TD 4 – Synapses & Dendrites

Practical Information

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TD Material
https://github.com/esther-poniatowski/2223_UlmM2_ThNeuro

Goals of the TD

This TD aims to study **synaptic transmission** through the lens of **signal processing**.
Indeed, synapses actively contribute to neuronal *computations* by transforming pre-synaptic spike trains into post-synaptic inputs with potentially different features. They can be conceived as *filters* endowed with a large computational power, because their transmission properties (i.e. the type of information conveyed from pre- to post-synaptic signals) can be affected by the history of pre- and post-synaptic firing in various ways. Understanding neural coding and information processing thus requires to take into account signal transformations performed at multiple steps during synaptic transmission.

In order to predict post-synaptic responses triggered by pre-synaptic spike trains, models can incorporate several mechanisms :

① Pre-synaptic release

In the pre-synaptic neuron, the arrival of an action potential (membrane depolarization) causes the opening of voltage-gated calcium channels. The subsequent elevation of the intra-cellular calcium concentration [Ca^{2+}] elicits the fusion of vesicles with the membrane, thereby releasing neurotransmitters in the synaptic cleft.
► The variable of interest is **synaptic efficacy**, i.e. the amount of transmitters released in response to one spike. Synaptic efficacy is subject to short and long term **plasticity**, which deploy over hundreds of milliseconds to seconds for the former and hours or longer for the latter.

② Post-synaptic input

Neurotransmitters diffuse in the cleft and bind to post-synaptic receptors. Those ligand-gated ion channels generate input currents in the post-synaptic neuron, which cause a subsequent change in its membrane potential. Different types of receptors exist, with different activation times scales.
► The variable of interest is **receptors conductance** and their activation time courses in response to the variations of neurotransmitter concentration in the cleft.

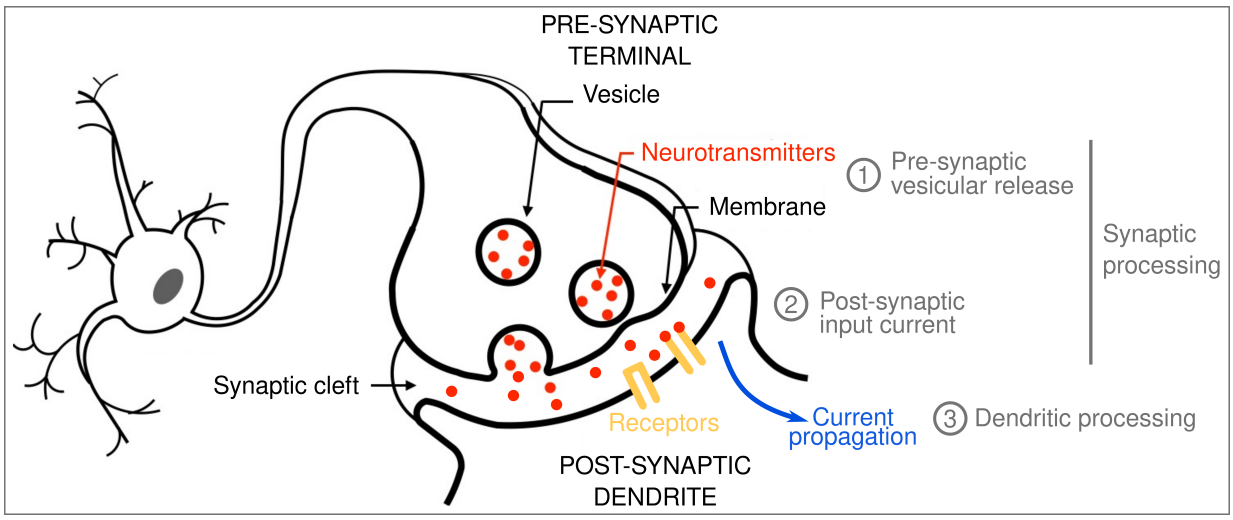
③ Dendritic processing

Finally, in the post-synaptic neuron, the synaptic input currents generated across the whole dendritic tree spread to the soma, where their integration leads to the elaboration of a new spike train. Signals can be further altered during their propagation along the dendrites, which constitutes an additional step of computation.
► The variable of interest is the **spatio-temporal membrane potential** at different locations of the neuron's morphology.

Part **1** *studies different kinds of synaptic plasticity : short term depression (STD) and facilitation (also named potentiation) (STP), and associative spike-timing-dependent plasticity (STDP).*

Part **2** *focuses on receptor kinetics to account for different receptor types.*

Part **3** *investigates dendritic processing through the influence of the spatial separation of inputs and outputs. It derives a spatially continuous model using the cable equation and a discrete model of multiple compartments.*



1 Synaptic plasticity

1.1 Short term depression and facilitation (STD, STP)

Modeling short-term pre-synaptic plasticity

Short-term plasticity refers to the **activity-dependent** variation of **synaptic efficacy** on short time scales (milliseconds to seconds). Short term plasticity can be distinguished between **facilitation** (enhancement of synaptic efficacy with past activity) and **depression** (reduction of synaptic efficacy with past activity), which can coexist in the same synapse with different weights.

In the lens of signal processing, facilitation and depression have functional relevance because they can modulate the *type of information* conveyed in post-synaptic responses about pre-synpatic inputs, especially the amount of *contextual information* about the past spiking history. Modulations can impact both *temporal coding* (when the post-synaptic response preferentially reacts to the occurrence of each individual pre-synaptic spike) and *rate coding* (when the post-synaptic response most strongly varies with the pre-synaptic firing frequency). By possessing both facilitating and depressing synapses, a single axon might be able to convey different messages to its different target post-synaptic neurons.

Models are valuable to assess temporal and rate coding capacities of synapses with various facilitation and depression regimes. Specifically, rate coding can be investigated by the **synaptic transfer function**, which captures the relationship between the pre-synaptic firing frequency and the post-synaptic response amplitude.

Models of synaptic transfer focus on **synaptic efficacy**, which reflects the amount of vesicles released in response to one spike arriving at the axon terminal of the pre-synaptic neuron. This quantity depends on two factors, associated with their own variables in the model :

① Resources pool

The vesicular pool is partitioned into three states, modeled by distinct variables : effective $E(t)$, inactive $I(t)$, and recovered $R(t)$ (all comprised in $[0, 1]$). Each pre-synaptic spike exhausts the available resources by triggering the release of a fraction of vesicles in the recovered pool. Those vesicles immediately become effective, and then quickly inactivate with a time constant τ_i of a few milliseconds. The pool of available resources is replenished by the recovery of inactivated vesicles with a time constant τ_r of about 1 sec.

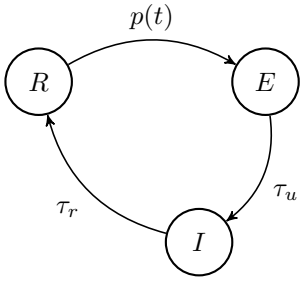
② Calcium concentration

The elicitation of vesicular release thanks to pre-synaptic spikes is modeled by a variable $p(t)$, which stands for the release probability. It corresponds to the fraction of the recovered vesicles released by a single spike. The baseline release probability U is incremented by each spike by a similar amount U. This facilitative effect decays with a time constant τ_p.

Post-synaptic response

On the post-synaptic side, the net input current is assumed to be directly proportional to the fraction of resources in the effective state $E(t)$ by a factor A_{SE} (absolute synaptic efficacy). The latter parameter reflects the maximal possible response which would be generated if all the resources were activated by a pre-synaptic spike.

$$I_{syn}(t) = A_{SE}E(t)$$



1.1.1 Dynamics of the vesicular pool

① Express the amount of vesicles mobilized from the recovered pool in response to a spike as a function of the model's variables.

② By a law of mass, establish kinetic equations for the fraction of resources in each of the three states (i.e. express the dynamics of the variables R, E, I).

③ Solve the dynamical system established at question ② *after* the occurrence of a pre-synaptic spike, assuming that the system is in a state (R_0, E_0, I_0) just after this event.

④ Compare the time constants of inactivation and recovery. Propose an approximation for reducing the vesicular pool system to one single variable.

1.1.2 Depressive synapse – Rate & Temporal coding

In the following questions, the release probability is assumed to be constant to its baseline value U across spiking events.

⑤ Prove the recurrence relation between the amplitudes of two successive post-synaptic input currents elicited by two pre-synaptic spikes separated by an interval T :

$$I_{syn,n+1} = A_{SE}U(1 - e^{-T/\tau_r}) + I_{syn,n}(1 - U)e^{-T/\tau_r} \tag{1}$$

The following questions focus on *rate coding*. It can be investigated once the post-synaptic current has reached a *stationary* (periodic) behavior.

⑥ In the stationary regime, express the post-synaptic current amplitude as a function of the pre-synaptic spiking rate r :

$$I_{\infty}(r) = A\frac{U(1 - e^{-1/r\tau_r})}{1 - (1 - U)e^{-1/r\tau_r}} \tag{2}$$

⑦ Show that it asymptotically decreases in inverse proportion of the pre-synaptic spiking rate, such that :

$$I_{syn}(r) \approx \frac{A_{SE}}{\tau_r}\frac{1}{r} \tag{3}$$

⑧ Comment about the limitation of the synapse to transmit information about the pre-synaptic firing rate.

9 How does the baseline release probability U influence this synaptic transfer function ? Comment on the importance of the parameter U for rate coding.

The following questions focus on *temporal coding*. It can be investigated during the *transient* phase of the response of the post-synaptic current, starting from the first spike to the stationary regime.

10 Express the post-synaptic current after n spikes as a function of its asymptotic value I_∞ :

$$I_{syn,n} = I_\infty + (A_{SE}U - I_\infty)\beta^n \qquad \text{with } \beta = (1-U)e^{-T/\tau_r} \tag{4}$$

11 How does the baseline release probability U influence the time window of transient docidng (time to reach the stationary state) ? Comment on the importance of the parameter U for temporal coding.

1.1.3 Facilitative synapse – Three coding regimes

In the following questions, the dynamics of the release probabilty are taken into account.

12 Express the dynamics of the probability $\frac{\mathrm{d}p}{\mathrm{d}t}$. Solve its temporal evolution between two successive spikes arriving in the pre-synaptic terminal separated by an interval T :

$$p_{n+1} = p_n e^{-T/\tau_p} + U(1 - p_n e^{-T/\tau_p}) \tag{5}$$

13 Show that the stationary values p_∞ and I_∞ as a function of the pre-synaptic firing rate are :

$$p_\infty(r) = \frac{U}{1-(1-U)e^{-1/r\tau_p}} \qquad I_\infty(r) = A\frac{p_\infty(1-e^{-1/r\tau_r})}{1-(1-p_\infty)e^{-1/r\tau_r}} \tag{6}$$

14 Study the limits of both functions (6) for $T \to 0$, $T \to +\infty$.<
Study the limits of I_∞ for a fixed frequency when $p_\infty \to 0$, $p_\infty \to +1$.

15 Sketch the corresponding surface in a graph of axes (T, p_∞, I_∞). Deduce qualitatively that the transfer function of a facilitative synapse could display a maximum at an intermediate frequency. Propose method(s) which could allow to find this maximum.

16 What does the existence of a maximum imply for rate coding ? Justify that a facilitative synapse can function on three coding schemes in different frequency bands : the encoding of absolutes frequencies, of frequencies 'derivatives' (i.e. variations in frequencies), and of frequencies 'integrals' (i.e. number of spikes emitted).

17 With a qualitative biological argument, how does the parameter U influence the relative weights of depression and facilitation in a given synapse ? How could it be modified by learning ? Comment on the effect of learning in switching the coding properties of a synapse.

1.2 Spike-timing-dependent plasticity (STDP)

Modeling spike-timing-dependent plasticity

Spike-timing-dependent plasticity is a class of *long term* modulation of synaptic strength, which depends on both *pre-synaptic and post-synaptic* mechanisms. In this sense, this is an *associative* process, which can be seen as an implementation of the *hebbian learning rule* for adjusting the strength of connections between neurons. This process reinforces or weakens synaptic strengths based on relative spike timings, which might constitute a proxy for causality.

Modeling STDP phenomenologically requires to define a **rule** which specifies how to modify the synaptic strength depending on the time interval between pre- and post-synaptic spikes.

To formalize, pre-synaptic and post-synaptic neurons emit trains of n_{pre} and n_{pre} spikes respectively :

$$(t_{\mathrm{pre},1}, t_{\mathrm{pre},2}, \ldots, t_{\mathrm{pre},n_{pre}}) \qquad (t_{\mathrm{post},1}, t_{\mathrm{post},2}, \ldots t_{\mathrm{post},n_{post}})$$

Each pair of *nearest-neighbor* spikes $(t_{\mathrm{pre},i}, t_{\mathrm{post},j})$ induces the following modification of the synaptic weight w :

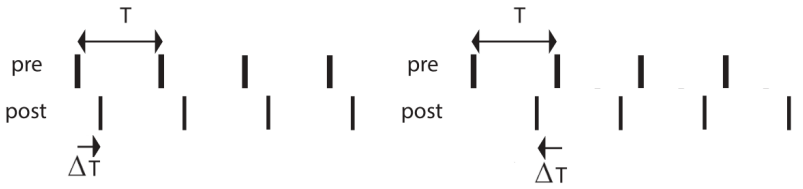
$$\Delta w = f(t_{\mathrm{post},j} - t_{\mathrm{pre},i}) \qquad \text{with} \quad f(s) = \begin{cases} A^+ e^{-s/\tau^+} & \text{if } s \geq 0 \\ -A^- e^{s/\tau^-} & \text{if } s < 0 \end{cases} \tag{7}$$

with A^+, A^-, τ^+ and τ^- positive parameters.

Pairs of spikes are considered *nearest-neighbors* if and only if there is no other spike in the interval between the two spikes $]t_{\mathrm{pre},i}, t_{\mathrm{post},j}[$ (or $]t_{\mathrm{post},j}, t_{\mathrm{pre},i}[$). The synaptic modification is the sum of all modifications induced by the individual nearest-neighbor pairs.

1.2.1 Regular pre-synaptic train

In the following questions, both neurons fire n spikes periodically with a frequency $F = 1/T$, with T the inter-spike interval of each neuron.
Pre-synaptic and post-synaptic spikes are separated by a fixed interval $\Delta T = t_{\mathrm{post},i} - t_{\mathrm{pre},i}$ for all $i = 1, \ldots n$. The sign of ΔT is chosen such that $\Delta T \in [-T/2, T/2]$.



18 Compute the total synaptic modification W induced by these spike trains, distinguishing for $\Delta T \in [-T/2, 0]$ and $\Delta T \in [0, T/2]$.

19 Compute the synaptic modification W when the inter-spike interval T is much longer than the widths of the STDP windows τ^+ and τ^-, for both $\Delta T > 0$ and $\Delta T < 0$. Sketch how W depends on ΔT.

20 Compute the synaptic modification when the inter-spike interval T is much shorter than the widths of the STDP windows. Sketch again the dependence of W on ΔT.

1.2.2 Stochastic pre-synaptic train

In the following questions, spikes are produced randomly. For the sake of simplification, spikes still alternate between pre-synpatic and post-synaptic neurons, but the duration between successive spikes is stochastic. In total, $2n$ spikes are generated, n per neuron. In practice, spikes are produced following a Poisson process of mean frequency $R = 1/T$ and assigned to each neuron in alternation.
In a Poisson process, the probability of $k \in \mathbb{N}$ spikes occurrences in a duration $\delta t > 0$ is given by :

$$\mathbb{P}(k, \delta t) = \frac{(R\delta t)^k}{k!} e^{-R\delta t}$$

21 Compute the distribution of the inter-(pre-post) spike interval ΔT.

(22) Compute the average total synaptic modification W at the end of the spike trains, as a function of n, R, A^+, A^-, τ^+ and τ^-.

(23) Determine equivalents of W in the low ($R \to 0$) and high ($R \to \infty$) frequency limits.

(24) In the *BCM learning rule*, the synaptic modification is negative at low frequencies, and positive at high frequencies. Determine the conditions on parameters for implementing this rule.

(25) Compute the slope at 0 and the limits of the synaptic modification W obtained at question (22). Deduce the shape of this function when the conditions (24) hold.

(26) Determine the frequency at which the total synaptic modification changes sign.

2 Receptors kinetics & Post-synaptic current

Ligand-gated ion channels

In a post-synaptic neuron, input currents are induced by the neurotransmitters released in the cleft, through the activation of **ligand-gated ion channels** called *receptors*. Receptors can be conceived as a global conductance $g_{syn}(t)$, which varies in time according to the amount of neurotransmitters in the cleft $L(t)$.

As a first approximation, a range of models assume that the input conductance is merely proportional to the amount of neurotransmitters in the cleft :

$$g_{syn}(t) = \overline{g} L(t)$$

with $\overline{g}$ the maximal conductance.

However, different receptors exist with distinctive time courses, which might have a functional importance. For instance, AMPA receptors provide fast transient responses, whereas NMDA receptors foster slower and more sustained responses. Different types of models account for this response diversity.

Alpha functions and **double-exponentials** are phenomenological models which describe the time course of the post-synaptic input current as a function of time :

$$g_{syn}(t) = \frac{1}{\tau} \left(e^{-t/\tau_{slow}} - e^{-t/\tau_{fast}} \right) \tag{8}$$

Markov kinetic models are more detailed descriptions of the receptors' conformations (states). Generally, the types of states included in receptor models are the following :

- Open state O : The receptor is bound to ligands, which allows ionic flow through the membrane.
- Close state C : The receptor is not bound, but is ready to capture ligands and to open.
- Bound state C^* : The receptor is bound to ligands but not open yet.
- Desensitized D : The receptor cannot return immediately in the open state before transitioning through the close state.

Those models consist in dynamical systems which predict the distribution of the receptors among the different states, and the variables C, O, D or C^* can be seen as proportions among the whole receptor pool.

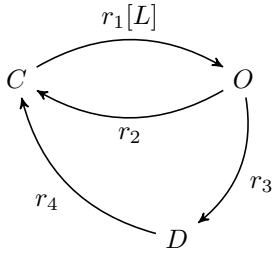
Neurotransmitters released in the synapse act by modulating the **transition rates** between the states, thereby favoring the probability of residence in the open state.

Finally, the conductance g_{syn} is equated to the proportion of receptors in the open state.

2.1 Comparing alpha functions and Markov kinetics

The following questions study the three-states Markov model below.
Initially, the system is in conditions (O_0, D_0, C_0). The concentration of neurotransmitters in the synaptic cleft is suddenly set to a fixed value L. The transition r_1 depends linearly on the concentration of neurotransmitters :

$$r_1([L]) = \overline{r}_1[L]$$



27 Write the dynamical equations for the variables O and D. Justify that the system is fully characterized by only those two variables.

28 Determine the equilibrium (O_∞, D_∞).

29 Solve this system, to obtain solutions of the form :

$$O(t) = O_\infty + \alpha_O \, e^{-t/\tau_1} + \beta_O \, e^{-t/\tau_2} \tag{9}$$
$$D(t) = O_\infty + \alpha_D \, e^{-t/\tau_1} + \beta_D \, e^{-t/\tau_2} \tag{10}$$

$$\tau 1 \geq \tau_2 \tag{11}$$
$$\alpha_O = -\frac{(O_0 - O_\infty)(a + \frac{1}{\tau_2}) + b(D_0 - D_\infty)}{\frac{1}{\tau_2} - \frac{1}{\tau_1}} \tag{12}$$
$$\beta_O = (O_0 - O_\infty) - \alpha_1 \tag{13}$$

with a and b to be determined as a function of the transition rates.
Note : It is not necessary to determine the constants for the variable D.

Experiments suggest that under physiological conditions, the exact time course of neurotransmitter concentrations in the synaptic cleft is not a main determinant of the kinetics of postsynaptic responses at many synapses. In experiments using a fast-perfusion technique, Colquhoun et al. (1992) and Hestrin (1992) found that 1 ms pulses of glutamate applied to patches containing AMPA/kainate receptor-gated channels produced responses that closely matched the time course of synaptic currents.
Therefore, in the following questions, the model is submitted to square pluses of neurotransmitters, separated by longer intervals. During pulses, the concentration is set to a constant value L, and between pulses, it is set to 0.
Initially, all channels are close.

30 Transition rates are set such that $|\alpha_O| \gg 1$, $|\beta_O| \gg 1$ whatever the values of O and D. Justify that $\alpha_0 \approx -\beta_0$.

31 Compare the time constants τ_1 and τ_2 when $[L] = 0$ and $[L] \neq 0$. What does it imply for the state of the system before the second pulse ?

32 Justify that the constant α_0 has a decreasing magnitude for each successive pulse.

33 Trace the time course of the post-synaptic current for successive pulses of neurotransmitters, and show that the response displays desensitization.
Compare with the double-exponential model.

2.2 From kinetic models to phenomenological models

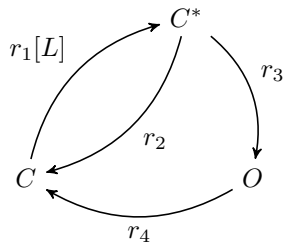
In the following questions, analogous forms of the double-exponentials model and the alpha function will be derived from the three-states Markov model below.
The following approximations will be considered :

- The neurotransmitter concentration occurs as an instantaneous pulse :

$$r_1([L]) = \overline{r}_1 \delta(t)$$

- The state C is always in excess compared to the other states, which is valid if few receptors bind to the neurotransmitters. With this assumption, the variable C can be considered constant : $C \approx 1$.

The following questions propose to use the Laplace transform to solve the dynamical system with Dirac input more rigorously.



34 Compute the Laplace transform of an exponential function :

$$\mathcal{L}[e^{\lambda t}](s) = \int_0^{+\infty} e^{-st} e^{\lambda t} dt \tag{14}$$

35 By integrating by parts, show that the Laplace transform of a differentiable function f is :

$$\mathcal{L}[f'(t)](s) = s\mathcal{L}[f(t)](s) - f(0^+) \tag{15}$$

36 Establish the kinetic equations of the model.

37 Take the Laplace transform of both sides of the differential equation for the variable C^*.

38 Express the function $\mathcal{L}[C^*(t)](s)$ a function of the variable s. Identify the function $C^*(t)$ by considering and (14).

39 Solve for the function $O(t)$ by applying the same method.

40 Conclude about the analogy with the double-exponential model. Which range of parameters might lead to the alpha function model ? Interpret in terms of receptor kinetics.

3 Dendritic processing – From synaptic inputs to somatic integration

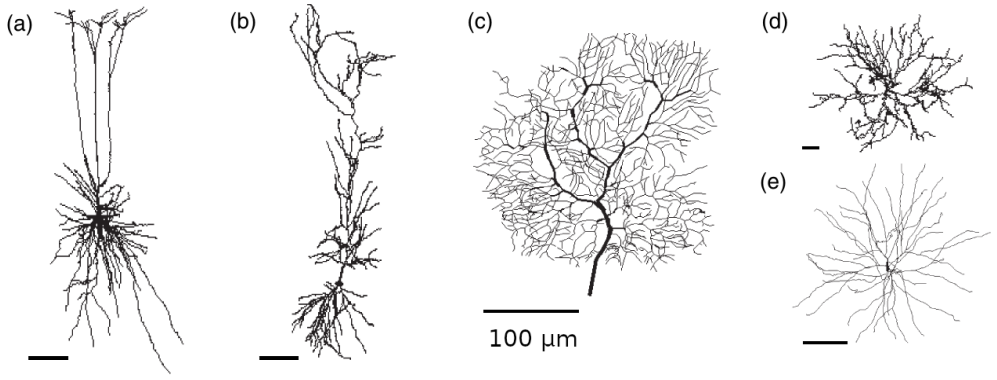
Spatially extended models

Neurons often exhibit highly developed **dendritic trees** which can extend over several hundred microns. Synaptic inputs along those branches are propagated up to the soma, where they are integrated and may trigger action potentials. Before reaching the soma, those inputs may undergo attenuation or cancellation with other inputs while they propagate along the dendritic branches.

This motivates the modeling of more detailed spatial morphologies, beyond the simple point neuron models.

Continuous spatio-temporal models aim to predict the membrane potential $V(x,t)$ at any location x and any time t along the dendrite.

Compartment models reduce the dendrite and the soma to coupled compartments, without considering spatial continuity.



Reconstructed morphology of various types of neurons.
(a) Pyramidal neuron from a deep cortical layer (Contreras et al., 1997).
(b) Pyramidal neuron from the CA1 layer of the hippocampus (Golding et al., 2005).
(c) Purkinje cell from the cerebellum (Rapp et al., 1994).
(d) Motoneuron from the spinal cord (Cullheim et al., 1987).
(e) Stellate neuron from the neocortex (Mainen, Sejnowski, 1996)

3.1 Continuous spatial modeling – Cable equation

3.1.1 Establishing the cable equation

Model of a passive dendrite

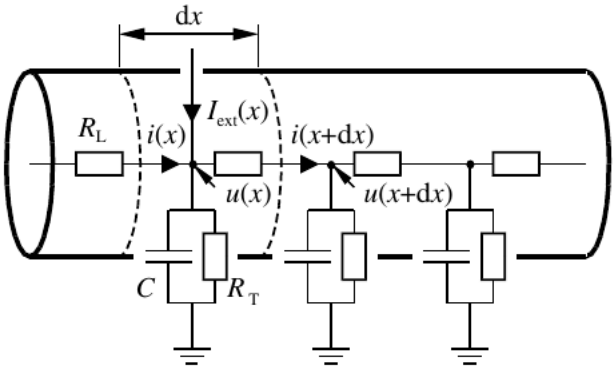
The dendrite is modeled as a long homogeneous cylinder, which is conceived as a succession of adjacent cells of infinitely narrow length $dx \to 0$.

At each location x, the membrane can be crossed by transversal leak currents I_L (through leak ion channels) and synaptic currents I_{ext} (through ligand-gated channels). The membrane is modeled as a capacitor of capacitance C, in parallel with a *transversal resistance* R_T (as in point neurons models ▷[*TDs 1,2,3*]).

Internal currents also propagate along the dendrite in the intra-cellular media, driven by the non-uniform distribution of the membrane potential between the dendritic tree and the soma. The intra-cellular media is modeled by an *longitudinal resistance* R_L.

The goal is to derive the **cable equation** under the standard form :

$$\frac{\partial u}{\partial t}(x,t) = \frac{\partial^2 u}{\partial x^2} u(x,t) - u(x,t) + i_{ext}(x,t) \tag{16}$$



41 Write Ohm's law for the longitudinal current $i(x,t)$ passing through the dendrite at point x and the local membrane potentials u in adjacent cells.

42 Use Kirchoff laws at point x to express the relation between the 'output' current $i(x+dx,t)$ emerging from this point and the 'input' currents received at this point.

The values of the longitudinal resistance, the capacitance, the leak current as well as the externally applied current can be expressed in terms of specific quantities per unit length :

$$R_L = r_L\,dx \quad C = c\,dx \quad I_l(x,t) = i_L(x,t)\,dx \quad I_{ext}(x,t) = i_e xt(x,t)\,dx$$

43 Explain the physical meaning of those scaling relations. Justify that the longitudinal current $i(x,t)$ and transversal resistance R_T cannot be expressed per unit length similarly.

44 Take the limit $dx \to 0$ in equations **41** and **42** to obtain coupled partial differential equations for $\frac{\partial u}{\partial x}$ and $\frac{\partial u}{\partial x}$.

45 Differentiate the expression for u to obtain a single partial differential equation.

46 Express the leak current as a function of the leak conductance per unit length $g_l := \frac{1}{r_T}$ and the leak potential E_l.

47 By considering physical dimensions and homogeneity, show that the model yields a *characteristic length scale* $\lambda^2 = \frac{r_T}{r_L}$ ("electrotonic length scale").
Rewrite the equation under the form $\lambda^2 \frac{\partial u}{\partial x} = ...$
By considering physical dimensions and homogeneity, show that the model yeilds a *characteristic time scale* $\tau = r_T c$.
Comment in relation with point neurons models.

48 Perform the following transformation to unit-free coordinates :

$$x \to \widehat{x} = \frac{x}{\lambda} \qquad t \to \widehat{t} = \frac{t}{\tau}$$

and the following rescaling of the current and voltage variables :

$$i \to \widehat{i} = \sqrt{r_T r_L}\, i \qquad i_{ext} \to \widehat{i}_{ext} = r_T i_{ext} \qquad u \to \widehat{u} = u - E_l$$

49 Interpret the cable equation by giving a physical meaning to the three contributions to the variation of the membrane potential at a given location.

3.1.2 Solving the cable equation

Green's functions for an infinite cable

The cable equation is a partial differential equation which admits solutions for a variety of boundary conditions. In a first approach, the dendrite is considered as a cable extending to infinity in both directions. A short synaptic current i_{ext} is injected at time $t = 0$ at location $x = 0$.

Green's function is defined as the solution of a linear partial differential equation with a **Dirac δ-pulse** as its input. In the case of the cable equation :

$$\left[\frac{\partial}{\partial t} - \frac{\partial^2}{\partial x^2} + 1\right] G_\infty(x,t) = \delta(x)\delta(t) \tag{17}$$

In the case of the cable equation, Green's function has the following expression :

$$u(x,t) = G_\infty(x,t) = \frac{1}{\sqrt{4\pi t}} e^{-t-\frac{x^2}{4t}} \mathbb{1}_{[0,+\infty[}(t) \tag{18}$$

with $\mathbb{1}_{[0,+\infty[}$ the Heaviside function or 'step' function :

$$\mathbb{1}_{[0,+\infty[}(t) = \begin{cases} 1 & t \geq 0 \\ 0 & t \leq 0 \end{cases}$$

Green's function corresponds to as an *elementary solution* of the differential equation because, owing to linearity, the solution for any arbitrary input can be built as a superposition of these Green's functions, as an integral over (hypothetical) pulse-inputs at all places and all times.

$$u(x,t) = \int_{-\infty}^{t} ds \int_{-\infty}^{+\infty} dx\; G_\infty(x-y, t-s) i_{ext}(y,s) \tag{19}$$

50 Apply the Fourier transformation with respect to the spatial variable over the following partial differential equation :

$$\frac{\partial}{\partial t} u(x,t) - \frac{\partial^2}{\partial x^2} u(x,t) + u(x,t) = \delta(x)\delta(t) \tag{20}$$

to obtain the following *ordinary differential equation* :

$$\frac{\partial}{\partial t} \widehat{u}(k,t) - k^2 \widehat{u}(k,t) + \widehat{u}(k,t) = \frac{1}{\sqrt{2\pi}} \delta(x) \tag{21}$$

Note : The Fourier transform of a function f is defined as $\widehat{f}(k) = \mathcal{F}[f](k) = \int_{-\infty}^{+\infty} f(x) e^{-ikx} dx$

51 Solve this ordinary differential equation in variable t by applying the Laplace transform over the temporal variable, to obtain :

$$\widehat{u}(k,t) = \frac{1}{\sqrt{2\pi}} e^{-(1+k^2)t} \mathbb{1}_{[0,+\infty[}(t) \tag{22}$$

52 Apply the inverse Fourier transformation over the frequency variable k to get the expression of the Green's function (17).

Note : The inverse Fourier transform of a function $\widehat{f}$ is defined as $f(x) = \mathcal{F}^{-1}[\widehat{f}](k) =< \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{+\infty} \widehat{f}(k) e^{ikx} dk$

53 Sketch the Green's function as a function of space at different times, and as a function of time at different locations. Comment.

54 Check the validity of equation (19).

3.2 Discrete spatial modeling – Compartment model

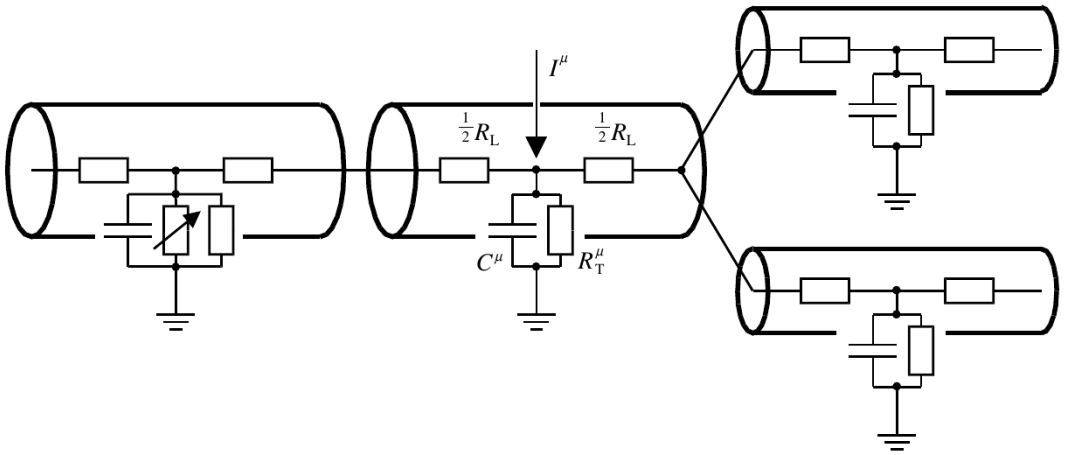
Compartments models

Analytical solutions of the cable equation hold for *uniform geometrical and electrical properties*.

However, a dendritic tree can be assimilated to a uniform cable only *locally*, as it is affected by numerous bifurcations and variations in diameter and electrical properties along the dendrites.

Moreover, the dendrite's behavior is not fully passive. On the contrary, it is endowed with non-linear voltage-gated ion channels which are necessary for the regeneration of the membrane potential depolarization and its propagation up to the soma.

Compartmental models provide a framework to solve for the membrane potential in more complex dendritic models. It consists in dividing the neuron morphology into cylinders of homogeneous properties and a single membrane potential variable. Adjacent compartments are coupled by the longitudinal resistance determined by their geometrical properties.



(55) **num** In case more complex aspects are added to the model and the cable equation cannot be solved analytically, propose a method to simulate the cable equation numerically.