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The effects of pooling on spike train correlations

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Neurons integrate inputs from thousands of afferents. Similarly, some experimental techniques record the pooled activity of large populations of cells. When cells in these populations are correlated, the correlation coefficient between the collective activity of two subpopulations is typically much larger than the correlation coefficient between individual cells: The act of pooling individual cell signals amplifies correlations. We give an overview of this phenomenon and present several implications. In particular, we show that pooling leads to synchronization in feedforward networks and that it can amplify and otherwise distort correlations between recorded signals.

Keywords: correlation, pooling, synchrony, feedforward networks

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1 INTRODUCTION

To characterize the neural code it is essential to understand how information is represented in the collective response of neurons. The **correlation** between cell pairs is a fundamental statistic that can be extracted from concurrent recordings of multiple cells. It has therefore frequently been used to characterize the dependence between neuronal responses. Cells at different stages of processing, from periphery (Mastronarde, 1983; Meister et al., 1995; Schneidman et al., 2006), through sensory (Zohary et al., 1994; Kohn et al., 2009) and motor areas (Lee et al., 1998) display correlated firing. Correlations can be important in sensory coding (Romo et al., 2003; Jones and Gabbiani, 2010), can carry information about movement direction (Nicolelis et al., 1995; Maynard et al., 1999; Kilavik et al., 2009), and can significantly affect the amount of information in neuronal responses (Zohary et al., 1994; Abbott and Dayan, 1999; Sompolinsky et al., 2001; Averbeck et al., 2006). However, the strength of these dependencies, and the impact they may have on the neural code are hotly debated (Ecker et al., 2010; London et al., 2010; Renart et al., 2010). It is therefore essential to understand the mechanisms that shape correlations between neurons in a population.

The total input to a cortical neuron often represents the pooled activity of hundreds to thousands of afferent cells. Similarly, voltage sensitive dye (VSD) and multi-unit (MU) recordings can represent the pooled activity of many nearby cells (Gray et al., 1995; Grinvald and Hildesheim, 2004). Here, we discuss the effects of such **pooling** on correlations and explore several implications.

Correlations can be dramatically amplified by pooling: Weak correlations between pairs of cells in two populations can result in high correlations between the summed activity of these two populations (Bedenbaugh and Gerstein, 1997; Chen et al., 2006; Renart et al., 2010; Rosenbaum et al., 2010). An illustration is provided in **Figure 1A**: Two electrodes each record the ensemble activity of a population of weakly correlated cells. Even in the absence of overlap, the recorded signals are much more strongly correlated than the activity of individual cells. The same effect can cause strong correlations between the activity of two neurons that receive inputs from a population of weakly correlated cells. Correlations between excitatory and inhibitory cells can modulate this

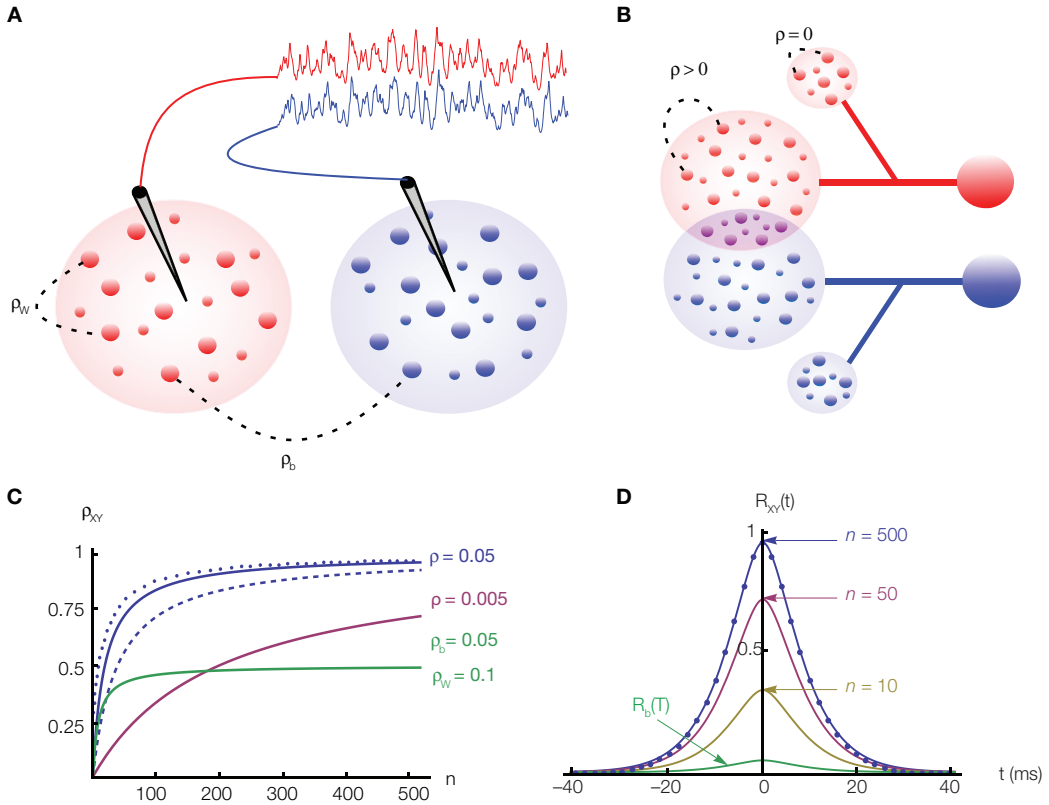

FIGURE 1 | The effects of correlations on pooled signals. (A) Two electrodes record from non-overlapping populations. Cells from separate (same) populations are correlated with coefficient ρ_b (ρ_w). The traces above the populations were obtained by convolving the pooled spike trains with an exponential kernel. Here $\rho_b = \rho_w = 0.050$ and $n = 500$. Although ρ_b is small, the traces are strongly correlated. **(B)** Two cells receiving input from overlapping populations. Each of the two subpopulations on the left contain n cells. All pairs of cells within these subpopulations are correlated with coefficient ρ. The two cells on the right share np of their inputs from these subpopulations (purple intersection). Additionally, each cell receives nq uncorrelated inputs (smaller populations on top and bottom). **(C)** The dependence of the pooled correlation, ρ_{XY}, on population size, n, for the examples in **(A,B)**. Green line corresponds to population model **(A)** with $\rho_b = 0.05$ and $\rho_w = 0.1$, while the blue line corresponds to **(B)** with $\rho = 0.05$ and $p = q = 0$ (solid line); $p = 0$ and $q = 1$ (dashed line); $p = 0.25$ and $q = 0$ (dotted line). A moderate amount of overlap between the populations or independent inputs do not significantly affect the pooled correlation when n is large. The pink line corresponds to model **(A)** with $\rho_b = \rho_w = 0.005$. **(D)** The cross-correlation function from the population model in **(A)** with $R_b(t) = R_w(t) = 0.05e^{-|t|/5}(1 + |t|/5)$ and for various values of n. The case $n = 500$ corresponds to the traces in **(A)** and the filled circles are from simulations.

effect, but only when excitation and inhibition are nearly perfectly balanced (Hertz, 2010; Renart et al., 2010; Rosenbaum et al., 2010).

This amplification of correlations has a simple mathematical explanation and has been noticed a number of times in different contexts (Bedenbaugh and Gerstein, 1997; Super and Roelfsema, 2005; Chen et al., 2006; Stark et al., 2008; Renart et al., 2010). We review, synthesize, and extend several existing results that pertain to this phenomenon and discuss several implications. In particular, we show that the effects of pooling on correlations is the primary mechanism responsible for the synchronization of feedforward chains. We also show that the effects of pooling can conceal the stimulus dependence of correlations as measured by MU recordings and otherwise distort relations between recorded signals.

2 THE IMPACT OF POOLING ON CORRELATIONS

We start by examining the effects of pooling in a simple setting where two signals each represent the summed activity of a population. We will first look at how pooling affects the correlation coefficient between such signals, and then examine the impact on their **cross-correlation function**.

THE IMPACT OF POOLING ON CORRELATION COEFFICIENTS

We represent the activity of cells in two populations by $\{x_i\}_{i=1}^n$ and $\{y_i\}_{i=1}^m$ respectively, where x_i and y_i are random numbers that can represent spike counts or some other scalar measure of neuronal response. The pooled activity from the two populations is assumed to be $X = \sum_{i=1}^n x_i$ and $Y = \sum_{i=1}^m y_i$, which can represent the total input

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spike counts to a pair of downstream cells. The following discussion applies to any pair of signals that represent an approximately linear combination of individual cell activity.

To simplify the exposition we assume homogeneity in the populations: All variables have the same variance, $\sigma^2 = \mathrm{var}(x_i) = \mathrm{var}(y_i)$, and the populations have equal size, $n = m$. To illustrate the impact of correlations between individual variables, i.e., the x_i's and y_i's, on the pooled quantities, X and Y, we consider two idealized population models. As discussed below, the effects of pooling are similar under more general assumptions (Rosenbaum et al., 2010).

The first population model (**Figure 1A**) captures the fundamental effects of pooling on correlations between two populations. For simplicity, we assume that the populations are non-overlapping. The correlation coefficients between two cells from separate populations (the **between correlations**) are denoted by $\rho_b = \mathrm{cov}(x_i, y_j)/\sigma^2$. The correlation coefficients between pairs from the same population (the **within correlations**) are $\rho_w = \mathrm{cov}(x_i, x_k)/\sigma^2 = \mathrm{cov}(y_i, y_k)/\sigma^2$, for $i \neq k$. The correlation coefficient between the pooled variables is then given by (Bedenbaugh and Gerstein 1997; Rosenbaum et al., 2010)

$$\rho_{XY} = \frac{\rho_b}{\rho_w + \frac{1}{n}(1-\rho_w)} = \frac{\rho_b}{\rho_w} - \mathcal{O}(1/n). \quad (1)$$

Hence, for large n, the correlation between the pooled signals approaches the ratio of the between and within correlations (see **Figure 1C**). More generally, $|\rho_{XY}| \geq |\rho_b|$ so that pooling amplifies correlations for any value of n.

If the recordings are from two subsets of a larger, homogeneous population then $\rho_b = \rho_w = \rho$. When pooling from a smaller number of neurons, $\rho_{XY} = n\rho + \mathcal{O}(\rho^2)$, and pooled activity increases approximately linearly with population size (Renart et al., 2010). For large populations correlations saturate and $\rho_{XY} = 1 - \mathcal{O}(1/n)$.

This analysis also provides simple bounds on pairwise correlations in a population. For example in the population model considered in **Figure 1A**, the fact that $|\rho_{XY}| < 1$ combined with Eq. (1) tells us that that $|\rho_b| \leq |\rho_w| + \mathcal{O}(1/n)$. That is, pairwise correlations *between* two populations are bounded by the correlations *within* the two populations. As the input population size grows, this bound becomes tighter and ρ_b cannot be much larger than ρ_w.

The second population model (**Figure 1B**), illustrates the case when X and Y represent the activity of overlapping populations. We assume that a proportion p of the n recorded cells in a population are shared between the populations. This implies that $\mathrm{cov}(x_i, y_j)/\sigma^2 = 1$ for $n\,p$ separate x_i, y_j pairs. The remaining $n\,(n - np)$ pairs have correlation $\rho = \mathrm{cov}(x_i, y_j)/\sigma^2$. For simplicity, assume that the *within* correlations are the same as the *between* correlations: $\rho = \mathrm{cov}(x_i, y_j)/\sigma^2 = \mathrm{cov}(x_i, x_k)/\sigma^2 = \mathrm{cov}(y_i, y_k)/\sigma^2$ for $i \neq k$. We also include inputs from two external, statistically independent populations, modeled by $m = qn$ independent variables. Hence, $X = \sum_{i=1}^{n} x_i + \sum_{j=1}^{m} w_j$ and $Y = \sum_{i=1}^{n} y_i + \sum_{j=1}^{m} z_j$ where z_j and w_j are independent from all other variables, i.e., $\mathrm{cov}(w_j, u) = 0$ for all $u \neq w_j$ and $\mathrm{cov}(z_j, u) = 0$ for all $u \neq z_j$. The correlation coefficient between the pooled variables is then given by (Rosenbaum et al., 2010)

$$\rho_{XY} = \frac{\rho + \frac{p}{n}(1-\rho)}{\rho + \frac{1}{n}(1-\rho+q)} = 1 - \mathcal{O}(1/n). \quad (2)$$

Overlap between the two populations, as well as uncorrelated input, does not significantly affect the pooled correlation, ρ_{XY}, when n is large (see **Figure 1C**). For smaller values of n and when ρ is small, correlations are dominated by overlap and $\rho_{XY} \approx p$.

The equations discussed above have been studied in the context of multiunit recordings (Bedenbaugh and Gerstein, 1997) and VSD signals (Chen et al., 2006). They can be generalized to arbitrary heterogeneous populations (Rosenbaum et al., 2010) yielding an equation that is nearly identical to Eq. (1) with ρ_b and ρ_w replaced by weighted averages of the correlations between and within each population. Thus, the main ideas that we discuss are not fundamentally impacted by heterogeneity. In **Figure 1C**, we illustrate the dependence of ρ_{XY} on the population size, n, for the population models discussed above.

THE IMPACT OF POOLING ON CROSS-CORRELATION FUNCTIONS

It is frequently of interest to determine correlations over different timescales (Bair et al., 2001; Smith and Kohn, 2008). For instance, the filtering of recorded spike trains by synapses or recording devices can affect the timescale over which correlations occur (Tetzlaff et al., 2008; Rosenbaum et al., 2010; Tetzlaff and Diesmann, 2010) and downstream cells with short membrane time constants may be more sensitive to tightly synchronous inputs (Moreno et al., 2002; Gutnisky and Josić, 2010). Assuming two signals, $x(t)$ and $y(t)$, are jointly stationary, this temporal correlation structure is captured by the cross-correlation function (Perkel et al., 1967),

Correlation
The Pearson correlation coefficient is a measure of dependence between two random quantities. The correlation coefficient between spike counts is frequently used to quantify the statistical dependence between two spike trains. The degree of correlation can impact stimulus coding and network dynamics.

Pooling
A neuron combines inputs from thousands of afferent cells. Similarly, signals obtained using some recording techniques represent the combined activity of many neurons. We refer to this act of combining cellular activity as "pooling." Here we assume that the pooled signal represents approximately a linear combination of the component signals.

Cross-correlation function
The spiking activity of neurons can be correlated over a broad timescale. The cross-correlation function quantifies the degree of correlation between two signals over different time lags. In particular, the cross-correlation function evaluated at a time lag τ represents the correlation between one signal at time t and the other at time $t + \tau$.

Within versus between correlations
When looking at the correlation between the pooled activity of two subpopulations, it is necessary to distinguish correlations between elements of the same population (*within* correlations) from correlations between elements of different populations (*between* correlations).

Feedforward network
A layered network of neurons in which cells in a layer only receive inputs from cells in a previous layer. Frequently, neurons in deeper layers of such networks spike synchronously. Such synchronization is primarily due to the effects of pooling.

$$R_{xy}(\tau)=\frac{\mathrm{cov}(x(t),y(t+\tau))}{\sqrt{\mathrm{var}(x(t))\mathrm{var}(y(t))}}.$$

Due to stationarity, $\mathrm{var}(y(t)) = \mathrm{var}(y(t+\tau))$ so that $-1 < R_{xy}(\tau) < 1$ is simply the correlation coefficient between the random variables $x(t)$ and $y(t+\tau)$. Thus, the impact of pooling on cross-correlation functions can be understood in terms of the results in the previous section.

We derive the analog of Eq. (1) for cross-correlation functions. Assume that $\{x_i(t)\}_{i=1}^n$ and $\{y_i(t)\}_{i=1}^n$ are populations of stationary stochastic processes with $\sigma^2 = \mathrm{var}(x_i(t)) = \mathrm{var}(y_i(t))$, $R_b(\tau)=R_{x_iy_j}(\tau)$, and $R_w(\tau)=R_{x_ix_k}(\tau)=R_{y_iy_k}(\tau)$ for $i \neq k$. The cross-correlation function between the pooled processes, $X(t)=\sum_{i=1}^n x_i(t)$ and $Y(t)=\sum_{i=1}^n y_i(t)$, is given by

$$R_{XY}(\tau)=\frac{R_b(\tau)}{R_w(0)+\frac{1}{n}\left(1-R_w(0)\right)}=\frac{R_b(\tau)}{R_w(0)}-\mathcal{O}(1/n). \quad (3)$$

This equation can be related to Eq. (1) intuitively by recalling that $R_{XY}(\tau)$ is the correlation coefficient between $X(t) = \Sigma_i x_i(t)$ and $Y(t+\tau) = \Sigma_j y_j(t+\tau)$. The "between" correlations in this case are given by the correlation coefficient between $x_i(t)$ and $y_j(t+\tau)$, i.e., $R_b(\tau) = \mathrm{cov}(x_i(t), y_j(t+\tau))/\sigma^2$. Similarly, the "within" correlations are given by $R_w(0) = \mathrm{cov}(x_i(t), x_j(t))/\sigma^2 = \mathrm{cov}(y_i(t+\tau), y_j(t+\tau))/\sigma^2$.

From Eq. (3) we see that pooling scales the entire cross-correlation function by $R_w(0) + (1 - R_w(0))/n$ so that correlations over all time lags are scaled by the same factor. We also see that the cross-correlation function is generally amplified by pooling in the sense that $|R_{XY}(\tau)| \geq |R_b(\tau)|$. For homogeneous populations, where $R_b(\tau) = R_w(\tau) = R(\tau)$, the zero-lag cross-correlation, $R_{XY}(0)$, approaches 1 for large n, as illustrated in **Figure 1D**.

3 POOLING INDUCES SYNCHRONIZATION IN FEEDFORWARD NETWORKS

Layered **feedforward networks** (**Figure 2**), provide a simple setting to study the propagation of neuronal activity (Kumar et al., 2010). In general, neurons in the deeper layers of such networks tend to synchronize (Diesmann et al., 1999; van Rossum et al., 2002; Litvak et al., 2003; Reyes, 2003; Tetzlaff et al., 2003; Doiron et al., 2006; Kumar et al., 2008). Propagation of synchronous activity is important for some neural codes (Abeles, 1991; Abeles et al., 1994; Diesmann et al., 1999), but the tendency of feedforward to synchronize in feedforward networks generally reduces information encoded in deeper layers (van Rossum et al., 2002; Kumar et al., 2010).

The amplification of correlations due to pooling underlies the development of synchrony

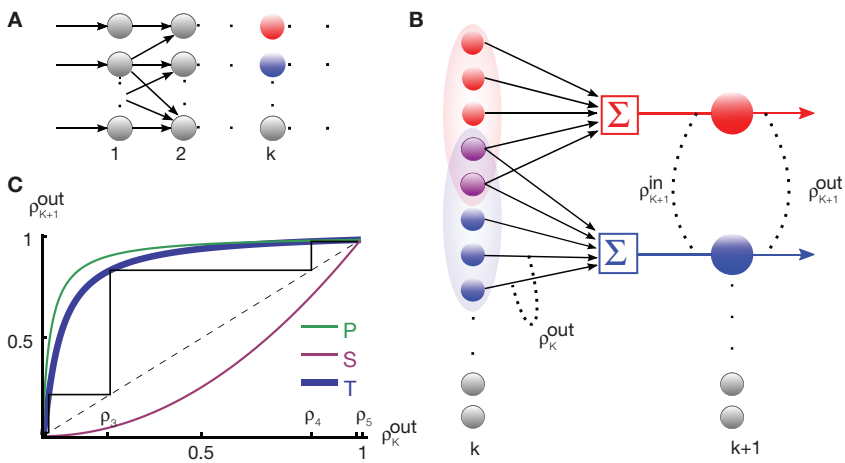

FIGURE 2 | The effect of pooling in feedforward networks. (A) A schematic diagram of a feedforward network with random connectivity. Each layer consists of N cells. Each cell in layer $k+1$ receives a fixed number of randomly selected inputs from layer k. **(B)** The stages of processing in the network pictured in **(A)**. Outputs from layer k are pooled to form the input to each cell in layer $k+1$. These inputs are, in turn, decorrelated by the cells in layer $k+1$. The combined effect can lead to large gains in correlation from layer-to-layer. **(C)** Iteration of the dynamical model described in the text. The green line represents the pooling map P, the pink line is the decorrelating transfer map, S (here chosen to be $S(\rho) = \rho^2$). The solid blue line represents their composition, $T = S \pm P$, which maps output correlations from layer k to output correlations from layer $k+1$. The solid black line shows the trajectory obtained by iterating the map with $\rho_1^{in} = 0$, $n_e = 600$, $n_i = 400$, $p = 0.05$.

in feedforward networks. This effect can be understood using the diagram in **Figure 2B**: The input to layer $k+1$ is obtained by pooling the output of layer k, leading to a large gain in correlations. This pooled input is then passed through the cells of layer $k+1$. Due to cellular dynamics and the effects of thresholding, a layer of neurons typically reduces correlations, especially when the cells are operating in a fluctuation dominated regime (Shea-Brown et al., 2008; Rosenbaum and Josić, 2011). However, the correlating effects of pooling will often outweigh the decorrelating effects of cellular dynamics. Correlations between cells in layer $k+1$ will therefore be greater than those in layer k.

The development of synchrony can be illustrated more quantitatively using a mean-field model. We follow a construction similar to those in Aviel et al. (2003), Tetzlaff et al. (2003), but highlight the effects of pooling. In addition, we oversimplify the input–output correlation transfer of a neuron. For a more detailed study of the interplay between correlation transfer and firing rates of cells, see Tetzlaff et al. (2003). Consider a randomly connected feedforward network with excitatory and inhibitory cells, and denote the input correlations to and output correlations from cells in the kth layer by ρ_k^{in} and ρ_k^{out} respectively. In a network with random connectivity, the number of inputs to a cell in a layer, as well as the overlap in the pools projecting to two cells are random quantities. We replace these quantities with their means to obtain a tractable model. Hence each cell receives input from exactly n_e excitatory and n_i inhibitory cells, and each pair of cells share a fraction p of their excitatory and inhibitory input pools.

The inputs to layer $k+1$ are obtained by pooling the outputs from layer k. The effect of this pooling on the correlation, ρ_{k+1}^{in}, between the inputs to layer $k+1$ is captured by a mapping P such that $\rho_{k+1}^{in} = P(\rho_k^{out})$. This mapping can be derived using Eq. (4) (see Tetzlaff et al., 2003; Rosenbaum et al., 2010),

$$P(\rho) = \frac{\rho(\beta-1)^2 + \frac{p}{n_i}(1-\rho)(1+\beta)}{\rho(\beta-1)^2 + \frac{1}{n_i}(1-\rho)(1+\beta)}, \qquad (4)$$

where β measures the balance of excitation and inhibition. Assuming for simplicity that excitation and inhibition have equal synaptic weights, $\beta = n_e/n_i$. As illustrated in **Figure 2C**, P is strongly correlating when n_e and n_i are large and $\beta \neq 1$. To complete the dynamical model, we must map input correlations to output correlations. As a simplifying approximation, we assume that ρ_k^{out} only depends on ρ_k^{in} and write $\rho_k^{out} = S(\rho_k^{in})$. As mentioned above, the mapping from input to output correlations is typically decorrelating, i.e., $|S(\rho)| \leq |\rho|$. The composite map, $T = S \pm P$, combines the correlating effects of pooling and the decorrelating effects of cell transfer. This mapping induces the discrete dynamical system, $\rho_{k+1}^{out} = T(\rho_k^{out})$ that describes the propagation of correlations across layers (Aviel et al., 2003; Tetzlaff et al., 2003; Rosenbaum et al., 2010).

The correlating effects of pooling typically outpace the decorrelating effects of cell filtering so that T is correlating (see **Figure 2C**). Precise balance between excitation and inhibition ($\beta = 1$) can prevent runaway synchrony in this simple dynamical model, but this cancelation is difficult to achieve in feedforward networks of spiking cells due to the fragile stability of this asynchronous state (Rosenbaum et al., 2010). However, recurrent networks can dynamically stabilize the asynchronous state under certain conditions (Renart et al., 2010).

We argue that the development of synchrony in large feedforward networks is primarily due to the pooling of correlated inputs. Overlapping inputs introduce correlations in early layers, but the layer-to-layer increase in correlations downstream is primarily a result of *pooling* and not overlap. This point is illustrated by comparing a network with overlapping inputs (**Figure 3A**) to a network without overlap (**Figure 3B**). In **Figure 3B**, correlations are introduced in the input to the first layer, whereas in **Figure 3A** input to the first layer are uncorrelated, but correlations are introduced to the second layer by overlap. Comparing layer k in **Figure 3B** to layer $k+1$ in **Figure 3A**, we see that spiking in the two networks becomes correlated at about the same rate, suggesting that pooling, not overlap, is the mechanism most responsible for the gain in correlations across layers.

The fact that pooling dominates overlap in synchronizing feedforward networks can also be explained quantitatively by appealing to Eq. (4). The effect of overlap in the input population is of order $\mathcal{O}(1/n_e, 1/n_i)$ when upstream correlations are non-zero, but pooling has an order unity effect, and is therefore the dominant factor in determining input correlations when input populations are large and upstream correlations are non-zero.

In **Figure 3** we see that the activity in deeper layers is not only highly correlated, but tightly synchronous. We can explain this fact by appealing to Eq. (3) which shows that if the "within" and "between" correlation coefficients at lag

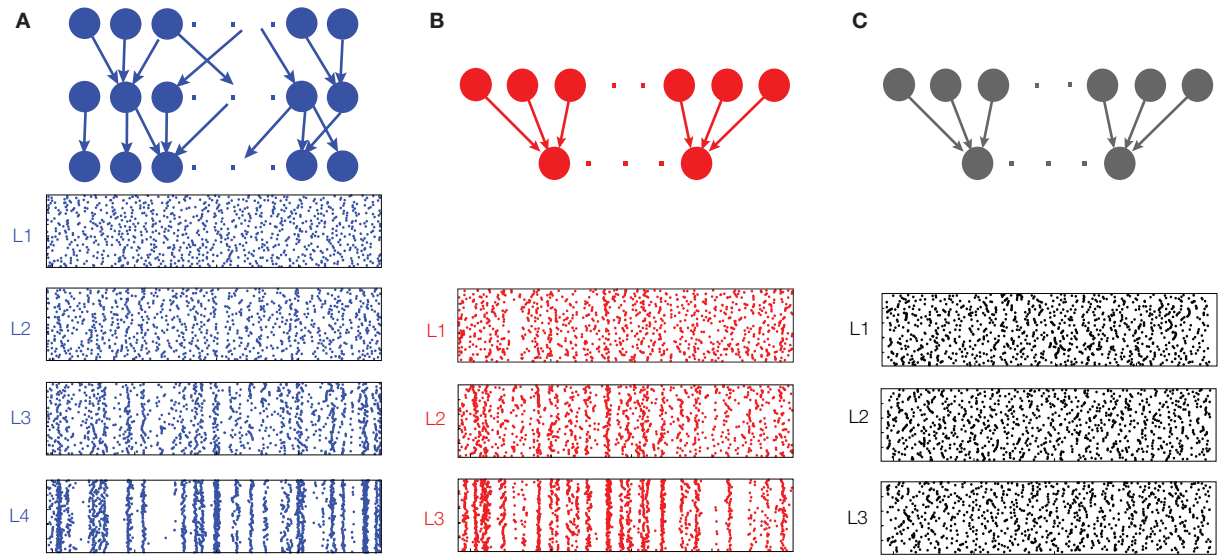

FIGURE 3 | Development of synchrony in feedforward networks. (A) Spike rasters from a simulation of a randomly connected feedforward network. Each cell receives $n_e = 1400$ excitatory and $n_i = 600$ inhibitory inputs. In addition, two cells in a layer share, on average, a proportion $p = 0.05$ of their inputs. Each cell in layer 1 receives an independent Poisson excitatory input, so that outputs from the first layer are uncorrelated. **(B)** A feedforward network with no overlap. Each cell receives the same number of inputs as in **(A)**, but there are no shared inputs ($p = 0$). Correlated inputs are introduced to the first layer, $\rho_1^{in} = 0.05$, to match the level of correlation introduced by overlap in the input to layer 2 in **(A)**. **(C)** A feedforward network with no overlap receiving independent input. All model parameters are the same as in **(B)**. However, the input to the first layer is uncorrelated ($\rho_1^{in} = 0$), and synchrony does not develop. The spike count correlation over a window of width 50 ms averaged over all pairs is $\rho = 0.02$, 0.18, and 0.59 for layers 2, 3, and 4 in **(A)**; and $\rho = 0.03$, 0.21, and 0.63 for layers 1, 2, and 3 in **(B)**. Cells in all other layers are not correlated.

zero are not significantly different, then $R_{XY}(0)$ approaches unity (see **Figure 1D**) for large input populations. In a feedforward network, this effect is compounded across layers and cells in deeper layers will tend to spike synchronously.

Synchrony in feedforward networks has received much attention, especially in the context of the propagation of pulse packets (Diesmann et al., 1999; Kumar et al., 2008). While synchrony may benefit temporal codes, it can make rate coding difficult (van Rossum et al., 2002). The tuning of feedforward networks for rate or temporal coding and the impact on information transmission is reviewed in Kumar et al. (2010). An alternative to the present approach is to use Fokker-Planck equations to describe the evolution of the size and shape of pulse packets (Câteau and Fukai, 2001; Doiron et al., 2006). Closer to the present approach, one can develop probabilistic models of randomly connected feedforward networks of binary threshold neurons (Nowotny and Huerta, 2003). However, this approach makes the effects of pooling difficult to isolate.

The lack of recurrence in feedforward networks makes them more amenable to mathematical analysis. However, biophysically realistic layered neuronal networks are embedded within larger, recurrent networks. Moreover, connectivity between cells is not random. Additional structure can lead to richer dynamics and functionality. For instance, the inclusion of disynaptic inhibitory circuits (which amounts to adding lateral inhibitory-to-excitatory and inhibitory-to-inhibitory connections to the purely feedforward network) allows the network to selectively propagate only strongly synchronous inputs (Kremkow et al., 2010). Hence, the details of the feedforward network architecture can significantly impact the propagation of synchronous activity.

4 IMPACT OF POOLING ON VSD AND MU RECORDINGS

We next explore the effects that pooling can have on recorded signals. First, we show that pooling can mask stimulus dependent changes in spiking correlations. Second, we show that poor discrimination between cells when sorting spikes can artificially increase measured correlations.

4.1 POOLING CAN CONCEAL STIMULUS DEPENDENT CHANGES IN CORRELATION

A stimulus (Kohn and Smith, 2005; de la Rocha et al., 2007; Gutnisky and Dragoi, 2008; Churchland et al., 2010), as well as the behavioral state of the animal (Riehle et al., 1997; Greenberg et al., 2008; Cohen and Maunsell,

Stimulus dependent changes in correlation

The structure and magnitude of correlations in a population of cells can change in response to stimuli, as well as changes in behavioral states. Such changes in correlation can modulate information encoded in the cells' spike trains. We show that these changes can be masked by the effects of pooling.

2009; Kilavik et al., 2009) can modulate the firing rates and correlations in neuronal responses. **Stimulus dependent changes in correlation** can have a significant impact on the neural code (Shamir and Sompolinsky, 2004; Josić et al., 2009). However, such changes may be masked in recordings that reflect the pooled activity of large groups of cells.

As discussed above, the correlation, ρ_{XY}, between the pooled signals from two large populations of cells reflects the ratio of the "between" and "within" correlations (ρ_b and ρ_w), but does not reflect the actual scale of these pairwise correlations. Thus, changes in correlation structure that scale ρ_b and ρ_w by the same factor are difficult to detect by looking at the correlation between the pooled recordings.

To illustrate this effect, we consider a simple, experimentally motivated model. Using VSDs, Chen et al. (2006) imaged the response of primary visual cortex in monkey during an attention task. The imaged area was divided into 64 pixels, each pixel capturing the pooled activity of $n \approx 10^4$ neurons. To model such recordings we assume that, in the presence of a stimulus, the firing rate of individual cells decays with the distance from the center of the retinotopic image of that stimulus. When a stimulus is absent, the background firing rate is assumed constant. Additionally, the correlation between the responses of two neurons increase with their firing rates (see de la Rocha et al., 2007; Shea-Brown et al., 2008) and correlations decay exponentially with cell distance (Smith and Kohn, 2008; see however Poort and Roelfsema, 2009; Ecker et al., 2010). In particular, we assume that the correlation between two cells at distance d is given by $\rho_{xy} = e^{-\alpha d}$ for some $\alpha > 0$. See Rosenbaum et al. (2010) for more details about our model and derivations.

We consider the recordings from two pixels, X and Y. In response to a stimulus, correlation between cells in the pixels increase due to an increase in firing rates, however all pairwise correlations are increased by the same factor so that the ratio of *between* and *within* correlations is unchanged. Thus, the correlation between the recordings is nearly unchanged by the presence of a stimulus when n is large. More precisely, the correlation between the pooled signals is of the form $\rho_{XY} = e^{-\alpha D}\,\mathcal{O}\,(1/n)$ where D is the distance between the pixels (Rosenbaum et al., 2010). This holds whether a stimulus is present or not. Thus, even significant stimulus dependent changes in correlations could be masked in the recorded signals. This overall trend is consistent with the results in Chen et al. (2006; compare **Figure 4B** to their Figure 2F).

However, in Supplementary Figure 3 of Chen et al. (2006) the presence of a stimulus apparently results in a slight decrease in correlations between more distant pixels. In **Figure 4C** this effect is reproduced using the model described above with the additional assumption that the activity of cells not tuned to a stimulus is suppressed in the presence of that stimulus. The imaged area was divided into 64 pixels, each pixel capturing the pooled activity of n ≈ 104 neurons (See **Figure 4A**). The effect can also be reproduced by assuming that the spatial correlation decay constant, α, increases when a stimulus is present.

As this example shows, care needs to be taken when inferring underlying correlation structures from pooled activity. The statistical structure of the recordings can depend on pairwise correlations between individual cells in a subtle way, and different underlying correlation structures may be difficult to distinguish from the pooled signals. The fine structure of correlations may be similarly masked if recordings from many cells are used in

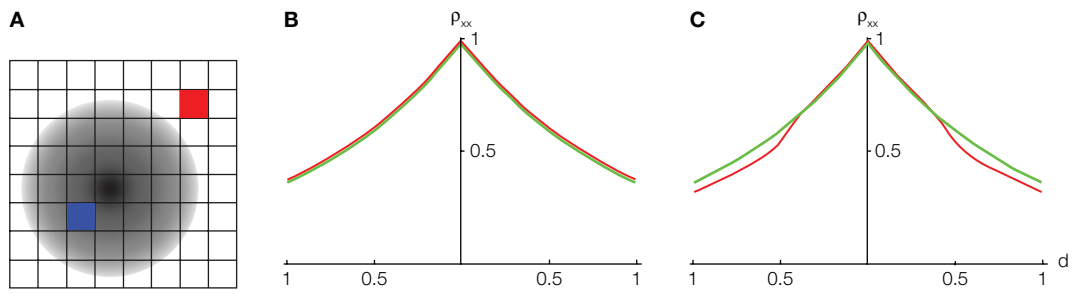

FIGURE 4 | The effect of pooling on recordings of stimulus dependent correlations. (A) A diagram of our model. Signals $X(t)$ and $Y(t)$ are recorded from two pixels (red and blue squares). The activity in response to a stimulus is shown as a gradient centered at some pixel (the center of the retinotopic image of the stimulus). **(B)** The prediction of the correlation between two pixels obtained using the model considered in the text with stimulus present (red) and absent (green). We assumed that one pixel is located at the stimulus center ($d_i = 0$). A stimulus dependent change in correlations is undetectable. **(C)** Same as in **(C)**, except that the activity of cells not tuned to the stimulus is decreased by 50% in the presence of stimulus. Compare to Figure 2F in Chen et al. (2006).

obtaining estimates. However, as downstream neurons are driven by the pooled input from many afferents, they may also be insensitive to the precise structure of pairwise correlations.

4.2 POOLING AMPLIFIES CORRELATIONS WHEN SPIKES ARE POORLY DISCRIMINATED IN MULTI-CELL RECORDINGS

Spike sorting methods are used to assign action potentials recorded by a single electrode to different cells. Insufficient separation may result in treating spikes from different cells as coming from a single cell (Lewicki, 1998). Thus the response attributed to a single cell can reflect the pooled activity of a small population. Errors in spike sorting can therefore affect estimates of correlations (Gerstein, 2000; Pazienti and Grün, 2006; Ecker et al., 2010; Cohen and Kohn, private communication).

To illustrate this effect, consider an example where $m+n$ cells with equal spike count variance, σ^2, are recorded using an extracellular electrode (or several electrodes). Assume that the spikes from m of the cells are mistakenly attributed to a single cell and spikes from the other n are mistakenly attributed to a separate single cell, so that the experimenter sees two cells where there are actually $m + n$. For simplicity, assume that the spike count correlation between all of the cells is identically ρ. Then the correlation, ρ_{rec}, between the recorded spike counts is given by

$$\begin{aligned}\rho_{\text{rec}} &= \frac{\rho}{\sqrt{\left(\rho+\frac{1}{m}(1-\rho)\right)\left(\rho+\frac{1}{n}(1-\rho)\right)}} \\ &= \sqrt{mn}\rho+\mathcal{O}(\rho^2).\end{aligned}$$

Thus, when cells are weakly correlated, the correlation coefficient between the recorded spike counts is a factor of $\sqrt{mn}$ larger than the actual spike count correlation. In practice, it is unlikely that m and n would be large, but even in the simplest case where two cells are mistaken for one and another cell is isolated correctly ($m = 2$, $n = 1$), the recorded correlation is a factor of $\sqrt{2}$ larger than the actual correlation.

5 DISCUSSION

We have illustrated how pooling can impact correlations between the inputs to pairs of cells, as well as recordings that represent the summed activity of neuronal populations. These effects have been discussed in a variety of settings (Bedenbaugh and Gerstein, 1997; Super and Roelfsema, 2005; Chen et al., 2006; Stark et al., 2008; Renart et al., 2010), and similar ideas were also developed for the variance alone (Salinas and Sejnowski, 2000; Moreno-Bote et al., 2008). The saturation of the signal-to-noise ratio with increasing population size observed in Zohary et al. (1994) has a similar origin. We have extended these results by generalizing the population models and by giving a combined analysis of the effects of pooling and overlap (Rosenbaum et al., 2010). We also reviewed the impact of pooling on the development of synchrony in feedforward networks and the interpretation of results obtained from recordings of population activity. While pooling increases correlations, it may also mask stimulus dependent changes in correlations because of saturation.

Although feedforward connectivity appears constraining, neuronal architectures may harbor hidden feedforward structures (Ganguli et al., 2008; Goldman, 2009; Murphy and Miller, 2009). However, there are other mechanisms that can modulate correlated activity which we did not address here. For instance, recurrent connections between cells can increase or decrease correlations (Schneider et al., 2006; Ostojić et al., 2009; Renart et al., 2010). Moreover, the activity of groups of neurons may become entrained to network oscillations, thus resulting in more synchronous firing (Womelsdorf et al., 2007). A full understanding of the statistics of population activity will require an understanding of how these mechanisms interact to shape the spatiotemporal properties of the neural response.

In addition to looking at the impact of pooling on correlation coefficients, we also looked at the impact on cross-correlation functions. We found that correlations are amplified by the same factor at all time lags. This effect gives rise to tight synchrony between spiking in deeper layers of feedforward networks.

Although all equations remain valid in the presence of negative correlations, we did not consider them here. Negative correlations can be introduced to the inputs of two cells by negatively correlated afferents or by positively correlated excitatory and inhibitory inputs (Renart et al., 2010). Pooling can amplify negative correlations. However, negative and positive correlations can also cancel between signals that represent the collective activity of cell populations. Only when positive and negative contributions are precisely balanced will such cancelation be exact. Theoretical and experimental studies suggest that such a decorrelated state may be stable in neuronal networks (Ecker et al., 2010; Hertz, 2010; Renart et al., 2010). The nonnegative definiteness of covariance matrices also imposes theoretical bounds on their magnitude. Additionally, there are bounds on the magnitude of negative input correlations that can result from correlations between excitatory and inhibitory afferents. These bounds are discussed in the context of pooling in Rosenbaum et al. (2010).

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