Midterm next week. Take Home (at least in part).
Spike timing

- What is the ‘neural code’?

**Trial 1**

**Trial 2**

**Trial 3**

**Trial 4**

**Trial 5**

**Unit 1**

**Unit 2**

**Unit 3**

**Unit 4**

**Unit 5**

5 x Stimulus

1 x Stimulus
- Two ‘competing’ theories: Rate Vs. Temporal code

(Kumar et al, 2010; Ainsworth et al, 2012)
Spike timing

- Why would one need precise spike timing?... Elicit a spike

Presynaptic strength is small.

- Paired recordings: 1 EPSP \( \sim 1-3 \) mv \( \rightarrow \) need 3-5 *almost simultaneous* presynaptic synaptic releases to trigger a spike in a postsynaptic cell (cortex).
- Synapses fail \( \sim 3 \) out of 4 times \( \rightarrow \) need 12 to 20 *almost simultaneous* neurons to trigger a postsynaptic cell (hippocampus).
- In *vivo*, synchrony occurs with \( \sim 3-20 \) ms jitter \( \rightarrow \) realistically need \( \sim 50-100 \) *synchronous* presynaptic neurons to trigger a postsynaptic cell.
- Not accounting for synaptic dynamics (depression, facilitation) or dendritic synaptic location.

*Figures and references:* (Furhman et al. 2004) (Williams and Stuart 2002)
Why would one need spike timing: … Synaptic plasticity

Spike-Timing-Dependent-Plasticity (STDP)

Repeated pairings: spike/epsp

\[ \Delta t = \text{Post}_{\text{spike}} - \text{Pre}_{\text{epsp}} \]

Post \(\rightarrow\) Pre

Pre \(\rightarrow\) Post

Long Term Depression (LTD)

Long Term Potentiation (LTP)

(Bi & Poo, 2001)
What is the experimental evidence that spike timing may carry information: Reliable spiking *in vitro*

Determinism: Same stimulus → Same spike times
Spike timing

- What is the experimental evidence for spike timing: Reliable spiking *in vivo*

Different animals!

Visual Stimulation (grey levels)

(Reinagel & Reid 2002)
- What is the experimental evidence for spike timing: Reliable spiking *in vivo*

Stimulus → Eye → LGN → V1 → V2 → V4 → MT

>12 synapses from the stimulus!

(Buracas, Zador, DeWeese, Albright, 1998)
- Analyzing spike timing: **Reliability** (‘repeatability’) and **precision** (‘tightness’)

- **Step 1**: histogram

- Spike timing

```plaintext
Spike timing

- Analyzing spike timing: Reliability (‘repeatability’) and precision (‘tightness’)

- Step 1: histogram

bin size ?
```
Spike timing

- Analyzing spike timing: Reliability and Precision

- **Step 2**: smoothing the histogram

Rule of thumb…Smoothing window= ~1x/2x bin size
Also see *smooth()* in Matlab for a simple ‘moving average’ smoothing method
Spike timing

- Analyzing spike timing: Reliability and Precision

- **Step 3**: Finding ‘events’

  ![Graph showing 4 peaks found]

  Threshold?

- **Step 4**: Computing (average) Reliability and Precision

  ![Graph showing 4 events, Reliability: 0.56, Precision: 13.12 (ms), Event-rel: 0.81]
Spike timing: Reliability and Precision

- Analyzing spike timing: Reliability and Precision

  ● Precision

  \[ P = \left( \sum_e \sigma_e \right)^{-1} \]
  
  (average) jitter

  ● Reliability

  \[ R = \frac{\sum_e N_e}{N} \]
  
  With \( N_e = \) number of spikes within event \( e \)
  
  \( N = \) total number of spikes

  ● Average event-reliability

  \[ r = \frac{1}{e} \sum_e \frac{N_e}{N_t} \]
  
  With \( N_t = \) number of trials/units
Spike timing

- Computing Reliability and Precision *in vivo*

(Reinagel and Reid 2002)
Spike timing

- Comparing the firing of two cells

\[ \Delta t = \frac{\mu_1 - \mu_2}{<\sigma>} \]

Mean time of the events

\[
\begin{align*}
0.2 & \quad 0.1 & \quad -0.1 & \quad 0.6 & \quad 0.9 & \quad 0.2 & \quad 0.2 & \quad -0.9 & \quad 0.3 & \quad -0.3 & \quad -0.1 \\
\end{align*}
\]

ON cells

OFF cells

(Reinagel and Reid 2002)
Spike timing

- Analyzing spike timing: Spike train distances

What is D? (metric)

Side bar: Distance Vs Metric
Spike timing

- Distances: Vectorial approach

  ● Binning

  0000000101000000100001000000000100000000110000000000000000100001…

  N-dimensional vectorial space

  ● Use Euclidian Distance in N-Dimensional space (a.k.a L2 norm)

  \[ D(v, w) = \sqrt{\sum_{i=1}^{N} (v_i - w_i)^2} \]

  2 spike trains \( v \) and \( w \):

  ● Problem: High dimensional space (computationally expensive)
  small spike jitter ➔ discrete shifts in new dimensions
- Metric: Bin-less approach

\[ D(V, W) = 1 - \sum_{i=1}^{N} V_i \cdot W_i / \|V\| \cdot \|W\| \]

(Kruskal et al, 2007; Lyttle and Fellous, 2011)
How is information represented in the brain?

- Spike Count
- Firing Rate
- Spike Timing
-...??...
- Stimulus-dependent sensory information (e.g. Vision) is represented by precise and reliable firing events. Recall:
Reliability in Vitro

- Same *in vitro* (i.e. no synaptic activity)

(Fellous et al, 2004)
- Neurons receive thousands of background (noise) synaptic inputs.
- Synaptic transmission is unreliable ($p \approx 0.2-0.3$).
- Network configurations are different from animal to animal.

How can a neuron *in vivo*, several synapses away from a stimulus, fire reliably with millisecond precision?

What are some of the characteristics of *in vivo* reliable and precise firing?
In Vitro: Reliabilities

- Response to a stimulus is non-stationary and (in at least some cases) non deterministic

(Fellous et al, 2004)
- Limited non-determinism: Cycle skipping

(Fellous et al, 2004)
Assumption: trials are independent

Re-sorting (by hand)

Same information
Two different spike patterns

(Fellous et al, 2004)
- Can one hide/find different spike patterns?
- Surrogate set: Jitter, Noisy-spikes, missing spikes

(Fellous et al, 2004)
Clustering

Find spike patterns

Find cluster centers, and cluster radii to maximize correct classification
- Real Data: No knowledge of the cluster structure – ‘unsupervised learning’

- Find cluster centers, and cluster radii to minimize the number of outliers

- Find cluster centers \{C\}, and radii \{R\} to maximize an ‘objective function’

\[ O(C, R) = \frac{D_{\text{between clusters}}}{D_{\text{within clusters}}} \]
- **K-means clustering**
  
  - 1: Start with random guess: K cluster centers.
  - 2: Assign each data point to the nearest cluster (also called ‘Centroidal Voronoi tesselation’). If no new assignments: STOP
  - 3: Move each cluster center to the mean of the data assigned to it.
  - 4: Go to 2.

- Other algorithms: Mixture of Gaussian (EM-algorithm), Fuzzy K-Means …
Recoding: ‘Everything is Relative’

- Problem: Space of spike trains is large and infinite.
- $\rightarrow$ Recode in a smaller, finite space.

\[(Fellous et. al. 2004)\]
Clustering Method: Clustering

- Maximize Spike train space occupancy

(Fellous et. al. 2004)
Spike Patterns In Vitro

- → Surrogate sets: As expected…
- In *vitro* data: As expected …

(Fellous et. al. 2004)
- Complex inputs *in vitro* (prefrontal cortex, rat)

(Fellous et. al. 2004)
- Complex inputs in vitro (prefrontal cortex, rat)
  → Discrete clusters in response to the same stimuli

(Fellous et al. 2004)
Spike Patterns in Vivo

- Behaving monkey, Area MT
- Visual stimulation, moving Gabor patches

Is there more to ‘global alignments’?

(Buracas, Zador, DeWeese, Albright, 1998)
- Is there more to ‘global alignments’?
In Vivo: Behaving Monkey, MT

1

3 clusters

~50% empty!

2

5 clusters

~25% empty!
Spike Patterns in Vivo

- Is there more to ‘global alignments’?

Within cells Vs Across cells
In Vivo: Anesthetized Cat, LGN

- 2 Clusters
- Long-term determinism
Multi-unit spike patterns

From Multiple Trials to Multiple Neurons
Spike Patterns \textit{in vitro}?

- Population dynamics in vitro: Are there spatio-temporal patterns of spiking?

Mice visual cortical slices, Fura2-AM, 2-photon imaging:

(Ikegaya, Aaron, Cossart, Aronov, Lampl, Ferster, Yuste 2004)
Spike Patterns *in vitro*/*in vivo*?

- Record spontaneous post-synaptic events
  \(\Rightarrow\) Single cell receives repeating patterns of (near identical) synaptic inputs


(Env, Layer 5, mice)
Spike Patterns *in vitro*?

Repeating pattern of synaptic inputs

\[\leftrightarrow\] Repeating pattern of (presynaptic) firing

Problem: Need to record from neurons!
- Recording from >800 neurons simultaneously.
  -> Use calcium imaging
  -> ‘Bursts’ detection

Spike Patterns *in vitro*?

- Repeated Motifs across cell populations

10 cells x 2

4 cells x 4

Warning: bursts… not spikes!
Significance and Surrogate Datasets

- Motifs by chance?

Surrogate datasets for controls

‘Frame jitter’ = ‘temporal jitter’ in terms of image frames

A: Destroys temporal correlations within cells (e.g. oscillations) – Preserves firing rate.
B: Destroys motif cell composition - Preserves partial synchronization.
C: Destroys spike orders within motif - Preserves number of spikes per cell, and population firing modulations.

For more on the debate: ➔ (Mokeichev et al, 2007) ➔ (Ikegaya et al 2008)
Spike Patterns *in vitro*?

- Is there topographic (spatial) organization for each Motif?
  → classification problem (no theory… yet)
- Motifs of Motifs….Cortical songs

➤ 2 major issues: detecting songs, and assessing their (statistical) significance
Spike Patterns *in vitro*?

- Is there temporal compression?

Most motifs compress in time