Membrane noise sources

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- Koch, C. Biophysics of Computation, Information Processing in Single Neurons
- Johnson&Wu. Foundation of Cellular Neurophysiology

Background

- Neuron as communication device, efficacy of neuron (MacKay&McCulloch, 1952)
- Information transmission: random input-spike output
- Nature of neural codes
- Capacity of neural codes
- From black-box-type studies to more thorough modelling:
  - Identify a role of each stage: synapse, the dendritic tree, the soma, the spike initiation zone, the axon (Koch, Manwani, Steinmetz, 1999->)
Background

- Aim of study of Manwani and Koch
  - Biophysically faithful model of a single neuron
  - Theoretical analysis of the information loss of signal propagating along a linear, one-dimensional, weakly active, passive or quasiactive cable
  - In the future analysis with active nonlinear membrane conductance via numerical simulations

Why important to analyse?

- Statement: Noise limits the precision, speed and accuracy of neural computation
- Noise affects strongly to neural computation
  - Can change the spiking behavior of neurons
    - Distribution of response latencies
    - Spike propagation
    - Spontaneous action potentials
    - Reliability and precision of spike timing
Why important to analyse?

- Causes fluctuation in subthreshold voltage
- Affects also to the operations in nonspiking neurons
- May improve signal transmission
  - Stochastic resonance
    - Noise enhancement of input-output transmission of signal applied to an individual nonlinear system

Noise sources

- Noise and signal transfer
  - Synapse
    - Release probability
    - Variability in vesicle size and available receptors
  - Dendrite
    - Stochastic ion channels
    - Background synaptic activity
  - Axon
    - Stochastic spiking mechanism
    - Spike propagation
Noise sources

- Thermal noise
- Channel noise
- Synaptic noise
- Other sources

Thermal noise

- Arises from Brownian motion
  - Every material if temperature above absolute zero
  - Motion of particles: step to the right and left as equal
  - Phenomenon observed 1785
  - Rediscovered by Brown 1828
- Johnson noise, Nyquist noise, white noise
  - Johnson was first to measure 1928
  - Mathematical format by Nyquist 1928
Thermal noise

- White noise
  - Power is independent of spectral location
    \[ P_{th} = k \cdot T \cdot \Delta f \]
    \[ k = \text{Boltzman constant} = 1.38 \times 10^{-23} \text{Ws/K} \]
    \[ T = \text{Temperature (K)} \]

- Distribution Gaussian
- Variance \[ \sigma^2 = \int_{-B}^{B} S_{th}(f) df \]

Thermal noise

- Power spectral density

\[ S_{V_{th}} = 2 \cdot k \cdot T \cdot R \quad \left[ \frac{V^2}{Hz} \right] \]
\[ S_{I_{th}} = 2 \cdot k \cdot T \cdot \frac{1}{R} \quad \left[ \frac{A^2}{Hz} \right] \]

[Diagram of Voltage Noise Model and Current Noise Model]
Thermal noise

- Example. Semi-infinite passive cable

\[ S_{\text{th}}(f) = 2kT \Re\{Z(f)\} \]

\[ = \frac{2kT}{\sqrt{r_i \cdot r_m}} \cdot \cos \left( \frac{\tan^{-1} \left( \frac{2\pi f \tau_m}{2} \right)}{2} \right) \]

\[ = kT \sqrt{2r_m r_m} \left[ \frac{1}{1 + (2\pi f \tau_m)^2} + \frac{1}{\sqrt{1 + (2\pi f \tau_m)^2}} \right]^{1/2} \]

Thermal noise

- For large \( f \)

\[ S_{\text{th}}(f) \propto f^{-\frac{1}{2}} \]

- This is said to be divergent?

- If intracellular capacitance is considered

\[ S_{\text{th}}(f) \propto f^{-2} \]

- This is said to be convergent?
Thermal noise

- Is that true?
- P-test:
  - The following integral is convergent if and only if $p<1$
    \[ \int_0^1 \frac{1}{x^p} \, dx \]
  - The following integral is convergent if and only if $p>1$
    \[ \int_1^{\infty} \frac{1}{x^p} \, dx \]
Thermal noise

- Parameters in previous figure
  Diameter 25e-4 cm, length 2 cm
  \( R_m = 40000 \ \Omega\text{-cm}^2, \ C_m = 1 \mu\text{F/cm}^2, \ R_i = 200 \ \Omega\text{-cm} \)
  \( r_m = \frac{R_m}{2\pi r}, \ c_m = C_m * 2\pi r, \ r_i = \frac{R_i}{\pi r^2} \)
  \( \tau_m = 30\text{ms}, \ \tau_i = 3\mu\text{s} \)

Channel noise

- Stochasticity in voltage-dependent ion channels
  - Random opening and closing of ion channels
- Analysis
  - Channel kinetics with HH-like models of voltage-gated K⁺ and Na⁺ channels
  - Markov process
Channel noise

- HH channel kinetics
  - $K^+$-channel
    \[
    C_0 \frac{\alpha_n}{\beta_n} \quad C_1 \quad \frac{\alpha_m}{\beta_m} \quad C_2 \quad \frac{\alpha_i}{\beta_i} \quad C_3 \quad \frac{\alpha_e}{\beta_e} \quad \mathcal{O} \quad (1) \quad (2) \quad (3) \quad (4) \quad (5)
    \]
  - $Na^+$-channel
    \[
    \alpha_k \beta_k \quad \alpha_k \beta_k \quad \alpha_k \beta_k \quad \alpha_k \beta_k \quad \alpha_k \beta_k \quad (1) \quad (2) \quad (3) \quad (4)
    \]

- $Na^+$-channel
  \[
  \begin{align*}
  \alpha_n &= \frac{3\alpha_m}{\beta_m} \quad \alpha_m &= \frac{2\alpha_n}{3\beta_n} \quad C_3 &= \frac{\alpha_m}{3\beta_m} \quad \mathcal{O} \\
  \alpha_i &= \frac{2\alpha_m}{3\beta_m} \quad \alpha_i &= \frac{\alpha_m}{3\beta_m} \\
  \alpha_e &= \frac{\alpha_m}{3\beta_m} \quad \alpha_e &= \frac{\alpha_m}{3\beta_m} \\
  \alpha_n &= \frac{\alpha_m}{3\beta_m} \quad \alpha_n &= \frac{\alpha_m}{3\beta_m} \\
  \alpha_m &= \frac{2\alpha_n}{3\beta_n} \quad \alpha_m &= \frac{3\alpha_n}{2\beta_n} \quad \alpha_m &= \frac{3\alpha_n}{2\beta_n} \quad \alpha_m &= \frac{3\alpha_n}{2\beta_n} \\
  \alpha_i &= \frac{2\alpha_m}{3\beta_m} \quad \alpha_i &= \frac{\alpha_m}{3\beta_m} \quad \alpha_i &= \frac{\alpha_m}{3\beta_m} \quad \alpha_i &= \frac{\alpha_m}{3\beta_m} \\
  \alpha_e &= \frac{\alpha_m}{3\beta_m} \quad \alpha_e &= \frac{\alpha_m}{3\beta_m} \quad \alpha_e &= \frac{\alpha_m}{3\beta_m} \quad \alpha_e &= \frac{\alpha_m}{3\beta_m} \\
  \end{align*}
  \]

Channel noise

- Autocovariance
  - $K^+$ channel
    \[
    C_{\beta\beta}(\tau) = \eta_{\beta\beta}^2 \left( V_m - E_K \right)^2 \sum_{i=1}^{4} \left( \frac{4}{1-n_i} \right) (1-n_i) e^{-\frac{\tau}{\theta}}
    \]
  - $Na^+$-channel
    \[
    C_{\beta\beta}(\tau) = \eta_{\beta\beta}^2 \left( V_m - E_{Na} \right)^2
    \]
    \[
    \left[ m^2 h_n \left( m_n + (1-n_n) e^{-\frac{\tau}{\theta_n}} \right) \left[ h_n + (1-h_n) e^{-\frac{\tau}{\theta_n}} \right] - m^2 h^2 \right]
    \]
Channel noise

- Variables

\( \eta = \) ion channel density in the membrane
\( \gamma = \) Open conductance of single channel
\( E = \) Reversal potential of ion
\( n_\infty = \) Steady state open probability of K\(^+\) channel
\( m_\infty = \) Steady state value of subunit m of Na\(^+\) channel
\( h_\infty = \) Steady state value of subunit h of Na\(^+\) channel
\( \theta_i = \) Relaxation time constant of the i subunit (i = n, m or h) = \(1/(\alpha_i + \beta_i)\)
\( \alpha_i \) and \( \beta_i = \) Rate constants of the i subunit

Channel noise

- Power spectrum of K\(^+\) channel current noise
  - Wiener-Khinchine theorem (Papoulis, 1991?): Power spectrum is the Fourier transform of autocovariance
    \[
    S_{\eta K}(f) = \eta K^2 (V_m - E_K)^2 \eta n_\infty \sum_{i=0}^{4} (1 - n_\infty)^i n_\infty^{i+1} \frac{2^\theta_k/i}{1 + (2\pi f \theta_k/4)^2}
    \]
  - For \( n_\infty \ll 1 \)
    \[
    S_{\eta K}(f) = \eta K^2 (V_m - E_K)^2 \eta n_\infty (1 - n_\infty)^i \frac{2^\theta_k/4}{1 + (2\pi f \theta_k/4)^2}
    \]
    \[
    = S_{\eta K}(0) \frac{1}{1 + (f / f_\kappa)^2}
    \]
  - Single lorentzian with \( S_{\eta K}(0) \) amplitude and cutoff frequency \( f_\kappa \),
    bandwidth \( B_\kappa \approx 1/\theta_k \)
  - Approximation holds near resting potential.
Channel noise

- Power spectrum of Na\(^+\) channel current noise
  - For \(m_\infty \ll 1\) and \(h_\infty \approx 1\)

\[
S_{B_{Na}}(f) = \eta_{Na} \gamma_{Na}^2 (V_m - E_{Na})^2 m_\infty^3 (1 - m_\infty)^3 \ h_\infty^2 \ \frac{2 \theta_m / 3}{1 + (2 \pi f \theta_m / 3)^2}
\]

\[
= \frac{S_{B_{Na}}(0)}{1 + (f / f_{Na})^2}
\]

→ Single lorenzian with \(S_{INa}(0)\) amplitude and cutoff frequency \(f_{Na}\), bandwidth \(B_{Na} = \frac{3}{4} \theta_m\)

→ approximation holds near resting potential.

Channel noise

- Variance
  - K\(^+\)-channel
    \[
    \sigma^2_{IK} = \eta_{K} \gamma_{K}^2 (V_m - E_{K})^2 \ n_\infty^4 (1 - n_\infty)^4
    \]
  - Na\(^+\)-channel
    \[
    \sigma^2_{INa} = \eta_{Na} \gamma_{Na}^2 (V_m - E_{Na})^2 \ m_\infty^3 h_\infty (1 - m_\infty^3 h_\infty)
    \]
Synaptic noise

- Study of mEPP (miniature end-plate potential)
  - Variance in amplitude
    - Amount of transmitter in vesicle varies
    - Amount of molecules binding to the receptors
    - The number of postsynaptic receptors
    - Probability of channel opening after binding

Synaptic noise

- Analysis
  - Restricted to channels specialized for mediating fast chemical synaptic transmission, voltage-independent

- Time course of the postsynaptic change in response to presynaptic spike

\[ g_a(t) = \frac{g_{\text{peak}}}{t_{\text{peak}}} e^{-t/t_{\text{peak}}} u(t) \]

- \( g_{\text{peak}} \) = peak conductance change
- \( t_{\text{peak}} \) = time to peak conductance change
Synaptic noise

- Postsynaptic change and synaptic current
  \[ g_{\text{Syn}}(t) = \sum_j g_a(t-t_j) \]
  \[ i_{\text{Syn}}(t) = g_{\text{Syn}}(t)(V_m - E_{\text{Syn}}) \]
- If the presynaptic spike train is homogenous Poisson process with mean firing rate \( \lambda_n \):
  - variance
  \[ \sigma_{\text{Syn}}^2 = \eta_{\text{Syn}} \lambda_n \left( \frac{g_{\text{peak}} e}{2} \right) (V_m - E_{\text{Syn}})^2 t_{\text{peak}} \]

Synaptic noise

- Power spectral density
  \[ S_{\text{ISyn}}(f) = \eta_{\text{Syn}} \lambda_n \left( \frac{e g_{\text{peak}} f_{\text{peak}} (V_m - E_{\text{Syn}})}{1 + (2\pi f_{\text{peak}})^2} \right)^2 \]
  \[ S_{\text{ISyn}}(0) = \frac{S_{\text{ISyn}}(0)}{\left[ 1 + (f/f_{\text{Syn}})^2 \right]^2} \]
  \[ \Rightarrow \] Double lorentzian. Spectrum falls twice as fast as spectrum of single lorentzian
  \[ \Rightarrow \] Single lorentzian with \( S_{\text{ISyn}}(0) \) amplitude and cutoff frequency \( f_{\text{Syn}} \) bandwidth \( B_{\text{Syn}} \approx \pi/4 \)
Other Sources of Noise

- Several ionic channels with different kinetics
  - Ligand-gated channels (myriad? types)
- 1/f noise
- Shot noise
- Carrier-mediated transport noise in ionic pumps
- Burst noise

Not analysed:
- Lack of a theoretical understanding of their origin
- Insignificance of their magnitudes
Noise calculated for membrane patch

- Soma of neocortical pyramidal cell (1000µm²)
- Modeled as passive RC-filter
- HH type currents
  - Rapid sodium current
  - Delayed rectifier potassium current
- Current noise of patch
  \[ I_n = g_k (V_m - E_k) + g_{Na} (V_m - E_{Na}) + g_{Syn} (V_m - E_{Syn}) + I_{th} \]
  \[ g = \text{random component of conductance} \]

Noise calculated for membrane patch

- Noise sources independent:
  \[ S_{Vn} = S_{IK} (f) + S_{INa} (f) + S_{ISyn} (f) + S_{Ith} (f) \]
  \[ S_V = \frac{S_{Vn} (f)}{G [1 + (2\pi f \tau)^2]} \]
- Variance of the voltage noise
  \[ \sigma_V^2 = \frac{\pi}{G} \left[ S_{IK} (0) \frac{f_m f_K}{f_m + f_K} + S_{INa} (0) \frac{f_m f_{Na}}{f_m + f_{Na}} + S_{ISyn} (0) \frac{f_m f_{Syn} (f_m^2 + f_m f_{Syn} - 2 f_{Syn}^2)}{2 (f_m + f_{Syn}) (f_m^2 - f_{Syn}^2)} + S_{Ith} (0) f_m \right] \]
- \[ f_m = 1/2\pi \tau, \tau \text{ is the time constant of passive membrane} \]
Noise calculated for membrane patch

- Comparison of magnitudes of the power spectral densities and voltage standard deviation of the different noise sources

<table>
<thead>
<tr>
<th>Noise type</th>
<th>A * S_f(0) (A^2/Hz)</th>
<th>S_v(0) (V^2/Hz)</th>
<th>σ_v (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thermal</td>
<td>2.21 × 10^{-11}</td>
<td>3.14 × 10^{-11}</td>
<td>2.05 × 10^{-5}</td>
</tr>
<tr>
<td>K⁺</td>
<td>1.74 × 10^{-17}</td>
<td>2.46 × 10^{-8}</td>
<td>5.33 × 10^{-1}</td>
</tr>
<tr>
<td>Na⁺</td>
<td>1.67 × 10^{-28}</td>
<td>2.30 × 10^{-19}</td>
<td>5.59 × 10^{-2}</td>
</tr>
<tr>
<td>Synaptic</td>
<td>4.12 × 10^{-27}</td>
<td>5.84 × 10^{-9}</td>
<td>8.54 × 10^{-1}</td>
</tr>
<tr>
<td>Total</td>
<td>5.88 × 10^{-27}</td>
<td>8.33 × 10^{-8}</td>
<td>3.01</td>
</tr>
</tbody>
</table>

- dependence on area
  - Area increases → voltage fluctuation decreases
Discussion

- Deeper study on affects of noise
- Information theory
- Other theories
- Syncronization
- Correlation
- Stochastic resonance