Washington University in St. Louis
Office of Technology Management

ROBUST, SCALABLE PHASE CONTROL SYSTEM FOR NON-INVASIVE NEUROMODULATION DEVICES

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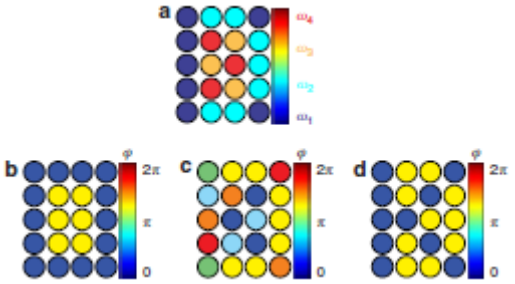
T-016206

Technology Description:

Researchers in Prof. Jr-Shin Li's laboratory have developed a robust, scalable, patented technology to control and entrain complex, noisy, non-linear oscillating systems such as neuronal firing and circadian rhythms. This system uses a single global, open-loop control to manipulate (e.g. synchronize or desynchronize) the phase of noisy, dynamic units with potential applications in neuromodulation devices to treat Parkinson's disease, epilepsy or jet lag.

Brain function, sleep cycles and other complex biological systems are noisy, non-linear and hard to characterize. Therefore, it is difficult to simultaneously synchronize or entrain the collection ("ensemble") of individual components (e.g., neurons) within the system. This technology overcomes this hurdle with a mathematical framework for constructing pulse signals inspired by MRI waveforms that drive nuclear spins. The system provides the appropriate periodic forcing signal to establish and maintain a coherent, stable pattern (e.g., synchrony, clustering) with an aim to regulate dynamic neural signaling, influence circadian rhythms or control other biological phenomena. Because this method can entrain an ensemble through a weak coupling signal, it is likely enable non-invasive devices for treating conditions such as sleep disorders or Parkinson's disease.



Proof of Concept: *Electrochemical pattern switching between "O" (b) and "K" (d) pattern with phase-selective entrainment.*

Stage of Research:

Using an electrochemical phase-switching system, the inventors have experimentally demonstrated that a single global input can control the complex oscillatory reactions of 20 different elements in an array (ensemble) to create target patterns. (*Nature Communications*)

Applications:

- **Neuromodulation devices –** pulse or waveform design for a brain entrainment system to control the phase (e.g., synchronizing or desynchronizing) of oscillating biological signals, with end-user applications such as treatment for:
  - Parkinson's disease and other movement disorders
  - sleep/circadian rhythm disorders (e.g., jet lag)

- epilepsy

Key Advantages:

- **Non-invasive** – single global signal can manipulate oscillation phases without coupling or feedback information, thus it has the potential for non-invasive interventions without direct connection to neurons deep within the brain
- **Robust** – entrainment system is resilient to noise, disturbances and model variability which is necessary for uncertain biological systems that can't be readily observed and feedback information is unavailable
- **Scalable** – based on a unified, systematic mathematical theory that is predicted to be effective for nonlinear oscillating system with up to thousands of elements

Patents: Phase-selective entrainment of nonlinear oscillator ensembles (U.S. Patent No. 10,693,416)

Publications:

- Zlotnik, A., Nagao, R., Kiss, I. Z., & Li, J. S. (2016). Phase-selective entrainment of nonlinear oscillator ensembles. *Nature communications*, 7(1), 1-7.
- Study sheds light on patterns behind brain, heart systems; circadian rhythms. *theSource*, March 18, 2016.

Related Web Links: Applied Mathematics Lab