Modeling the stochastic activity of recurrent balanced cortical circuits

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Outline:

1) Background: the “rate code” and the impact of spike correlations

2) Mechanism: shared inputs vs. correlated inputs.

3) Model: a densely-connected balanced asynchronous network

4) Experimental predictions. Correlations in large cortical populations in vivo.

5) Functional implications of an Asynchronous network.
An experimental Foundation of the Rate Code

Hubel & Wiesel ‘62
Neural responses show trial-to-trial variability

Average responses are informative

Information must be represented in the population response → spatial average

Shadlen & Newsome ’98
Neural responses are correlated

Correlation coefficient
spike count $n_i$:

$$r_{12} = \frac{\text{Cov}(n_1, n_2)}{\sqrt{\text{Var}(n_1) \text{Var}(n_2)}}$$

Neural responses are correlated

$< r > = 0.19$

Monkey MT awake

$Zohari et al. '94$

Correlation coefficient $r_{ij}$

$< r > = 0.18$

Monkey V1 anesthetized

$Kohn & Smith, 2005$
Correlations impair population coding

Population Activity: \[ m(t) = \frac{1}{N} \sum_{i=1}^{N} s_i(t) \]

Normalized Pop. Act. Variance:

\[
\frac{\text{Var}(m)}{\text{Var}(s_i)} = \frac{1}{N} + \langle r \rangle
\]

If \( \langle r \rangle > 0 \), firing rates are intrinsically inefficient

Britten et al. ’92; Shadlen & Newsome ’98; Zohari et al. ‘94
Correlations could limit sensory discrimination

Britten et al. ’92; Shadlen & Newsome ’98; Zohari et al. ‘94
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Mechanisms:
what causes correlations in a cortical circuit?

Shared Inputs
Shared input causes correlations.

Feed-forward network:

- A: 0% shared
- B: 10%
- C: 20%
- D: 30%
- E: 40%
- F: 50% shared

Output correlation $r_{out}$

Positive Correlations

Shadlen & Newsome ‘98
Mechanisms:
what causes correlations in a cortical circuit?
Correlated inputs do not cause output correlations.

Feed-forward network with correlated inputs.

"The finding contradicts the common assumption that synchronous spikes must exert an exaggerated influence on networks of neurons..."
“Status Quo”

• Spiking correlations are effectively set by the level of shared input in the network.

• Because shared input is a fact of the cortical anatomy, a significant amount of spiking correlation is inevitable.

• Estimation of firing rates in the cortex is intrinsically inefficient, i.e., noise cannot be averaged out.

• Such correlations constrain our ability to perform sensory discriminations!
But, recent work has shown...
i) Brain state modulates correlations

- Dual whole cell recordings in barrel cortex in awake mice:
ii) Attention modulates correlations

- Multi-unit recordings in V4 in behaving monkeys during an attention demanding task:

  - *Mitchell, Sundberg & Reynolds 2009*

  - *Cohen & Maunsell, 2009*
iii) Correlations can be very small…

- Multiple extracellular recordings in V1 in behaving monkeys passively viewing.

*Ecker et al, 2010.*
Do correlated inputs cause output correlations? [redux]

\[ I_1 = \sum_{i=1}^{N} s_i , \quad I_2 = \sum_{j=1}^{N} s_j ; \quad \text{CorrCoef} (s_i, s_j) = \frac{\text{Cov}(s_i, s_j)}{\text{Var}(s_i)} = \frac{\text{cov}}{\text{var}} = r_{in} \]

\[ \text{CorrCoef} (I_1, I_2) ? \]
Correlated inputs do cause output correlations (E inputs only)

\[ I_1 = \sum_{i=1}^{N} s_i, \quad I_2 = \sum_{j=1}^{N} s_j; \quad \text{CorrCoef} (s_i, s_j) = \frac{\text{Cov}(s_i, s_j)}{\text{Var}(s_i)} = \frac{\text{cov}}{\text{var}} = r_{in} \]

\[ \text{CorrCoef} (I_1, I_2) = \frac{\text{Cov}(I_1, I_2)}{\text{Var}(I_1)} = \frac{N^2 \text{cov}}{N \text{var} + N(N-1)\text{cov}} = \frac{Nr_{in}}{1 + (N-1)r_{in}} \]
Correlated inputs do cause output correlations \((E \text{ inputs only})\)

\[
I_1 = \sum_{i=1}^{N} s_i, \quad I_2 = \sum_{j=1}^{N} s_j;
\]

\[
\text{CorrCoef}(I_1, I_2) \approx \frac{p + Nr_{in}}{1 + (N-1)r_{in}}
\]

Output Correlation \(r_{out}\)

\[
\begin{align*}
r_{out} & \sim p + Nr_{in} \\
0.4 & \sim 0 + 1 \times 0.4
\end{align*}
\]
Correlated inputs do cause output correlations (E inputs only)

\[ I_1 = \sum_{i=1}^{N} s_i, \quad I_2 = \sum_{j=1}^{N} s_j; \]

\[ \text{CorrCoef}(I_1, I_2) \approx \frac{p + Nr_{in}}{1 + (N-1)r_{in}} \]

E inputs only

Output Correlation \( r_{out} \)

Input Correlation \( r_{in} \)

EPSCs

\( r_{in} = 0.025 \)
Correlated inputs do cause output correlations (*E inputs only*)

Fixed point: synchrony explosion!

\[ r_{in} = r_{out} \]
Correlated inputs do cause output correlations (*E and I inputs*).

**Positive output Correlations**

*E inputs only*

**Negative Correlations**

**EPSCs**

**IPSCs**
Correlated inputs do cause output correlations (*E and I inputs*).

\[ r_{out} \sim p + N \left( J_E - J_I \right)^2 r_{in} \]
Correlated inputs do cause output correlations (*E* and *I* inputs)

What happens in a generic recurrent network (i.e. no fine-tuning)?

\[ r_{out} \sim p + N (J_E - J_I)^2 r_{in} \]

*Shadlen & Newsome ’98: \( J_E = J_I \)
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5) Functional implications of an Asynchronous network.
1) Neurons are binary: $\sigma_i = 0$ (inactive), 1 (active). Analytically tractable.

2) Network is randomly and \textit{densely} connected.

3) Neurons are \textbf{strongly coupled}: only a small fraction of a neuron’s inputs are enough to make it fire.
Model of a recurrent network.

Connection probability $p$:

**SPARSELY CONNECTED:** $p \sim O(1/N)$

The mean fraction of *shared input* goes to zero as the network size $N$ increases: *trivially asynchronous!*

**DENSELY CONNECTED:** $p \sim O(1)$

The mean fraction of *shared input* is fixed and independent of the network size $N$ increases.

Van Vreeswijk & Sompolinsky ’96, Brunel & Hakim ‘99
Model of a recurrent network.

Synaptic Strength $J$:

- Mean current $\sim N J$
- Current Variance $\sim N J^2$

WEAKLY COUPLED: $J \sim O(1/N)$

No temporal fluctuations in the synaptic currents for large networks.

STRONGLY COUPLED: $J \sim O(1/\sqrt{N})$

Temporal fluctuations do not decay with the network size. Requires balancing excitation with inhibition.

Van Vreeswijk & Sompolinsky ’96
Rationale:

(1) Assume the network state is asynchronous: \( r \sim O(1/N) \)
   - Synaptic currents can be approximated as Gaussian for large \( N \)

(2) Calculate MICROSCOPIC equations that specify the firing rates and pair-wise correlations of every cell and pair on the steady-states. These equations depend on the specific realization of the synaptic weights \( J \).

(3) Calculate population-averages of rates and pair-wise correlations, by averaging over the distribution \( P(J) \). Obtain MACROSCOPIC equations for the spatial distribution of rates and pair-wise correlations.

(4) Check whether these equations have solutions in which the network is asynchronous.
Master equation:

\[
\frac{d}{dt} P(\tilde{\sigma}, t) = - P(\tilde{\sigma}, t) \sum_i w(\sigma_i) + \sum_i P(\tilde{\sigma}(\sigma_i^*), t)w(1 - \sigma_i)
\]

\[
\frac{d}{dt} \langle \sigma_i \rangle(t) \equiv \frac{d}{dt} \left( \sum_{\tilde{\sigma}} P(\tilde{\sigma}, t) \sigma_i \right) = \sum_{\tilde{\sigma}} \left( \frac{d}{dt} P(\tilde{\sigma}, t) \right) \sigma_i
\]

\[
\frac{d}{dt} \langle \sigma_i \rangle(t) = \sum_{\tilde{\sigma}} P(\tilde{\sigma}, t) \left[ w(\sigma_i)(1 - 2\sigma_i) \right]
\]

\[
w(\sigma_i^\alpha) = \frac{1}{\tau^\alpha} \left[ \sigma_i^\alpha - \Theta(h_i^\alpha) \right]^2 \quad \text{[transition probabilities]}
\]

\[
h_i^\alpha = \sum_{E,I,X} \sum_{N} J_{ij}^{\alpha\beta} \sigma_j^\beta - \theta_i^\alpha \quad \text{[synaptic input]}
\]

\[
m_i^\alpha(t) = \langle \sigma_i^\alpha \rangle(t) \quad \text{[synaptic input]}
\]

\[
\tau^\alpha \frac{d}{dt} m_i^\alpha(t) = -m_i^\alpha(t) + \langle \Theta(h_i^\alpha(t)) \rangle
\]

Van Vreeswijk and Sompolinsky '96
Stationary solution mean activity:

\[ m_i^\alpha = \langle \Theta(h_i^\alpha) \rangle \]

\[ m_i^\alpha = H \left( -\mu_i^\alpha / \sqrt{(s_i^\alpha)^2} \right) \]

\[ H(z) \equiv \frac{1}{\sqrt{2\pi}} \int_z^\infty dx \exp(-x^2/2) \]

Population averaged mean activities (Macroscopic description):

\[ m_\alpha \equiv \frac{1}{N} \sum_i m_i^\alpha = H \left( -\mu_\alpha / \sqrt{s_\alpha^2} \right) \]

\[ \mu_\alpha = \sum_\beta J_{\alpha\beta} m_\beta \]

\[ s_\alpha^2 = \sum_\beta J^{(2)}_{\alpha\beta} m_\beta + \sum_\beta J_{\alpha\beta}^2 (q_\beta - m_\beta^2) \]

\[ q_\alpha \equiv \frac{1}{N} \sum_i (m_i^\alpha)^2 \]

Van Vreeswijk and Sompolinsky '96
Balanced equations:

\[
\mu_E = \sqrt{N} \left( J_{EE} m_E - J_{EI} m_I + J_{EX} m_X \right) - \theta_E \sim O(1)
\]

must cancel within \(O(1/\sqrt{N})\)!

In the large \(N\) limit:

\[
m_E = \frac{J_{II} J_{EX} - J_{EI} J_{IX}}{J_{EI} J_{IE} - J_{II} J_{EE}} m_X = A_E m_X
\]

\[
m_I = \frac{J_{II} J_{EE} - J_{EX} J_{IE}}{J_{EI} J_{IE} - J_{II} J_{EE}} m_X = A_I m_X
\]

Van Vreeswijk and Sompolinsky ‘96
Stationary solution pair-wise correlation:

\[ r_{ij}^{\alpha \beta} (t) \equiv \langle \delta \sigma_i^\alpha (t) \delta \sigma_j^\beta (t) \rangle \quad \alpha_i \neq \beta_j \]

\[ (\tau_\alpha + \tau_\beta) r_{ij}^{\alpha \beta} = \tau_\alpha \langle \delta \sigma_i^\alpha \delta \Theta (h_j^\beta) \rangle + \langle \delta \Theta (h_i^\alpha) \delta \sigma_j^\beta \rangle \tau_\beta \]

Population averaged correlations (Macroscopic description):

\[ r_{\alpha \beta} \equiv \sum_{ij} r_{ij}^{\alpha \beta} / N^2 \]

\[ r_{EE} = \frac{1}{N} \left( A_E^2 (m_X - q_X) - (m_E^0 - q_E^0) \right) \]

\[ r_{II} = \frac{1}{N} \left( A_I^2 (m_X - q_X) - (m_I^0 - q_I^0) \right) \]

\[ r_{EI} = \frac{1}{N} \left| A_E A_I (m_X - q_X) \right| \]
Recurrence balanced network is asynchronous

If inhibition is not too weak or slow,...

1. the network is **BALANCED**

A Balanced network generates large $V_m$ fluctuations and irregular Poisson-like spiking.

2. the network is **ASYNCHRONOUS**:

Correlation decreases at fixed $p$ (avg. shared fraction).

Van Vreeswijk and Sompolinsky ‘96
Self-consistent Asynchronous state

Asynchronous firing: $r \sim O(1/N)$

Common input
Amplification due to strong coupling

Synchronous Currents: $c \sim O(1)$

Population Averaged Correlation

Currents $EE$
$c_{xx} = p = 0.2$

Spikes
The negative current correlations generated by tracking precisely cancel all sources of positive current correlations, including shared inputs.
Tracking of spontaneous E and I activity fluctuations generates strong EI correlations

\[ m_E(t) = A_E \, m_X(t) \]
\[ m_I(t) = A_I \, m_X(t) \]

Very fast and strong negative feedback!
Self-consistent Asynchronous state

Asynchronous firing: $r \sim O(1/N)$

Synchronous Currents: $c_{EE} \sim O(1)$

Weakly Synchronous Total Current $c \sim O(1/\sqrt{N})$

Fast Exc-Inh Tracking

Common input (Recurrent & External)
Amplification due to strong coupling

Spikes
Exc-Inh tracking delay decreases with N

$\tau = 10 \text{ ms}$
Exc-Inh tracking delay decreases with N

Tracking

\[
\begin{align*}
X & \quad E & \quad i \\
m & m_E & m_X \quad N=1024 \\
N=8192
\end{align*}
\]

\[\tau = 10 \text{ ms}\]

How many neurons need to fire for everyone to notice?
What fraction of the network firing synchronously creates a current \(\sim O(1)\)?

Network size: \(N=16\)
Fluctuation size: \(\sqrt{N}=4\)
Fraction network: \(1/\sqrt{N}=0.25\)

Network size: \(N=256\)
Fluctuation size: \(\sqrt{N}=16\)
Fraction network: \(1/\sqrt{N}=0.0625\)

Network size: \(N=4096\)
Fluctuation size: \(\sqrt{N}=64\)
Fraction network: \(1/\sqrt{N}=0.0156\)
Self-consistent Asynchronous state

$E_I - Lag$

$\tau = 10 \text{ ms}$
Both the amplitude and the time-scale of the (total) current correlations decrease as $\sim O(1/\sqrt{N})$.

The Area under the CCG $\sim O(1/N)$.
Self-consistent Asynchronous state

Asynchronous firing: \( r \sim O(1/N) \)

Synchronous Currents: \( c \sim O(1) \)

Weakly Synchronous Total Current \( c, \text{ width} \sim O(1/\sqrt{N}) \)

Integration of synaptic input with the biophysical time-constant

Common input (Recurrent & External)

Amplification due to strong coupling

Synchronous Currents: \( c_{EE} \sim O(1) \)

Integration of synaptic input with the biophysical time-constant

Fast Exc-Inh Tracking

Population Averaged CC

Population Averaged CC
Correlated inputs cancel the effect of shared inputs

\[ r_{EE}, r_{II}, r_{EI}, r_{EX}, r_{IX} \]

are dynamic variables

Exc  

Negative Correlations

Inh
Correlated inputs cancel the effect of shared inputs

\[ r_{EE}, r_{II}, r_{EI}, r_{EX}, r_{IX} \]

are dynamic variables

\[ r_{out} \sim p + N(J_{EE}^2 + J_{II}^2 + 2J_{E}J_{I}r_{EI} + \ldots) \]

Becomes \( < 0 \)

\[ r_{in} = r_{out} \]

Extremely low correlations \( r \sim 1/N \)

under stationary conditions.

\[ \text{Exc} \]

\[ \text{Inh} \]

Negative Correlations
Correlated inputs cancel the effect of shared inputs

![Diagram showing synaptic current correlation](image)
Correlated inputs cancel the effect of shared inputs
The sources of pair-to-pair heterogeneity in correlation are larger than the mean.

\[ \text{connection impact} \sim \frac{1}{\sqrt{N}} \]

\[ \text{mean} \sim \frac{1}{N} \]
The sources of pair-to-pair heterogeneity in correlation are larger than the mean. The distribution of $r$ is ‘wide’, meaning $\frac{\sigma_r}{\bar{r}} >> 1$. This implies that around half of the pairs have $r < 0$. 
The Asynchronous state with non-stationary inputs.

Non-Stationary Input

Stationary Input

Instantaneous activity $r\text{ condition on } \langle m(t) \rangle_{\text{trials}}$

Firing correlation $r\text{ condition on } \langle m \rangle_t$
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Experimental prediction 1:

In an asynchronous state, $E$ and $I$ currents are much more strongly correlated than the total synaptic current.
Experimental prediction 1:

- Recurrent balanced network of conductance-based integrate-and-fire (LIF) neurons. $N_E=4000$, $N_I=1000$, $N_X=4000$, $p=0.2$. 
**Experimental prediction 1:**

- Excitatory and Inhibitory currents should be much more strongly correlated than the total synaptic current.

Dual intracellular recordings in vivo
*(Hasenstaub et al 2005.)*

Ferret PFC; Correlations measured **inside** Up-states (Haider et al.)

Only 1 pair, **VERY** preliminary!
Experimental prediction 2:

The distribution of spiking correlations across the populations is ‘wide’, meaning \( \frac{\sigma_r}{\bar{r}} \gg 1 \).
In vivo population recordings

- 64 Ch. Silicon Probe. *NeuroNexus Tech.*
- Yield: > 100 single units
- Rat auditory (A1) and somatosensory (S1)
- Urethane Anesthesia
- Spontaneous Activity
Spontaneous brain state changes under urethane

Cortical Inactivation
Slow Wave Sleep; Drowsiness…

Cortical Activation
REM; attentive wakefulness…

LFP

Time (s)

CV Population Act. 0 0.6 1

Pop. Rate (spks/s)

1 s

1 s
Correlations during *Activated* and *Inactivated* states.

As predicted, $r$ distribution is **wide**: $\sigma_r >> \langle r \rangle$.
Correlations during the Activated state.
Correlations in rat PFC during behavior

Rat mPFC; Behavior during Working Memory Task

11% of all CCs > 0 have $p < 0.01$
5% of all CCs < 0 have $p < 0.01$

Data from Fujisawa et al. ‘08
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An asynchronous network produces Population activity with Variance $\sim 1/N$: Neurons behave effectively as independent!
Functional Consequences of the Asynchronous State

What is this network computing?

Input Population rate

Output Population rate

Synchronous Network

Output Population rate
Functional Consequences of the Asynchronous State

What is this network computing?

It is the first, biologically-plausible network model which is *not* an irreducible source of noise (i.e. correlations).
If shared input does not cause correlations, what generates correlations in the data?

1. Network state is non-stationary: the network exhibits slow global co-variations of the rates (e.g. oscillations, chaotic fluctuations).

3. There are variables which cannot be controlled for by the experimented which introduce spurious correlations.
If shared input does not cause correlations, what generates correlations in the data?

1. Network state is non-stationary: there exists slow global co-variations of the rates.
If shared input does not cause correlations, what generates correlations in the data?

2. Hidden variables introduce spurious correlations

... I’m hungry...

... can’t wait to get out of here.
Summary

1. In recurrent BALANCED networks the population-averaged correlation is fundamentally *not* about shared input. Instead, fast tracking of Excitation by Inhibition renders the network asynchronous.

3. The spatial organization of correlations during Activated states (under urethane) and in behaving rats is *wide* ($\sigma_r \gg \langle r \rangle$), as predicted by the model.
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