An Event-Driven Model for Estimation of Phase-Amplitude Coupling at Time Scales of Cognitive Phenomena
Phase-amplitude coupling (PAC) is a form of cross-frequency coupling (CFC) in which the amplitude of a fast signal is shown to depend on the phase of a slower signal. The fast signal is said to be “nested” within the cycles of the slow modulation signal.

PAC between distinct neural oscillations has been shown to play a critical role in the execution of cognitive functions that include cross-scale organization, selection of attention, routing the flow of information through neural circuits, memory processing, and information coding. PAC itself is thought to be a neural computation involved in regulating signal synchrony in the brain, and has been demonstrably identified in various species and across multiple brain areas.

Several methods exist for PAC estimation, but the physiological bases of PAC are not well understood, so there is not yet a singular "golden standard" presented by the neuroscience community for PAC estimation.

Researchers Dr. Andre Fenton and Ph.D student Dino Dvorak at NYU's Center for Neural Science have published a new approach to PAC estimation which extends PAC analysis beyond current methods, which are limited by filter parameters to analytical windows of no less than 10 seconds. The new approach can accurately estimate PAC phenomena within a single cycle of the modulation signal while still providing the same information as current PAC estimation techniques at larger time scales. Importantly, the extension of PAC analysis to smaller timescales enables the investigation of PAC at the time scales of cognitive phenomena.

It is not always certain before analysis which frequency bands are involved in PAC phenomena, so PAC estimation typically begins with the construction of a comodulogram to view the signal interactions for all detectable combinations of the phase signal \( \phi(t) \) and the amplitude signal \( A(t) \). Once the oscillatory events of the band being analyzed have been properly displayed in time-frequency space, the proper modulation index is estimated by using high power events as time locking points for the whole signal. It is often difficult to estimate the modulation index presented by the slow wave if the slow wave signal is not sinusoidal, which is currently a strong limitation for filtering techniques.

Andre Fenton's and Dino Dvorak’s work in this field describes another form of CFC called oscillation-triggered coupling (OTC) which is used to characterize PAC phenomena at the scale of individual oscillations. The OTC approach provides the same global estimates of PAC properties such as the frequencies of the modulatory rhythms, the frequencies of modulated bands, as well as the preferred phases of coupling for the individual modulated bands. OTC analysis extends beyond the global scale into the scale of individual oscillations by using frequency-specific oscillation events to view and estimate PAC patterns.
Oscillation triggered coupling (OTC) analysis.

(A) The OTC algorithm operates at two temporal scales – the “global” scale, which estimates the general properties of PAC (modulated bands, preferred phases of coupling) and the “local” scale of individual oscillations. Oscillations that are initially used to create the oscillation triggered comodulogram (OTCG) at the global scale can be filtered using various criteria (e.g. specific frequency, phase and power) in order to obtain the specific events that are responsible for generating phase–amplitude coupling. (B) In the first step, the raw LFP signal is transformed into (C) a z-score normalized wavelet spectra. Individual oscillations are detected as local maxima in time–frequency space. (D) Time stamps of large (>2 S.D. from mean power) and frequency-specific (f±delta-f) oscillations are then used as trigger points for summing the time windows of the raw LFPs centered at these time stamps. The development of the OTC signal is displayed as a function of increasing numbers of summed event windows N = 1, 50, 100 and 1000. Notice that the amplitude and smoothness of the resulting OTC signal increases with the number of events. This indicates there is a systematic relationship between the peaks of detected oscillations and the phase of the slow rhythm. The red dotted horizontal lines mark the significant amplitude threshold of the OTC signal, which was computed from a surrogate test using random trigger points. (E) The resulting OTC signal displays several important properties. Its peak-to-peak amplitude corresponds to the strength of coupling, its phase at time 0 (middle of the time window) corresponds to the preferred phase of the coupling and its frequency corresponds to the modulatory rhythm. (F) In order to obtain a significant amplitude of the modulatory signal, approximately 70 events (corresponding to approx. 30 s of data) need to be added to the summation. (G) The above process can be repeated for a range of frequency bands (e.g. 20–200 Hz) to obtain the oscillation-triggered comodulogram (OTCG). The profile of the modulation strength (peak-to-peak amplitude of the modulatory signal) across frequencies (G right) shows peaks in the slow (40 Hz) and fast (80 Hz) gamma bands (red arrows) and (H) the same peaks can be also observed in the FFT spectra computed from all frequency-specific modulatory signals. The FFT also shows that the wave pattern of the OTC corresponds to a single modulatory frequency of 8 Hz (theta) that is present across the whole frequency range (20–200 Hz). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)
Dr. Andre Fenton's and Ph.D student Dino Dvorak's work is published in the Journal of Neuroscience Methods titled, Toward a Proper Estimation of Phase-Amplitude Coupling in Neural Oscillations