TD 4 – Synapses & Dendrites

Practical Information

TD Assistant
eponiatowski@clipper.ens.psl.eu

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 currents, acting like *filters*. They are endowed with a large computational power, because their transmission properties can be affected by the history of pre- and post-synaptic firing in various ways.

Thus, understanding neural coding requires to take into account signal transformations performed at multiple steps during synaptic transmission.

Part 1 Overview of synaptic mechanisms.

Part 2 Short term synaptic plasticity : short term depression (STD), short term potentiation (STP).

Part 3 Long term synaptic plasticity : associative spike-timing-dependent plasticity (STDP).

Part 4 Receptor kinetics.

Part 5 Dendritic processing : spatially continuous model, compartments model.

1 Synaptic transmission

Overview of the synaptic stages

Several phenomena happen to transform one spike train in the pre-synaptic neuron into another spike train in the post-synaptic neuron.

① Pre-synaptic release of neurotransmitters

In the pre-synaptic neuron, the arrival of an action potential (membrane depolarization) at the axon terminal 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.

Synaptic efficacy, i.e. the amount of transmitters released in response to one spike, is subject to **plasticity**. Modulations can deploy either on the short term (hundreds of milliseconds to seconds) or on the long term (hours or longer).

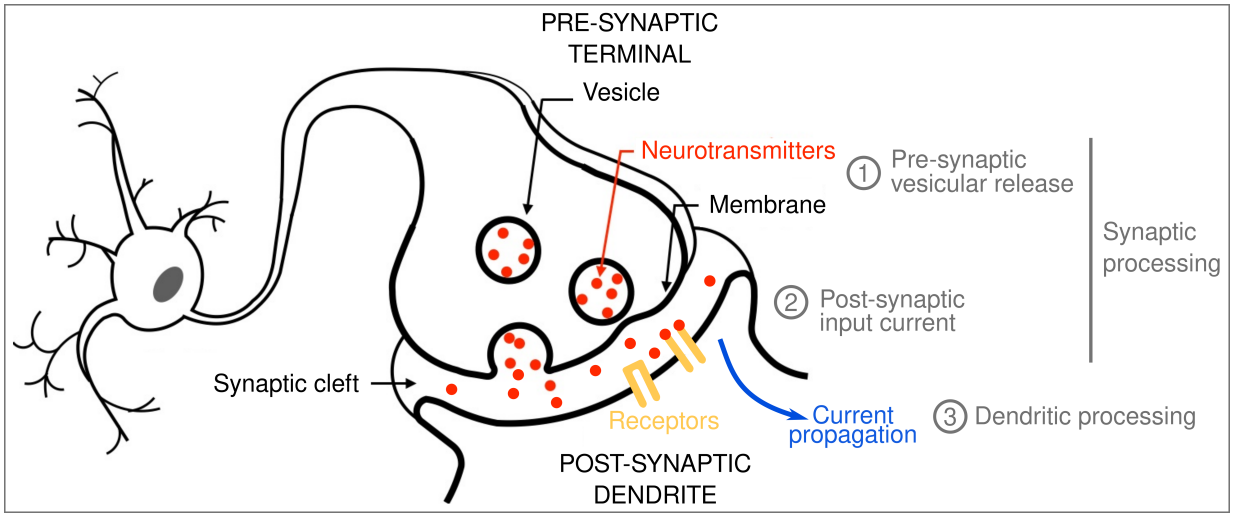
② Post-synaptic input currents

Neurotransmitters diffuse in the cleft and bind to post-synaptic **receptors**. Those ligand-gated ion channels which open when they bind to neurotransmitters. Their opening generates **input currents** in the post-synaptic dendrite, which cause a subsequent change in the membrane potential in at the synaptic location.

Different types of receptors exist, characterized by the activation times scales of their conductances in response to the variations of neurotransmitter concentration in the cleft.

③ Dendritic processing

Finally, in the post-synaptic neuron, the synaptic inputs generated at various locations across the whole dendritic tree propagate along the dendrites until reaching the soma. There, their integration triggers a new spike train. This constitutes an additional step of computation, because the **spatio-temporal evolution** of the membrane potential at different locations depends on the neuron's morphology.



2 Short term depression and facilitation (STD, STP)

Short-term pre-synaptic plasticity and Information coding

Short-term plasticity refers to the **activity-dependent** variation of synaptic efficacy on short time scales (milliseconds to seconds). Two main types of plastity can coexist in the same synapse :

- **Facilitation** (or potentiaton) : enhancement of synaptic efficacy with past activity.
- **Depression** : reduction of synaptic efficacy with past activity.

In terms of signal processing, plasticity has a functional relevance because it can switch the balance between two "coding schemes", which differ in the amount of "contextual information" conveyed to the post-synaptic neuron (information about the past spiking history) :

- **Temporal coding** : when the post-synaptic response preferentially reacts to the occurrence of each *individual* pre-synaptic spike.
- **Rate coding** : when the post-synaptic response most strongly varies with the pre-synaptic *firing frequency*.

The **synaptic transfer function** captures the relationship between the pre-synaptic firing frequency and the post-synaptic response amplitude. It can be investigated to assess temporal and rate coding capacities of synapses with various facilitation and depression regimes.

Modeling short term plasticity

Models of short term plasticity usually focus on the variation of synaptic efficacy, associated with the amount of vesicles released in response to one spike arriving at the axon terminal of the pre-synaptic neuron. Models usually include several components :

① Dynamics of the resources pool

• The total vesicular pool (fixed) is and partitioned into three states, modeled by distinct variables : effective vesicles $E(t)$, inactive vesicles $I(t)$, and recovered vesicles $R(t)$ (all comprised in $[0, 1]$).

• Each pre-synaptic spike exhausts the available resources by triggering the release of a fraction $p(t)$ of vesicles from the recovered pool (see ②).

• Those vesicles immediately become effective, and then quickly inactivate with a time constant τ_i (of the order of a few milliseconds).

• The pool of available resources is replenished by the recovery of inactivated vesicles with a time constant τ_r (of the order of 1 sec).

② Calcium concentration

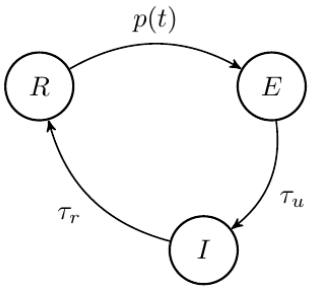
The variable $p(t)$ stands for the *release probability*, which corresponds to the fraction of the recovered vesicles released by a single spike arriving at the pre-synaptic axon terminal.

This probability evolves in time, reflecting the dynamics of the pool of calcium ions in the synapse which are mobilized to elicit vesicular fusion. In absence of spiking stimulation, the concentration of calcium ions in the synapse decays to a baseline U with a time constant τ_p. When a spike occurs, new calcium ions accumulate in the synapse, increasing the concentration by a fraction U of the unmobilized pool of calcium ions.

③ 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.

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



2.1 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).

Express those equations with only two variables among R, E, I (the most relevant ones), $p(t)$, and the time parameters.

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.

2.2 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 :

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

2.2.1 Rate coding

Rate coding 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 :

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

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

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

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.

2.2.2 Temporal coding

Temporal coding 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 codidng (time to reach the stationary state) ? Comment on the importance of the parameter U for temporal coding.

2.3 Facilitative synapse – Three coding regimes

In the following questions, the dynamics of the release probability are taken into account. The baseline release probability U (and the amount by which the release probability is increased by each spike) are considered small, so that several spikes are required to saturate at a value of $p = 1$.

(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.

(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.

3 Spike-timing-dependent plasticity (STDP)

Spike-timing-dependent plasticity

Spike-timing-dependent plasticity (STDP) is a class of **long term** modulation of synaptic efficacy, which depends on both *pre-synaptic and post-synaptic* mechanisms. In this sense, this is an *associative* process, which reinforces or weakens synaptic strengths between neurons based on their relative spike timings.

This biological mechanism can be considered as an implementation of the *Hebbian learning rule* for adjusting the strength of connections between neurons. This computational rule has been proposed as a proxy for causality.

Modeling spike-timing-dependent plasticity

Models of STDP usually propose a phenomenological description of the phenomenon, without focusing on the precise biological mechanisms.

In those models, pre-synaptic and post-synaptic neurons emit trains of n_{pre} and n_{post} spikes respectively :

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

The modification of the synaptic weight w is specified by a rule which depends on the time interval between each pair of *nearest-neighbor* pre- and post-synaptic spikes $(t_{\mathrm{pre},i}, t_{\mathrm{post},j})$:

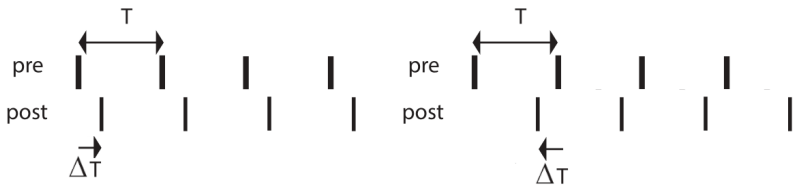
$$\Delta w = f(t_{\mathrm{post},j} - t_{\mathrm{pre},i}) \qquad \text{with} \quad f(s) = \begin{cases} A^+ e^{-s/\tau^+} & \text{if } s \geq 0 \\ -A^- e^{s/\tau^-} & \text{if } s < 0 \end{cases} \tag{7}$$

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.

3.1 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 between $\Delta T \in [-T/2, 0]$ 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.

3.2 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. 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 expected total synaptic modification W at the end of a spike train, as a function of n, R, A^+, A^-, τ^+ and τ^-.

23 Determine equivalents of $\mathbb{E}(W)$ 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 the parameters for implementing this rule.

25 Determine the frequency at which the total synaptic modification changes sign.

26 To compare with the results of the previous part (regular pre-synaptic train), deduce the shape of the expected synaptic modification $\mathbb{E}(W)$ (22) as a function of ΔT when the conditions (24) hold.

4 Receptors kinetics & Post-synaptic current

Modeling 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.

In biological systems, different receptors exist with distinctive time courses, which seems to have a functional importance. For instance, AMPA receptors provide fast transient responses, whereas NMDA receptors foster slower and more sustained responses.

Two main types of models can be distinguished.

On the one hand, some models propose a *phenomenological* description of the time course of the post-synaptic input current.

The **double-exponentials** model has the following shape :

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

The **alpha-function** model has the following shape :

$$g_{syn}(t) = \frac{1}{\tau}te^{-t/\tau} \tag{9}$$

On the other hand, some models propose to link the observed time course of the current to the *dynamics of the receptors*. In this view, **Markov kinetic models** attempt to account for the different conformations of the receptors and the transitions between those states. Generally, the types of states included in receptor models are the following :

- Open state O : The receptor is bound to ligands, which allows current 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. 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.

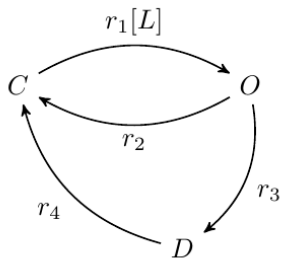
Finally, the conductance g_{syn} is equated to the proportion of receptors in the open state.

4.1 Comparing alpha functions and Markov kinetics

The following questions study the **three-states Markov model** schematized 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 the dynamics of the system, to obtain solutions of the form :

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

$$D(t) = D_\infty + \alpha_D \, e^{-t/\tau_1} + \beta_D \, e^{-t/\tau_2} \tag{11}$$

with $\begin{cases} \tau_1 & \geq \tau_2 \\ \alpha_O & = -\dfrac{(O_0 - O_\infty)(a + \frac{1}{\tau_2}) + b(D_0 - D_\infty)}{\frac{1}{\tau_2} - \frac{1}{\tau_1}} \\ & \text{with } a \text{ and } b \text{ to be determined as a function of the transition rates} \\ \beta_O & = (O_0 - O_\infty) - \alpha_O \end{cases}$

Note : It is not necessary to determine the constants for the variable D because only O is necessary to deduce the input current.

30 Trace an example time course of the post-synaptic current during a pulse of neurotransmitter, during which the concentration $[L]$ is assumed to remain constant.

4.2 From kinetic models to phenomenological models

⚠ The approach proposed below uses the Laplace transform to solve a dynamical system with Dirac input more rigorously than in the previous sections. For the final exam, it is **NOT** required to master this mathematical tool. ⚠

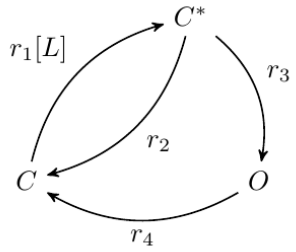
Analogous forms of the **double-exponentials model** and the **alpha function** can be derived from the **three-states Markov model** schematized below.

The following approximations are 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 : $C \approx 1$.



4.2.1 Generalities about the Laplace Transform

(31) Justify that the Laplace transform is a linear operator.

(32) Compute the Laplace transform of an exponential function :

$$\mathcal{L}[e^{\lambda t}](s) = \int_0^{+\infty} e^{-st} e^{\lambda t} dt \tag{12}$$

(33) Compute the Laplace transform of a Dirac function.

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

$$\mathcal{L}[f'(t)](s) = s\mathcal{L}[f(t)](s) - f(0^+) \tag{13}$$

4.2.2 Application to the model

(35) Establish the kinetic equations of the model.

(36) Take the Laplace transform of both sides of the differential equation for the variable C^*.

(37) Express the function $\mathcal{L}[C^*(t)](s)$ as a function of the variable s. Identify the function $C^*(t)$ by considering (12).

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

(39) 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.

5 Dendritic processing – From synaptic inputs to somatic integration

⚠ For the final exam, it is **NOT** required to master the models and the mathematical tools introduced in this part. ⚠

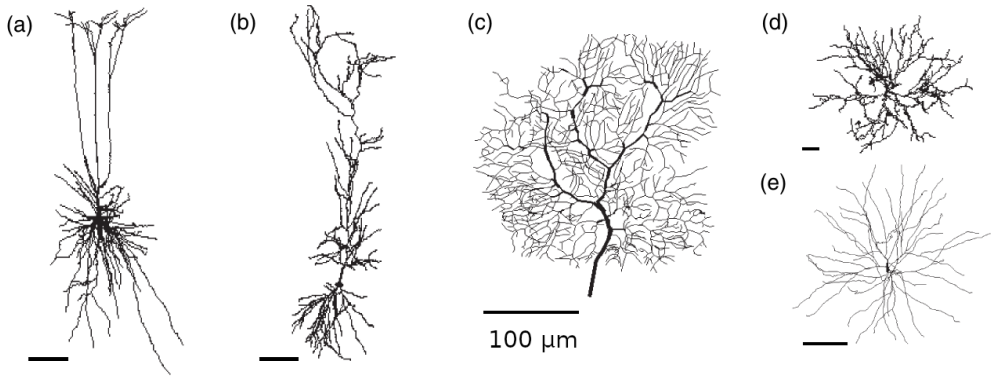
Spatially extended models

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.

Two approaches exist to encompass a spatial dimension :

- **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)

5.1 Continuous spatial modeling – Cable equation

5.1.1 Establishing the cable equation

Model of a passive dendrite

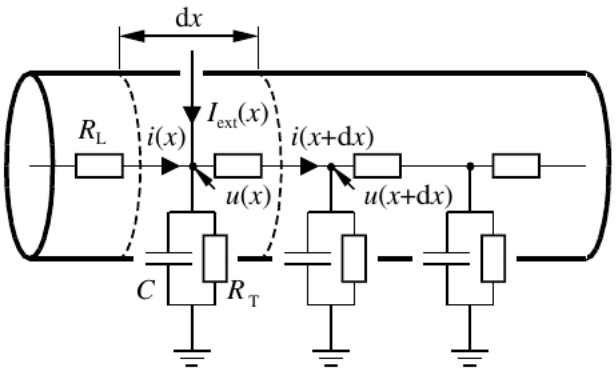
The dendrite is modeled as a long homogeneous cylinder, which is conceived as a succession of adjacent cells of infinitely narrow length $dx \to 0$.

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*]).

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 :

$$\frac{\partial u}{\partial t}(x,t) = \frac{\partial^2 u}{\partial x^2}u(x,t) - u(x,t) + i_{ext}(x,t) \tag{14}$$



40 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.

41 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 :

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

42 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.

43 Take the limit $dx \to 0$ in equations **40** and **41** to obtain coupled partial differential equations for $\frac{\partial u}{\partial x}$ and $\frac{\partial u}{\partial x}$.

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

45 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.

46 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.

47 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 :

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

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

5.1.2 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 :

$$\left[\frac{\partial}{\partial t} - \frac{\partial^2}{\partial x^2} + 1\right] G_\infty(x,t) = \delta(x)\delta(t) \tag{15}$$

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

$$u(x,t) = G_\infty(x,t) = \frac{1}{\sqrt{4\pi t}} e^{-t-\frac{x^2}{4t}} \mathbb{1}_{[0,+\infty[}(t) \tag{16}$$

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.

$$u(x,t) = \int_{-\infty}^{t} ds \int_{-\infty}^{+\infty} dx\; G_\infty(x-y, t-s) i_{ext}(y,s) \tag{17}$$

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

$$\frac{\partial}{\partial t} u(x,t) - \frac{\partial^2}{\partial x^2} u(x,t) + u(x,t) = \delta(x)\delta(t) \tag{18}$$

to obtain the following *ordinary differential equation* :

$$\frac{\partial}{\partial t} \widehat{u}(k,t) - k^2 \widehat{u}(k,t) + \widehat{u}(k,t) = \frac{1}{\sqrt{2\pi}} \delta(x) \tag{19}$$

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

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

$$\widehat{u}(k,t) = \frac{1}{\sqrt{2\pi}} e^{-(1+k^2)t} \mathbb{1}_{[0,+\infty[}(t) \tag{20}$$

51 Apply the inverse Fourier transformation over the frequency variable k to get the expression of the Green's function (15).

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

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

53 Check the validity of equation (17).

5.2 Discrete spatial modeling – Compartment model

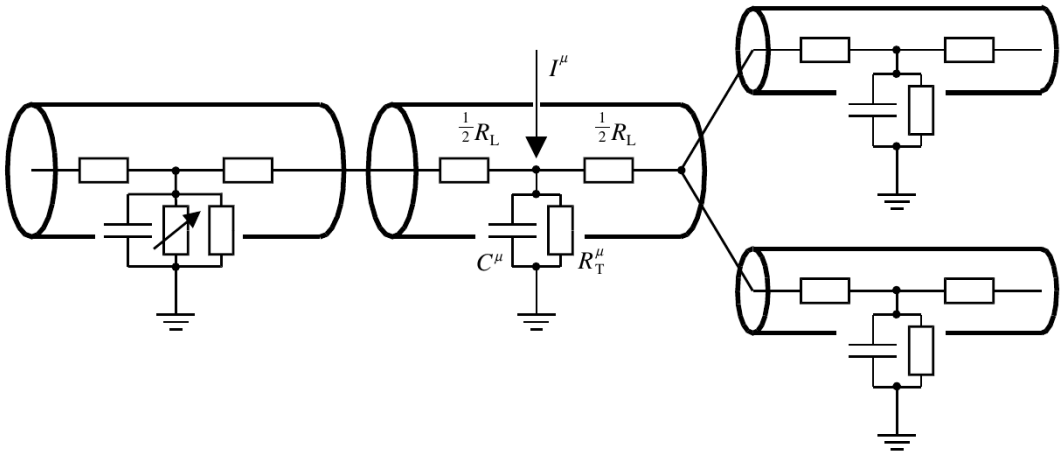
Compartments models

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 morphologies. 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.



(54) 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.