Dissecting the locust ear

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soon:
FB Biologie
Eberhard-Karls Universität
Tübingen
Neuroethology of electrosensory systems

Weakly electric fish

Electrophysiology

Natural stimuli in natural habitats
Ribbon synapse

Tuberous receptor synapse of *Eigenmannia virescens* (Wachtel & Szamier, 1966)
The auditory system of grasshopper

well defined acoustic stimuli:
courtship songs

well characterized behavior
The grasshopper’s ear

Tympanum and Müller’s organ

Bipolar receptor neurons
From sound to spike

Sound-wave with amplitude modulation:

Recording from the axon of an auditory receptor neuron:

Receptor neurons generate action potentials in response to sound wave
Tuning curve

- Two classes of receptor neurons:
  - Low-frequency receptors: best frequency at about 5 kHz
  - High-frequency receptors: best frequency at about 15 kHz
- Broad tuning
Auditory transduction chain

- Spectral integration
- Temporal integration

Intrinsic noise

- Receptor channel noise
- Adaptation channel noise
Auditory transduction chain

1. sound coupling
2. mechano transduction
3. electrical integration
4. spike generation
Auditory transduction chain

1. Sound coupling

2. Mechano transduction

3. Electrical integration

4. Spike generation

Linear filter $L(\Delta t)$

Non-linear function

Linear filter $Q(\Delta t)$

Non-linear function

LNLN cascade
Response to pure tone

Stimulus with sound frequency $f_1$ and amplitude $A_1$: $s_1(t) = A_1 \sin(2\pi f_1 t)$
Stimulus

Pure tone 1: $s_1(t) = A_1 \sin(2\pi f_1 t)$

Output

Firing rate 1: $r_1$
Spectral integration

Stimulus

Pure tone 1: \( s_1(t) = A_1 \sin(2\pi f_1 t) \)

Pure tone 2: \( s_2(t) = A_2 \sin(2\pi f_2 t) \)

Output

Firing rate 1: \( r_1 \)

Firing rate 2: \( r_2 \)
Spectral integration

**Stimulus**

Pure tone 1: $s_1(t) = A_1 \sin(2\pi f_1 t)$

Pure tone 2: $s_2(t) = A_2 \sin(2\pi f_2 t)$

Mixed tone:

$$s(t) = s_1(t) + s_2(t) = A_1 \sin(2\pi f_1 t) + A_2 \sin(2\pi f_2 t)$$

**Output**

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Spectral integration

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\[
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**Output**

Firing rate 1: \( r_1 \)

Firing rate 2: \( r_2 \)

Pressure: \( A_1 + A_2 \)

Energy: \( A_1^2 + A_2^2 \)

How are two sound frequencies combined?
Simplification: no temporal integration

Sound coupling $\rightarrow$ mechano transduction $\rightarrow$ electrical integration $\rightarrow$ spike generation

Linear filter $L(\Delta t)$ $\rightarrow$ Non-linear function $\rightarrow$ Linear filter $Q(\Delta t)$ $\rightarrow$ Non-linear function

Firing rate is time-averaged output activity
Simplification: no temporal integration

1. sound coupling
2. mechano transduction
3. electrical integration
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Linear filter $L(\Delta t)$
Non-linear function
Linear filter $Q(\Delta t)$
Non-linear function

Firing rate is time-averaged output activity

Still: two successive non-linearities — how to isolate the first one?
**Iso-response method**

<table>
<thead>
<tr>
<th>Hypothesis:</th>
<th>pressure summation</th>
<th>energy summation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. non-linearity:</td>
<td>$x = A_1 + A_2$</td>
<td>$x = A_1^2 + A_2^2$</td>
</tr>
<tr>
<td>2. non-linearity:</td>
<td>$r_1 = g(x)$</td>
<td>$r_2 = g(\sqrt{x})$</td>
</tr>
<tr>
<td>combined:</td>
<td>$r_1 = g(A_1 + A_2)$</td>
<td>$r_2 = g\left(\sqrt{A_1^2 + A_2^2}\right)$</td>
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Hypothesis: pressure summation

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2. non-linearity: \( r_1 = g(x) \)

combined: \( r_1 = g(A_1 + A_2) \)

energy summation

\( x = A_1^2 + A_2^2 \)
\( r_2 = g(\sqrt{x}) \)
\( r_2 = g\left(\sqrt{A_1^2 + A_2^2}\right)\)
Iso-response method

Hypothesis: pressure summation

1. non-linearity:
   \[ x = A_1 + A_2 \]

2. non-linearity:
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combined:
\[ r_1 = g(A_1 + A_2) \]

Iso-response:
\[ r_1 = \text{const} \]
\[ \Leftrightarrow A_1 + A_2 = \text{const} \]

energy summation

\[ x = A_1^2 + A_2^2 \]
\[ r_2 = g(\sqrt{x}) \]
\[ r_2 = g\left( \sqrt{A_1^2 + A_2^2} \right) \]

Iso-response:
\[ r_2 = \text{const} \]
\[ \Leftrightarrow A_1^2 + A_2^2 = \text{const} \]
Superposition of two pure tones

Hypothesis:

1. Pressure summation $A_1 + A_2$: linear iso-response curves
2. Energy summation $A_1^2 + A_2^2$: elliptic iso-response curves

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⇒ Mechano-transduction adds amplitudes quadratically

Predicting response to white-noise stimulus

Response curve for white noise stimulus

Prediction of response curve for white noise

Temporal integration: the full LNLN cascade

How to measure the two linear filters?
Double-click experiment

• Spike precision $\approx 1$ ms

• Much worse than stimulus timescales
  kHz $\leftrightarrow < 1$ ms

$\Rightarrow$ Iso-response on spike probability!
Iso-probability sets for double-click stimuli

Linear summation on short time scales
→ Summation on the tympanum before the squaring non-linearity

Iso-probability sets for double-click stimuli

Quadratic summation on longer time scales
→ Electrical integration after the squaring non-linearity

Iso-probability sets for double-click stimuli

How do the two filters look like?

Temporal filters

Measure amplitude $A_2$ of second click as a function of $t_{\text{gap}}$

Tympanal filter $L(t)$ and electrical integration $Q(t)$:

2 unknown filters

$\rightarrow$

2 experiments
one with “inverted” 2nd click

Temporal filters

Measure amplitude $A_2$ of second click as a function of $t_{\text{gap}}$

Tympanal filter $L(t)$ and electrical integration $Q(t)$:

2 unknown filters

→

2 experiments
one with “inverted” 2$^{\text{nd}}$ click

… some math …

Temporal filters

Temporal filters

\( L(t) \): Resonator
Tympanal membrane
Traditional: Laser interferometry

\( Q(t) \): Leaky integrator
Transduction & cell properties

Temporal filters

$L(t)$: Resonator
Tympanal membrane
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$Q(t)$: Leaky integrator
Transduction & cell properties

Summary I

- Squaring non-linearity at mechanical transduction
  “Energy integration”

- Rapid integration of input signal \((t < 1\,\text{ms})\)

- High-precision measurements \((t \approx 1\,\mu\text{s})\)
  despite large spike-time jitter \((t_{\text{spike}} \approx 1\,\text{ms})\)

- Simple phenomenological description
  → quantitative constraints for any mechanistic model
Neural noise
Spike-time variability

38 dB

Stimulus 6 kHz tone 500 ms
Spike-time variability

Stimulus 6 kHz tone 500 ms

38 dB

$Spike-time \ variability\n
38 \ dB\n
38 \ dB\n
38 \ dB\n
Stimulus \ 6 \ kHz \ tone \ 500 \ ms$
Variability depends on sound intensity

38 dB

44 dB

Stimulus 6 kHz tone 500 ms

$\text{ISI [ms]}$

$\text{f} = 35 \text{ Hz}$
$\text{CV} = 0.62$

$\text{f} = 93 \text{ Hz}$
$\text{CV} = 0.27$

$\text{CV} = 0.62$

$\text{CV} = 0.27$
Variability depends on sound intensity

- **38 dB**
  - Stimulus: 6 kHz tone 500 ms
  - CV: 0.62

- **44 dB**
  - Stimulus: 500 ms
  - CV: 0.27

- **50 dB**
  - Stimulus: 6 kHz tone 500 ms
  - CV: 0.18
Variability depends on sound intensity

![Graph 1: Spike frequency vs. Sound intensity (dB SPL)]

- Spike frequency $f$ [Hz]
- Sound intensity [dB SPL]

![Graph 2: CV vs. Sound intensity (dB SPL)]

- CV
- Sound intensity [dB SPL]
Variability depends on sound intensity

- What is causing this variability?
- What does it tell us about the underlying noise source?
ISI densities: Inverse Gaussian

Super-threshold constant input $\mu$

No noise:
- periodic spiking,
- limit cycle dynamics

$\Rightarrow$ canonical model:
- perfect integrator

$$\dot{V} = \mu$$
ISI densities: Inverse Gaussian

Super-threshold constant input $\mu$

No noise:
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$\dot{V} = \mu$

Additive white noise:
$\dot{V} = \mu + \sqrt{2D}\xi(t)$
ISI densities: Inverse Gaussian

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  $\dot{V} = \mu$

Additive white noise:

$\dot{V} = \mu + \sqrt{2D}\xi(t)$

$\Rightarrow$ Inverse Gaussian as ISI density:

$$p(T) = \frac{1}{\sqrt{4\pi DT^3}} \exp \left[ -\frac{(T-\langle T_i \rangle)^2}{4DT\langle T_i \rangle^2} \right]$$

$$D = \frac{CV^2}{2\langle T_i \rangle}$$

Gerstein & Mandelbrot (1964)
Experimental interspike-interval histograms

$I = 58$ dB SPL
$f = 51$ Hz
$CV = 0.59$

$I = 64$ dB SPL
$f = 127$ Hz
$CV = 0.3$

$I = 73$ dB SPL
$f = 173$ Hz
$CV = 0.2$
Experimental interspike-interval histograms

white noise (Inverse Gaussian)

\[
p(T) \quad \text{[Hz]}
\]

\[
I = 58 \text{ dB SPL} \\
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p(T) \quad \text{[Hz]}
\]

\[
I = 73 \text{ dB SPL} \\
f = 173 \text{ Hz} \\
CV = 0.2
\]

good match with inverse Gaussian

bad match
Simulations of channel noise

\[ \dot{C}V = -I_{Na} - I_{K} - I_{L} - I_{A} - I_{R} \]

Hodgkin-Huxley type single compartment model with

- Receptor current \( I_{R} = \bar{g}_{R} r (V - E_{R}) \)
- Sodium current \( I_{Na} = \bar{g}_{Na} m^{3} h (V - E_{Na}) \)
- Potassium current (delayed rectifier) \( I_{K} = \bar{g}_{K} n^{4} (V - E_{K}) \)
- Adaptation current (M-type current) \( I_{A} = \bar{g}_{A} a (V - E_{A}) \)

Conductances either

- deterministic
- stochastic channel opening and closing
Simulated interspike-interval histograms

Receptor

Sodium current

Adaptation

\[ p(T) \text{ [Hz]} \]

\[ 0 \quad 0.001 \quad 0.01 \quad 0.1 \quad 1 \]

simulated interspike-interval histograms

Receptor

Sodium current

Adaptation

\[ p(T) \text{ [Hz]} \]

\[ 0 \quad 0.001 \quad 0.01 \quad 0.1 \quad 1 \]
Simulated interspike-interval histograms

⇒ Stochastic adaptation currents generate peaked ISI histograms!
Adaptation currents
Adaptation currents

M-type current

\[ I_M = \bar{g}_M a (V - E_K) \]

\[ \tau_a \dot{a} = a_\infty (V) - a \]
Adaptation currents

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Adaptation currents

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\[ I_M = \bar{g}_M a (V - E_K) \]

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![Graphical representation of M-type current](image)
Adaptation currents

M-type current

\[ I_M = \bar{g}_M a (V - E_K) \]

\[ \tau_a \dot{a} = a_\infty (V) - a \]

\[
\begin{array}{c|c|c|c|c|c}
0 & 40 & 80 & 120 & 160 & f_0(I) \\
0 & 40 & 80 & 120 & 160 & f_\infty(I) \\
0 & 0.1 & 0.2 & 0.3 & a \\
0 & 40 & 80 & 120 & I_M [\mu A/cm^2] \\
-50 & 0 & 50 & 100 & 150 & 200 & 250 & 300 & Time [ms]
\end{array}
\]
Stochastic adaptation current

M-type current (slow, $\tau_a \approx 100$ ms, voltage gated potassium current)

Deterministic:

\[
I_M = \bar{g}_M a(V - E_K)
\]

\[
\tau_a \dot{a} = a_\infty(V) - a
\]

\[
a_\infty(V(t)) = \begin{cases} 
1 & t_i < t < t_i + \tau_{AP} \\
0 & \text{else}
\end{cases}
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Stochastic:

\[
I_M = \bar{g}_M a(V - E_K) \\
a = N_{\text{open}}/N_{\text{all}}
\]

Two-state channel:

\[
\alpha_a(V) \quad \text{open} \quad \text{close} \\
\beta_a(V)
\]
Stochastic adaptation current

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\end{cases}$$

Stochastic:

$$I_M = \bar{g}_M a (V - E_K)$$
$$a = \frac{N_{\text{open}}}{N_{\text{all}}}$$

Two-state channel:

Transition rates:

$$\alpha_a (V) = \frac{a_\infty (V)}{\tau_a} = \begin{cases} 
1/\tau_a & \text{spike} \\
0 & \text{else}
\end{cases}$$
$$\beta_a (V) = \frac{1 - a_\infty (V)}{\tau_a} = \begin{cases} 
0 & \text{spike} \\
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\end{cases}$$
Stochastic adaptation current

M-type current (slow, $\tau_a \approx 100$ ms, voltage gated potassium current)

Deterministic:

$$I_M = \bar{g}_M a \left( V - E_K \right)$$
$$\tau_a \dot{a} = a_\infty(V) - a$$

Slow state transitions

$$a_\infty(V(t)) = \begin{cases} 1 & t_i < t < t_i + \tau_{AP} \\ 0 & \text{else} \end{cases}$$

Stochastic:

$$I_M = \bar{g}_M a \left( V - E_K \right)$$
$$a = \frac{N_{\text{open}}}{N_{\text{all}}}$$

⇒ Colored noise with correlation time $\tau_a$

Two-state channel:

Transition rates:

$$\alpha_a(V) = \frac{a_\infty(V)}{\tau_a} = \begin{cases} 1/\tau_a & \text{spike} \\ 0 & \text{else} \end{cases}$$
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Diffusion approximation of adaptation noise

Stochastic adaptation channels

Diffusion approximation

Separation \( A = a + \eta \)

Stochastic adaptation \( \Rightarrow \) colored noise with correlation time \( \tau_a \)

Experimental interspike-interval histograms

white noise (Inverse Gaussian)

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Experimental interspike-interval histograms

white noise (inverse Gaussian)

$\tilde{\tau} = 1.3 \text{ ms}$

$\tilde{\tau} = 2.9 \text{ ms}$

$\tilde{\tau} = 104.9 \text{ ms}$

dominated by white-noise
dominated by colored-noise

$\tilde{\tau}$
Experimental spike-frequency adaptation

Effective time constant of adaptation $\tilde{\tau}$: $\sim$ 100 ms
Simulation of auditory receptor cell

\[ \dot{C}V = -I_{Na} - I_{K} - I_{L} - I_{A} - I_{R} \]

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Both
- receptor channels
- adaptation channels
stochastic.
Simulation of auditory receptor cell

Simulation: stochastic receptor and adaptation channels

Intracellular recording:

Spike frequency [Hz]

$\alpha_e, \alpha_s$

$\rho_1$
Summary II

- Deterministic adaptation with white-noise:
  - inverse Gaussian ISI distribution
  - negative ISI correlations
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- Stochastic adaptation is a colored noise source:
  - more peaked ISI distributions
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  - more peaked ISI distributions
  - positive ISI correlations

- Locust auditory receptor neurons:
  - white noise source at low spike frequencies $\Rightarrow$ receptor or sodium current
  - colored noise source at high spike frequencies $\Rightarrow$ adaptation current

![Graph showing Fano factor vs. counting time]
Final summary

- Auditory transduction chain:
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  - Squaring non-linearity
    “Energy integration”
  - Tympanum resonance filter
  - Electrical integration
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  - Measure with stimulus
  - Non-invasive!
  - Temporal precision independent on spike-timing variability
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- Intrinsic noise
  - …shapes ISI statistics
  - Stochastic adaptation generates colored noise
Thanks to

Iso-response

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