INTRODUCTION

Spontaneous activity is a principal mode of operation of the brain. It is defined as neuronal activity that is not directly tied to either sensory input or a behavioral task. Functionally, it has been suggested that cortical spontaneous activity underlies processes such as mental imagery (Kreiman et al., 2000; Kosslyn et al., 2001; Kraemer et al., 2005), cognition (Badagigiani et al., 2010), and the consolidation of memories (Buzsaki, 1989; Hoffman and McNaughton, 2002; Born et al., 2006). In recent years, a variety of recording techniques across multiple in vivo and in vitro models have documented a resemblance of stimulus-evoked activity patterns to those that occur spontaneously. Considering the synaptic requirement for propagation of neuronal activity, it is likely that cortical connectivity imposes common constraints on the activity structure seen within a cortical circuit.

The initial description of a significant overlap between spontaneous and evoked activity patterns was provided by studies using voltage-sensitive dyes. Visualizing ongoing activity in cat visual cortex, Evarts et al. (2003) showed that spontaneously emerging patterns of activity corresponded closely to functional orientation maps. Similarly, patterns of activity emerging in response to sensory stimulation were also found to occur spontaneously in mouse sensorimotor cortex (Frecou et al., 2006). Theoretical studies have shown a direct link between the connectivity in network models and the resultant dynamics (e.g., Honey et al., 2007; Galan, 2008; Rinzel, 2011). Consistent with these theoretical studies, recent experiments using either ultrastructural analysis (Bock et al., 2011) or paired patch clamp recording (Ko et al., 2011) have demonstrated that visually evoked neural activity patterns reflected synaptic connectivity.

Even in absence of sensory stimuli cortical networks exhibit complex, self-organized activity patterns. While the function of those spontaneous patterns of activation remains poorly understood, recent studies both in vivo and in vitro have demonstrated that neocortical neurons activate in a surprisingly similar sequential order both spontaneously and following input into cortex. For example, neurons that tend to fire earlier within spontaneous bursts of activity also fire earlier than other neurons in response to sensory stimuli. These “default patterns” can last hundreds of milliseconds and are strongly conserved under a variety of conditions. In this paper, we will review recent evidence for these default patterns at the local cortical level. We speculate that cortical architecture imposes common constraints on spontaneous and evoked activity flow, which result in the similarity of the patterns.

Keywords: neocortex, microcircuit, spontaneous, imaging, tetrode, default mode
The most distinguishable patterns of spontaneous spiking activity are observed during slow wave oscillations (SWO), which can be observed during slow wave sleep (Metherate and Ashe, 1993), quiet wakefulness (Petersen et al., 2003; Crochet and Petersen, 2006; Ferezou et al., 2006; Luczak et al., 2007, 2009), and under anesthesia (Steriade et al., 1993). SWO can also originate without pharmacological manipulation in vitro in slices of isolated cortex (Sanchez-Vives and McCormick, 2000; Cossart et al., 2003; Shu et al., 2003), showing a strong generalization of this rhythmic neuronal behavior to the cortex. During SWO, bursts of population activity called UP states last for 100 ms to several seconds and are interspersed with periods of neuronal silence (DOWN states; Metherate et al., 1992; Steriade et al., 1993; see example in Figure 1 middle column and in Figure 2A). UP states, whether spontaneous or evoked by external stimuli, occur simultaneously in nearby neurons (Lampl et al., 1999; Luczak et al., 2007, 2009) and exhibit complex spatiotemporal patterns of neuronal activity (Cossart et al., 2003; MacLean et al., 2005; Watson et al., 2008). Multiple studies have shown that those patterns occurring during spontaneous UP states are particularly similar to patterns produced by thalamic or sensory stimulation (Tsydynkova et al., 1999; Kenet et al., 2003; Fiser et al., 2004; MacLean et al., 2005; Eggermont, 2006; Watson et al., 2008; Luczak et al., 2009). These data suggest that spontaneous patterns resemble stimulus-evoked patterns because they propagate through the same microcircuits, and the architecture of synaptic weights and connections imposes significant ‘hardware’ constraints on activity patterns.

In this mini review, we will focus on the similarity of spontaneous and evoked activity patterns at the local circuit level. Although this similarity has also been observed on much larger spatial scales (Vincent et al., 2007; Mohajerani et al., 2010), we will focus on microcircuits that can be densely recorded from with single cell resolution. We term local patterns of neuronal activations that frequently repeat spontaneously or in response to stimuli as “default patterns” due to the preservation of their structure regardless of the source of initiation. Consistent with the theory that local cortical architecture plays a major role in generating these default patterns, we also introduce the term “default microcircuits.” Thus, default microcircuits give rise to default patterns, reflecting the concept that specific connectivity in a local network constrains and shapes the spontaneous and evoked activity. We speculate that default microcircuits are a network of strongly interconnected neurons embedded in network of weaker connections (Song et al., 2005; Perin et al., 2011), likely shaped by plasticity mechanisms (Han et al., 2008). These strong connections cause spontaneous or evoked signals to be more likely to travel along these stronger connections, which, in turn, results in similar activity patterns.

**DEFAULT PATTERNS: IN VITRO**

Far from being random, spontaneous circuit activity is precisely patterned in terms of the timing of a specific neuron within a sequence of neuronal activity (Cossart et al., 2003; Kenet et al., 2003; MacLean et al., 2005; Watson et al., 2008; Luczak et al., 2007, 2009). Further, the same circuits that are spontaneously active in sensory cortices can also be activated by thalamic input in vitro (Castro-Alamancos, 2009; MacLean et al., 2005; Watson et al., 2008). Here we define a circuit as a group of neurons that are likely synaptically interconnected and functionally related (Brock et al., 2011; Ko et al., 2011). Thus, any discrete population of neurons that are co-active (i.e., a circuit) will be repeatedly co-active to the exclusion of the majority of the surrounding neurons. This suggests that this activity is the byproduct of discrete/specific synaptic connectivity inherent to cortex (Sanchez-Vives and McCormick, 2000).

**FIGURE 1** Spatiotemporal precision of network activation: cells are activated in similar order spontaneously and following thalamic stimulation. (A) Light micrograph, with an overlaid cartoon, of a somatosensory (SI) thalamocortical slice preparation with intact thalamic input nucleus (ventral basal nucleus, VB), thalamocortical axons, and the somatosensory cortex. A stimulating electrode is placed in VB, as indicated by yellow square. The superimposed dashed-red box indicates the location, over layer 4, of the illustrated frame in (B). Scale bar: 1 mm. (B) Individual frames (300 ms) from representative movies of a thalamically evoked network activation (triggered, gray, left) and a spontaneous network activation (spontaneous, green, middle) in the same slice. Each movie progresses from top to bottom as indicated by the arrow. Core frames indicate cells active in the same order across all movies (n = 11) from this slice, indicated in red. Scale bar 50 μm (adapted from MacLean et al., 2005).
FIGURE 2 | Spontaneous UP states initiate sequential patterns homologous to evoked responses. (A) Representative raw data plot showing a tone response and spontaneous firing waves. DOWN states of complete silence alternate with UP states of generalized activity. Neurons are ordered vertically by the mean latency over all stimuli, to illustrate sequential spread of activity. Blue traces show local field potentials (LFPs) from four separate recording shanks; at bottom is the multiunit firing rate (MUA).

(B) Raster plots showing spike times for two representative neurons to repeated presentations of a pure tone stimulus. (C) Average activity of 90 simultaneously recorded neurons to tone stimuli. Gray bars show pseudocolor representations of each neuron’s peri-event time histogram normalized between 0 and 1; red dots denote each neuron’s latency in the 100 ms after tone onset. (D) Response of the same two neurons as in (B) triggered by UP state onsets. Note the similar temporal pattern. (E) Average upstate-triggered activity of all neurons, sorted in the same order as in C (adapted from Luczak et al., 2009).

(F) Cartoon illustration of default microcircuits – strongly connected neurons (solid arrows) embedded in pool of weaker connections (dashed arrows). Due to constraints on connectivity, different inputs may result in similar activity propagation through the network. Most typical patterns produced in such default microcircuit are termed default patterns. (G) Cartoon illustration of stimulus-evoked patterns. The overall structure of evoked patterns is similar to the spontaneous default patterns shown in panel (B), but the firing rate and to smaller degree spike timing of neurons encodes information about stimulus identity. For example: during spontaneous activity neuron 1 (green) tends to fire before neuron 2 (brown). In response to a stimulus that is preferred by neuron 1, neuron 1 fires at a higher rate (4 Hz) and with shorter delay (5 ms) after stimulus onset while neuron 2 fires at 2 Hz 25 ms after onset. For a different stimulus that is preferred by neuron 2, neuron 1 fires at a lower rate (1 Hz) and with longer delay (15 ms), while neuron 2 increases its firing rate by 3 Hz and shortens its delay by 5 ms. This exemplifies how external stimulation can evoke a stimulus-specific firing rate and timing of neurons and still maintain the overall structure of the default pattern (i.e., neuron 1 fires before neuron 2).
event was changed (different from bootstrap reshuffled data sets in which cell identity be around 70%. These repeating sequences were significantly dif-

same order both spontaneously and following thalamic input to the cortex. Comparing all possible pairs of core neuron sequences, it was found that the percent of core neurons that were activated in exactly the same circuit was maintained and only the time of activation during a circuit event was changed (Figure 1). Thus, cortical circuits that are activated by thalamic input significantly overlap with the activity that arises in these same circuits spontaneously. This result implies that intracortical connectivity plays a dominant role in determining the corticospinal response to sensory input.

DEFAULT PATTERNS: IN VIVO SENSORY CORTICAL CIRCUITS

To investigate if precise spatiotemporal sequences of activation also occur in vivo, Luczak et al. (2009) recorded simultaneously from 40–100 neurons in layer V of rat auditory cortex using silicon microelectrodes in both urethane anesthetized and awake rats. In response to tone stimulus as well as spontaneously, neurons showed sequential temporal firing patterns (Figure 2A). If the sequential structure of sensory responses is a reflection of a default dynamics of the circuit producing it, spontaneous patterns generated by the same circuit should show the same stereotyped sequential structure as sensory responses. In support of this prediction, individual neurons showed similar temporal relationships of their spiking activity to UP state onsets as they did to sensory stimuli, revealing a similar sequential structure at the population level (Figures 2B–E). The similarity of spontaneous and evoked patterns was also observed in somatosensory and visual areas (Jermakowicz et al., 2009; Luczak et al., 2009) and similar sequential patterns were also reported in prefrontal cortex (Peyrache et al., 2010). This suggests that default patterns are present in most cortical areas. Moreover, weak pair-wise correlations in neuronal circuits may cause major constraints not only on sequential structure of default patterns but also on firing rate correlations at the population level (Schneidman et al., 2006). Thus, default patterns not only demonstrate fine-scale temporal patterns, but also have similar firing rate correlations for both spontaneous and stimulus-evoked events (Luczak et al., 2009). These are important findings because it shows that population spike patterns in anesthetized and awake animals are much less diverse than previously assumed.

DISCUSSION

It is not surprising that the neuronal population patterns may show a certain level of similarity to each other, since more strongly connected neurons will be more likely to fire together across different conditions. Rather, the surprise is how highly conserved these activity patterns are under a variety of conditions. Considering that each cortical neuron receives input from potentially thousands of other neurons, any evoked or spontaneous activity pattern could have very different spatiotemporal dynamics from all other patterns. Contrary to this expectation, studies reviewed here show that neuronal responses are limited to a small subset of all possible activity patterns. We suggest that these “default patterns” are the functional manifestation of “default microcircuits”—local patterns of connectivity that impose similar spatiotemporal constraints on spontaneous and stimulus-evoked flow of activity, as illustrated in cartoon form in Figures 2F–H.

One profound question which comes to mind is: what would be the function of default patterns? We see it a little differently—that the system has to generate default patterns given the constraints imposed by synaptic connectivity. Thus, we feel it could be misguided to try to assign a specific function to this activity, rather default patterns reflect the circuit wiring diagram(s) in neocortex. Let’s use an analogy: the arm is composed of set of bones and joints which put together set constraints on possible movements. Thus, although spontaneous arm movements, reaching for a cup or writing are quite different actions—patterns of muscles activity during those actions share many similarities, because it uses the same “hardware.” Thus, default activity patterns are likely the manifestation of “hardware” constraints within the system. However, we believe that it is important to discuss the existence of default patterns because it can shed light on the structure of baseline activity, structure of stimulus-evoked patterns and thus will likely prove critical to our understanding of the informational coding scheme in cortex.

Although, results reviewed here indicate that the spatiotem-

da the number of possible patterns is still enormous, allow-

ing for the unique representation of different stimuli (Luczak et al., 2009). For instance, for a preferred stimulus, a neuron will tend to respond with higher firing rate and with slightly shorter latency but the overall structure of default pattern will be preserved (Figure 2H, see also Figure 3 in Luczak et al., 2009). It is also interesting to note that the highest precision of spike patterns is observed immediately after stimulus (Churchland et al., 2010) or UP state onset, after which timing precision progressively deteriorates (Luczak et al., 2007). Thus, those results are not fully consistent with concept of “synfire chains” which generally implies repeating patterns to have a millisecond-level precision for the entire duration of pattern (Abeles, 1991). It is conceivable that the reason for the highest precision of spiking observed immediately after onset could be that neurons firing earliest in the sequence would reflect an initial processing of information; and spiking activity at later times would reflect subsequent computations combined with feedback information from other areas. For example in several sensory systems, short-latency responses correlate with simple stimulus features, while later responses evolve to represent more complex...
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periods of SWO are interleaved with periods of REM sleep. Each
be due to differences in brain state. For instance, during sleep,
out what is the expected
problem resides in defining a null hypothesis: what is the expected
this fact may lead to incorrect interpretation of experimental data
especially when investigating temporal and firing rate relationships
between neurons.
Despite the fact that many labs have observed and reported
repeating patterns in neuronal activity, these results are not widely
accepted. One of the reasons for this is the statistical difficulty in
assessing the significance of reoccurring patterns. Specifically, the
problem resides in defining a null hypothesis: what is the expected
probability of a pattern arising by chance (Ikegaya et al., 2004;
Mokeicheva et al., 2007; Ikegaya et al., 2008; Rozin et al., 2008). For
example, should the analyzed spike trains be compared to a
homogeneous or inhomogeneous Poisson process, if inhomoge-
neous, what then should be an appropriate modulation function?
We would like to note that evidence showing consistent and repeat-
ing sequential neuronal activity in response to stimulation as well as
down-UP state transition as reviewed here are not subject to
these statistical difficulties.
Another potential source for discrepancy between results may be
due to differences in brain state. For instance, during sleep,
periods of SWO are interleaved with periods of REM sleep. Each
of those states has quite different dynamics. Moreover, the awake
state is different from sleep and has its own range of states ranging
from an animal at rest to an animal which is fully engaged while
performing a task. Probably during “quiescent” states (i.e., SWO in
thalamocortical slices, SWO in animals under anesthesia, “quiet”
wakefulness; Petersen et al., 2003) it is easier to detect default activity
patterns as opposed to the activated/attending state observed in
animals engaged in task. We speculate that in the more active
brain, i.e., attentive wakefulness, spatial and temporal overlap of
patterns propagating through the same default microcircuits may
obscure and complicate detection of any structured activity. By
analyzing only moving carousel it easy to see each of the seats,
but when the carousel is spinning fast we can no longer distin-
guish single seats from the blur of motion. Thus, the apparent
absence of patterns reported in some studies (e.g., Ecker et al.,
2010) could be the result of a more activated brain state. In studies
that densely sample from neuronal populations, as afforded by
2-photon imaging methods, significant correlation between
nearby and task related neurons has been observed even during
the activated state (e.g., Konigsmann et al., 2010). This observation
was made possible by imaging approaches that allow single cell
resolution. Without fine spatial resolution, task-engaged circuits
could be intermingled and overlapping, making it difficult to detect
meaningful correlations and preserved spatial-temporal structure
of local circuits. The other possible source of discrepancies in
detecting repeated patterns may be found in the size of the time
bin over which correlation is calculated, as it can lead to nega-
tive results if the time bin is too large or small. Regardless, we
suggest that it is of utmost importance that the role and activity
of neurons that comprise a default microcircuit be characterized
across different brain states ranging from deep sleep to awake
and engaged brain.
In summary, we describe current evidence for existence of
default patterns. We suggest that default microcircuits (strongly
connected neurons embedded in pool of weaker connections)
could cause similar propagation of activity through the network,
despite differences in spontaneous and stimulus-evoked inputs
(Figure 2F). As the result, certain types of activity patterns
(i.e., default patterns) are more prominent and more frequent
(Figure 2G).

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