Biological Modeling of Neural Networks

Week 7 – Variability and Noise: The question of the neural code

Wulfram Gerstner
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7.1 Variability of spike trains
- experiments

7.2 Sources of Variability?
- Is variability equal to noise?

7.3 Poisson Model
- Three definitions of Rate code

7.4 Stochastic spike arrival
- Membrane potential fluctuations

7.5. Stochastic spike firing
- stochastic integrate-and-fire
Neuronal Dynamics – 7.1. Variability

motor cortex

visual cortex

to motor output

frontal cortex
Variability in vivo

- of membrane potential?
- of spike timing?

awake mouse, cortex, freely whisking,

Crochet et al., 2011
Detour: Receptive fields in V5/MT

visual cortex

cells in visual cortex MT/V5 respond to motion stimuli
15 repetitions of the **same** random dot motion pattern

adapted from **Bair and Koch 1996; data from Newsome 1989**
Neuronal Dynamics – 7.1 Variability in vivo

Human Hippocampus

4 repetitions of the same time-dependent stimulus,
Neuronal Dynamics – 7.1 Variability

Fluctuations
-of membrane potential
-of spike times

- fluctuations=noise?

relevance for coding?

source of fluctuations?

model of fluctuations?

In vivo data
→ looks ‘noisy’

In vitro data
→ fluctuations
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- Intrinsic noise (ion channels)
  - Finite number of channels
  - Finite temperature
Review from 2.5 Ion channels

A. Traces from a patch containing several channels. Bottom: average gives current time course.

B. Opening times of single channel events

Na+ channel from rat heart (Patlak and Ortiz 1985)

Steps: Different number of channels

Stochastic opening and closing

Ions/proteins

Na+, K+, Ca^{2+}
- Intrinsic noise (ion channels)
  - Finite number of channels
  - Finite temperature

- Network noise (background activity)
  - Spike arrival from other neurons
  - Beyond control of experimentalist

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Check intrinsic noise by removing the network
Neuronal Dynamics — 7.2 Variability in vitro

neurons are fairly reliable

Image adapted from Mainen & Sejnowski 1995
REVIEW from 1.5: How good are integrate-and-fire models?

Aims: - predict spike initiation times
- predict subthreshold voltage

only possible, because neurons are fairly reliable

Badel et al., 2008
Neuronal Dynamics – 7.2. Sources of Variability

- Intrinsic noise (ion channels)
  - Finite number of channels
  - Finite temperature

- Network noise (background activity)
  - Spike arrival from other neurons
  - Beyond control of experimentalist

Check network noise by simulation!
The Brain: a highly connected system

High connectivity:
- systematic, organized in local populations
- but seemingly random

Distributed architecture
- $10^{10}$ neurons
- $10^4$ connections/neurons
Random firing in a population of LIF neurons

Population
- 50 000 neurons
- 20 percent inhibitory
- randomly connected

Network of deterministic leaky integrate-and-fire: ‘fluctuations’

Mayor and Gerstner, Phys. Rev E. 2005
Vogels et al., 2005
Random firing in a population of LIF neurons

Population
- 50 000 neurons
- 20 percent inhibitory
- randomly connected

Neuron # 32374

input \{ low rate, high rate \}
- Variability of interspike intervals (ISI)

Variability of spike trains: broad ISI distribution

here in simulations, but also in vivo

Mayor and Gerstner, Phys. Rev E. 2005
Vogels and Abbott, J. Neuroscience, 2005
Intrinsic noise (ion channels)

In vivo data
→ looks ‘noisy’

In vitro data
→ small fluctuations
→ nearly deterministic

- Network noise

**small contribution!**

**big contribution!**
A - Spike timing in vitro and in vivo
[ ] Reliability of spike timing can be assessed by repeating several times the same stimulus
[ ] Spike timing in vitro is more reliable under injection of constant current than with fluctuating current
[ ] Spike timing in vitro is more reliable than spike timing in vivo

B – Interspike Interval Distribution (ISI)
[ ] An isolated deterministic leaky integrate-and-fire neuron driven by a constant current can have a broad ISI
[ ] A deterministic leaky integrate-and-fire neuron embedded into a randomly connected network of integrate-and-fire neurons can have a broad ISI
[ ] A deterministic Hodgkin-Huxley model as in week 2 embedded into a randomly connected network of Hodgkin-Huxley neurons can have a broad ISI
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- 3 definitions of rate coding

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Homogeneous Poisson model: constant rate

Probability of finding a spike \( P_F = \rho_0 \Delta t \)

stochastic spiking \( \rightarrow \) Poisson model
Neuronal Dynamics – 7.3 Interval distribution

Probability of firing:

\[ P_F = \rho_0 \Delta t \]

(i) Continuous time

\[ \Delta t \rightarrow 0 \]

prob to ‘survive’

(ii) Discrete time steps

\[ \frac{d}{dt} S(t_1 \mid t_0) = -\rho_0 \ S(t_1 \mid t_0) \]

Blackboard: Poisson model
Exercise 1.1 and 1.2: Poisson neuron

1.1. - Probability of NOT firing during time t?
1.2. - Interval distribution $p(s)$?
1.3. - How can we detect if rate switches from
$$\rho_0 \rightarrow \rho_1$$

(1.4 at home:)
- 2 neurons fire stochastically (Poisson) at 20Hz. 
  Percentage of spikes that coincide within +/-2 ms?)
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Rate changes

Probability of firing \( P_F = \rho(t) \Delta t \)

Survivor function \( S(t | \hat{t}) = \exp(-\int_{\hat{t}}^{t} \rho(t') dt') \)

Interval distribution \( P(t | \hat{t}) = \rho(t) \exp(-\int_{\hat{t}}^{t} \rho(t') dt') \)
**A Homogeneous Poisson Process:**
A spike train is generated by a homogeneous Poisson process with rate 25Hz with time steps of 0.1ms.
[ ] The most likely interspike interval is 25ms.
[ ] The most likely interspike interval is 40 ms.
[ ] The most likely interspike interval is 0.1ms.
[ ] We can’t say.

**B Inhomogeneous Poisson Process:**
A spike train is generated by an inhomogeneous Poisson process with a rate that oscillates periodically (sine wave) between 0 and 50Hz (mean 25Hz). A first spike has been fired at a time when the rate was at its maximum. Time steps are 0.1ms.
[ ] The most likely interspike interval is 25ms.
[ ] The most likely interspike interval is 40 ms.
[ ] The most likely interspike interval is 0.1ms.
[ ] We can’t say.
3 definitions
- Temporal averaging
- Averaging across repetitions
- Population averaging (‘spatial’ averaging)
Variability of spike timing

rate as a (normalized) spike count:

\[ \nu(t) = \frac{n^{sp}}{T} \]

single neuron/single trial: temporal average

T=1s
Neuronal Dynamics – 7.3. Rate codes: spike count

single neuron/single trial: temporal average

\[ \nu(t) = \frac{n_{sp}}{T} \]

Variability of interspike intervals (ISI) measure regularity

ISI distribution
Neuronal Dynamics – 7.3. Spike count: FANO factor

Fano factor

\[ F = \frac{\left\langle n_k^{sp} - \langle n_k^{sp} \rangle^2 \right\rangle}{\langle n_k^{sp} \rangle} \]

Brain

stim

trial 1 \( n_1^{sp} = 5 \)

trial 2 \( n_2^{sp} = 6 \)

trial \( K \) \( n_K^{sp} = 4 \)
3 definitions

- Temporal averaging (spike count)
  - ISI distribution (regularity of spike train)
  - Fano factor (repeatability across repetitions)

- Averaging across repetitions

- Population averaging (‘spatial’ averaging)

Problem: slow!!!
Neuronal Dynamics – 7.3. Three definitions of Rate Codes

3 definitions

- Temporal averaging

  Problem: slow!!!

- Averaging across repetitions

- Population averaging
Neuronal Dynamics – 7.3. Rate codes: PSTH

Variability of spike timing

Brain

stim

trial 1
trial 2
trial $K$
Averaging across repetitions

single neuron/many trials: average across trials

$$PSTH(t) = \frac{n(t; t + \Delta t)}{K \Delta t}$$

$K$ repetitions

Stim$(t)$

$PSTH(t)$

$K=50$ trials
3 definitions

- Temporal averaging

- Averaging across repetitions
  
  Problem: not useful for animal!!

- Population averaging
population of neurons with similar properties

Neuronal Dynamics – 7.3. Rate codes: population activity

Brain

stim

neuron 1
neuron 2
Neuron $K$
population activity - rate defined by population average

\[ A(t) = \frac{n(t; t + \Delta t)}{N\Delta t} \]
Neuronal Dynamics – 7.3. Three definitions of Rate codes

Three averaging methods

- over time
  - Too slow for animal!!!

- over repetitions
  - Not possible for animal!!!

- over population (space)
  - ‘natural’
Neuronal Dynamics – 7.3 Inhomogeneous Poisson Process

inhomogeneous Poisson model consistent with rate coding

\[ PSTH(t) = \frac{n(t; t + \Delta t)}{K \Delta t} \]

\[ A(t) = \frac{n(t; t + \Delta t)}{N \Delta t} \]

population activity
Neuronal Dynamics – Quiz 7.3.

Rate codes. Suppose that in some brain area we have a group of **500 neurons**. All neurons **have identical parameters** and they all receive **the same input**. Input is given by sensory stimulation and passes through 2 preliminary neuronal processing steps before it arrives at our group of 500 neurons. Within the group, neurons are **not connected** to each other. Imagine the brain as a model network containing 100,000 nonlinear integrate-and-fire neurons, so that we know exactly how each neuron functions.

Experimentalist A makes a measurement in a **single trial on all 500 neurons** using a multi-electrode array, during a period of sensory stimulation.

Experimentalist B picks an arbitrary **single neuron and repeats** the same sensory stimulation 500 times (with long pauses in between, say one per day).

Experimentalist C **repeats** the same sensory stimulation 500 times (1 per day), but every day he **picks a random neuron** (amongst the 500 neurons).

All three determine the time-dependent firing rate.

- A and B and C are expected to find the same result.
- A and B are expected to find the same result, but that of C is expected to be different.
- B and C are expected to find the same result, but that of A is expected to be different.
- None of the above three options is correct.
Neuronal Dynamics: Computational Neuroscience of Single Neurons

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Neuronal Dynamics – 7.4 Variability in vivo

Spontaneous activity in vivo

Variability of membrane potential? awake mouse, freely whisking,

Crochet et al., 2011
Random firing in a population of LIF neurons

Population
- 50,000 neurons
- 20 percent inhibitory
- randomly connected

Input
{ low rate, high rate }

Neuron # 32374

A [Hz]
10
32440

Neuron #
32340
32440

Neuron # 32374

u [mV]
0
100
200

Time [ms]
50
100
200
Pull out one neuron from neuron’s point of view: stochastic spike arrival

‘Network noise’

big contribution!
Neuronal Dynamics – 7.4. Stochastic Spike Arrival

Total spike train of $K$ presynaptic neurons

Gradient $\Delta t$

Probability of spike arrival:

$$P_F = K \rho_0 \Delta t$$

Take $\Delta t \rightarrow 0$ expectation

$$S(t) = \sum_{k=1}^{K} \sum_{f} \delta(t - t_k^f)$$
A leaky integrate-and-fire neuron without threshold (=passive membrane) receives stochastic spike arrival, described as a homogeneous Poisson process.

Calculate the **mean membrane potential**. To do so, use the above formula.
A linear (=passive) membrane has a potential given by

\[ u(t) = \sum_{f} \int dt' f(t-t') \delta(t'-t^f_k) + a \]

Suppose the neuronal dynamics are given by

\[ \tau \frac{d}{dt} u = -(u - u_{rest}) + q \sum_{f} \delta(t-t^f) \]

[ ] the filter \( f \) is exponential with time constant \( \tau \)
[ ] the constant \( a \) is equal to the time constant \( \tau \)
[ ] the constant \( a \) is equal to \( u_{rest} \)
[ ] the amplitude of the filter \( f \) is proportional to \( q \)
[ ] the amplitude of the filter \( f \) is \( q \)
Neuronal Dynamics – 7.4. Calculating the mean

\[ RI^{syn}(t) = \sum_{k} w_k \sum_{f} \alpha(t - t^f_k) \]

\[ I^{syn}(t) = \frac{1}{R} \sum_{k} w_k \sum_{f} \int dt' \alpha(t - t') \delta(t' - t^f_k) \]

mean: assume Poisson process

\[ x(t) = \sum_{f} \int dt' f(t - t') \delta(t' - t^f_k) \]

\[ I_0 = \langle I^{syn}(t) \rangle = \frac{1}{R} \sum_{k} w_k \int dt' \alpha(t - t') \left( \sum_{f} \delta(t' - t^f_k) \right) \]

\[ \langle x(t) \rangle = \int dt' f(t - t') \left( \sum_{f} \delta(t' - t^f_k) \right) \]

\[ I_0 = \frac{1}{R} \sum_{k} w_k \int dt' \alpha(t - t') \nu_k \]

\[ \langle x(t) \rangle = \int dt' f(t - t') \rho(t') \]

use for exercise
rate of inhomogeneous Poisson process
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Neuronal Dynamics – 7.5. Fluctuation of current/potential

![Neuronal network diagram]

### Synaptic current pulses of shape $\alpha$

$$R I^\text{syn}(t) = \sum_k w_k \sum_f \alpha(t - t^f_k)$$

**EPSC**

### Passive membrane

$$\tau \frac{d}{dt} u = -(u - u_{\text{rest}}) + RI^\text{syn}(t)$$

→ Fluctuating potential

$$I^\text{syn}(t) = I_0 + I^\text{fluct}(t)$$

- Fluctuating input current
for a passive membrane, we can analytically predict the mean of membrane potential fluctuations

\[ \tau \frac{d}{dt} u = -(u - u_{\text{rest}}) + RI^{\text{syn}}(t) \]

\textit{Passive membrane} = \textit{Leaky integrate-and-fire without threshold}
neuronal dynamics – 7.5. stochastic leaky integrate-and-fire

noisy input/ diffusive noise/ stochastic spike arrival

subthreshold regime:
- firing driven by fluctuations
- broad ISI distribution
- in vivo like

\[ u(t) \]
Reading: W. Gerstner, W.M. Kistler, R. Naud and L. Paninski, *Neuronal Dynamics: from single neurons to networks and models of cognition*. Ch. 7,8: Cambridge, 2014
OR W. Gerstner and W. M. Kistler, Spiking Neuron Models, Chapter 5, Cambridge, 2002