Trends in Neurosciences

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Feature Review

Diverse Phase Relations among Neuronal Rhythms and Their Potential Function

Eric Maris,[1,*] Pascal Fries,[1,2] and Freek van Ede[1,3]

Neuronal oscillations at nearby sites in the brain often show phase relations that are consistent across time, yet diverse across space. We discuss recent demonstrations of this phase relation diversity, and show that, contrary to earlier beliefs, this diversity is a general property of oscillations that is neither restricted to low-frequency oscillations nor to periods outside of stimulus processing. Arguing for the computational relevance of phase relation diversity, we discuss that it can be modulated by sensory and motor events, and put forward the idea that phase relation diversity may support effective neuronal communication by (i) enhancing selectivity and (ii) allowing for the concurrent segregation of multiple information streams.

Trends

Neuronal oscillations are a prominent feature of neuronal population activity. Across populations, oscillations exhibit stable phase relations that can be highly diverse across nearby sites.

Phase relation diversity is prominent even for high-frequency (>40 Hz) oscillations during sustained visual stimulation, and is therefore neither restricted to low frequencies nor to periods outside of sensory processing.

Arguing for its computation relevance, this diversity is modulated by both sensory and motor events and, for hippocampal theta oscillations, it even allows for reconstructing a rat's location.

Phase relation diversity may enhance selectivity of neuronal communication and allow for the concurrent segregation of multiple information streams. This may be particularly relevant for beta oscillations that are coherent across frontal and parietal brain areas.

Existence and Potential Relevance of Phase Relation Diversity

A central question in neuroscience is how the billions of neurons in the human brain are coordinated such that they perform useful computations. Looking for an answer, it is obvious to consider the fact that neuronal activity is usually coordinated across time and space. This holds both for subthreshold **membrane potentials** (see Glossary; reflecting the inputs to a neuron) and action potentials (spikes, the neuronal output). Correlations among neuronal output, such as spike synchrony and relative spike timing, have a substantial impact on neuronal function [1–7]. Correlations across time often occur within a limited frequency band, as typically identified by a rhythmic pattern in the **autocorrelation**. This rhythmic neuronal activity is typically denoted as a **neuronal oscillation**. Neuronal oscillations are involved in a whole range of sensory [8], motor [9,10], and cognitive processes [11–13]. They have been described in terms of their frequency, amplitude, synchronization, and between-site **phase relations**. Here, we focus on the surprising diversity in their between-site phase relations, even between nearby sites (see Box 1 for a description of how these phase relations can be assessed empirically). Historically, this diversity has mainly been studied in the context of **traveling waves**, and was considered typical for ongoing oscillations in the absence of stimulus processing. In this review article, we discuss recent demonstrations of **phase relation diversity**, showing that it is a general property of oscillations that is neither restricted to low-frequency oscillations nor to periods outside of stimulus processing.

To argue for the functional relevance of phase relation diversity, it is important to demonstrate (i) that it can be modulated by sensory and motor events, and (ii) that it plays a role in the flow of neuronal information. With regard to the role of neuronal oscillations in the flow of neuronal information, much attention has been focused on interactions between communicating sites. Specifically, it has been proposed that effective communication between two oscillating neuronal populations depends, at least in part, on their phase relation [14–17]. Communication is most effective when the neuronal output of the sending population arrives at the receiving population at its most **excitable phase**. Because oscillations in both the sending and the receiving populations may be characterized by local diversity in their phase relations (as we will review), it makes sense to incorporate this type of

[1]Radboud University, Donders Institute for Brain, Cognition, and Behaviour, 6525 EZ, Nijmegen, The Netherlands
[2]Ernst Strüngmann Institute (ESI) for Neuroscience in Cooperation with Max Planck Society, 60528, Frankfurt, Germany
[3]Oxford Centre for Human Brain Activity, Department of Psychiatry, University of Oxford, OX3 7JX, Oxford, UK

*Correspondence: e.maris@donders.ru.n (E. Maris).

Box 1. Calculating Phase Relations, Their Diversity, and Their Coherence

In a first step, the phases of single sites are obtained from a Fourier (or wavelet) transform of some epoch of the recorded signal (Figure IA). The Fourier coefficients are frequency indexed complex numbers whose phase angle and magnitude are the elements for several derived quantities. First, from the single site phases obtained from multiple sites, one can calculate the between-site phase relations (Figure IB). In Figure IC, we consider an example situation involving three sites (color-coded blue, green, and red), resulting in two site pairs (blue–green and green–red), for which we obtained recordings in a series of trials/epochs. The phase relations are shown in the gray middle columns. They are obtained as the product of the immediate left and the conjugate of the immediate right column. This operation produces complex numbers whose phase angles equal the phase differences (phase relations) between the two sites, and magnitudes that equal the product between the magnitudes of the single site coefficients. Importantly, one must distinguish the epoch-specific phase relations from their average across all epochs, which is also called the average phase relation. Phase relation diversity pertains to the diversity in the average phase relations across the site pairs (here illustrated for two pairs – the minimum number). Crucially, this across-site pair diversity only makes sense if the average phase relations are also reliable, implying that the corresponding epoch-wise phase relations are similar to the average phase relation. This reliability can be quantified using a split-half procedure (see Figure 1A in main text), as well as by coherence, which is obtained by normalizing the cross-spectrum (the average of the complex numbers in the middle columns in Figure IB) by the square roots of the power of the sites (the average of the squared magnitudes of the numbers in the outer columns). Thus, phase relation diversity is only relevant for sites that are coherent, because otherwise the diverse average phase relations are not representative of the epoch-wise phase relations.

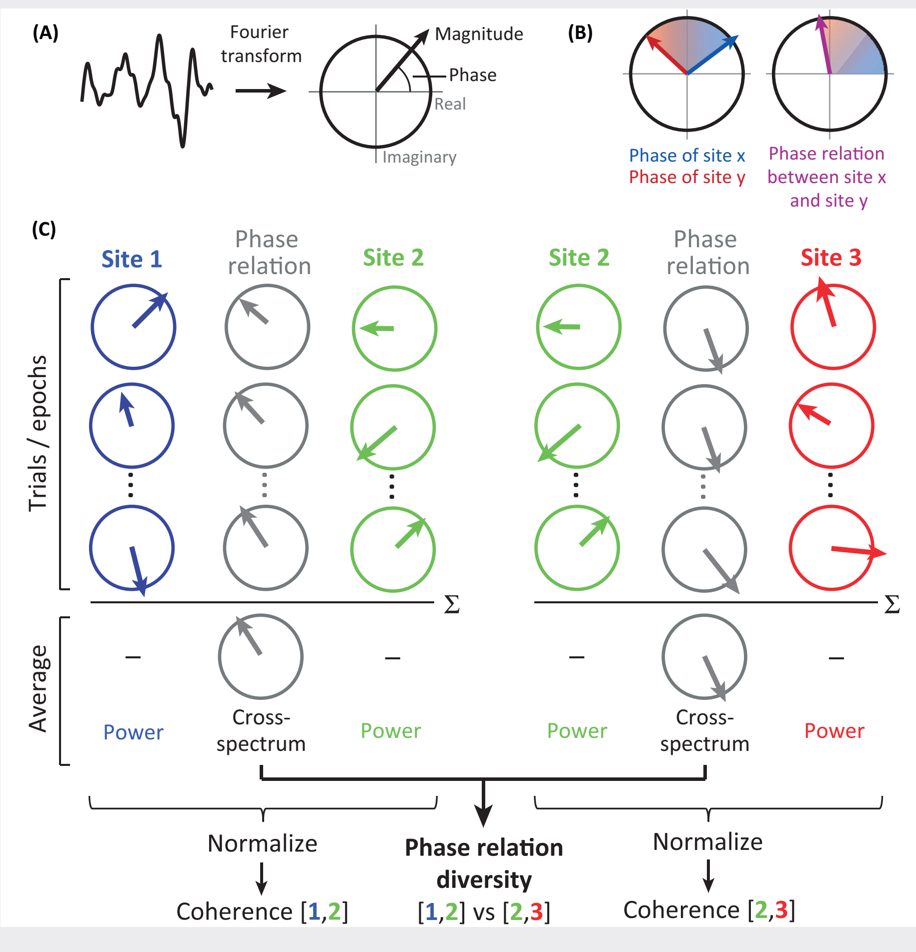

Figure I. Calculating Phase Relations, Their Diversity, and Their Coherence.

Glossary

Autocorrelation: correlation across time between a signal and a time-shifted copy of that same signal.
Coherence: degree to which the phase relations between two signals are consistent across non-overlapping time windows.
Crosscorrelation: correlation across time between a signal and a time-shifted copy of another signal.
Decoding: data analytic technique that estimates a variable (e.g., the current position of an animal) on the basis of a set of other variables (e.g., neuronal signals).
Excitable phase: phase at which a neuron with an oscillating membrane potential has the highest probability of generating an action potential in response to excitatory synaptic input.
Membrane potential: the difference in electric potential between the interior and the exterior of a cell. The membrane potential is especially relevant for cells with voltage-sensitive ion channels, such as neurons: the more positive the membrane potential, the higher the probability that an excitatory synaptic input results in an action potential (produced by a massive opening of voltage-sensitive sodium channels).
Neuronal oscillation: neuronal signal with a repeating waveform. Such a signal is also said to exhibit periodicity or rhythmicity, and it is reflected in the fact that the autocorrelogram has multiple peaks.
Phase–amplitude coupling: particular relation between a low- and a high-frequency signal component, involving that the time-varying amplitude of the high-frequency component predominantly occurs at a particular phase of the low-frequency component.
Phase relation: time relation between two periodic signal components, expressed as the fraction of the repeating waveform by which the signals are shifted.
Phase relation diversity: variability across signal pairs with regard to their phase relations.
Traveling wave: waveform over (as a function of) space that changes its position over time.
Voltage-sensitive dye: dye that changes its spectral properties in response to voltage changes, allowing it to be used for optical imaging of potential distributions.