An introduction to mathematical neuroscience

Gemma Huguet
Dept. Matemàtiques, UPC

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I. Synaptic transmission
The Neuron

Synapsis: pre-synaptic and post-synaptic neuron.
Neurotransmitters and receptors

Neurotransmitters:

- **Excitatory**: Glutamate. It activates two kinds of receptors:
  - AMPA. Fast synapsis (rise time is less than 1ms)
  - NMDA. Slower than AMPA. Involved in short-term memory.

Both AMPA and NMDA receptors produce mixed-cation conductances with reversal potential around 0mV.

- **Inhibitory**: GABA (γ-aminobutyric acid). It activates two kinds of receptors:
  - GABA\(_A\). Fast. Produce a fast \(Cl^-\) conductance.
  - GABA\(_B\). Slower than GABA\(_A\). Activates the conductance indirectly through an intracellular pathway (G-protein that activates a \(K\) channel). It produces a slower and long-lasting \(K\) conductance.
Kinetics of various types of synaptic currents

A. AMPA

B. NMDA

C. $\text{GABA}_A$

D. $\text{GABA}_B$
Synaptic currents:

\[ \dot{V} = -l_{ion}(V, w) - I_{syn} \]

\[ I_{syn} = g_{syn}(t)(V_{post} - E_{syn}) \]

where \( E_{syn} \) is the synaptic reversal potential: \( E_{syn} = 0 \text{mV (EXC)} \) and \( E_{syn} = -80 \text{mV (INH)} \) and

\[ g_{syn}(t) = \sum_{k} \bar{g}_{syn}F(t - t_k) \]

where \( t_k \) are the pre-synaptic spike times.
Models of synaptic currents

- Instantaneous: $F(t) = \delta(t - D)$, $D$ transmission delay.
- Sudden jump with exponential decay: $F(t) = e^{-t/\tau_d} \Theta(t)$
- $\alpha$-function (difference of exponentials): $F(t) = (e^{-t/\tau_d} - e^{-t/\tau_r}) \Theta(t)$
- Dynamics: $F(t) = s(t)$

$$\frac{ds}{dt} = \alpha_s [T](1 - s) - \beta_s s,$$

$[T] =$ neurotransmitter concentration

$[T] =: f(V_{pre}) = \frac{T_{max}}{1 + \exp(-(V_{pre} - \theta)/k_p)}$. 
Simple modelling of conductances

The conductances depend on the spiking times of the presynaptic neurons:

\[ g(t) = \bar{g}_{\text{max}} \sum_k \alpha(t - t_j^k), \]

\[ t_j^k = \text{time of the } j\text{th spike of the } k\text{th presynaptic neuron.} \]

\[ \alpha(t) = \frac{a_d a_r}{a_r - a_d} \left( e^{-a_d t} - e^{-a_r t} \right), \]

\( a_r = \text{rise rate}; \ a_d = \text{decay rate}. \) Assuming \( a_r = a_d \) (usual),

\[ \alpha(t) = a_d^2 t e^{-a_d t}, \]

with constants chosen under some normalization criterion (e.g. \( \int_0^\infty \alpha(t) dt = 1 \)). Assuming \( a_r \to \infty \), it reduces to a single exponential.
Simple modelling of conductances

\[
\begin{align*}
\left\{
  g(t) &= \bar{g}_{\text{max}} \sum_k \alpha(t - t^k_j), \\
  \alpha(t) &= a_d^2 t e^{-a_d t}
\right.
\end{align*}
\]
It is modeled as the voltage-gated ionic channels:

\[ I_{syn} = \bar{g}_{max} s(t) (V - V_{syn}), \]

where \( s \) is the fraction of channels opened by the neurotransmitter. We model \( s \) as:

\[ \frac{ds}{dt} = \alpha_s [T] (1 - s) - \beta_s s, \]

where \([T]\) = concentration of neurotransmitter.

We assume \([T]\) jumps to \( T_{max} \) when pre-syn neuron spikes and \([T]\) falls back to 0 after a short time \( \Delta t \).

A usual model is

\[ [T] =: f(V_{pre}) = \frac{T_{max}}{1 + \exp\left(-\left(V_{pre} - \theta\right)/k_p\right)}. \]
Short-term synaptic plasticity - Synaptic depression and Facilitation

Graph showing the dynamics of synaptic changes over time with labels for R1, R2, and Recovery Response, and waveforms for Pre Vm and Post Vm with annotations for stationary EPSP, A1 Experiment, and 30Hz frequency.
Vesicles can be in two possible states, 'available for release' (A) or 'refractory' (R).

\[ \dot{x} = \frac{1 - x}{\tau_D} - a_d x \sum_k \delta(t - t_k) \]

- \( a_d (u) \) = fraction of vesicles released by a presynaptic AP
- \( \tau_D \) = recovery time constant
Tsodyks-Markram model - dynamic $u$

\[
\begin{align*}
\dot{x} &= \frac{1 - x}{\tau_D} - u^+ x^- \sum_k \delta(t - t_k) \\
\dot{u} &= \frac{-u}{\tau_F} + a_f (1 - u^-) \sum_k \delta(t - t_k)
\end{align*}
\]

- $x =$ fraction of available vesicles after neurotransmitter depletion, decreases by an amount $u x$ at each spike and then recovers with time constant $\tau_D$.
- $u =$ fraction of vesicles released by a pre-synaptic AP is now a dynamic variable, increases by an amount $a_f (1 - u)$ at each spike and then decays with time constant $\tau_F$.
- $\tau_D =$ recovery time constant
- $\tau_F =$ facilitation time constant
Depressing vs Facilitation synapses

- $x =$ fraction of available vesicles, decreases by an amount $ux$ at each spike and then recovers with time constant $\tau_D$.
- $u =$ utilization variable (release probability), increases by an amount $a_f(1 - u)$ at each spike and then decays with time constant $\tau_F$. 
Long-term memory

- Structural changes in synaptic connections
- Long-term changes in synaptic strength (long-term potentiation LTP or long-term depression LTD) depend on the activity of neurons.
- STDP rule:
  - If the pre-synaptic spike arrives at the postsynaptic neuron before the postsynaptic neurons fires the synapsis is potentiated.
  - If the pre-synaptic spike arrives at the postsynaptic neuron after the postsynaptic neurons fires the synapsis is depressed.

Froemke et al, 2006
II. Network Dynamics
What are networks made of?

- How many types of neurons? How many neurons in each type?
- How are neurons connected (what is the connectivity matrix)?
- What are the external inputs?
- Which neuron models?
- Which synapse models?
What are networks made of?

- How many types of neurons? How many neurons of each type?
  - Excitatory, Inhibitory
  - 1, 2, ... populations
  - $N \approx 10s, 100s, 1000s, \ldots N \to \infty$
What are networks made of?

- How many neurons connected (what is the connectivity matrix)?
  - Fully connected (all-to-all)
  - Randomly connected (e.g. Erdos-Renyi)
  - Spatial structure
  - With a structure imposed by learning
What are networks made of?

- What are the external inputs?
  - Constant
  - Stochastic (e.g. independent Poisson processes; independent white noise)
  - Temporally/spatially structured
Poisson process

- pdf of ISIs: \( P(T) = \nu e^{-\nu T} \)
- mean: \( \langle 1/T \rangle = \nu \)
- Number of spikes \( k \) in an interval of duration \( T \) is given by a Poisson distribution.

\[
P(k) = (\nu T)^k e^{-\nu T} / k!
\]
What are networks made of?

- Which are the neuron models?
  - Binary
  - Spiking (LIF, HH-type, etc...)
What are networks made of?

- Which are the synapse models?
  - Number (synaptic weight, binary networks)
  - Temporal kernel (spiking networks)
What are the questions?

- **Dynamics**: What are the intrinsic dynamics of networks (spontaneous activity, in the absence of structured inputs)?

- **Coding**: What is the effect of external inputs on network dynamics? How do networks encode external inputs?

- **Learning and memory**: How are external inputs learned/memorized?
  - How do external inputs modify network connectivity through synaptic plasticity? How is learning implemented?
  - What is the impact of structuring in the connectivity on network dynamics?

- **Computation**: How do networks perform computations?
Different types of asynchronous/synchronous states

Synchronous regular (SR)

Asynchronous regular (AR)

Synchronous irregular (SI)

Asynchronous irregular (AI)
Neuronal network

- $N$ integrate-and-fire (IF) neurons.
- Each neuron receives $C$ randomly chosen connections from other neurons (sparsely connected network with $C/N \ll 1$) and $C_{\text{ext}}$ connections from excitatory neurons outside the network.
- $V_i$ of neuron $i$: $\tau \dot{V}_i = -V_i + RI_i$
- $I_i$ synaptic currents at cell $i$: $RI_i = \tau \sum_{j=1}^{C} J_{ij} \sum_k \delta(t - t_j^k)$
- $J_{ij} = J > 0$ for all synapses.
- External synapses are activated by independent Poisson processes with rate $\nu_{\text{ext}}$. 
The current that enters through the neuron’s membrane is highly noisy (Gaussian noise).

It can be described with two parameters: the mean current $\mu$ and the standard deviation $\sigma$.

The neuron’s membrane potential has an irregular shape.

$|S|$: interspike interval (time between two spikes or action potentials)
Mean field reduction

- ISI of an integrate-and-fire neuron can be computed as a function of $\mu$ and $\sigma$ using the Fokker-Planck formalism.
- $\nu$: Discharge frequency or firing rate of the post-synaptic neuron

$$\nu = \frac{1}{<\text{ISI}>} \quad \nu = \phi(\mu, \sigma)$$
The synaptic current is generated by the activity of the presynaptic neurons and thus the mean and the standard deviation $\sigma$ depend on their discharge frequency $\nu$:

$$\mu = CJ\nu + \mu_{\text{ext}}$$
$$\sigma = CJ^2\nu + \sigma_{\text{ext}}^2$$

where $C$ is the number of presynaptic neurons that our neuron has, $J$ is the strength of connections and the parameters $\mu_{\text{ext}}$ and $\sigma_{\text{ext}}$ describe the input current to the neuron that do not depend on other neurons that we are simulating, but are the result of interactions with neurons in the external circuit.
Mean field reduction

- Self-consistency equation: impose the discharge frequency of the pre and postsynaptic to be the same.

\[ \nu = \phi(\mu(\nu), \sigma(\nu)) = \phi(CJ\nu + \mu_{\text{ext}}, CJ^2\nu + \sigma^2_{\text{ext}}) \]

- Graphical study.

- Dynamics: \( \dot{\nu} = -\nu + \phi(\mu(\nu), \sigma(\nu)) \).
• $N$ integrate-and-fire (IF) neurons, $N_E = 0.8N$ excitatory, $N_I = 0.2N$ inhibitory.

• Each neuron receives $C$ randomly chosen connections from other neurons ($C_E$ from Exc neur and $C_I$ from Inh neurons; sparsely connected network with $C_E/N_E = C_I/N_I << 1$) and $C_{ext}$ connections from excitatory neurons outside the network.

• $V_i$ of neuron i: $\tau \dot{V}_i = -V_i + RI_i$

• $I_i$ synaptic currents at cell i: $RI_i = \tau \sum_j J_{ij} \sum_k \delta(t - t_{jk} - D)$

• $J_{ij} = J > 0$ for all E synapses and $J_{ij} = -gJ$ for I synapses.

• External synapses are activated by independent Poisson processes with rate $\nu_{ext}$. It is compared with the frequency needed for a neuron to reach the threshold in the absence of network feedback $\nu_{thr}$. 
III. Rate models
Models of populations of neurons

- **Networks of spiking neurons**: describe the activity of a population of \( N \) neurons by \( \mathcal{O}(N) \) coupled differential equations, coupled through network connectivity matrix.

- **Rate model (firing rate model, neural mass model)**: describe the activity of a whole population of neurons by a single 'average firing rate' variable \( r(x, t) \)

![Raster plot](image1)

![Firing rate](image2)

Wang, 2002
The simplest rate model

f-I curve of a specific spiking neuron model

Thus,

\[ r = S(I(t)), \quad I(t) = \text{overall neuron's input} \]

Fake dynamics:

\[ \tau \frac{dr}{dt} = -r + S(I(t)) \]
The transfer function

Threshold linear \( S(x) = [x - \theta]^+ \)

Sigmoidal \( S(x) = \frac{1}{1 + \exp\left(-\frac{x - \theta}{k}\right)} \)

f-I curve of a specific spiking neuron model

\( \tau_r = 6.6 \text{ ms} \quad \tau_m = 27.1 \text{ ms} \)
\( C = 257 \text{ pF} \quad V_r = 1.7 \text{ mV} \)
\( \alpha = 5.1 \text{ pA s} \)
\( P = 0.3202 (*) \)
\( d = 0.85 \text{ Hz} \)
Wilson-Cowan equations (1972)

E-I network (Wilson-Cowan equations, 1972)

\[
\begin{align*}
\tau_E \frac{dr_E}{dt} &= -r_E + S_e(J_{EE} r_E - J_{EI} r_I + I_E) \\
\tau_I \frac{dr_I}{dt} &= -r_I + S_i(J_{IE} r_E - J_{II} r_I + I_I),
\end{align*}
\]

where

\[
S_i(x) = \frac{1}{1 + \exp(-a_i(x - \theta_i))}
\]
\[ \tau_E \frac{dr_E}{dt} = -r_E + S(J_{EE} r_E + I_E) \]
I-network with delays - oscillations

\[ \tau_I \frac{d r_I}{d t} = -r_I + S(-J_{II} r_I(t - D) + I_I) \]
E-I network (Wilson-Cowan equations, 1972)

\[
\begin{align*}
\tau_E \frac{dr_E}{dt} &= -r_E + S_e (J_{EE} r_E - J_{EI} r_I + I_E), \\
\tau_I \frac{dr_I}{dt} &= -r_I + S_i (J_{IE} r_E - J_{II} r_I + I_I),
\end{align*}
\]
E-I network - oscillations

E-I network (Wilson-Cowan equations, 1972)

\[
\begin{align*}
\tau_E \frac{dr_E}{dt} &= -r_E + S_e(J_{EE} r_E - J_{EI} r_I + I_E), \\
\tau_I \frac{dr_I}{dt} &= -r_I + S_i(J_{IE} r_E - J_{II} r_I + I_I),
\end{align*}
\]
E-I network - oscillations

E-I network (Wilson-Cowan equations, 1972)
E-I network - oscillations

E-I network (Wilson-Cowan equations, 1972)
I-I network - Winner-take-all (WTA)

\[
\begin{aligned}
\tau_1 \frac{dr_1}{dt} &= -r_1 + S(-w r_2 + I_1), \\
\tau_2 \frac{dr_2}{dt} &= -r_2 + S(-w r_1 + I_2),
\end{aligned}
\]

Ermentrout & Terman, 2010
Applications of firing rate models

- Decision making
- Working memory
- Perceptual bistability in ambiguous visual stimuli
IV. Decision making
Decision making
The two alternative forced choice task (TAFC)

Random dots (Newsome)

Visit http://monkeybiz.stanford.edu/research.html
The physiological task

Behavioral measures: reaction time (RT) distribution, error rate (ER)

Physiological measures: fMRI (humans), direct recordings in visual processing and motor areas (monkeys: MT, LIP, FEF)
Neural correlates

Where in the brain do we find neural correlates of choice/decision... dynamics of temporal integration?

Shadlen & Newsome, 2001
Motion coherence and MT neurons

Motion stimulus

Responses of MT neurons

no coherence  50% coherence  100% coherence
Experiment of Roitman and Shadlen, 2002

Diagram showing stages of a visual experiment:
- Fixation
- RF
- Targets
- Motion
- Saccade
- Reaction Time (RT)

Time axis runs vertically.
Experiment of Roitman and Shadlen, 2002

A: Firing rate vs. Time (ms) with select T1 and T2.

B: Firing rate vs. Motion strength (% coherence) with a* and b*.

C: Firing rate vs. Motion strength (% coherence) with c and d.
Experiment of Roitman and Shadlen, 2002

A. Firing rate (sp/s) vs. time (ms)
- Select T1
- Select T2

B. Firing rate (sp/s) vs. motion strength (% coherence)
- Motion strength:
  - 51.2
  - 25.6
  - 12.8
  - 6.4
  - 3.2
  - 0

C. Firing rate (sp/s) vs. motion strength (% coherence)
- Motion strength (% coherence)
- 0
  - 10
  - 20
  - 30
  - 40
  - 50

Probability correct vs. motion strength (% coherence)
- Motion Strength (% coh)
  - 0
  - 2.5
  - 5
  - 10
  - 20
  - 40

RT (ms) vs. motion strength (% coherence)
- RT (ms)
  - 0
  - 400
  - 600
  - 800

Fixation
- RF
- Targets
- Motion
- Saccade
- RT

Gemma Huguet
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Probabilistic Decision Making by Slow Reverberation in Cortical Circuits

Wang, 2002

Spiking neuronal network model

I_1 \rightarrow 1 \xrightarrow{w_+} \text{Background} \xrightarrow{w_+} \text{I} \rightarrow 7200

I_2 \rightarrow 2 \xrightarrow{w_+} \text{NS} \xrightarrow{w_+} \text{I}
Decision dynamics for $c' = 0$
Model reduction and predictions (Wong & Wang '06)

Spiking neuronal network model

Mean-field approach

Simplified P-I curves
Constant activity of NS cells

Slow NMDA gating variable

Reduced two-variable model
Model reduction and predictions (Wong & Wang '06)

Spiking neuronal network model

Mean-field approach

Simplified P-I curves
Constant activity of NS cells

Slow NMDA gating variable

Reduced two-variable model

Experimental data

Spiking neuronal network model

Reduced two-variable model
Ad-hoc reduced model

\[ \tau r_1 = -r_1 + S(\alpha r_1 - \beta r_2 + I_1 + n_1) \]
\[ \tau r_2 = -r_2 + S(\alpha r_2 - \beta r_1 + I_2 + n_2) \]

Reduced two-variable model
Memory of a choice during delay

Stimulus with $c' = 6.4\%$

Weak $c' \rightarrow$ slight asymmetry

Decision phase plane

resting state

error trial
Biased competition, $c' > 0$

c' = 51.2\% 

c' = 75\%
V. Working Memory

https://wm.crm.cat
V. Perceptual Bistability
Perceptual bistability

Binocular rivalry

Ambiguous figures

- Necker Cube
- Rubin vase

- Same visual stimulus; different perception
- Perception changes along time

Young Old woman
Common features of perceptual multistability

1. **Exclusivity.** Conflicting visual representations are never simultaneously present.
2. **Inevitability.** Perception changes along time
3. **Randomness**

Hupé & Rubin, 2003
Neural correlates of alternations

Leopold & Logothetis, 1999

Physiological recordings from area V4

Percentage of percept-related cells in different brain areas

Leopold & Logothetis, 1999
Neural correlates of alternations

fMRI signal in the LGN

Wunderlich et al, 2005
The model

\[ \tau \dot{r}_C = -r_C + f(-\beta r_T - a_C + I_C) \]
\[ \tau \dot{r}_T = -r_T + f(-\beta r_C - a_T + I_T) \]
\[ \tau_a \dot{a}_C = -a_C + J_{a r_C} \]
\[ \tau_a \dot{a}_T = -a_T + J_{a r_T} \]

Bifurcation diagram

The function \( f(x) \) is defined as:

\[ f(x) = \frac{1}{1 + e^{-(x-\theta)/k}} \]
Dynamical properties of the model

Figure 3. Bifurcation diagrams and examples of activity timecourses for neuronal competition model (2.1) with parameter values $g = 0.5$, $\tau = 100$, $r = 10$, $\theta = 0.2$, and $\beta = 1.1$ (A–G), respectively, $\beta = 0.75$ (H–I). Timecourses of $u_1$, $u_2$ corresponding to panel F for different values of $I$: (A) $I = 1.86$, (B) $I = 1.5$, (C) $I = 1$, (D) $I = 0.5$, and (E) $I = 0.08$. Bifurcation diagrams of period $T$ of the network oscillation versus input strength $I$ (F and H). Bifurcation diagram of population activity $u_1$ versus $I$ (G and I).
The role of noise and adaptation

- Add noise term (noise-driven switching or not)

Ornstein-Uhlenbeck process

\[ \tau \dot{r}_C = -r_C + f(-\beta r_T - a_C + I_C + n_C) \]
\[ \tau \dot{r}_T = -r_T + f(-\beta r_C - a_T + I_T + n_T) \]
\[ \tau_a \dot{a}_C = -a_C + J_a r_C \]
\[ \tau_a \dot{a}_T = -a_T + J_a r_T \]

\[ \dot{n}_i = -\frac{n_i}{\tau_s} + \sigma \frac{\sqrt{2}}{\tau_s} \xi(t) \]

\[ \langle \xi(t), \xi(t') \rangle = \delta(t - t') \]

Ornstein-Uhlenbeck process

Moreno-Bote et al., 2007
Closing remarks

- Showroom of classical models
- Different mathematical tools (dynamical systems theory, stochastic differential equations, statistics, etc.)
- Open questions (memory, decisions, encoding information, etc.)
- Contact: gemma.huguet@upc.edu
Thank you for your attention
Some references


[4] Nicholas Brunel. Slides from the course 'Network dynamics and computation'.
https://galton.uchicago.edu/ nbrunel/teaching/winter2015.html

