# **Structure of Correlations in Neuronal Networks**

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### The Connectome



Van J. Wedeen, MGH/Harvard

Monday, May 21, 2012

#### The Connectome  $\sim$ cortex to subcorting  $\sim$  $\mathcal{S}(\mathcal{A}(\mathcal{A}))$  in each potential potentials in each potential potentials in each potential potentials in each potential poten  $\bullet$  to four cells and measuring the averaged peak excitation  $\bullet$

 $\begin{picture}(20,20) \put(0,0){\line(1,0){10}} \put(15,0){\line(1,0){10}} \put(15,0){\line(1$ 





of the local cortical network, in which a skeleton of stronger

Van J. Wedeen, MGH/Harvard

Song, et al. 2004

(C) Average EPSP waveform measured in the postsynaptic neuron (bottom) while evoking action potentials in the presynaptic neuron (top).

PLoS Biology | www.plosbiology.org March 2005 | Volume 3 | Issue 3 | e68 0508

classifying all simultaneously recorded pairs of neurons into  $\tau_{\rm eff}$  classes: unconnected, unconnected, unconnected, and bidirectionally connected. Given connection probability p and total number of pairs  $N$  the expected number of pairs  $N$ 

of unidirectionally connected pairs shown be 2Np(1  $\mu$ ), and and  $2N_{\rm eff}$  $\mathbf{t}$  the expected number of bidirectional ly connected pairs of bidirectional ly connected pairs of  $\mathbf{t}$ 

tionally connected pairs is four times that of the expected pairs is four times that of the expected pairs is four numbers (p , 0.0001) (Figure 2B). The observed overrepresentation of reciprocally connected layer 5 neurons  $\sigma$  previous reports  $\sigma$  for  $\sigma$ . Such over also been observed in layer 2/3 of the rate visual cortex  $\mathcal{I}_1$  $H_{\rm eff}$  and  $\sigma_{\rm eff}$  projections between layers observe this between layers observe this between layers observe this between layers observed that

Can the overrepresentation of reciprocal connections reflect an experimental artifact? Indeed, such overrepresen-

. We find that the actual number of bidirec-

. The expected number  $\mathcal{I}$ 

















#### Are neuronal responses dependent or independent?

Tolias, Dragoi, Smirnakis, Angelaki, ....





#### How are structure and dynamics related in neuronal networks?



How are structure and dynamics related in neuronal networks?

Synchrony - is probably atypical

#### Correlation - a measure of dependence

when the humble neuron

1 Mww.mundumy.humbumlul neuron 2











neuron 1



*n* - (random) number of spikes of neuron *i* during a time T. Correlation coefficient of the output is i

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

![](_page_16_Figure_0.jpeg)

*n* - (random) number of spikes of neuron *i* during a time T. Correlation coefficient of the output is i

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

![](_page_16_Figure_3.jpeg)

low correlation

![](_page_17_Figure_0.jpeg)

*n* - (random) number of spikes of neuron *i* during a time T. Correlation coefficient of the output is i

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

![](_page_17_Figure_3.jpeg)

high correlation

## Short vs long timescale correlations

![](_page_18_Figure_1.jpeg)

#### Cross-Correlation Function some size. Choose a spike in train *A* at some time *t*<sup>0</sup> (dashed vertical line in the figure below). **NOSS-CONGREGION FUNCION**  $\overline{\phantom{0}}$ **CIUSS-CUILEIANUILI UILLIU**

![](_page_19_Figure_1.jpeg)

It is easy to see that *hA,B*(*t*) = *hB,A*(−*t*) when the rates of the two processes are equal. It is

also easy to see from the definition how to compute *hB,A*(*t*): Separate the timeline into bins of

below *t<sup>i</sup>* stands for the relative time between this and the *i*th spike following it). Increase the

 $E = \frac{1}{2}$ Conditional probability of spike in B, given spike in A.

intensity function with the cross-covariance density *cA,B*(*t*) = *rBhA,B*(*t*)−*rArB*, where *r<sup>A</sup>* and

*r<sup>B</sup>* are the respective rates of the two processes. Here *cA,B*(*T*)(∆*t*)<sup>2</sup> can again be interpreted

as the approximate covariance of *NA*(*t* + *T,t* + *T* + ∆*t*) and *NB*(*t, t* + ∆*t*).

The argument used in proving relation  $\mathbb{R}^n$  can again be used to relate the cross-cr

value in the bin by this amount.

Input correlation *c* 

0.1 0.2 0.3

0 40

*µ* (mV)

#### Cross-Correlation Function some size. Choose a spike in train *A* at some time *t*<sup>0</sup> (dashed vertical line in the figure below). **NOSS-CONGREGION FUNCION**  $\overline{\phantom{0}}$ **CIUSS-CUILEIANUILI UILLIU**

![](_page_20_Figure_1.jpeg)

It is easy to see that *hA,B*(*t*) = *hB,A*(−*t*) when the rates of the two processes are equal. It is

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#### Exercise: How do you need to normalize the resulting histogram to get *hB,A*(*t*)? Conditional probability of spike in B, given spike in A.

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![](_page_20_Figure_3.jpeg)

Short-timescal (synchrony)

value in the bin by this amount.

Input correlation *c* 

0.1 0.2 0.3

0 40

*µ* (mV)

#### Now compute the relative times between this spike and all spikes in train *B* (in the figure below *t<sup>i</sup>* stands for the relative time between this and the *i*th spike following it). Increase the  $\overline{\phantom{0}}$ Input correlation *c*   $\sim$  0.1 0.2  $\sim$  0.1  $C$  ross-Correlation Function  $C_{i,i}(\tau)$ where  $\bullet$  defined and  $\bullet$  are  $\bullet$  in particular,  $\circ$   $\bullet$   $\bullet$   $\bullet$ Cross-Correlation Function,  $C_{i,j}(\tau)$

(J*ij* ∗ *y<sup>j</sup>* )(*t*)*,* where J*ij* (*t*) =

![](_page_21_Figure_1.jpeg)

also easy to see from the definition how to compute *hB,A*(*t*): Separate the timeline into bins of

*<sup>f</sup>i*(*t*) = #

some size. Choose a spike in train *A* at some time *t*<sup>0</sup> (dashed vertical line in the figure below).

#### Exercise: How do you need to normalize the resulting histogram to get *hB,A*(*t*)? Conditional probability of *the spite conditional* probability of spike in B, given spike in A.  $\overline{a}$  defined as

intensity function with the cross-covariance density *cA,B*(*t*) = *rBhA,B*(*t*)−*rArB*, where *r<sup>A</sup>* and

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7

cov<br>,

as the approximate covariance of *NA*(*t* + *T,t* + *T* + ∆*t*) and *NB*(*t, t* + ∆*t*).

The argument used in proving relation  $\mathbb{R}^n$  can again be used to relate the cross-cr

<sup>W</sup>*ij* '

*S,j* (

0 *t <* τ*D,j*

-*.*

C*ij* (*s*)(τ − *|s|*)*ds.*

$$
\mathbf{C}_{ij}(\tau) = \text{cov}\left(y_i(t+\tau), y_j(t)\right)
$$

We assume stationarity of the spiking processes so that ρ*ij* does not depend on *t*. The spike count

covariance is related to the cross-correlation function by [Bair et al., 2001, Shadlen and Newsome,

-

=

*Ny<sup>i</sup>* (*t, t* + τ )*, Ny<sup>j</sup>* (*t, t* + τ )

value in the bin by this amount.

Input correlation *c* 

0.1 0.2 0.3

0 40

*µ* (mV)

#### and using redundancy to compute reduces to content to content in the counterpart of large  $\alpha$ the optimal coupling has a sign opposite to the input correlation. **Correlations Impact Neural Computation**

 $\mathbb{R}^n$ , the optimal coupling  $\mathbb{R}^n$  as the same sign as the same sign as the input correla-same sign as the input correl

tion, as in the binary input case, thus enhancing input correlations

and using redundancy to counteract noise. However, for large β,

 $\mathbb{R}^n$ , the optimal coupling  $\mathbb{R}^n$  as the same sign as the same sign as the input correla-same sign as the input correl

tion, as in the binary input case, the binary input case, thus enhancing input case, thus enhancing input corr

![](_page_22_Figure_1.jpeg)

Tkačił<br>Tkačił Tkačik, et al. 2010

DEF

Cov h **J** Cov

## Models of Neurons - Integrate and Fire

$$
\frac{dV}{dt} = -\frac{V}{\tau_m} + \Psi(V) + \mu + \sqrt{2D\eta(t)}
$$

$$
V(t) = V_{\theta} \Rightarrow V(t^{+}) = V_{\text{reset}}
$$

Subthreshold membrane potential

Fire and Reset

![](_page_23_Figure_5.jpeg)

*Rate r -* number of spikes per second

![](_page_24_Figure_1.jpeg)

![](_page_25_Figure_1.jpeg)

![](_page_26_Figure_1.jpeg)

![](_page_27_Figure_1.jpeg)

The membrane potential of an IF neuron receiving input *X*(*t*), with vanishing temporal average,

![](_page_28_Figure_1.jpeg)

Linear response in recurrent networks

#### Structure or correlations in networks  $\frac{1}{2}$   $\frac{1}{2}$ Here *E<sup>i</sup>* represents the mean input from parts of the system not explicitly modeled. A spike-To illustrate the results we consider a network of *N* nonlinear integrate-and-fire (IF) neurons with

!

to *v*r*,* and held constant for an absolute refractory period τref. The output of cell *i* is characterized

![](_page_29_Figure_1.jpeg)

 $y_j(t) = \sum \delta(t - t_i^j)$  output spike train of cell j  $f_i(t) = \sum$ *j*  $f_i(t) = \sum_{i,j} (\mathbf{J}_{ij} * y_j)(t)$  synaptic coupling  $\left(\mathbf{W}_{ii}\left(\frac{t-\tau_{D,j}}{2}\right)_{\text{exp}}\left[-\frac{t-\tau_{D,j}}{2}\right]\right)$  t  $>$   $\tau_{D,i}$  contains the synaptic syn  $\mathbf{J}_{ij}(t) = \left\{ \begin{array}{c} \nabla^{ij} \left( \begin{array}{c} \tau_{S,j}^2 \end{array} \right)^{\text{exp}} \left[ \begin{array}{c} \tau_{S,j} \end{array} \right] \end{array} \right. \qquad \qquad \text{where} \qquad \mathbb{R} \rightarrow \mathbb{R} \rightarrow \mathbb{R} \rightarrow \mathbb{R}$  $\begin{pmatrix} 0 \end{pmatrix}$  $\sum_{i,j} \delta(t - t^j)$  $\frac{U_{j}(\gamma)}{i}$  and  $\frac{U_{j}}{i}$  is the members of the members potential is result. to *v*r*,* and held constant for an absolute refractory period τref. The output of cell *i* is characterized  $\dot{J}$  ${\bf J}_{ij}(t) =$  $\sqrt{ }$  $\int$  $\overline{a}$  $\mathbf{W}_{ij}\bigg($  $\frac{t-\tau_{D,j}}{a}$  $\left[ \frac{-\tau_{D,j}}{\tau_{S,j}^2} \right] \exp \left[ -\frac{t-\tau_{D,j}}{\tau_{S,j}} \right]$   $t \geq \tau_{D,j}$ 0  $t < \tau_{D,j}$  $y_j(t) = \sum \delta(t-t_i^j)$  output spike train of cell *j* synaptic coupling i  $\delta(t-t_i^j)$ 

![](_page_29_Figure_3.jpeg)

Nykamp

of a synaptic connection from cell *j* to cell *i*.

modelled [Renart et al., 2004]. We model both by independent, Gaussian, We model both by independent, Gaussian,

The *N* × *N* matrix J contains the synaptic kernels, while the matrix W contains the synaptic

weights, and hence defines the network architecture. In particular, W*ij* = 0 represents the absence

membrane potentials modeled by

proach using current-based IF neurons, and explain how it can be generalized to other models in

The output of a model neuron is a spike train *X*  $\left| \begin{array}{ccc} \text{if } & \text{if } & \text{if } \\ \text{if } & \text{if } & \text{if } & \text{if } \\ \text{if } & \text{if } & \text{if } & \text{if } & \text{if } \\ \text{if } & \text{if } & \text{if } & \text{if } & \text{if } \\ \text{if } & \text{if } \\ \text{if } & \text{if } \\ \text{if } & \$ 

The membrane potential of an IF neuron receiving input *X*(*t*), with vanishing temporal average,

$$
y_j(t) = \sum_i \delta(t - t_i^j)
$$

*if*  $\frac{1}{2}$  *timear response gives the output rate as* 

$$
r(t) = r_0 + (A \ast X)(t)
$$

where *r*<sup>0</sup> is the stationary firing rate in the absence of the signal *X*(*t*). The linear response kernel,

*A*(*t*)*,* characterizes the firing rate response to first order in the strength of the input *X*(*t*). A rescal-

ing of the function *A*(*t*) gives the spike-triggered average of the cell, to first order in input strength,

and is hence equivalent to the optimal Weiner kernel in the presence of the signal ξ(*t*). [Barreiro

et al., 2010, Gabbiani and Cox, 2010] In Fig. 1A, we compare the approximate firing rate obtained

of the statistics of the input, *X*(*t*). In particular, *A*(*t*) is sensitive to the value of the mean input

current, *E*. We emphasize that the presence of noise in Eq. (3) is essential to the theory.

The linear response kernel *A*(*t*) depends implicitly on model parameters, but is independent

from Eq. (4) to that obtained numerically from Monte Carlo simulations.

The time-dependent firing rate,

approximates the firing rate by

the Discussion.

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The output of a model neuron is a spike train *X*  $\left| \begin{array}{ccc} \text{if } & \text{if } & \text{if } \\ \text{if } & \text{if } & \text{if } & \text{if } \\ \text{if } & \text{if } & \text{if } & \text{if } & \text{if } \\ \text{if } & \text{if } & \text{if } & \text{if } & \text{if } \\ \text{if } & \text{if } \\ \text{if } & \text{if } \\ \text{if } & \$ 

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#### *A* How do we use this to compute the cross-correlation?

![](_page_31_Figure_6.jpeg)

![](_page_31_Figure_7.jpeg)

feedback of their spike trains. This feedback consists of the sum o

lumped into the current, and the voltage variable and current are rescaled by a typical value such that all variables and parameters are nondimensional. The dynamics Eq. !1" is complemented by the well-known fire-and-reset rule: whenever the voltage reaches a prescribed constant threshold *vT*, the neuron fires and the voltage is kept fixed for an absolute refractory period !*<sup>R</sup>* and then reset to a value *vR*. In the following we set *vT*= 1 and *vR*= 0. The output of the *i*th LIF neuron is a " spike train determined by the *j*th instants of

threshold crossing of the *i*th neuron *ti*,*<sup>j</sup>*

The input current *Ii*

LINDNER, DOIRON, AND LONGTIN PHYSICAL REVIEW E **72**, 061919 !2005"

The time-dependent firing rate,

approximates the firing rate by

the Discussion.

$$
\frac{dV}{dt} = -\frac{V}{\tau_m} + \Psi(V) + \mu_0 + \sqrt{2D}\eta(t)
$$

$$
y_0(t) = \sum_i \delta(t - t_i^0)
$$

$$
\frac{dV}{dt} = -\frac{V}{\tau_m} + \Psi(V) + \mu_0 + \sqrt{2D}\eta(t) + X(t)
$$

$$
y_0(t) = \sum_i \delta(t - t_i^0)
$$

$$
\frac{dV}{dt} = -\frac{V}{\tau_m} + \Psi(V) + \mu_0 + \sqrt{2D}\eta(t) + X(t)
$$

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$$

$$
y(t) = \sum_i \delta(t - t_i)
$$

#### **Can we estimate the correlation structure?** of the statistics of the input, *X*(*t*). In particular, *A*(*t*) is sensitive to the value of the mean input

$$
\frac{dV}{dt} = -\frac{V}{\tau_m} + \Psi(V) + \mu_0 + \sqrt{2D}\eta(t) + X(t)
$$

$$
y(t) = \sum_i \delta(t - t_i)
$$

Use linear response to obtain a mixed point/continuous process the approach introduced by Lindan introduced by Lindan instead of using the linear response kernel to using the l approximate the first rate of a cell and the first rate of approximate a realization of its output  $\alpha$ 

$$
y(t) \approx y^1(t) = y^0(t) + (A \ast X)(t)
$$

Here *y*0(*t*) represents a realization of the spike train generated by an integrate-and-fire neuron

obeying Eq. (3) with *X*(*t*) = 0.

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$$
y(t) \approx y^1(t) = y^0(t) + (A \ast X)(t)
$$

Which averages out to the right thing Here *y*0(*t*) represents a realization of the spike train generated by an integrate-and-fire neuron

 $r(t) \approx r_0 + (A*X)(t)$ 

obeying Eq. (3) with *X*(*t*) = 0.

#### Approximate network correlations *j <sup>i</sup>* (*t*) = *y*<sup>0</sup> *<sup>i</sup>* (*t*) +" (K*ij* <sup>∗</sup> [*y*<sup>0</sup> *<sup>j</sup>* − *r<sup>j</sup>* ])(*t*)*.* (8)

 $W$  can use  $E$  approximate the cross-correlation between a pre-synaptic cell with index  $\mathbb{R}^n$ 

We next extend this approach to approximate this approximate the full impact of recurrent connections in the full impact of recurrent connections in the full impact of recurrent connections in the full impact of recurrent

The linear response approximation now takes the form

*y*1

$$
y_i^1(t) = y_i^0(t) + \sum_{\text{all inputs}} (\mathbf{K}_{i,j} * [y_j^0 - r_j]) (t)
$$

$$
\mathbf{K}_{i,j} = (A_i * \mathbf{J}_{i,j})(t)
$$

*<sup>i</sup>* (*t*) in Eq. (8) gives a first approximation We can use this to approximate the cross-covariances

$$
\mathbf{C}_{ij}(\tau) \approx \mathbf{C}_{ij}^1(\tau) = \mathbf{E}\left\{ (y_i^1(t+\tau) - r_i)(y_j^1(t) - r_j) \right\}
$$
  
=  $\delta_{ij}\mathbf{C}_{ii}^0(\tau) + (\mathbf{K}_{ij} * \mathbf{C}_{jj}^0)(\tau) + (\mathbf{K}_{ji}^T * \mathbf{C}_{ii}^0)(\tau) + \sum_k (\mathbf{K}_{ik} * \mathbf{K}_{jk}^T * \mathbf{C}_{kk}^0)(\tau)$ 

Ostojic, Brunel, Hakim, 2009, Trousdale, Yu, Shea-Brown, Josić, 2011 *j* ,

(10)

#### Impact of non-immediate neighbors C˜ *<sup>n</sup>*(ω) = E[˜y*n*(ω)˜y*n*∗(ω)] = # K˜ *<sup>k</sup>*(ω)E[˜y0(ω)˜y0∗(ω)](K˜ <sup>∗</sup>)

*n*

We use an iterative construction se an it K˜ *<sup>k</sup>*(ω) ens<br>S  $\begin{picture}(180,10) \put(0,0){\line(1,0){10}} \put(10,0){\line(1,0){10}} \put(10,0){\line($ 

$$
\mathbf{y}^{n+1}(t) = \mathbf{y}^{0}(t) + (\mathbf{K} * [\mathbf{y}^{n} - \mathbf{r}]) (t)
$$

$$
= \mathbf{y}^{0}(t) + \sum_{k=1}^{n+1} (\mathbf{K}^{(k)} * [\mathbf{y}^{0} - \mathbf{r}]) (t)
$$

(ω)

*<sup>i</sup>* of the spiking

Which gives the *n*-th approximation to the cross-correlation<br>After taking the Fourier transform and the limit  $n \to \infty$ After taking the Fourier transform, and the limit  $n\to\infty$  $\Delta$ 1995,  $\Delta$ 1995,

$$
\tilde{\mathbf{C}}^{\infty}(\omega) = \lim_{n \to \infty} \tilde{\mathbf{C}}^n(\omega) = (\mathbf{I} - \tilde{\mathbf{K}}(\omega))^{-1} \tilde{\mathbf{C}}^0(\omega) (\mathbf{I} - \tilde{\mathbf{K}}^*(\omega))^{-1}
$$

see [Beck et al., 2011]). In the limit  $\rho$  – ∞, directed paths of arbitrary length contribute to the limit of arbitrary length contribute to the limit of arbitrary length contribute to the limit of arbitrary length contri

approximation. Eq. (15) therefore takes into account the full recurrent structure of the network.

We will use the norm *|| · ||*2, and assume that in the networks we study *||*K˜ *||*<sup>2</sup> *<sup>&</sup>lt;* 1. This condition

is confirmed numerically when we use Eq. (15).

*<sup>i</sup>* is defined by ˜*y<sup>n</sup>*

#### Impact of non-immediate neighbors C˜ *<sup>n</sup>*(ω) = E[˜y*n*(ω)˜y*n*∗(ω)] = # K˜ *<sup>k</sup>*(ω)E[˜y0(ω)˜y0∗(ω)](K˜ <sup>∗</sup>)

*n*

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$$
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$$

$$
\mathbf{K}_{i,j} = (A_i * \mathbf{J}_{i,j})(t)
$$

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*<sup>i</sup>* is defined by ˜*y<sup>n</sup>*

### The iterative construction

![](_page_41_Figure_1.jpeg)

Figure 1: A) Illustrating Eq. (4). i) The input to the neuron is a spike train which is convolved with

a synaptic kernel. ii) The output firing rate, *r*(*t*), is obtained by averaging over realizations of the

output spike train with fixed input, and independent realizations of noise, ξ(*t*). The rate obtained

using Monte Carlo simulations (shaded in gray) matches predictions of linear response theory

 $B_{2D}$ gan  $2009$ Pernice, Staube, Cardanobile, Rotter 2011 cell. Bloodey, May 21, 2012. Compare records and a sequence of graphs of graphs determines the successive May 21, 2012.  $R<sub>20032</sub>$  matches  $R<sub>20032</sub>$  matches predictions of  $R<sub>20032</sub>$  response to  $R<sub>20032</sub>$ Trousdale, Yu, Shea-Brown, Josić, 2011 cell. B) An example recurrent network. C-E) A sequence of graphs determines the successive of  $\epsilon$ from the rest of the network, and all approximations involve only its unperturbed output, *y*<sup>0</sup> Rangan 2009

### The iterative construction

![](_page_42_Figure_1.jpeg)

Figure 1: A) Illustrating Eq. (4). i) The input to the neuron is a spike train which is convolved with

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output spike train with fixed input, and independent realizations of noise, ξ(*t*). The rate obtained

using Monte Carlo simulations (shaded in gray) matches predictions of linear response theory

 $B_{2D}$ gan  $2009$ Pernice, Staube, Cardanobile, Rotter 2011 cell. Bloodey, May 21, 2012. Compare records and a sequence of graphs of graphs determines the successive May 21, 2012.  $R<sub>20032</sub>$  matches  $R<sub>20032</sub>$  matches predictions of  $R<sub>20032</sub>$  response to  $R<sub>20032</sub>$ Trousdale, Yu, Shea-Brown, Josić, 2011 cell. B) An example recurrent network. C-E) A sequence of graphs determines the successive of  $\epsilon$ from the rest of the network, and all approximations involve only its unperturbed output, *y*<sup>0</sup> a synaptic kernel. *ii*) The output first first

### The iterative construction

![](_page_43_Figure_1.jpeg)

Rangan 2007<br>Pernice, Staube, Cardanobile, Rotter 2011 cell. Bloodey, May 21, 2012. Compare records and a sequence of graphs of graphs determines the successive May 21, 2012. termee, educee, editieene, tredien<br>Trousdale, Yu, Shea-Brown, Josić, 2011 cell. B) An example recurrent network. C-E) A sequence of graphs determines the successive of  $\epsilon$ output spike train with fixed input, and independent realizations of noise, ξ(*t*). The rate obtained

## The approximation works well

![](_page_44_Figure_1.jpeg)

Cross-correlation between two excitatory cells as we shift between two excitatory cells in an all–to-all network (*N<sup>E</sup>* = 80*, N<sup>I</sup>* = 20) obtained using Eq. (27) (Solid – balanced network with ˜*µ* ≡ 0 (*G<sup>E</sup>* = 175 mV*·*ms*, G<sup>I</sup>* = (*NE/N<sup>I</sup>* )*G<sup>E</sup>* = 700 mV*·*ms*,* τ*<sup>E</sup>* = from balance to excess inhibition

contributing to contributing to contributing to correlations in the all-to-all-to-all-to-all-to-all-to-all-to-<br>The all-to-all-to-all-to-all-to-all-to-all-to-all-to-all-to-all-to-all-to-all-to-all-to-all-to-all-to-all-to-a

τ*<sup>I</sup>* = 10 ms), dashed – unbalanced network with ˜*µ* "=0(*G<sup>E</sup>* = 210 mV*·*ms*, G<sup>I</sup>* = 1050 mV*·*ms*,* τ*<sup>E</sup>* =

10 ms*,* τ*<sup>I</sup>* = 5 ms). B) Comparison of first and second order contributions to the cross-correlation

function in panel A in the balanced (left) and unbalanced (right) network. C) Some of the submotifs

#### **Expansion in terms of paths through the graph** the power spectra of the power spectra of the operation of the operation of the operation of the operation of <br>The operation of the operation of the operation point plays of the operation of the operation of the operation  $\frac{1}{2}$  in tarme of nathe through the aranh input. Using linear response theory, these changes are reflected in the response functions *Ai*, and

The operating point of a cell is set by its parameters (τ*i, EL,i*, etc.) and the statistics of

the power spectra of the isolated cells, C $0.000$ . To highlight the operating point plays of the operating point plays  $\mu$ 

represents the effects of an indirect common input *n* steps removed from cell *i* and *m* steps removed

from cell *j*. This corresponds to a submotif of the form *i* ← *an*−<sup>1</sup> ← *···* ← *a*<sup>0</sup> → *b*<sup>1</sup> → *···* →

did not capture such corrections [Ostojic et al., 2009].

The operating point of a cell is set by its parameters (τ*i, EL,i*, etc.) and the statistics of

its input (*Ei,* σ*i*). A change in operating point can significantly change a cell's response to an

in the approximation of the approximation structure given by Eq. (15), we electron structure given

**a**0a0k™ ∗a0

*<sup>a</sup>*0*b*<sup>1</sup> *···* K˜ <sup>∗</sup>

*<sup>b</sup>m*−2*bm*−<sup>1</sup>K˜ <sup>∗</sup>

$$
\mathbf{C}^{\infty}(\tau) = \lim_{n \to \infty} \sum_{k,l}^{n} \left( \mathbf{K}^{(k)} * \mathbf{C}^{0} * \mathbf{K}^{(l)T} \right) (\tau)
$$

![](_page_45_Figure_2.jpeg)

#### How does local structure determine correlations? recording 19 pyramid 1 neur are in projection in projection in the cerebral projection in the cerebral projection in the cerebral pro the expected number of bidirectional  $\mathbf{r}$ ncal structure det tionally connected pairs is four times that of the expected representation of  $\lambda$ confirms previous reports [5,6]. Such overrepresentation has  $\sim$  the data from 14 to 16-def measurements were performed (see Figure S5). We found that bidirectional connections are also overrepresented in this  $\blacksquare$

three classes: unconnected, unconnected, unconnected,  $\alpha$  and  $\alpha$ 

![](_page_46_Figure_1.jpeg)

small numbers of recordings have precluded statistical

connections is immersed in a sea of weaker ones.

![](_page_46_Figure_2.jpeg)

 $\circledR$ 

Song, et al. 2005  $\mathcal{L}$  Raw (open bars) and multiple-hypothesis testing corrected (filled (f bars) p-values bars) p-values above 0.5 are not shown.  $\mathbf{0}^{\prime}$ 

#### How do small motifs impact the correlation structure? adjacency matrix, so the indicate the presence of the presence of the presence of  $\mathcal{L}_{\mathbf{A}}$  $\frac{1}{2}$  $\beta$  . We first contribution the total number of times at which the motif occurs, and dividends at numbers, the (relative) motif counts for such regular graphs agree with those in the classical model of random graphs, the Erdios-Royal model in the limit of large network in the limit of large  $\sim$ we refer to the prevalence of network motion to  $\sim$

by the total number if of possible occurrences in a graph of the given size. For first order  $\mathcal{L}_\mathcal{D}$ 

motif occurs in the network can accurately predict levels of correlation across the network.

outgoing connections (i.e, the same *in and out degree*). Importantly, due to the law of large

We next introduce notation that will allow us to make these ideas precise. Let W<sup>0</sup> be

![](_page_47_Figure_1.jpeg)

!"

(W<sup>0</sup>

W<sup>0</sup>

 $\mathbf{F}_{\mathbf{r}}$  is the different types of second order motifs ( $\mathbf{F}_{\mathbf{r}}$  ). (Left)  $\mathbf{F}_{\mathbf{r}}$  is a second order motifs in a second order m

across the network. Here, we simulate 265 (give number of dots) different networks of

excitatory and inhibitory [Dayan and Abbot, 2001], exponential integrate and fire cells (this

Figure 2 illustrates the importance of network motifs in setting the average correlation

)*i,j*#

*/*<br>*/N*3 *− p*22 − *p*22 − *p*2

Sporns and Kötter, 2004<br>The dynamics of corresponding to the dynamics of the dynamics of the dynamics of the dynamics of the dynamics o is a frequently used model of spiking cells that has been shown to give an accurate description

*,* (15)

*/N3 − p2* (14) − *p2* (14) −

*.* (12)

*/N*<sup>3</sup> <sup>−</sup> *<sup>p</sup>*<sup>2</sup> (13)

cell *j* to cell *i*, and W<sup>0</sup>

Erd¨os-R´enyi graph.

#### How do small motifs impact the and a matrix, so the south world was the presence of the presence of the presence of  $\mathbf{z}_i$ numbers, the (relative) motif counts for such regular graphs agree with those in the classical model in the Erdios-Room graph, the limit of the Erdïos-Room in the limit of the Erdïos-Room in the limit of the limit of the limit of the limit numbers, the (relative) motif counts for such regular graphs agreement agreement agreement agreement those in<br>Those in the classical graphs agreement agreement agreement agreement agreement agreement agreement agreement mnant tha

given graph, we first count the total number of times at which the motif occurs, and divide occurs, and divide<br>The motif of times at which the motif of times at which the motif of times at which the motif of times at which

we refer to the prevalence of network motifs, this means in comparison to either a regular or the prevalence o<br>This means in comparison to either a regular or the prevalence or the prevalence of the prevalence of the prev

 $\sqrt{ }$ 

motif occurs in the network can accurately predict levels of correlation across the network.

outgoing connections (i.e, the same *in and out degree*). Importantly, due to the law of large

outgoing connections (i.e, the same *in and out degree*). Importantly, due to the law of large

we refer to the prevalence of network motifs, this means in comparison to either a regular or the prevalence o<br>This means in comparison to either a regular or the prevalence or the prevalence or the prevalence of the prev

We next introduce notation that will allow us to make these ideas precise. Let W<sup>0</sup> be

2,287.6,\*"

![](_page_48_Figure_1.jpeg)

!"

(W<sup>0</sup>

W<sup>0</sup>

 $\mathbf{F}_{\mathbf{r}}$  is the different types of second order motifs ( $\mathbf{F}_{\mathbf{r}}$  ). (Left)  $\mathbf{F}_{\mathbf{r}}$  is a second order motifs in a second order m

across the network. Here, we simulate 265 (give number of dots) different networks of

excitatory and inhibitory [Dayan and Abbot, 2001], exponential integrate and fire cells (this

Figure 2 illustrates the importance of network motifs in setting the average correlation

)*i,j*#

*/*<br>*/N*3 *− p*22 − *p*22 − *p*2

 $F_{\rm eff}$  is the different types of second order motifs (Right). (Left)  $\Delta E$  and  $\Delta E$  in a analysis in a analysis in a second order motifs in a s

across the network. Here, we simulate 265 (give number of dots) different networks of

excitation and inhibitory  $\mathbb{D}^2$  and  $\mathbb{D}^2$  and  $\mathbb{D}^2$  and fire cells (this integrate and fire cells (this integrate

is a frequently used model of spiking cells that has been shown to give an accurate description

Figure 2 illustrates the importance of network motifs in setting the average correlation

![](_page_48_Picture_2.jpeg)

*i,j* = 0 indicates its absence. To quantify the frequency of a motif in a

*/* $ch$   $\frac{1}{2}$ 

!"

 $\mathcal{O}(\frac{1}{2})$ 

(W<sup>0</sup>*<sup>T</sup>*W<sup>0</sup>

*p* =

*j,k*)*/N*<sup>3</sup> <sup>−</sup> *<sup>p</sup>*<sup>2</sup>

The preponderance of second order motifs is measured by similar motifs in  $\mathbb{R}^n$  , the motifs is measured by similar motifs in  $\mathbb{R}^n$ 

where W<sup>0</sup>*<sup>T</sup>* denotes the transpose of W<sup>0</sup>. Consider the expression defining *q*div: the sum

others (*i* and *j*), and divides by the total number of possible connections of this type. This

count, but then subtracting the value expected in a reference graph,

 $\int_{\alpha}$  $q_{\rm con}$ <sup>W</sup><sup>0</sup>*<sup>T</sup>* )*i,j*#  $\frac{1}{\sqrt{1}}$ 

d Kötter, 2004 is a frequently used model of spiking cells that has been shown to give an accurate description of the dynamics of the dynamics of corresponding to the dynamics  $\frac{1}{\sqrt{2}}$  Kotter, 2004 *i,j* in the first equality of Kötter, 2004

 $q_{\rm ch}$ 

*,* (15)

*/N3 − p2* (14) − *p2* (14) −

cell *j* to cell *i*, and W<sup>0</sup>

network.

Erd¨os-R´enyi graph.

Erd¨os-R´enyi graph.

### Mean correlations in structured networks

![](_page_49_Figure_1.jpeg)

#### How do small motifs impact the  $normal$ ation etructura? div is much improved, achieving an *R*<sup>2</sup> measure of 0.99, up from 0.8 in the correlation structure?

![](_page_50_Figure_1.jpeg)

![](_page_50_Figure_2.jpeg)

becomes

![](_page_50_Picture_3.jpeg)

%#&'()#\*)" +,\*&'()#\*)" +-.#\*" %#&'()#\*)" +,\*&'()#\*)" +-.#\*"

#### *<sup>y</sup>*˜(ω)=(<sup>I</sup> <sup>−</sup> K˜ (ω))−<sup>1</sup> *y*˜0 (ω)*,* (7) Correlations with homogeneity  $\bigcap$  simplifies the network. In the network,  $\bigcap$ instance, we consider *homogeneous networks* in which cells have identical (unperturbed)

power spectra, linear response functions, and synaptic kernels. In this case the diagonal

timescales. The weighted connectivity matrix W, defines the structure of the network.

$$
\tilde{\mathbf{C}}^{\infty}(\omega) = (\mathbf{I} - \tilde{\mathbf{K}}(\omega))^{-1} \langle \tilde{y}^{0}(\omega) \tilde{y}^{0*}(\omega) \rangle (\mathbf{I} - \tilde{\mathbf{K}}^{*}(\omega))^{-1}
$$

= (<sup>I</sup> <sup>−</sup> AW˜ F˜) (<sup>I</sup> <sup>−</sup> F˜<sup>∗</sup> structure from the effects of neuronal responses on network activity. The resulting cross-Assuming homogeneity in uncoupled cells, and evaluating at  $\omega = 0$ 

$$
\widetilde{\mathbf{C}}^{\infty}(0) = \widetilde{C}^0(0)(\mathbf{I} - \widetilde{A}\mathbf{W})^{-1}(\mathbf{I} - \widetilde{A}\mathbf{W}^T)^{-1}
$$

is the Fourier transform of the synaptic coupling kernel from cell *i*. As noted later, our results

*ii*(ω) =

 $\mathcal{L}_{\mathcal{L}}$ Anet expanding and truncating at second order in connection strength,  $\vert$  $\frac{1}{2}$  is a spin-directed on window size  $\frac{1}{2}$  in addition window size  $\frac{1}{2}$ After expanding and truncating at second order in connection strength, writing  $wW^0=W$ To relate second-order motif frequencies to mean correlations between pairs of cells, we

$$
\left[\frac{\tilde{C}^{\infty}}{\tilde{C}^{0}} \approx I + \tilde{A}w\mathbf{W}^{0} + \tilde{A}w\mathbf{W}^{0T} + \left(\tilde{A}w\right)^{2}\mathbf{W}^{0}\mathbf{W}^{0T} + \left(\tilde{A}w\right)^{2}\left(\mathbf{W}^{0}\right)^{2} + \left(\tilde{A}w\right)^{2}\left(\mathbf{W}^{0T}\right)^{2}\right]
$$

*N*(*N* − 1)

To obtain the empirical average of pairwise covariances in the network, "C˜ <sup>∞</sup>#, we multiply

both sides of Eq. (25) on the left and right by L*<sup>T</sup>* and L*,* respectively. Making use of

spectral quantities at ω = 0, suppressing the dependence on ω. Finally, we define average

and matrix of cross-spectra

*i*(ω)˜*y*<sup>0</sup><sup>∗</sup>

#### Averagd network correlations between pairs and correlations can truncate Eq. (20) at second order in (*A*˜W), giving can truncate Eq. (20) at second order in (*A*˜W), giving C˜ <sup>∞</sup> *C*˜0 *<u>Ad</u> network correlations* !

To relate second-order motif frequencies to mean correlations between pairs of cells, we call  $\alpha$ 

W<sup>0</sup>*<sup>T</sup>* \$<sup>2</sup> (25)

*Aw*˜ "<sup>2</sup>

*Aw*˜ "<sup>2</sup>

$$
\frac{\tilde{C}^{\infty}}{\tilde{C}^{0}} \approx I + \tilde{A}w\mathbf{W}^{0} + \tilde{A}w\mathbf{W}^{0T} + \left(\tilde{A}w\right)^{2}\mathbf{W}^{0}\mathbf{W}^{0T} + \left(\tilde{A}w\right)^{2}\left(\mathbf{W}^{0}\right)^{2} + \left(\tilde{A}w\right)^{2}\left(\mathbf{W}^{0T}\right)^{2}
$$

 $\Delta$ *veraning over the network*  $\mathcal{L}_{\mathcal{L}}$  (22-24), we obtain the obtained by  $\mathcal{L}_{\mathcal{L}}$ Averaging over the network ayıny<br>"  $\overline{\phantom{a}}$ over the network

$$
\frac{\langle \tilde{\mathbf{C}}^{\infty} \rangle}{\tilde{C}^0} \approx \frac{1}{N} + 2 \tilde{A}wp + 3N \left( \tilde{A}w \right)^2 p^2 + N \left( \tilde{A}w \right)^2 q_{\text{div}} + 2N \left( \tilde{A}w \right)^2 q_{\text{ch}}
$$

![](_page_52_Figure_4.jpeg)

C˜ <sup>∞</sup>

*C*˜0

 $\mathbb{E}_{\mathcal{L}}[Z_{\mathcal{L}}(2,2)]$ 

![](_page_53_Figure_0.jpeg)

Figure 8: Estimating the number of occurrence of  $\mathcal{A}$  fourth order motif. Eq. (31) can be number of a fourth order motif. Eq. (31) can be numbered in the number of a fourth order motif. Eq. (31) can be numbered in the

understood by decomposing this motif into the constituent first and second order motifs.

## Resumming

$$
\frac{\langle \tilde{\mathbf{C}}^{\infty} \rangle}{\tilde{C}^{0}} = \frac{1}{N} \left( 1 - \sum_{n=1}^{\infty} (N \tilde{A} w)^{n} \mathbf{L}^{T} \mathbf{W}_{n}^{0} \mathbf{L} \right)^{-1} \left( 1 + \sum_{n,m=1}^{\infty} (N \tilde{A} w)^{n+m} \mathbf{L}^{T} \mathbf{W}_{n,m}^{0} \mathbf{L} \right)
$$

$$
\cdot \left( 1 - \sum_{m=1}^{\infty} (N \tilde{A} w)^{m} \mathbf{L}^{T} \mathbf{W}_{m}^{0T} \mathbf{L} \right)^{-1},
$$

*Keeping contribution of second order motifs* Eq. (33), we obtain an expression which involves only first and second order motif frequencies: W<sup>0</sup>  $\overline{\phantom{0}}$ *<sup>N</sup><sup>n</sup>*−<sup>1</sup> <sup>W</sup><sup>0</sup> Keeping contribution of second order motifs

$$
\frac{\langle \tilde{\mathbf{C}}^{\infty} \rangle}{\tilde{C}^{0}} = \frac{1}{N} \frac{1 + \left(N \tilde{A} w\right)^{2} q_{\text{div}}}{\left[1 - \left(N \tilde{A} w\right) p - \left(N \tilde{A} w\right)^{2} q_{\text{ch}}\right]^{2}}.
$$

To approximate the impact of motifs up to order *r*, we would similarly keep terms with

Figure 9 shows that this approximation to the covariance provides a significant improve-

 $W$  offer an intuitive explanation for the effective explanation for the effectiveness of  $r$ 

*n,m* where *n, n* + *m* ≤ *r* in Eq. (34).

ment over the second order truncation approximation in Eq. (26) (See Fig. 6).

 $\overline{\phantom{a}}$ 

 $\overline{\phantom{a}}$ 

(connection probability), W<sup>0</sup>

*n*

*n,m*

## Resumming

$$
\frac{\langle \tilde{\mathbf{C}}^{\infty} \rangle}{\tilde{C}^{0}} = \frac{1}{N} \left( 1 - \sum_{n=1}^{\infty} (N \tilde{A} w)^{n} \mathbf{L}^{T} \mathbf{W}_{n}^{0} \mathbf{L} \right)^{-1} \left( 1 + \sum_{n,m=1}^{\infty} (N \tilde{A} w)^{n+m} \mathbf{L}^{T} \mathbf{W}_{n,m}^{0} \mathbf{L} \right)
$$

$$
\cdot \left( 1 - \sum_{m=1}^{\infty} (N \tilde{A} w)^{m} \mathbf{L}^{T} \mathbf{W}_{m}^{0 T} \mathbf{L} \right)^{-1},
$$

#### *Keeping contribution of second order motifs* Eq. (33), we obtain an expression which involves only first and second order motif frequencies: W<sup>0</sup>  $\overline{\phantom{0}}$ Keeping contribution of second order motifs

$$
\frac{\langle \tilde{\mathbf{C}}^{\infty} \rangle}{\tilde{C}^{0}} = \frac{1}{N} \frac{1 + \left(N \tilde{A} w\right)^{2} q_{\text{div}}}{\left[1 - \left(N \tilde{A} w\right) p - \left(N \tilde{A} w\right)^{2} q_{\text{ch}}\right]^{2}}.
$$

 $W$  offer an intuitive explanation for the effective explanation for the effectiveness of  $r$ 

![](_page_55_Figure_4.jpeg)

 $\sim$ 

 $\mathcal{F}_{\mathcal{F}}$  and  $\mathcal{F}_{\mathcal{F}}$  comparison of the mean correlation obtained using Eq. (8) ( $\mathcal{F}_{\mathcal{F}}$ 

approximation in Eq. (34) (y-axes). Each panel corresponds to a different scaling of coupling of coupling of co

strength for the same set of  $512$  adjacency matrices. The effective coupling strength is  $\sim$ 

*n,m* where *n, n* + *m* ≤ *r* in Eq. (34).

ment over the second order truncation approximation in Eq. (26) (See Fig. 6).

 $\overline{\phantom{a}}$ 

 $\overline{\phantom{a}}$ 

(connection probability), W<sup>0</sup>

*n*

*n,m*

#### Theory extends to EI  $\mathbf{S}$  in Fig. 14 we compare the block-wise mean correlations from IF simulations from IF simulatio the predication based on non-linear resumming theory. We find  $\mathcal{L}_\text{S}$  and  $\mathcal{L}_\text{S}$

**Excitatory-Excitatory Average** 

+ *A*˜<sup>2</sup>

 $\overline{\phantom{a}}$ 

Resumming

<sup>I</sup> <sup>−</sup> *<sup>A</sup>*˜D2M*<sup>T</sup>*

 

*Property* 

 $\sim$ 

 

![](_page_56_Figure_2.jpeg)

the case of two interacting populations.

## Conclusion

- Linear response theory can be used to understand the statistical structure of population activity.

- Cross-correlation functions can be understood in terms of contributions from paths through the network. Thus architecture and population activity can be related.

- This local theory applies to any network where interactions can be linearized

- There is a lot more to do - see Bullmore and Sporns, *Nat Neurosci*, 2009

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