Leaky integrate and fire model

\[ \dot{u} = \left( E_L + R_M \cdot I(t) - u \right)/\tau \]

At threshold \( \vartheta \), the neuron fires a spike (usually modelled as dirac pulse), and the membrane potential is reset to \( u_r \).

Thus, the time course of the membrane potential in response to a constant current \( I_0 \) can be calculated analytically by integrating the differential equation.

The solution is:

\[ u(t) = R \cdot I_0 \cdot \left( 1 - \exp \left( - \frac{t - t_f}{\tau} \right) \right) - u_r \]
Leaky integrate and fire model

\[ \vartheta = R \cdot I_0 \cdot \left(1 - \exp\left(-\frac{t_2 - t_1}{\tau}\right)\right) - u_r \]

\[ \Delta t = t_2 - t_1 = -\tau \cdot \ln\left(1 - \frac{\vartheta - u_r}{R \cdot I_0}\right) \]

To calculate the firing rate of the neuron in response to a constant input current, we simply set \( u(t) = \vartheta \), and calculate the time between two successive spikes. The firing rate is then \( f = 1/\Delta t \).

In many applications, an absolute refractory time \( t_{\text{abs}} \) is introduced to account for the fact that two spikes cannot follow each other immediately.
Spike rate adaptation

Many real neurons show spike rate adaptation, i.e., the firing rate in response to a constant current decreases over time ($\tau=100\text{ms}$). The original integrate and fire neuron can be modified to account for this behaviour by adding an additional current with a time-dependent conductance $g_{rsa}$ (modelled as $K^+$ conductance).

When the neuron fires, the conductance is increased by a constant amount.

\begin{align*}
\dot{u} &= \left( E_L + R_M \cdot I(t) - r_m \cdot g_{rsa} \cdot (u - E_K) - u \right) / \tau \\
\dot{g}_{rsa} &= -\frac{g_{rsa}}{\tau_{rsa}} \\
\lim_{t \to t_f, t > t_f} g_{rsa}(t) &= g_{rsa}(t_f) + \Delta g_{rsa}
\end{align*}
Refractory period

Instead of introducing an artificial absolute refractory period, a more realistic relative refractory period can be simulated by the same mechanism as spike rate adaptation, but with a much shorter time constant ($\tau=2\text{ms}$) and larger increase of the leak conductance following an action potential.
Synaptic transmission

Information is collected via the dendritic tree.

Increase in membrane potential leads to an action potential at the axon hillock.

The action potential is actively moving along the axon.

It arrives at the synapses, causes release of neurotransmitters.

Neurotransmitters open ion channels at the postsynaptic neuron.

This leads to a change in conductance, and consequently to a change in the membrane potential of the postsynaptic neuron.
Action potential causes Ca\textsuperscript{2+} channels to open. Calcium influx causes vesicles to fuse with the membrane and release transmitter. Transmitter causes receptor channels to open, an excitatory postsynaptic potential (EPSP) can be observed.
Synaptic transmission: transmitters and receptors

Excitatory

Transmitter: glutamate
Results in opening of Na⁺ and Ka⁺ channels at the postsynaptic membrane
Reversal potential is at 0 mV (i.e., at 0 mV, no EPSP is visible)

Ionotropic glutamate receptors: AMPA, kainate, NMDA
AMPA: \(\alpha\)-amino-3-hydroxy-5-methylisoxazole-4-propionic acid
NMDA: \(N\)-methyl-D-aspartate

**AMPA**
short time constant (2 ms)

**NMDA**
long time constants (rise: 2 ms, decay 100 ms)
voltage dependent: Mg²⁺ blocks channel at –65 mV and opens upon depolarization
needs extracellular glycine as cofactor

Metabotropic glutamate receptors: indirectly gate channels through second messengers
Synaptic transmission: transmitters and receptors

Inhibitory

Transmitter: GABA and glycine
Results in opening of Cl⁻ channels at the postsynaptic membrane
Reversal potential is at -70 mV (i.e., at -70 mV, no IPSP is visible)

GABA-receptors: GABAₐ (ionotropic) and GABAₐ (metabotropic)

GABAₐ
longer time constant 10 ms, Cl⁻ conductance

GABAₐ
Opening of K⁺ channels, reversal potential –80 mV

Single channel conductance of glycine is larger (46 pS) than that of GABA (30 pS)
Synaptic transmission can be modelled by lowpass filter dynamics. The dynamics of the EPSP can be described by one or multiple time constants.
Numerical simulation

\[ \tau \frac{du}{dt} = E + R \cdot I - u \]

Basic differential equation.

\[ \frac{du}{dt} \approx \frac{u(t) - u(t - \Delta t)}{\Delta t} \]

Express the derivative by a difference.

\[ u_i := u(t_i) \quad t_{i+1} := t_i + \Delta t \]

For convenience, use indices.

\[ \dot{u}_{i+1} = \left( E + R \cdot I_i - u_i \right)/\tau \]

Calculate derivative \( du_{i+1}/dt \) at time \( t_{i+1} \) from values at time \( t_i \).

\[ \dot{u}_{i+1} \approx \frac{u_{i+1} - u_i}{\Delta t} \]

Integration step: calculate \( u_{i+1} \) from the known value \( u_i \) and the derivative.

(Euler one-step method)

\[ \Rightarrow u_{i+1} = u_i + \dot{u}_{i+1} \cdot \Delta t \]

Note: for good convergence, \( \Delta t \) has to be much smaller than \( \tau \).
Basic equation for synaptic input

\[ C_m \frac{dV}{dt} = -g_l \cdot (V - E_l) - g_s \cdot w_s \cdot p_s \cdot (V - E_s) \]

\[ \frac{dp_s}{dt} = -\frac{p_s}{\tau_s} + \sum_k \delta(t - t_k) \]

*\( p_s \) : fraction of open channels
*\( w_s \) : synaptic weight
*\( E_s \) : synaptic resting potential
*\( \tau_s \) : synaptic time constant

Basic differential equation of the leaky integrate and fire model with synaptic input.

The fraction of open channels determines the synaptic conductivity.

The product of conductivity and difference between membrane potential and synaptic resting potential determines the synaptic current.
Numerical simulation in MATLAB

1) Script-based numerical simulations

- Uses MATLAB programming language
- Various solvers for ordinary differential equations available
- Sometimes much more flexible than Simulink
- Requires some programming skills

2) Simulink-based numerical simulations

- Simulink graphical user interface
- Very convenient for rapid development
- Provides inbuilt visualization (scopes)
- Subsystems for modular architectures
- Vectorization for simulation of large numbers of neurons
Synaptic transmission: change in conductance

Synapse as change in input current: the effective afferent current $I(t)$ of a neuron depends on the input from $N$ synapses with weights $w_i$. The $k^{th}$ spike arrives at time $t_{ik}$ at synapse $i$.

$$\dot{I}(t) = \left( \sum_{i=1}^{N} w_i \cdot \sum_k \delta(t_{ik} - t) - I(t) \right) / \tau'$$

More realistic: change in conductance; involves not only the arriving spikes, but also the membrane potential of the postsynaptic neuron.

If the reversal potential of the synapse $u_E$ is sufficiently high (true for excitatory synapses, e.g. $u_E=0$), then the dependence of the postsynaptic current on the membrane potential can be neglected.

The effect of inhibitory spikes depends on the membrane potential of the postsynaptic neuron.

$$I(t) = g \cdot (u_E - u(t)) \cdot \sum_{i=1}^{N} s_j(t)$$

$$\dot{s}_j(t) = \sum_k \delta(t - t_{ik}) - s_j(t) / \tau'$$

For inhibitory synapses, this is not the case: $u_E$ is usually equal to the reversal potential of the neuron itself.
Synaptic transmission

Train of input spikes
(from one or more neurons, s is linear!)

Change in conductance s (blue)
Change in input current (red)

Membrane potential

Output spikes
Synaptic transmission: shunting inhibition

excitation only  "silent" inhibition  shunting inhibition

Strong inhibitory inputs do not need to generate an IPSP to affect output.
Inhibition changes the conductance of the membrane: the neuron becomes leakier!
Spike timing makes a difference!

Left: uncorrelated input spikes (i.e., spikes do not occur at the same time) from 3 neurons do not cause the postsynaptic cell to fire

Right: the same number of input spikes, again from 3 neurons, lead to firing of the postsynaptic cell, if spike times are correlated
From real spikes to spike events

Get spikes from measured data:

Determine a threshold for spike discrimination

Detect maxima above threshold
Probability distribution of time between action potentials (inter-spike interval, ISI) shows two peaks. This indicates that the neuron responded to some external events.

Another way to look at it: scatter plot of successive ISIs.

How can we describe spiking in terms of statistics?
Distribution of inter-spike intervals

Probability that a neuron discharges \( n \) spikes in the time interval \( t \) can be described by the Poisson distribution (\( \lambda \): mean and variance):

\[
P(t, n) = \frac{(\lambda \cdot t)^n}{n!} \cdot e^{-\lambda \cdot t}
\]

Probability that the neuron does not fire in the time interval \( T \):

\[
P(t < T) = 1 - P(T, 0) = 1 - e^{-\lambda \cdot T}
\]

Hence, the probability to find an ISI of \( T \) is:

\[
P(T) = \frac{d}{dT} P(t < T) = \lambda \cdot e^{-\lambda \cdot T}
\]

This is the exponential distribution
(see, e.g., Shadlen & Newsome 1998).

Better description: the Gamma distribution (assume that the neuron discharges only after \( k \) events, or, in other words, only every \( k \)'th time):

\[
P(T) = \frac{T^{k-1}}{\Gamma(k)} \cdot \lambda^k \cdot e^{-\lambda \cdot T}
\]

\( k \) can thus be conceived as neuronal threshold.
Distribution of inter-spike intervals

Empirical probability distribution of ISIs of a real neuron fitted with the gamma distribution.
From spikes to firing rate

Compute the instantaneous firing rate from spike events

\[ f_{i+1} = \frac{1}{t_{i+1} - t_i} \]

\( f \) : firing rate

\( t_i \) : time of \( i \)th spike

The instantaneous firing rate is assumed to be constant between spikes.

Technically, however, it does not exist between spikes.
From spikes to firing rate

Different methods to approximate firing rate. A: spike train, B: discrete rate, bins of 100ms, C: sliding window (100ms), D: Gaussian window ($\sigma=100$ms), E: alpha function window ($1/\alpha=100$ms)

Convolution (Faltung):

$$f(t) = r \ast s = \int_{-\infty}^{\infty} r(\tau) \cdot s(t-\tau) d\tau$$

Dayan & Abbott 2000
Top: Firing rate computed via interspike interval or convolution with a Gaussian window (corresponding to a probability distribution of each spike).
Bottom: Synaptic current computed from spike train or from firing rate.
From spiking neurons to firing rate

The current due to synaptic input is approximately described by leaky integration of the incoming spikes.

\[
\dot{I}(t) = w \cdot \sum_k \delta(t_k - t) - I(t) / \tau'
\]

The average firing rate \(r\) can be expressed as convolution (filtering) of the spike train with a window function (kernel) \(W(t)\), or as sum over the window functions at the times where spikes occur.

\[
r(T) = \int_{-\infty}^{\infty} \sum_k \delta(t_k - t) \cdot W(T - t) \cdot dt
\]

\[
\Rightarrow r(T) = \sum_k W(t_k - T)
\]

The sum over the incoming spikes can thus be replaced by the respective firing rate, if the interspike intervals are short compared to the synaptic time constant.

\[
\dot{I}(t) = w \cdot r_{pre}(t) - I(t) / \tau'
\]

\[
r_{post}(t) = F(I(t))
\]

The firing rate of the postsynaptic neuron is determined by the neuron’s response function \(F(I(t))\), which can be approximated by a threshold-linear function for the ideal integrate-and-fire neuron.
From spiking neurons to firing rate

Firing rate networks come in various flavours.

Usually, the dynamics are modelled by a single time constant, which may vary among neuron populations or for different types of synapses.

The time constant describes either the dynamics of synaptic transmission, or that of the neuron itself. In the latter case, the time constant will usually will smaller than the membrane time constant.

A combination of both is possible, of course.

\[ \dot{I} = \left( w \circ r_{\text{pre}} - I \right) / \tau_s \]

\[ r_{\text{post}} = F(I) \]

\[ \dot{r}_{\text{post}} = \left( F(w \circ r_{\text{pre}}) - r_{\text{post}} \right) / \tau_m \]
From spiking neurons to firing rate

For long synaptic time constants, the spike rate response of the postsynaptic neuron is determined by the synaptic time constant.