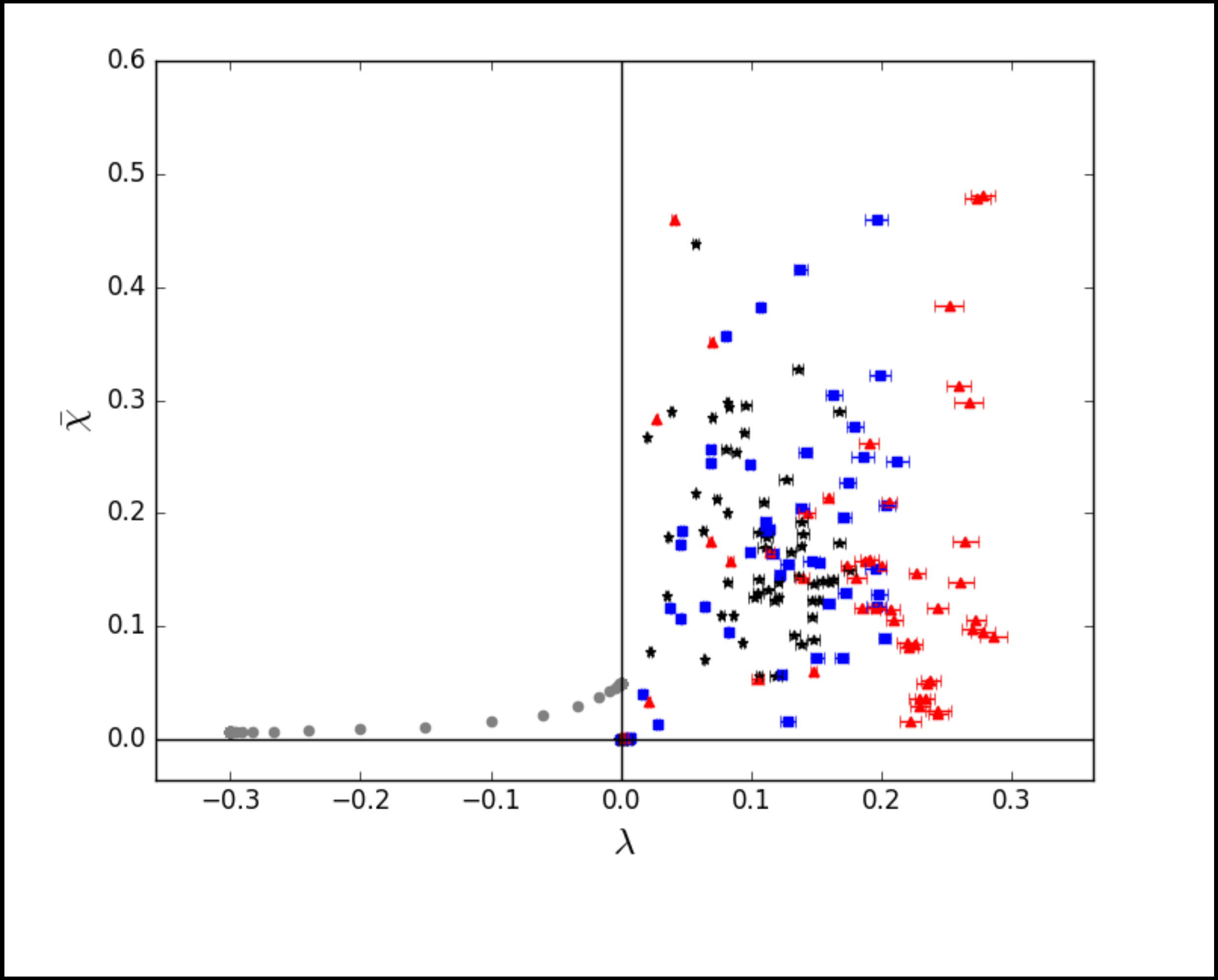


increasing stimulus amplitudes, below resonance

How does chaos affect the sensitivity of response?

-Vary parameters in the model, and determine the Lyapunov exponents. This provides a simple metric for the degree of chaos in the bundle.

-Calculate the sensitivity of the response χ, which measures the phase locked amplitude of the response, for a *given* forcing strength.



High gains are observed even at extremely small forcing amplitudes ($f_A=10^{-5}$). Blue, red, and black points correspond to variations in parameters k_{on}, k_{off}, and x_o. Grey points represent variations in *A*, in the limit cycle regime. Plot shows scaled sensitivity, defined as $|\chi-\chi_o|/\chi_o$.

Summary

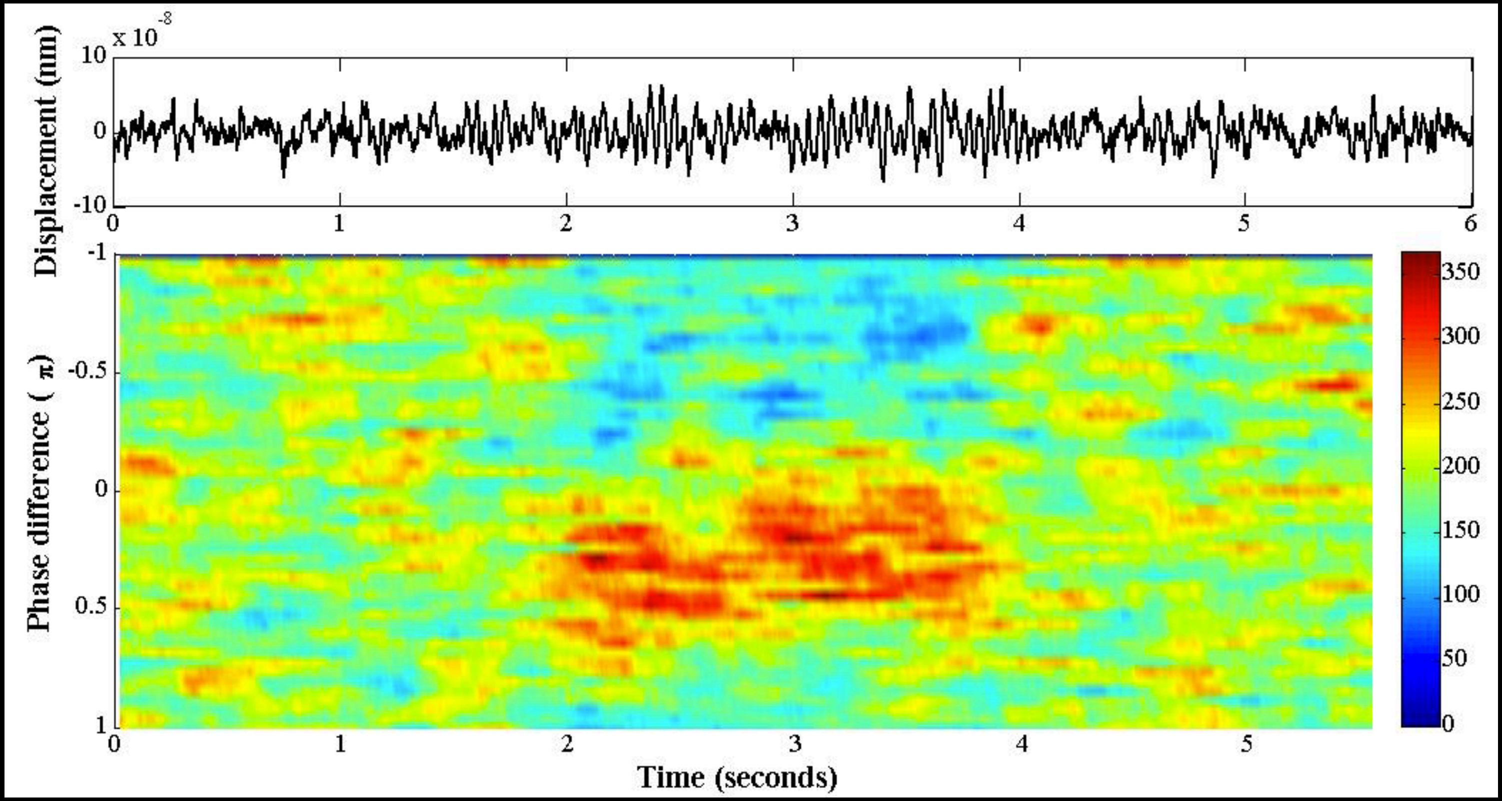
Active bundle motility exhibits chaos.

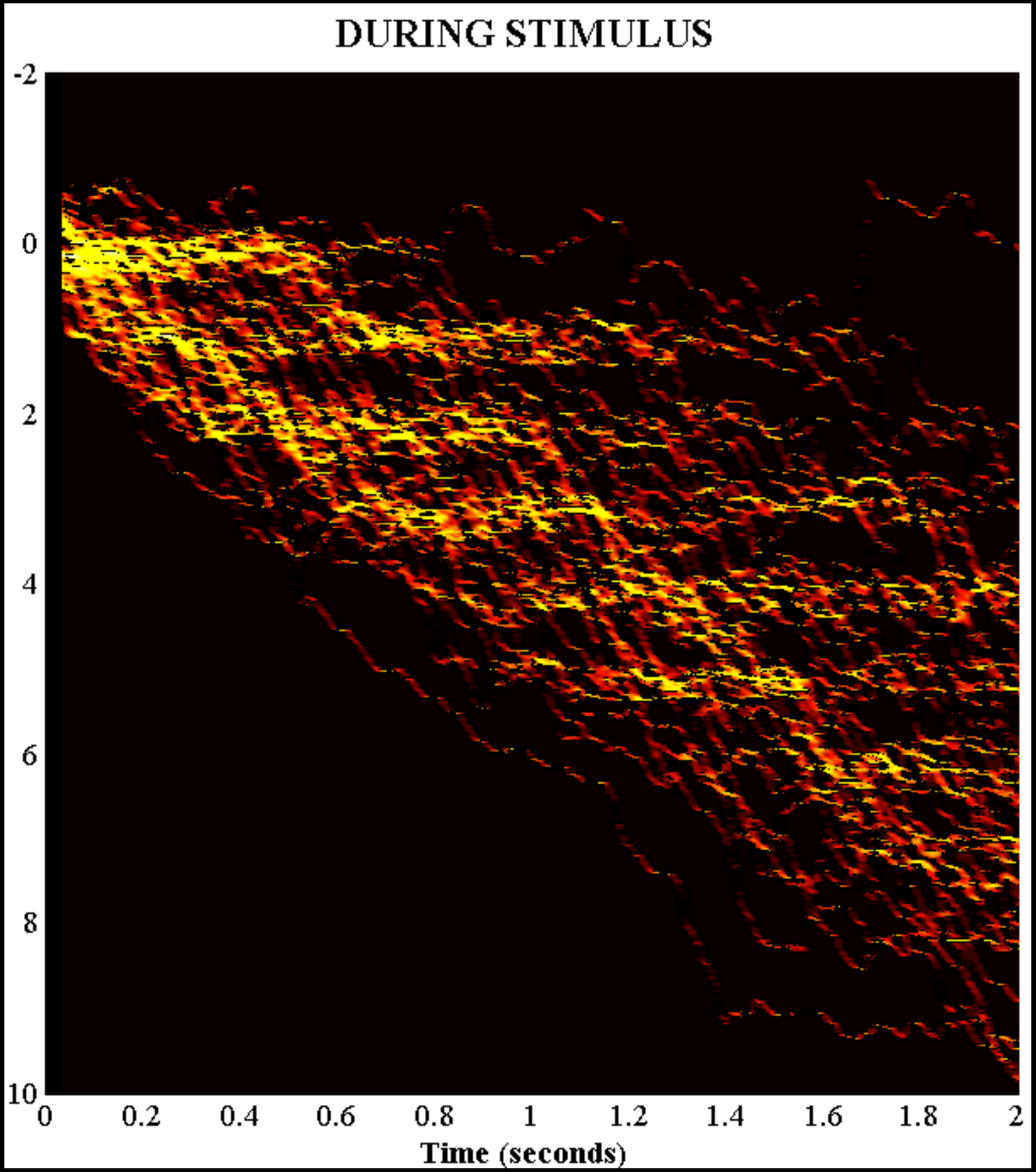
Degree of chaos is reduced by the application of an external signal. The quasi-periodic transition from chaos corresponds to the steepest gain in mutual information.

Numerical simulations indicate that weakly chaotic regime could be highly sensitive.

Effects of stochastic noise

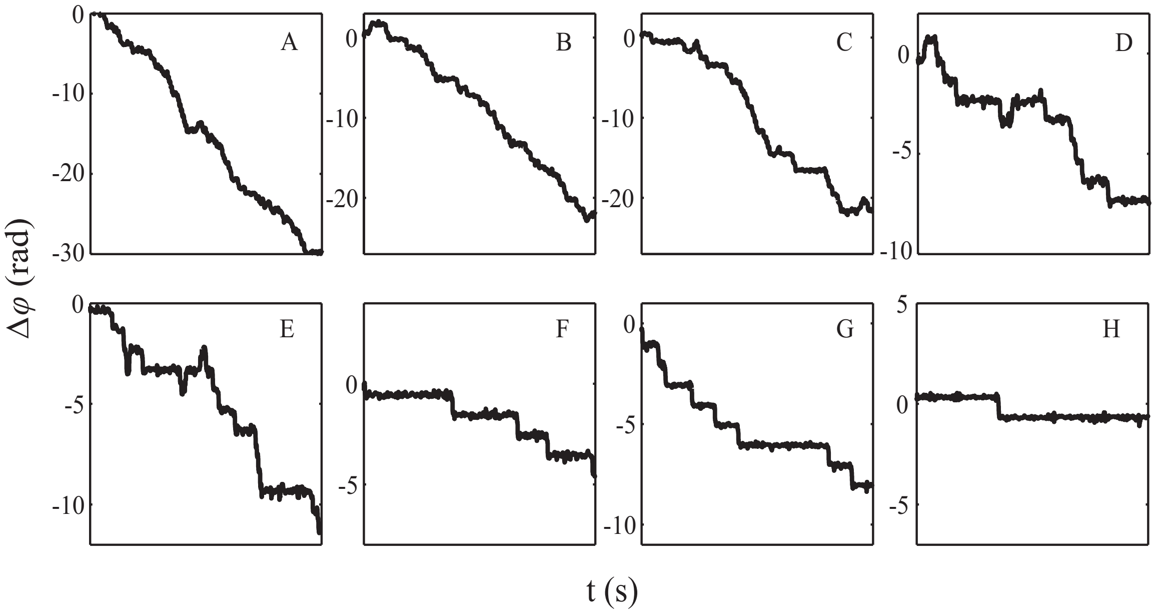
Phase-locking to low-amplitude sinusoidal stimuli





Roongthumskul, Y. et al, *Phys. Rev. Lett.*, **110**, 148103 (2013).

Phase slips

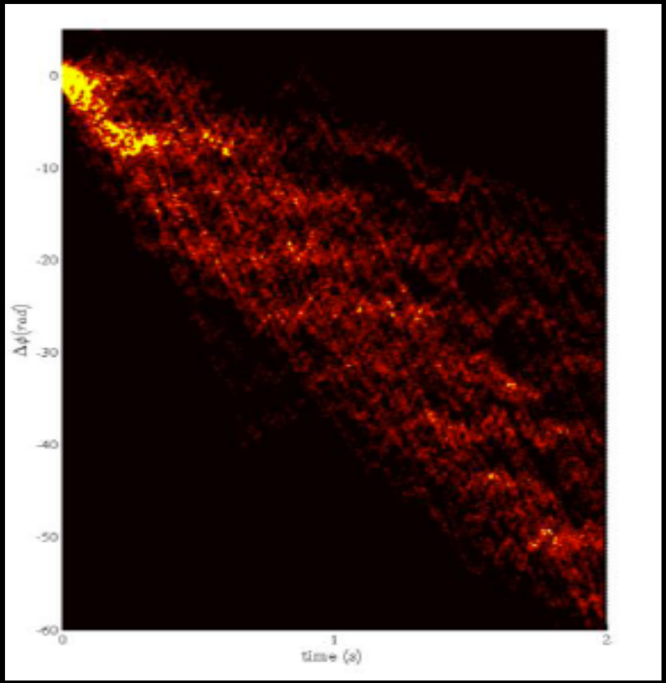


amplitudes: 0.2, 0.35, 0.5, 0.6, 0.7, 0.8, 1.0, 1.2 pN

Stochastic Adler equation

$$\frac{d\Delta\phi(t)}{dt} = -\Delta\omega + \epsilon \sin(\Delta\phi(t)) + \eta(t),$$

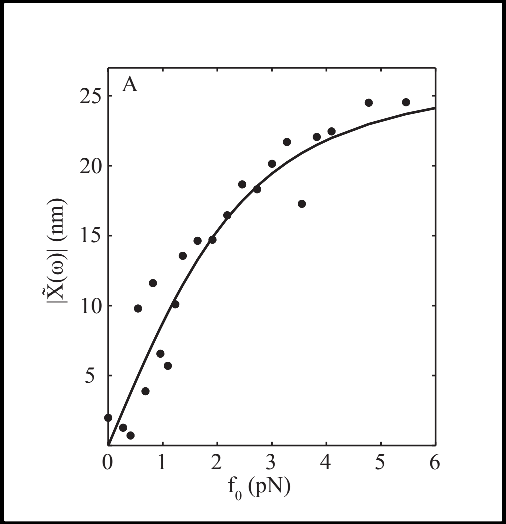
$$\langle \eta(t)\eta(t') \rangle = 2T\delta(t - t')$$



numerical simulation

Stochastic Adler equation

At low stimulus amplitudes: growth of the phase-locked component with driving force is well described by the Adler equation.

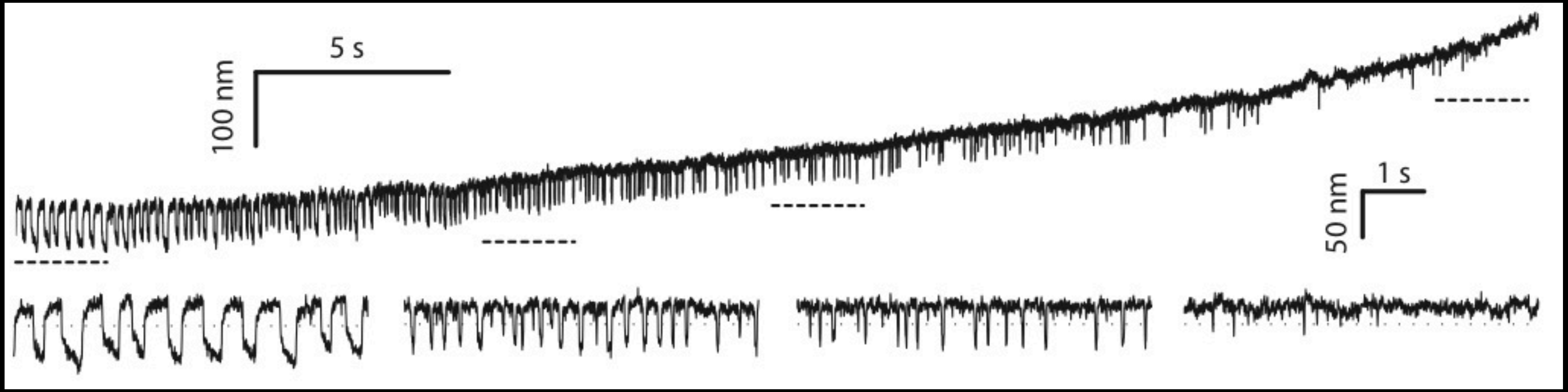


$$\left|\tilde{X}(\omega)\right| = r\, I_1\!\left(\frac{\varepsilon}{T}\right) \Big/ I_0\!\left(\frac{\varepsilon}{T}\right)$$

r = oscillation amplitude

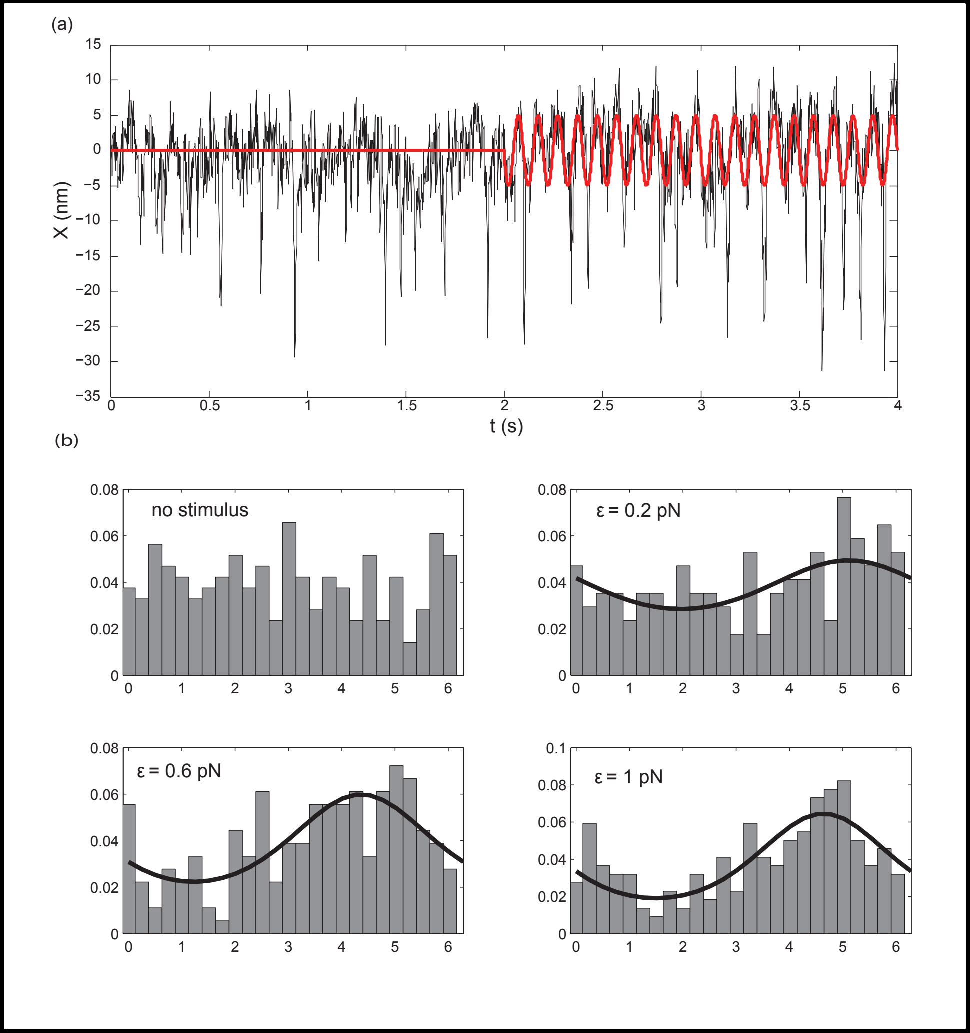
I: modified Bessel functions

Can the bundle amplify from the non-oscillatory state?



Near the transition between spontaneous oscillation and quiescence, the hair bundle exhibits sharp spike-like excursions.

Roongthumskul et al, *Biophys. J.*, **108**, 53 (2015)

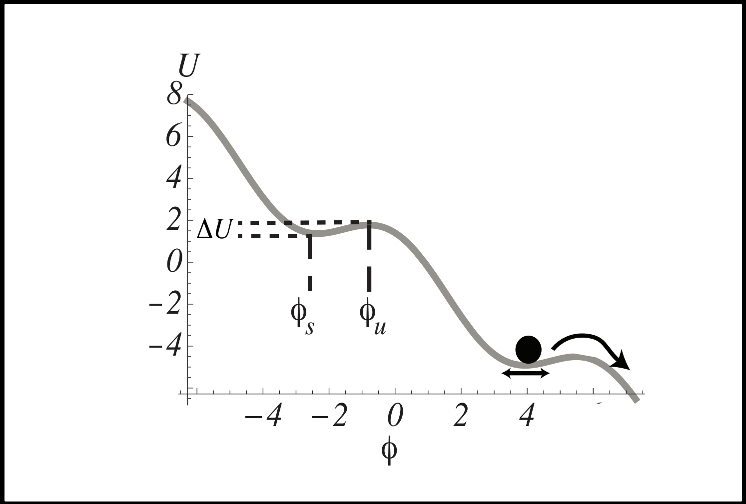


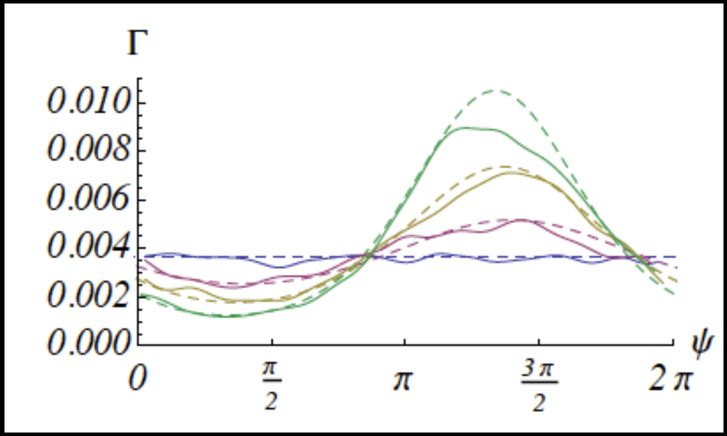
Without stimulus, the occurrence of spikes is stochastic. With an applied signal, they occur at a preferred phase.

Shlomovitz, R. et al, *Interface Focus*, **4**, 2014022 (2014).

Adler equation predicts phase slips (spikes) in the quiescent regime

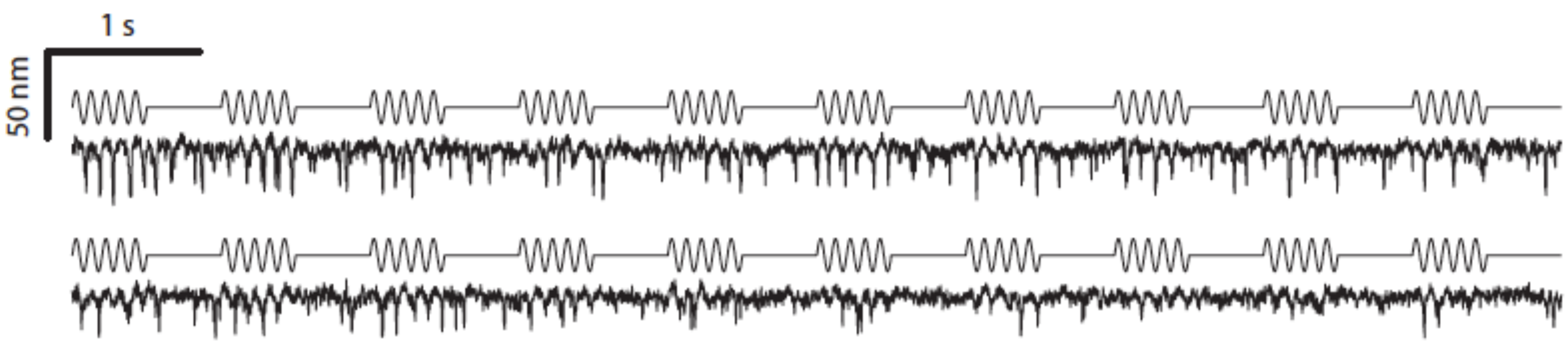
$$\dot{\phi} \simeq \omega_0 + F\sin(\phi) + \epsilon \sin(\phi - \omega_f t) + \sqrt{2D}\eta(t)$$





Preferential phase of spiking is predicted by the equations.

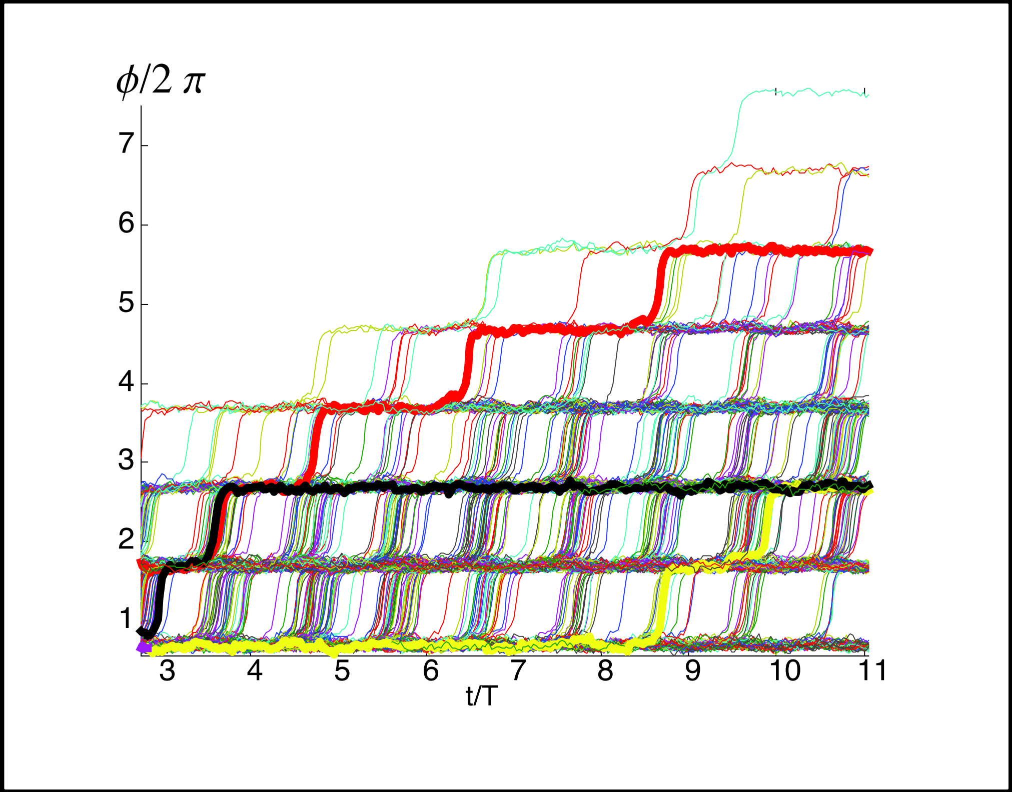
Active response from the spiking regime



In the absence of a stimulus, the occurrence of spikes is stochastic.

Even very weak drives can phase-lock the spikes, leading to 10-100x enhancement in the amplitude of the bundle movement.

Ensemble response



Summary

Mode-locking to weak signals is well described by the stochastic Adler equation. The transition is characterized by the occurrence of phase slips.

Spiking regime allows for a significant enhancement of the signal. Occurrence of spikes from the quiescent state exhibits a preferential phase. This allows the ensemble to encode the frequency of the stimulus.

Open problems

Interaction between noise and chaos

Role of both or either in coupled system

In vivo effects

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Janaki Sheth
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Dr. Lea Fredrickson

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Nonlinear dynamics
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