Spiking neurons and response variability

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Integrate-and-fire neurons

\[
\tau_m \frac{du(t)}{dt} = -u(t) + RI(t). \quad (3.1)
\]

\[
I(t) = \sum_j \sum_{t_f^j} w_j \alpha(t - t_f^j). \quad (3.2)
\]

\[
u(t_f^j) = \vartheta. \quad (3.3)
\]

\[
\lim_{\delta \to 0} u(t_f^j + \delta) = u_{\text{res}}. \quad (3.4)
\]
Response of IF neurons to constant input currents

[1] very short current input: \[ \tau_m \frac{du(t)}{dt} + u(t) = 0. \]  
\[ u(t) = e^{-t/\tau_m}. \]

[2] low, constant input current: \[ \frac{du}{dt} = 0. \]
\[ u = RI. \]
\[ u(t) = RI(1 - e^{-t/\tau_m} + \frac{u(t = 0)}{RI} e^{-t/\tau_m}), \]
Constant input current in IF neuron: low vs. high
Gain functions

The time when the membrane reaches the firing threshold:

\[ t^f = -\tau_m \ln \frac{\vartheta - RI}{u_{res} - RI}. \quad (3.10) \]

Firing rate: inverse of this time

\[ \bar{r} = \left( t^{ref} - \tau_m \ln \frac{\vartheta - RI}{u_{res} - RI} \right)^{-1}, \quad (3.11) \]

: Gain function

Output:
Firing rate

U_{res}: reset potential (resting potential)
The spike-response model

Time-varying input currents $I(t)$

\[ u(t) = R \int_0^\infty e^{-s/\tau_m} I(t - s) ds. \]  

\[ u(t) = \sum_j \sum_{t^j_i} w_j \epsilon(t - t^f_j, t^f_j, t - t^f_i) + \sum_{t^f} \eta(t - t^f). \]  

\[ \epsilon(t - t^f_j) = R \int_0^\infty e^{-s/\tau_m} \alpha(t - t^f_j - s) ds \]  

Summed spike responses from presynaptic spikes

\[ \eta(t - t^f) = -\vartheta e^{-(t-t^f)/\tau_m}. \]  

The reset of the membrane potential after a postsynaptic spike

\[ RI_{res} = -\vartheta \delta(t - t^f). \]
### Spike response functions

Table 3.1 Examples of spike response functions (right column) describing the membrane potential in response to the corresponding forms of PSPs (left column) used in simulations and analytical models. \( t^f \) is the firing time of the presynaptic neuron and \( t^d \) is the duration of the \( \alpha \)-pulse in the second example. \( \tau_m \) and \( \tau_s \) are time constants.

<table>
<thead>
<tr>
<th>Effective potential after a single presynaptic spike</th>
<th>Spike-response function</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ \alpha(t) = \delta(t - t^f) ]</td>
<td>[ \epsilon(t) = \begin{cases} 0 &amp; t \leq t^f \ \frac{1}{\tau_m} e^{-\frac{(t-t^f)}{\tau_m}} &amp; t^f &lt; t \leq t^d \ 0 &amp; t &gt; t^d \end{cases} \text{ for } t \leq t^f \ \begin{cases} 1 - \frac{1}{\tau_m} e^{-\frac{(t-t^f)}{\tau_m}} &amp; t^f &lt; t \leq t^d \ (1 - \frac{1}{\tau_m}) e^{-\frac{(t-t^f)}{\tau_m}} - \frac{1}{\tau_s} e^{-\frac{(t-t^f)}{\tau_s}} &amp; t &gt; t^d \end{cases} \text{ for } t &gt; t^f ]</td>
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<tr>
<td>[ \alpha(t) = \begin{cases} 0 &amp; t \leq t^f \ \frac{1}{\tau_s} e^{-\frac{(t-t^f)}{\tau_s}} &amp; t^f &lt; t \leq t^d \ 0 &amp; t &gt; t^d \end{cases} ]</td>
<td>[ \epsilon(t) = \begin{cases} 0 &amp; t \leq t^f \ \frac{1}{1 - \frac{1}{\tau_s/\tau_m}} (e^{-\frac{(t-t^f)}{\tau_m}} - e^{-\frac{(t-t^f)}{\tau_s}}) &amp; t &gt; t^f \end{cases} ]</td>
</tr>
</tbody>
</table>
Spike time variability

\[ C_V = \frac{\sigma}{\mu}. \]  

(3.18)

A. ISI-histogram from cell data

B. ISI-histogram from Poisson spike train

Biological Irregularity: sensory inputs, structural irregularity
Stochastic modeling: Normal distribution vs. Exponential distribution

\[ \text{pdf}_\text{normal}(x; \mu, \sigma)(x) = \frac{1}{\sqrt{2\sigma}} e^{-(x-\mu)^2/2\sigma^2}, \quad (3.19) \]

\[ \text{pdf}_\text{exponential}(x; \lambda)(x) = \lambda e^{-\lambda x}. \quad (3.20) \]

\[ \text{pdf}_\text{Poisson}(x; \lambda)(x) = \sum_{i=1}^{x} \frac{\lambda^i e^{-\lambda}}{i!}. \quad (3.21) \]
Noise model for IF neurons

Stochastic channel opening and closing

Stochastic expression of channel proteins.

Not recorded yet.

Random noise inputs + thermal noise

\[
\vartheta \rightarrow \vartheta + \eta^{(1)}(t)
\]

\[
\tau_m \frac{du}{dt} = -u + R I_{\text{ext}} + \eta^{(3)}(t)
\]

\[
u_{\text{res}} \rightarrow u_{\text{res}} + \eta^{(2)}(t)
\]
Simulating variability of real neurons

\[ I_{\text{ext}} = \bar{I}_{\text{ext}} + \eta \quad \text{with} \quad \eta \in N(0, 1). \quad (3.25) \]

\[ \text{pdf}^{\text{lognormal}}(x; \mu, \sigma) = \frac{1}{x\sigma\sqrt{2\pi}} e^{-\frac{(\log(x) - \mu)^2}{2\sigma^2}}. \quad (3.26) \]
Simulation of an IF neuron

Amplitude of incoming spike: \( w = 0.5 \) vs. \( w = 0.25 \)

Average firing rate: 118 Hz vs. 16 Hz
The gain function of an IF neuron

Output firing rates

Mean firing rates of inputs

\[ \bar{\tau} = (t_{\text{ref}} + \tau_m) \int_{(u_{\text{res}} - R\bar{I}_{\text{ext}})/\sigma}^{(\theta - R\bar{I}_{\text{ext}})/\sigma} \sqrt{\pi} e^{u^2} [1 + \text{erf}(u)] du^{-1} \]  \hspace{1cm} (3.27)

\[ \bar{\tau} = \bar{\tau}(\mu, \sigma, \ldots) \]  \hspace{1cm} (3.28)
Stochastic neuron modeling of Circadian Rhythms
BETTY DISCOVERS HER BIOLOGICAL TIME CLOCK IS TICKING
Biological Rhythms

Most animals and plants exhibit a **24-hour periodic** behavior in endocrinial and behavioral activity including hormone secretion, temperature, behavioral activity.
Where is the biological clock in the brain?

Suprachiasmatic nucleus (SCN)
The molecular mechanism of the SCN
Why do Physicists work on circadian rhythms?

- Circadian rhythm generation: Complex spiking patterns
- Synchronization
- Entrainment
- Phase resetting (the phase response curve)
- The origin and implications of neural oscillation
- The SCN contains pacemaker neurons imposing **circadian rhythmicity** in mammals.
- This circadian modulation is known to be associated with rhythmic changes in endogenous and behavioral activity in mammals.
SCN neurons exhibit irregular spontaneous firing patterns, accompanied by intermittent bursts, and thus generate complex ISI patterns, although the average SFR seems to maintain a circadian rhythm.
The aim of the study

- How this irregular spontaneous spiking activity of individual SCN neurons eventually produces the long-range circadian rhythm is poorly understood.

- As a first step toward understanding this issue, we investigate the firing pattern of individual SCN neurons and its underlying dynamics.

- In this study, we used nonlinear time series methods to determine whether the complex ISI patterns of SCN neurons are random or deterministic, a critical issue for understanding its underlying cellular mechanism.
SCN neurons exhibit irregular spontaneous firing patterns, accompanied by intermittent bursts, and thus generate complex ISI patterns, although the average SFR seems to maintain a circadian rhythm.
Slice preparation

1. 42 male Sprague-Dawley rats (40-100g) were housed in a temperature-controlled room under a 12h light- 12h dark cycle (light on at 7hr) for at least 2 weeks prior to use.

2. During the daytime of subjects, rats were anesthetized with Nembutal, decapitated and the brains were quickly removed.

3. A block of hypothalamic tissue was cut and sectioned with a vibrating tissue slicer (Vibratome) to thickness of 150-200um.

4. Coronal tissue slices containing the SCN were transferred to recording chamber and artificial cerebrospinal fluid (ASCF) constantly perfused at 1-1.5 ml/min. ASCF was maintained to room temperature 25-27 ℃.
Extracellular recording

• After 1-hr incubation in the recording chamber, extracellular recordings were commenced at room temperature (25-27 °C).
• Cell-attached patch (CAP) configuration without membrane rupture was achieved for extracellular, single-unit recording. In a CAP mode, a single action potential caused a transient capacitive current over the patch of membrane sucked into the pipette tip.
• The mean number of data points was 7,356 ± 2,961 (range: 1,422 - 19,213). For each recording, first two minute of data were discarded to ensure the stationarity of the ISI sequences as possible.
Dynamical Heterogeneity of spiking Patterns of the Rat Suprachiasmatic Nucleus \textit{in vitro}.

Jeong et al., J Computational Neuroscience (2004)
Fano factor (Allan Factor)

The Fano factor (FF) is the ratio of the variance of the number of spiking events in a counting number to the mean.

\[ F(T) = \frac{\text{var}[N_i(T)]}{<N_i(T)>} \]

The FF of a fractal stochastic process takes the power-law form \((0 < \alpha_F < 1)\) for large counting time \(T\), while it tends to stay in a constant value independent of \(T\) for a renewal process. The \(\alpha_F\) is considered as the fractal exponent (scaling exponent) of the point process. The power-law form implies that the fluctuations in the firing rate converge relatively slowly as \(T\) is increased.
Fractal stochastic modeling spiking patterns of the rat suprachiasmatic nucleus *in vitro*.

Kim et al., J. Comp. Neurosci. (in press)
Fractal stochastic process is one example of non-renewal processes having dependencies among ISIs. This process exhibits power-law behavior of one or more statistics. The dependencies (or correlation) among ISIs generated by the fractal stochastic process can be quantified by various fractal measures.
Temporal Dynamics Underlying Spiking Patterns of the Rat Suprachiasmatic Nucleus *in vitro*.

Kim et al. J. Computational neuroscience (in press)
Conclusion

• The suprachiasmatic nucleus (SCN) is known to be the master biological clock in mammals. Despite the periodic mean firing rate, interspike interval (ISI) patterns of SCN neurons are quite complex and irregular.

• Circadian rhythm and nonlinear dynamics of SCN are also important research issues in physics as well as chronobiology including synchronization, neural oscillations, and phase resetting.

• Physical analysis and computational modeling might provide insight into physiological mechanisms underlying circadian rhythms.
The Izhikevich neuron model was developed as an efficient, powerful alternative to the integrate-and-fire model.

The model uses ‘two variables’, a variable representing voltage potential and another representing membrane recovery (activation of potassium currents and inactivation of sodium currents).

This is a spiking neuron, so when the voltage passes a threshold value, a spiking event occurs, and the voltage and recovery variable are reset.
Izhikevich neuron

• Since $a$ is a parameter of the model, we use $v$ to represent activation (voltage potential). $u$ represents the recovery variable. Voltage is computed by integrating the following two differential equations using Euler's method:

$$\frac{dv}{dt} = .04v^2 + 5v + 140 - u + W \quad \frac{du}{dt} = a(bv - u)$$

• $W$ is weighted inputs; $a$ and $b$ are abstract parameters of the model. When the voltage exceeds a threshold value, which is preset at 30, both $v$ and $u$ are reset, as follows:

$$v \rightarrow c \quad u \rightarrow u + d$$

"The model can exhibit firing patterns of all known types of cortical neurons with [a suitable] choice of parameters"
Izhikevich neuron
McCulloch-Pitts neuron

- This neuron model was the boolean neuron for neural networks, firstly proposed by McCulloch and Pitts.
- As depicted, this neuron, with a threshold ($\theta$) of 1, can act as an inclusive-or logic gate. With weights assumed to be 1, inputs from either or both axon a and axon b will cause the neuron to fire and produce an output of 1. Only if both axons are quiet (0), will the neuron not fire.
(a) precession

(b) disjunction

(c) conjunction

(d) conjoined negation

(e) (a)~(d)의 합

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The neural code

• Neural coding is a neuronal scheme to explain how sensory and other information is represented in the brain by networks of neurons.

• The main goal of studying neural coding is to characterize the relationship between the stimulus and the individual or ensemble neuronal responses and the relationship among electrical activity of the neurons in the ensemble.

• It is thought that neurons can encode both digital and analog information.
Encoding and decoding

• The link between stimulus and response can be studied from two opposite points of view.

• **Neural encoding** refers to the map from stimulus to response. The main focus is to understand how neurons respond to a wide variety of stimuli, and to accurately construct models that attempt to predict responses to other stimuli.

• **Neural decoding** refers to the reverse map, from response to stimulus, and the challenge is to reconstruct a stimulus, or certain aspects of that stimulus, from the spike sequences it evokes.
Coding Schemes

- A sequence, or 'train', of spikes may contain information based on different coding schemes. In motor neurons, for example, the strength at which an innervated muscle is flexed depends solely on the 'firing rate', the average number of spikes per unit time (a 'rate code').

- At the other end, a complex 'temporal code' is based on the precise timing of single spikes. They may be locked to an external stimulus such as in the auditory system or be generated intrinsically by the neural circuitry.

- Whether neurons use rate coding or temporal coding is a topic of intense debate within the neuroscience community, despite the absence of clear definition of these terms.
Rate coding

• Rate coding is a traditional coding scheme, assuming that most, if not all, information about the stimulus is contained in the firing rate of the neuron.

• Because the sequence of action potentials generated by a given stimulus varies from trial to trial, neuronal responses are typically treated statistically or probabilistically. They may be characterized by firing rates, rather than as specific spike sequences.

• In most sensory systems, the firing rate increases, generally non-linearly, with increasing stimulus intensity. Any information possibly encoded in the temporal structure of the spike train is ignored. Consequently, rate coding is inefficient but highly robust with respect to the ISI 'noise.'
Spike trains and average response over trials
Rate coding

• The concept of firing rates has been successfully applied during the last 80 years. It dates back to the pioneering work of ED Adrian who showed that the firing rate of stretch receptor neurons in the muscles is related to the force applied to the muscle.

• In the following decades, measurement of firing rates became a standard tool for describing the properties of all types of sensory or cortical neurons, partly due to the relative ease of measuring rates experimentally.

• However, this approach neglects all the information possibly contained in the exact timing of the spikes.
Rate coding

- During recent years, more and more experimental evidences have suggested that a straightforward firing rate concept based on temporal averaging may be too simplistic to describe brain activity.
- During rate coding, precisely calculating firing rate is very important. In fact, the term “firing rate” has a few different definitions, which refer to different averaging procedures, such as an average over time or an average over several repetitions of experiment.
- In rate coding, learning is based on activity-dependent synaptic weight modifications.
Brain-Machine Interface
How accurate is spiking timing?

A. Constant stimulus

B. Rapidly changing stimulus
Temporal coding

- When precise spike timing or high-frequency firing-rate fluctuations are found to carry information, the neural code is often identified as a temporal code.

- A number of studies have found that the temporal resolution of the neural code is on a millisecond time scale, indicating that precise spike timing is a significant element in neural coding.

With correlation, Coincidence detector
Perfect integrator and Coincident detector
Temporal coding

- Temporal codes employ those features of the spiking activity that cannot be described by the firing rate.

- For example, time to first spike after the stimulus onset, characteristics based on the second and higher statistical moments of the ISI probability distribution, spike randomness, or precisely timed groups of spikes (temporal patterns) are candidates for temporal codes.

- As there is no absolute time reference in the nervous system, the information is carried either in terms of the relative timing of spikes in a population of neurons or with respect to an ongoing brain oscillation.
Temporal coding

- The temporal structure of a spike train or firing rate evoked by a stimulus is determined both by the dynamics of the stimulus and by the nature of the neural encoding process.
- Stimuli that change rapidly tend to generate precisely timed spikes and rapidly changing firing rates no matter what neural coding strategy is being used.
- Temporal coding refers to temporal precision in the response that does not arise solely from the dynamics of the stimulus, but that nevertheless relates to properties of the stimulus.
- The interplay between stimulus and encoding dynamics makes the identification of a temporal code difficult.
Temporal coding

• In temporal coding, learning can be explained by activity-dependent synaptic delay modifications.

• The modifications can themselves depend not only on spike rates (rate coding) but also on spike timing patterns (temporal coding), i.e., can be a special case of spike-timing-dependent plasticity.
Temporal and Rate coding

(A) Waveform illustrating phase shifts over time.

(B) Scatter plot showing phase of firing against position.

(C) Graph depicting firing frequency against position.
Population coding

- Population coding is a method to represent stimuli by using the joint activities of a number of neurons. In population coding, each neuron has a distribution of responses over some set of inputs, and the responses of many neurons may be combined to determine some value about the inputs.

- From the theoretical point of view, population coding is one of a few mathematically well-formulated problems in neuroscience. It grasps the essential features of neural coding and yet, is simple enough for theoretic analysis.
Population coding

- Experimental studies have revealed that this coding paradigm is widely used in the sensor and motor areas of the brain. For example, in the visual area medial temporal (MT), neurons are tuned to the moving direction.

- In response to an object moving in a particular direction, many neurons in MT fire, with a noise-corrupted and bell-shaped activity pattern across the population. The moving direction of the object is retrieved from the population activity, to be immune from the fluctuation existing in a single neuron’s signal.
Population coding

- Population coding has a number of advantages, including reduction of uncertainty due to neuronal variability and the ability to represent a number of different stimulus attributes simultaneously.

- Population coding is also much faster than rate coding and can reflect changes in the stimulus conditions nearly instantaneously.

- Individual neurons in such a population typically have different but overlapping selectivities, so that many neurons, but not necessarily all, respond to a given stimulus.
Correlation coding

- The correlation coding model of neuronal firing claims that correlations between action potentials, or "spikes", within a spike train may carry additional information above and beyond the simple timing of the spikes.

- It has been theoretically demonstrated that correlation between spike trains can only reduce, and never increase, the total mutual information present in the two spike trains about a stimulus feature.

- Any degree of correlation reduces the total entropy; thus, by Fisher's Information Theorem, correlations can only reduce information.
Correlation coding

• However, this does not prevent correlations from carrying information not present in the average firing rate of two pairs of neurons.

• A good example of this exists in the pentobarbital-anesthetized marmoset auditory cortex, in which a pure tone causes an increase in the number of correlated spikes, but not an increase in the mean firing rate, of pairs of neurons.
Spike-triggered rate encodes the stimulus, rather than rates of individual spike trains.
Population dynamics: modeling the average behavior of neurons:

**Population averages**

A

B

rate = average over pool of equivalent neurons (several neurons, single run)

\[
\begin{align*}
A(t) &= \lim_{\Delta T \to 0} \frac{1}{\Delta T} \frac{1}{N} \sum_{i=1}^{N} \delta(t' - t_{i}^f)dt'. \\
&= \lim_{\Delta T \to 0} \frac{1}{\Delta T} \int_{t-\Delta T/2}^{t+\Delta T/2} \frac{1}{N} \sum_{i=1}^{N} \delta(t' - t_{i}^f)dt'.
\end{align*}
\]
Population dynamics: modeling the average behavior of neurons:

Population averages

\[
A(t) = \lim_{\Delta T \to 0} \frac{1}{\Delta T} \frac{\text{number of spikes in population of size } N}{N} \\
= \lim_{\Delta T \to 0} \frac{1}{\Delta T} \int_{t-\Delta T/2}^{t+\Delta T/2} 1 \sum_{i=1}^{N} \delta(t' - t^f_i) dt'.
\]

(4.7)

\[
A(t) dt = \frac{1}{N} \sum_{i=1}^{N} \delta(t' - t^f_i),
\]

(4.8)

\[
\tau \frac{dA(t)}{dt} = -A(t) + g(RI^{\text{ext}}(t)).
\]

(4.9)

\[
A(t) = g(RI^{\text{ext}}(t)).
\]

(4.10) : Asymptotic stationary states
Motivations for Population dynamics

\[ u_i(t) = \sum_{t^f} \eta(t - t^f) + \sum_{j} \sum_{t_j^f} w_{ij} \epsilon(t - t_j^f). \quad (4.11) \]

\[ w_{ij} = \frac{w_0}{N}. \quad (4.12) \]

\[ u_{\epsilon}(t) = w_0 \int_0^{\infty} \epsilon(t') A(t - t') dt'. \quad (4.13) \]

\[ A(t) = \int_{-\infty}^{t} P_u(t|t^f) A(t^f) dt^f. \quad (4.14) \]

\[ g(x) = \frac{1}{t^{\text{ref}} - \tau \log(1 - \frac{1}{\tau x})}, \quad (4.15) \]

- Probability density
- Activation function (or gain function)
- mean influence of the postsynaptic potential using the rate of the population
Similar activation functions of neuronal populations and a single cell

A. Gain function for population average in adiabatic limit

Activation

\[ g(x) \]  

Inputs

B. Gain function of hippocampal pyramidal neuron

Discharge frequency [Hz]  
Current [nA]
Frequently used activation functions

<table>
<thead>
<tr>
<th>Type of function</th>
<th>Graph</th>
<th>Mathematical formula</th>
<th>Matlab implementation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear</td>
<td>![Linear Graph]</td>
<td>$g_{lin}(x) = x$</td>
<td><code>x</code></td>
</tr>
<tr>
<td>Step</td>
<td>![Step Graph]</td>
<td>$g_{step}(x) = \begin{cases} 1 &amp; \text{if } x &gt; 0 \ 0 &amp; \text{elsewhere} \end{cases}$</td>
<td><code>floor(0.5*(1+sign(x)))</code></td>
</tr>
<tr>
<td>Threshold-Linear</td>
<td>![Threshold-Linear Graph]</td>
<td>$g_{th-lin}(x) = x \Theta(x)$</td>
<td><code>x.*floor(0.5*(1+sign(x)))</code></td>
</tr>
<tr>
<td>Sigmoid</td>
<td>![Sigmoid Graph]</td>
<td>$g_{sigmoid}(x) = \frac{1}{1+\exp(-x)}$</td>
<td><code>1./(1+exp(-x))</code></td>
</tr>
<tr>
<td>Radial-basis</td>
<td>![Radial-basis Graph]</td>
<td>$g_{rb}(x) = \exp(-x^2)$</td>
<td><code>exp(-x.^2)</code></td>
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</tbody>
</table>