Spontaneous Activity

- Definition: Spiking activity that is not (temporally) related to a stimulus.
- E.g. Subthreshold ‘noise’:

![Graph showing synaptic and membrane noise with voltage levels and standard deviations](image.png)

Noise is non-linear voltage-dependent

(rat cortex, pyramidal cell, in vitro)
- Does membrane noise matter?

Unstructured inputs

(Mainen and Sejnowski, 1995)

Accumulating effects of membrane noise

Structured inputs

Even
Odd

Apparently stationary membrane noise effects

Rat prefrontal cortex pyramidal cells, in vitro, synaptic transmission blocked

(Fellous et al. 2004)

(Fellous et al. 2004)
Spontaneous activity

- But!... What if the inputs are ‘synaptic-like’

‘Frozen’ noise

(Apparently NO effect of membrane noise)

However…. Two Synaptic inputs are NEVER identical…

(Mainen and Sejnowski, 1995)
Spontaneous Activity

Sources of noise: Intrinsic? Or Synaptic?
- Thermal noise (‘Johnson’ noise).
  White noise, Gaussian amplitude distribution: ~< 0.5 mV
- Stochastic opening/closing of membrane channels: ~< 0.5 mv

- Synaptic noise: ~2-10 mV

In vitro

0 nA

(Temperature dependent)

(Hille 2001)

(Pare et. al. 1998)
Spontaneous Activity: **Standard deviation** of membrane potential

Quantifying synaptic noise (in *vivo*)

- 64 mV

- 82 mV

(hyperpolarized to better visualize spontaneous EPSPs)

Note: convention:
EEG downward $\rightarrow$ depolarizing potentials

- NMDA antagonist
- GABAA agonist

Noise is anesthetics dependent

(Pare et. al. 1998)
The subthreshold effects of synaptic activity

TTX = blocks synaptic transmission

Synaptic Stimulation → Pulse

V_m = R_{in} I

⇒ Synaptic activity decreases Input Resistance

(Pare et al. 1998)
Burstiness (in mammalian cortex) is (mostly) a network phenomenon: Analyses of simultaneously sampled EEG and spike recordings.

(Pare et al. 1998)

EEG

Spikes

‘up’/’down’ states
‘slow oscillations’

Study of a cell at different holding voltages:

~Lower voltage (less GABA synaptic effects)
~Higher voltage (less AMPA synaptic effects)
Spontaneous Activity: **Histogram** of Membrane Potential

Is the standard deviation the best measure….?

Ketamine-Xylazine

> ‘visualizing’

**Distribution** shape change

**Distributions:**

Relative

**Vs**

Cumulative

(Pare et. al. 1998)
- Is there a number that can indicate whether a cell is firing regularly, randomly (single spikes) or randomly with bursts?
Coefficient of Variation of ISIs

\[ CV = C_V = \frac{\sigma_{ISI}}{\langle ISI \rangle} \]

\[ \sigma_{ISI} = \sqrt{\frac{\sum_{i=1}^{N} (ISI_i - \langle ISI \rangle)^2}{N}} \]

(note: biased Vs. unbiased estimate of the variance)

\[ \sigma_{ISI} = \sqrt{\frac{\sum_{i=1}^{N} (ISI_i - \langle ISI \rangle)^2}{N - 1}} \]

CV=0

ISI\(_i\)=\langle ISI \rangle

Oscillation

Poisson: \( CV_{isi} = 1 \)

Gamma: \( CV_{isi} = 1/\sqrt{k+1} \)

\[ p(\tau) = \frac{a(\tau)^k e^{-a\tau}}{k!} \]
Coefficient of Variation of ISIs

- Is CV the best measure of variability/regularity?

- The ‘significance’ of a variation should depend on the mean.
- Slow variations in firing rate should not ‘count’ as Poisson.

→ One possibility is to ‘average’ consecutive ISIs.

\[
CV_2 = \frac{\sum_{i=1}^{N-1} 2|ISI_{i+1} - ISI_i|}{\sum_{i=1}^{N-1} \frac{ISI_{i+1} + ISI_i}{N - 1}}
\]

(Holt et. al. 1996)
Coefficient of Variation of ISIs

- When do we know we have a meaningful firing rate, CV, CV2? when do we know we have **enough data**?

- Cumulative statistics approach:

(Example: 200 spikes of a 20Hz Poisson train)

Algorithm…..

Take the first n spikes
compute/plot FR, CV, CV2
append the next (p) spikes to the list
stop if curve is ‘stable’, otherwise
Coefficient of Variation of ISIs

- What is the shortest mean ISI that will be representative of the variability of the whole dataset? What is the time scale of variability?

- Part I: create and study a surrogate dataset

\[ CV^2 = \frac{\text{mean ISI pair}}{t_r} \]

(Holt et. al. 1996)

uniform distribution \(\Rightarrow\) Poisson

Is the data ‘truly’ random?

(2000 spikes, 50 Hz Poisson, 4ms refractory period)

\( t_r = \text{refractory period} \)
Coefficient of Variation of ISIs

- Part II: Compare surrogate set with data

- No apparent differences between current injection and visual stimulation? same FR, CV, mean CV$_2$

- Subtle (significant?) differences between CV$_2$ curves

(Holt et. al. 1996)
Coefficient of Variation of ISIs

- Part III: Understand individual cases

$$CV_2 = \sum_{i=1}^{N} \frac{2|ISI_{i+1} - ISI_i|}{ISI_{i+1} + ISI_i}$$

Not uniform!

(Holt et. al. 1996)

Bursty cell with visual stimulation, but not with current injection.
Coefficient of Variation of ISIs

- Check…. Non bursty cell

For cells that are not bursty, CV2 decrease during current injections (i.e. cells are more regular at short mean ISIs)
Coefficient of Variation of ISIs

Population analyses: What do the differences mean?

- Long ISIs
  (more bursty during visual stimulation)

- Short ISIs
  (relative refractory period differences?)

- Same

(Coefﬁcient of Variation of ISIs

Visual stimulation
Current injection

Long ISIs
(1,1)
(1,4)

Short ISIs
(4,1)
(4,4)

Same

(Holt et. al. 1996)
Distribution of ISIs

Side Note: Warning!: Beware of Binning artifacts…

binsize > Refractory_Period

10ms refractory period, 5ms bins

10ms refractory period, 25ms bins

More on this later….
Goal: Detecting irregular (i.e. not visible ‘by eye’) temporal structure in spike trains

⇒ Poincaré map – ISI return map

- FR, CV, CV₂ are ‘overall’ spike train measurements

- (20 Hz Poisson train)
ISI return map

Figure 1

$\text{ISI}_{i+1}$ vs $\text{ISI}_i$

10ms

10ms
ISI return map

\[ ISI_{i+1} \]

\[ ISI_i \]
ISI return map

![Figure 1](image.png)

- ISI return map with scatter plot showing the distribution of ISI values.
- The x-axis represents ISI$_i$, and the y-axis represents ISI$_{i+1}$.
- The plot includes a horizontal line indicating a 100 ms interval.
ISI return map… for real

Pyloric neuron lobster STG

Two types of bursts

(Szucs et. al. 2005)
ISI return map… for real

Attractor

Two types of bursts

(Szucs et. al. 2005)
Other real ISI return maps

Stimulus-triggered Return Map

(Siegel, 1990)
Fano Factor – a.k.a. ‘index of dispersion’

- Measure the presence (and time scale) of intrinsic temporal correlations in a spike train.

- If one measures the distribution of the number of spikes occurring in T seconds (as a result of different experimental conditions for example):

\[
FF(T) = \frac{\sigma^2(T)}{\mu(T)}
\]

- For a Poisson distribution: FF(T)=1
- For a renewal process and large enough T

\[
\mu(T) \approx \frac{T}{<\text{ISI}>}
\]

\[
\sigma(T) \approx \sqrt{\frac{T\sigma^2_{ISI}}{<\text{ISI}>^3}}
\]

\[
FF(T) = \left(\frac{\sigma_{ISI}}{<\text{ISI}>}\right)^2 = CV_{ISI}^2
\]
Fano factor uses spike counts, not ISIs

(ISIs) 'Recoding' (spike = 1 time point)

Fano Factor

(ISI Vs. Count) (Teich. al. 1996)
‘Cheap’ Surrogate Dataset: Shuffled ISI

Shuffling does not change ISI distribution (Poisson $\Rightarrow$ Poisson)
Fano Factor

- Data (cat V1) Vs. Shuffled data Vs. Poisson: Testing significance

Spontaneous - T=2 sec

\( \text{Spike count} \rightarrow \text{Spike count} \)

\( F(T=2\text{sec)} \)

\( F(T=2\text{sec)} \)

\( L \text{sec} \)

\( L \text{sec} \)

(\text{Teich. al. 1996})

\( \Rightarrow \text{FF jumps when spikes cluster, or when spikes ‘de-cluster’} \)
- Because FF depends on T, one can study the statistics of the spontaneous activity at *specific* time scales.
- Use of shuffled ISIs as a surrogate dataset.

Spontaneous activity

(Reichl et al. 1996)
- Fano factor during visual stimulation at 1 Hz, 5 Hz and 10 Hz
- \( FF > 2 \iff CV > 1.4 \) … Presence of ‘clustering’ in spike train

Optimum (~40 Hz)

Stimulation artifact (phase locking with stimulus)
Fano Factor

- Allows for the uncovering of frequency/time scale preferences

(Teich et al. 1996)

(Entrainment, Resonant frequency)

(Fellous et al. 2001)
Fano Factor

- Measuring the variability of neural responses to the same stimuli, across multiple brain areas

Simultaneous recordings in anesthetized cat: retina, LGN, V1

(Kara et al. 2000)

➔ Activity is less and less regular from sensation to perception


Homework 2 – due Next week

- Q1: Using the simpleneuron model: Record the membrane potential (type ‘RecordMEMPOT(0)’). Run the model for 10 seconds (spontaneous activity). Use SaveMEMPOT() to save the voltage values of the simulation.
  > Compute the mean and standard deviation of the membrane potential and compare with (Pare et.al. 1998).

- Q2: Write a routine that takes a spike train and returns the firing rate, the CV and the CV2.

- Q3: Increase the level of noise of the model (in the shell, type ‘neurs[0].noise.g_e0=0.02’). Record the action potentials of neuron 0 (type ‘RecordAP(0)’). Run the Neuron model for 150 seconds (spontaneous activity). Use SaveAP() to save the times of the action potentials.
  > Compute the cumulative firing rate, CV and CV2. Plot the CV2 Vs mean ISI (see Holt et al. 1996, fig 2). What do you see?

- Q4 (optional):
  Generate 2000 spikes Poisson distributed at 20 Hz with a 4 ms absolute refractory period.
  > Modify the spike train to produce as ‘strange’ of a return map as possible. Plot the return map and a sample of the spike train. Make sure to explain the features of the map, and how they relate to the modifications you introduced.