

Laboratorio de Sistemas Dinámicos



# Lecture 2

# Dynamical models for single neurons. Measuring experimental neural data. Ana Amador

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SCHOOL ON NONLINEAR DYNAMICS, COMPLEX NETWORKS, INFORMATION THEORY AND MACHINE LEARNING IN NEUROSCIENCE ICTP-SAIFR - São Paulo, Brasil – May 22 - 26, 2023

# The Hodgkin – Huxley model

Using **pioneering experimental techniques** of that time, Hodgkin and Huxley (1952) determined not only the equations but **measured all the parameters values** :

$$C\dot{V} = I - \overbrace{\bar{g}_{\mathrm{K}}n^{4}(V - E_{\mathrm{K}})}^{I_{\mathrm{K}}} - \overbrace{\bar{g}_{\mathrm{Na}}m^{3}h(V - E_{\mathrm{Na}})}^{I_{\mathrm{Na}}} - \overbrace{g_{\mathrm{L}}(V - E_{\mathrm{L}})}^{I_{\mathrm{L}}}$$
  

$$\dot{n} = \alpha_{n}(V)(1 - n) - \beta_{n}(V)n$$
  

$$\dot{m} = \alpha_{m}(V)(1 - m) - \beta_{m}(V)m$$
  

$$\dot{h} = \alpha_{h}(V)(1 - h) - \beta_{h}(V)h ,$$

Values of shifted Nernst equilibrium potentials (so that  $V_{rest} = 0$ ):

$$E_{\rm K} = -12 \,\,{\rm mV} \,, \qquad E_{\rm Na} = 120 \,\,{\rm mV} \,, \qquad E_{\rm L} = 10.6 \,\,{\rm mV};$$

Values of maximal conductances:

$$ar{g}_{
m K} = 36 \ {
m mS/cm}^2 \ , \qquad ar{g}_{
m Na} = 120 \ {
m mS/cm}^2 \ , \qquad g_{
m L} = 0.3 \ {
m mS/cm}^2 \ .$$

Value of membrane capacitance:

 $C=1\,\mu\mathrm{F/cm^2}$ 

$$\begin{aligned} \alpha_n(V) &= 0.01 \frac{10 - V}{\exp(\frac{10 - V}{10}) - 1} ,\\ \beta_n(V) &= 0.125 \exp\left(\frac{-V}{80}\right) ,\\ \alpha_m(V) &= 0.1 \frac{25 - V}{\exp(\frac{25 - V}{10}) - 1} ,\\ \beta_m(V) &= 4 \exp\left(\frac{-V}{18}\right) ,\\ \alpha_h(V) &= 0.07 \exp\left(\frac{-V}{20}\right) ,\\ \beta_h(V) &= \frac{1}{\exp(\frac{30 - V}{10}) + 1} .\end{aligned}$$

4-dimensional system: difficult to study the dynamics

A lot of parameters to be determined to model a neuron! This is generally hard to measure!

# The Hodgkin – Huxley model, simplified

Many interesting features of single neuron dynamics can be illustrated using two-dimensional systems

$$C\dot{V} = I - \overbrace{g_{\rm L}(V - E_{\rm L})}^{\text{leak } I_{\rm L}} - \overbrace{g_{\rm Na}(V)(V - E_{\rm Na})}^{\text{instantaneous } I_{\rm Na,p}} - \overbrace{g_{\rm K}(n)(V - E_{\rm K})}^{I_{\rm K}},$$
  
$$\dot{n} = (n_{\infty}(V) - n)/\tau(V),$$
  
$$\frac{\text{Definition: } x\text{-Nullcline:}}{\text{curve such that } \frac{dx}{dt} = \dot{x} = 0}$$

The V-nullcline is given by the equation  $I - g_{\rm L}(V - E_{\rm L}) - g_{\rm Na} m_{\infty}(V) (V - E_{\rm Na}) - g_{\rm K} n (V - E_{\rm K}) = 0$ 

which has the solution

$$n = \frac{I - g_{\rm L}(V - E_{\rm L}) - g_{\rm Na} m_{\infty}(V) (V - E_{\rm Na})}{g_{\rm K} (V - E_{\rm K})}$$

The equation  $n_{\infty}(V) - n = 0$  defines the *n*-nullcline

$$n = n_{\infty}(V)$$



# The Hodgkin – Huxley model, simplified

Nullclines:

$$n = \frac{I - g_{\rm L}(V - E_{\rm L}) - g_{\rm Na} m_{\infty}(V) (V - E_{\rm Na})}{g_{\rm K} (V - E_{\rm K})}$$

$$n = n_{\infty}(V)$$





I,

The system

$$V = V(a-V)(V-1) - w + \dot{w} = bV - cw ,$$

imitates generation of action potentials by Hodgkin-Huxley-type models having cubic (N-shaped) nullclines (similar to the Figure in the previous slide)

- Parameter *I* mimics the injected current. For the sake of simplicity, we set I = 0
- Parameter *a* describes the shape of the cubic parabola V(a-V)(V-1)

The nullclines of the FitzHugh-Nagumo are: w = V(a - V)(V - 1) + I (V-nullcline), w = b/cV (w-nullcline),



# FitzHugh-Nagumo model

The nullclines of the FitzHugh-Nagumo are:

w = V(a - V)(V - 1) + I (V-nullcline) w = b/cV (w-nullcline),







# Recording neural activity

Now that we have a model for spikes, we want to record real spikes!

Or is it the other way around?

We first make **recording of spikes** and propose to use **dynamical models of spikes to make sense of our recordings** (we are just measuring few spikes out of many, many more!)







# probes

### NeuroNexus

Micromachined silicon

### Value: around USD 1000

















### In-house manufactured tetrodes



- Diameter 0.0005" (12.7 μm)
- Tungsten, HML coating
- Impedances: 500k to 3 MOhm







- ultra-lightweight
   customizable
- compact

Iow-cost

### Connector





- Tetrodes manufactured in-house
- Diameter 0.0005" (12.7 μm)
- Tungsten, HML coating
  - Impedances: 500k to 3 MOhm



# Lightweight recording device

- ultra-lightweight customizable
- compact

Iow-cost

### Connector





- Pitch 90 TPI = 282 µm/turn (manual step ≈25 µm)
- Mass <1g</li>
- 15mm tall, 13mm<sup>2</sup> footprint
- Tetrode geometry easy to modify.



- Tetrodes manufactured in-house
- Diameter 0.0005" (12.7 μm)
- Tungsten, HML coating
  - Impedances: 500k to 3 MOhm



- 4-tetrode array (16ch) + Ref
- 2x2 geometry

Credits: Cecilia T. Herbert





Work with Santiago Boari











# Different neurons may present different spike shapes







### Spike sorting: PCA analysis





# Neural recordings: LFP and MUA



### MUA (Multi-Unit Activity)

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1UA,		1		hanger and a second and the second a	FP,
2		Ch	, #	5 sec	_

### LFP (Local Field Potential)

Boari, Mindlin and Amador, EJN 2021



# Neural recordings: LFP and MUA



5 sec



# Neural recordings: LFP and MUA





# Rhythms in the Brain

# Ø

# Speech perception exhibits rhythmicity

# When presented with an acoustic stimulus

(speech or modulated white noise) the auditory cortex tracks the amplitude modulation of the input.

The speech rhythm enhances perception

### nature neuroscience

ARTICLES https://doi.org/10.1038/s41593-019-0353-z

# Spontaneous synchronization to speech reveals neural mechanisms facilitating language learning





# Rhythms in the Speech

# $\mathcal{O}$

### Speech production exhibits rhythmicity



# Speech rhythms and their neural foundations

David Poeppel<sup>™</sup><sup>1,2™</sup> and M. Florencia Assaneo<sup>™</sup><sup>2,3</sup>

### NATURE REVIEWS | NEUROSCIENCE

# Rhythms in the Brain of a Songbird?



### nature neuroscience

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# Spontaneous synchronization to speech reveals neural mechanisms facilitating language learning

M. Florencia Assaneo <sup>1,7\*</sup>, Pablo Ripollés<sup>1,7</sup>, Joan Orpella<sup>2,3,4,7</sup>, Wy Ming Lin<sup>1</sup>, Ruth de Diego-Balaguer<sup>2,3,4,5,8</sup> and David Poeppel<sup>1,6,8</sup>









# Rhythms in the Brain of a Songbird?



### Pallial Striatal C Modern view Pallidal Cerebrum (telencephalon) Lateral ventricle Cerebrum (telencephalon) Mesopallium Amygdaloid, Hp Striatum CDL Hyperpallium complex Six-layered cortex L2 Nidopallium Claustrum ateral MV entricle Striatum Ho Thalamus Cerebellum Midbrain B Thalamus Cerebellum Hindbrain Piriform TuO TuO cortex Midbrain Hindbrain Pallidum Piriform cortex Pallidum Amygdala

Similar structures mean similar properties?

### nature neuroscience

ARTICLES

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# Rhythms in the Brain of a Songbird !





LFP oscillations are phase-locked (synchronization)

### nature neuroscience

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# Rhythms in the Brain of a Songbird !





# LFP and coding of behavior (birdsong)





LFP oscillations occur at the song syllabic rate





# LFP vs. MUA vs. SUA



single units isolated in each protocol.



# LFP vs. MUA vs. SUA

Freq. Env. (kHz) (norm)

Freq.

Sound

í.

(arb.

-6B -6A -5B -5A

-4B -4A

-3B -3Ā -2B

-1A

-3/

-2A

0.15

0.1 0.05

0

0

0.5 t/τ<sub>syll</sub>

Prob.

0





# Gracias por su atención!





### Thanks for the support

- ♦ National Institute of Health (NIH, USA)
- ♦ University of Buenos Aires (Argentina)
- Ational Council for Science and Technology (CONICET, Argentina)
- Agencia Nac. de Promoción Científica y Tecnológica (ANPCyT, Argentina)

### Collaborators

- $\diamond$  Gabriel B. Mindlin (UBA, CONICET)
- $\diamond$  Daniel Margoliash (Univ. of Chicago)

### PhD Students

- ♦ Cecilia T. Herbert (UBA, Biology)
- ♦ Fiamma L. Leites (UBA, Biology)

### Postdocs

♦ Santiago Boari (UBA, Physics)

