# Introduction to Focus Issue: Rhythms and Dynamic Transitions in Neurological Disease: Modeling, Computation, and Experiment

Tasso J. Kaper,[1,a)] Mark A. Kramer,[1,b)] and Horacio G. Rotstein[2,c)]
[1]*Department of Mathematics and Statistics, Boston University, Boston, Massachusetts 02215, USA*
[2]*Department of Mathematical Sciences, New Jersey Institute of Technology, Newark, New Jersey 07102, USA*

(Received 11 December 2013; accepted 11 December 2013; published online 23 December 2013)

Rhythmic neuronal oscillations across a broad range of frequencies, as well as spatiotemporal phenomena, such as waves and bumps, have been observed in various areas of the brain and proposed as critical to brain function. While there is a long and distinguished history of studying rhythms in nerve cells and neuronal networks in healthy organisms, the association and analysis of rhythms to diseases are more recent developments. Indeed, it is now thought that certain aspects of diseases of the nervous system, such as epilepsy, schizophrenia, Parkinson's, and sleep disorders, are associated with transitions or disruptions of neurological rhythms. This focus issue brings together articles presenting modeling, computational, analytical, and experimental perspectives about rhythms and dynamic transitions between them that are associated to various diseases.  [http://dx.doi.org/10.1063/1.4856276]

**To have and to hold—and to oscillate—in sickness and in health.**

## INTRODUCTION

Dynamic phenomena, such as rhythmic oscillations and waves, are ubiquitous in the nervous system and have been associated with cognition and motor behavior in both health and disease.[1–5] Oscillations in different frequency ranges have been associated with healthy brain function, including learning, memory, spatial navigation, attention, sleep, and motor behavior.[2,6–14] Wave-like phenomena have been associated with sensory processing[15] and working memory.[16]

Rhythmic neuronal activity—and transitions between rhythms—are also central phenomena in neurological disease.[5,17] Perhaps the most famous manifestations occur in epilepsy, which is characterized as a paroxysmal cerebral dysrhythmia (see, e.g., Ref. 18). More recently, similar phenomena have been proposed in other neurological disorders, including schizophrenia (see, e.g., Refs. 19–22), Alzheimer's disease (see, e.g., Ref. 23), Parkinson's disease (see, e.g., Refs. 24 and 25), and sleep disorders (see, e.g., Ref. 26).

A broad range of rhythms, and transitions between different rhythmic regimes, have been observed for these diseases. In epilepsy, the rhythms range from extremely fast (e.g., hundreds of Hertz[27–30]) to slow (e.g., a few Hertz[31,32]) and are bracketed by abrupt transitions at the onset and termination of seizure events.[33–36] Schizophrenia—characterized as a failure of cognitive integration—manifests in brain rhythms as altered beta and gamma band (15–70 Hz) synchronization.[22,37] In Alzheimer's disease, brain rhythms shift to power at lower frequencies, and the coherence of fast rhythms decreases.[23,38,39] In Parkinson's disease, pathologically exaggerated beta oscillations characterize the abnormal rhythms.[25,40–44] Transitions between dynamic regimes have been observed during sleep, and abnormal transitions have been associated with sleep disorders.[26,45–51] Finally, the slow waves of cortical spreading depression[52] underlie the reduction of excitability in neuronal tissue associated with migraine,[53,54] in particular, migraine with aura.[52]

On the three fronts of modeling, computation, and experiment, there have been a series of important recent advances, and many new avenues of research have emerged. These include: (1) new techniques to record high-density brain activity;[55–57] (2) theoretical advances and clinical application of deep brain stimulation methods;[58] (3) sophisticated biophysical models of rhythms and disease;[59,60] (4) novel optogenetic techniques that permit interrogation of neural circuits *in vivo*;[61] and, (5) increasingly-sophisticated data-analysis techniques.[62] The modeling and computational work—both deterministic and stochastic—have focused in part on reproducing experimental results, and on the investigation of the underlying biophysical and dynamical mechanisms, especially when experiments are not possible or very difficult to perform.

The dynamic transitions between healthy and diseased regimes may occur in many ways, including through alterations in the intrinsic properties of the participating neurons, changes in the network connectivity between neurons, modulation in the extracellular environment, or combinations of these and other mechanisms. Dynamic transitions may involve bifurcations or abrupt transitions, which do not involve local bifurcations but rather result from the multiplicity of time scales present in neurons and neuronal networks. The basic ingredients of dynamic transitions may exist at the individual cell level or, alternatively, may result from circuit interactions (i.e., at the network level). The complexity of these interactions spanning spatial and temporal scales often leads to counterintuitive results. Identifying the mechanisms that govern these transitions and where these transitions originate is one of the challenges of systems

[a)]Electronic mail: tasso@bu.edu
[b)]Electronic mail: mak@bu.edu
[c)]Electronic mail: horacio@njit.edu

 

neuroscience that may shed light on the cellular and network substrate of diseases of the nervous system.

## THIS FOCUS ISSUE

This focus issue brings together scientists from widely disparate fields, who collectively apply a variety of techniques to assess the features of rhythmic neuronal activity and the transitions between rhythms. Despite the different objects of study and terminologies, common underlying mechanisms and similarities exist. We think that both experimental and theoretical scientists will benefit from exploring the mechanisms and ideas described in the presented articles. Also, we hope that this focus issue will further foster cross-fertilization of techniques and ideas between different fields, and promote continued collaboration between these fields.

Rhythms and dynamical changes of states are of critical importance in the development of migraines, as has been known for over 70 years. Significant current research is devoted to determining the upstream mechanisms, including cortical spreading depression, responsible for the onset of various types of migraines. Miura *et al.*[63] present a thorough review of eight of the mathematical models that have been used to study the physiological and dynamical mechanisms underlying the development of cortical spreading depression, and its role in migraine with aura. These models incorporate ion diffusion, membrane currents and pumps, spatial buffering, osmosis, and cell swelling. The authors also identify some important open questions. Dahlem[64] develops a novel mathematical model of the migraine generator network that takes into account the chemical imbalances associated with the generation of migraine. This network model incorporates the trigeminal nerve, which innervates the cranial circulation, an associated network of brainstem nuclei, and parasympathetic vasomotor efferents. It also includes the important physiological process of cortical spreading depression, as a spatio-temporal perturbation of homeostasis. The author shows how this extended network model may be used to understand the nonlinear interactions between the key physiological processes and to develop new experiments involving noninvasive and minimally-invasive neuromodulation techniques.

The intrinsic properties of individual cells, and synaptic connections between cells, typically affect network behavior in complicated ways. Proddutur *et al.*[65] use network models of fast spiking basket cells to examine how biophysical changes occurring in inhibitory synaptic interactions in epileptic-like (pilocarpine-treated) animals modulate network activity in the gamma frequency range (30–100 Hz). These synaptic changes consist mostly in the enhancement of extra synaptic gamma-amino butyric acid (GABA) currents and the depolarization of the GABA reversal potential. Cabral *et al.*[66] examine the effects of alterations in the connectivity properties that underlie the development of schizophrenia. These authors examine whether changes in the functional connectivity necessarily result from changes in the structural connectivity or whether other dynamic mechanisms are involved. Rotstein[67] investigates the conditions under which the interaction between E1-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid excitation and the intrinsic properties of neurons leads to abrupt transitions between low and high firing frequencies. This has been associated to the phenomenon of hyperexcitability in medial entorhinal cortex layer II stellate cells in pilocarpine treated rats.

How synaptic connections support robust neuronal dynamics remains an active research area. Jalil *et al.*[68] consider a mathematical model of a central pattern generator, a small network of synaptically-coupled interneurons, governing various motor behaviors in animals. The authors develop a four-cell network of biophysically-motivated model neurons, and examine the observed phase-locked activity states using Poincare return maps. Through variations of the model parameters, the authors match the model dynamics with observed electrophysiology, and thereby investigate the minimal wiring of synaptic connections supporting robust neuronal dynamics observed in experimental studies.

While brain disease is often characterized by intervals of strongly correlated activity, healthy brain activity is typically irregular and neuronal activity uncorrelated. Terman *et al.*[69] use conductance-based models to describe a novel mechanism by which irregular neuronal activity emerges in a two-cell network reciprocally connected by synaptic inhibition.

In addition to the computational modeling of neuronal activity, a fundamental issue in understanding the brain's rhythmic dynamics is the development of statistical tools to assess the data associated to these rhythms and their changes. To this end, Deng *et al.*[70] develop a point process modeling framework to characterize rhythmic spiking dynamics, test for significant changes in those dynamics, and track the temporal evolution of those changes. The authors apply this approach to spike train data recorded from patients with Parkinson's disease.

In a related vein, it is important to understand the relationships between results obtained from computational models and experiments. In particular, when models are built to address specific experimental questions, but the subsequent construction of hypotheses and the testing of predictions involve details not included in the original models, techniques are required to modify the original models. Skinner and Ferguson[71] propose a multi-level integrative approach to address the cyclic interactions between modeling and experiments. Using whole hippocampus *in vitro* preparations as a prototypical system, they show how to incorporate experimental measurements made at the cellular- and network-levels into a computational model and simultaneously how model output can be used to control the experiments. Their proposed cycling dynamically in real-time between experiment and model may help with resolving the accuracy of the models and for hypothesis testing regarding the transitions observed between rhythms in healthy organisms and those observed in neurological disease.

More broadly, these latter two research topics fall in the broader category of "data assimilation," which is also playing an increasingly-important role in other fields of science and engineering, including Lagrangian mixing in geophysical fluid mechanics, complex turbulent flows, among many others.

The two final articles focus on complicated dynamic activities that emerge in single cells. Osinga and Tsaneva-

Atanasova[72] study spike-adding as a transient response in fast-slow models of transmembrane voltage. Based on the classical Hindmarsh-Rose system, their model consists of one slow and two fast variables with a polynomial vector field, and its underlying structure is similar to that of models of pyramidal CA1 and CA3 excitable cells. They demonstrate how an applied current can take the cell out of the globally-attracting quiescent state and lead to the formation of spikes. They also analyze how the number of spikes in the transient response is determined by the amplitude of the applied current and by the geometry of the system's slow manifold. Desroches *et al.*[73] analyze a novel mechanism that governs the abrupt transitions between two oscillatory modes: subthreshold oscillations (STOs) and bursting. A key ingredient is the slow passage through a spike-adding bifurcation. These results extend previous work on mixed-mode oscillatory behavior between sub- and supra-threshold activity, which has almost exclusively focused on abrupt transitions between STOs and spikes.

## ACKNOWLEDGMENTS

This work was partially supported by NINDS R01NS072023 (MAK), NSF DMS-0817241 (HGR), NSF DMS-1313861 (HGR), and NSF DMS-1109587 (TJK). M.A.K. holds a Career Award at the Scientific Interface from the Burroughs Wellcome Fund.

[1]G. Buzsáki and A. Draguhn, "Neuronal oscillations in cortical networks," Science **304**, 1926–1929 (2004).
[2]G. Buzsáki, *Rhythms of the Brain* (Oxford University Press, 2006).
[3]S. Coombes, "Waves, bumps, and patterns in neural field theories," Biol. Cybern. **93**, 91–108 (2005).
[4]G. B. Ermentrout and J. D. Cowan, "A mathematical theory of visual hallucination patterns," Biol. Cybern. **34**, 137–150 (1979).
[5]R. D. Traub and M. A. Whittington, *Cortical Oscillations in Health and Disease* (Oxford University Press, 2010).
[6]R. D. Traub and R. Miles, "Pyramidal cell-to-inhibitory cell spike transduction explicable by active dendritic conductances in inhibitory cell," J. Comput. Neurosci. **2**, 291–298 (1995).
[7]X. J. Wang, "Neurophysiological and computational principles of cortical rhythms in cognition," Physiol. Rev. **90**, 1195–1268 (2010).
[8]R. D. Traub, J. G. R. Jefferys, and M. A. Whittington, *Fast Oscillations in Cortical Circuits* (The MIT Press, 1999).
[9]J. O'Keefe and M. L. Recce, "Phase relationship between hippocampal place units and the EEG theta rhythm," Hippocampus **3**, 317–330 (1993).
[10]S. Raghavachari, J. J. Kahana, D. S. Rizzuto, J. B. Caplan, M. P. Kirschen, M. Bourgeois, J. R. Madsen, and J. E. Lisman, "Gating of human theta oscillations by a working memory task," J. Neurosci. **21**, 3175–3183 (2001).
[11]A. K. Engel, P. Fries, and W. Singer, "Dynamic predictions: Oscillations and synchrony in top-down processing," Nat. Rev. Neurosci. **2**, 704–716 (2001).
[12]W. Singer and C. Gray, "Visual feature integration and the temporal correlation hypothesis," Annu. Rev. Neurosci. **18**, 555–586 (1995).
[13]V. N. Murthy and E. E. Fetz, "Oscillatory activity in sensorimotor cortex of awake monkeys: Synchronization of local field potentials and relation to behavior," J. Neurophysiol. **76**, 3949–3967 (1996).
[14]J. Sanes and J. Donoghue, "Oscillations in local field potentials of the primate motor cortex during voluntary movement," Proc. Natl. Acad. Sci. U.S.A. **90**, 4470–4474 (1993).
[15]G. B. Ermentrout and D. Kleinfeld, "Traveling electrical waves in cortex: Insights from phase dynamics and speculation on a computational role," Neuron **29**, 33–44 (2001).
[16]D. Golomb and Y. Amitai, "Propagating neuronal discharges in neocortical slices: Computational and experimental study," J. Neurophysiol. **78**, 1199–1211 (1997).
[17]A. Schnitzler and J. Gross, "Normal and pathological oscillatory communication in the brain," Nat. Rev. Neurosci. **6**, 285–296 (2005).
[18]F. A. Gibbs, E. L. Gibbs, and W. G. Lennox, "Epilepsy: A paroxysmal cerebral dysrhythmia," Epilepsy behav. **3**, 395–401 (2002).
[19]K. M. Spencer, P. G. Nestor, M. A. Niznikiewicz, D. F. Salisbury, M. E. Shenton, and R. W. McCarley, "Abnormal neural synchrony in schizophrenia," J. Neurosci. **23**, 7407–7411 (2003).
[20]C. S. Herrmann and T. Demiralp, "Human EEG gamma oscillations in neuropsychiatric disorders," J. Clin. Neurophysiol. **116**, 2719–2733 (2005).
[21]A. K. Roopun, M. A. Kramer, L. M. Carracedo, M. Kaiser, C. H. Davies, R. D. Traub, N. J. Kopell, and M. A. Whittington, "Period concatenation underlies interaction between gamma and beta rhythms in neocortex," Front. Cell. Neurosci. **2**, 1–8 (2008).
[22]D. Vierling-Claassen, P. Siekmeier, S. Stufflebeam, and N. Kopell, "Modeling GABA alterations in schizophrenia: A link between impaired inhibition and altered gamma and beta range auditory entrainment," J. Neurophysiol. **99**, 2656–2671 (2008).
[23]J. Jeong, "EEG dynamics in patients with Alzheimer's disease," J. Clin. Neurophysiol. **115**, 1490–1505 (2004).
[24]J. L. W. Bosboom, D. Stoffers, C. J. Stam, B. W. van Dijk, J. Verbunt, H. W. Berendse, and E. C. Wolters, "Resting state oscillatory brain dynamics in Parkinson's disease: An MEG study," Clin. Neurophysiol. **117**, 2521–2531 (2006).
[25]R. J. Moran, N. Mallet, V. Litvak, R. J. Dolan, P. J. Magill, K. J. Friston, and P. Brown, "Alterations in brain connectivity underlying beta oscillations in parkinsonism," PLoS Comput. Biol. **7**, e1002124 (2011).
[26]Y. Dagan, "Circadian rhythms sleep disorders (CRSD)," Sleep Med. Rev. **6**, 45–54 (2002).
[27]E. Urrestarazu, R. Chander, F. Dubeau, and J. Gotman, "Interictal high-frequency oscillations (100-500 hz) in the intracerebral EEG of epileptic patients," Brain **130**, 2354–2366 (2007).
[28]R. D. Traub, "Fast oscillations and epilepsy," Epilepsy Curr. **3**, 77–79 (2003).
[29]G. Alarcon, C. D. Binnie, R. D. Elwes, and C. E. Polkey, "Power spectrum and intracranial EEG patterns at seizure onset in partial epilepsy," Electroencephalogr. Clin. Neurophysiol. **94**, 326–337 (1995).
[30]R. S. Fisher, W. R. Webber, R. P. Lesser, S. Arroyo, and S. Uematsu, "High-frequency EEG activity at the start of seizures," J. Clin. Neurophysiol. **9**, 441–448 (1992).
[31]R. S. Fisher and S. C. Schachter, "The postictal state: A neglected entity in the management of epilepsy," Epilepsy Behav. **1**, 52–59 (2000).
[32]S. J. Schiff, D. Colella, G. M. Jacyna, E. Hughes, J. W. Creekmore, A. Marshall, M. Bozek-Kuzmicki, G. Benke, W. D. Gaillard, J. Conry, and S. R. Weinstein, "Brain chirps: Spectrographic signatures of epileptic seizures," J. Clin. Neurophysiol. **111**, 953–958 (2000).
[33]F. da Silva, W. Blanes, S. Kalitzin, J. Parra, P. Suffczynski, and D. N. Velis, "Epilepsies as dynamical diseases of brain systems: Basic models of the transition between normal and epileptic activity," Epilepsia **44**, 72–83 (2003).
[34]L. Topolnik, M. Steriade, and I. Timofeev, "Partial cortical deafferentation promotes development of paroxysmal activity," Cereb. Cortex **13**, 883–893 (2003).
[35]K. Schindler, C. E. Elger, and K. Lehnertz, "Increasing synchronization may promote seizure termination: Evidence from status epilepticus," J. Clin. Neurophysiol. **118**, 1955–1968 (2007).
[36]M. A. Kramer, W. Truccolo, U. T. Eden, K. Q. Lepage, L. R. Hochberg, E. M. Eskandar, J. R. Madsen, J. W. Lee, A. Maheshwari, E. Halgren, C. J. Chu, and S. S. Cash, "Human seizures self-terminate across spatial scales via a critical transition," Proc. Natl. Acad. Sci. U.S.A. **109**, 21116–21121 (2012).
[37]K. M. Spencer, P. G. Nestor, R. Perlmutter, M. A. Niznikiewicz, M. C. Klump, M. Frumin, M. E. Shenton, and R. W. McCarley, "Neural synchrony indexes disordered perception and cognition in schizophrenia," Proc. Natl. Acad. Sci. U.S.A. **101**, 17288–17293 (2004).
[38]P. M. Rossini, C. Del Percio, P. Pasqualetti, E. Cassetta, G. Binetti, G. Dal Forno, F. Ferreri, G. Frisoni, P. Chiovenda, C. Miniussi, L. Parisi, M. Tombini, F. Vecchio, and C. Babiloni, "Conversion from mild cognitive impairment to Alzheimer's disease is predicted by sources and coherence of brain electroencephalography rhythms," Neuroscience **143**, 793–803 (2006).

[39]J. Dauwels, F. Vialatte, T. Musha, and A. Cichocki, "A comparative study of synchrony measures for the early diagnosis of Alzheimer's disease based on EEG," Neuroimage **49**, 668–693 (2010).
[40]D. Terman, J. E. Rubin, A. C. Yew, and C. J. Wilson, "Activity patterns in a model for the subthalamopallidal network of the basal ganglia," J. Neurosci. **22**, 2963–2976 (2002).
[41]M. D. Bevan, J. Mcgill, D. Terman, J. P. Bolam, and C. J. Wilson, "Move to the rhythm: oscillations in the subthalamic nucleus-external globus pallidus network," Trends Neurosci. **25**, 525–531 (2002).
[42]R. Courtemanche, N. Fujii, and A. M. Graybiel, "Synchronous, focally modulated beta-band oscillations characterize local field potential activity in the striatum of awake behaving monkeys," J. Neurosci. **23**, 11741–11752 (2003).
[43]A. Priori, G. Foffani, A. Pesenti, F. Tamma, A. M. Bianchi, M. Pellegrini, M. Locatelli, K. A. Moxon, and R. M. Villani, "Rhythm-specific pharmacological modulation of subthalamic activity in Parkinson's disease," Exp. Neurol. **189**, 369–379 (2004).
[44]M. M. McCarthy, S. Ching, M. A. Whittington, and N. Kopell, "Dynamical changes in neurological disease and anesthesia," Curr. Opin. Neurobiol. **22**, 693–703 (2012).
[45]M. M. McCarthy, C. Moore-Kochlacs, X. Gu, E. S. Boyden, X. Han, and N. Kopell, "Striatal origin of the pathologic beta oscillations in Parkinson's disease," Proc. Natl. Acad. Sci. U.S.A. **108**, 11620–11625 (2011).
[46]M. M. McCarthy, E. N. Brown, and N. J. Kopell, "Potential network mechanisms mediating electroencephalographic beta rhythm changes during propofol-induced paradoxical excitation," J. Neurosci. **28**, 13488–13504 (2008).
[47]J. Best, C. Diniz-Behn, G. R. Poe, and V. Booth, "Neuronal models for sleep-wake regulation and synaptic reorganization in the sleeping hippocampus," J. Biol. Rhythms **22**, 220–232 (2007).
[48]M. Steriade, D. A. McCormick, and T. J. Sejnowski, "Thalamocortical oscillations in the sleeping and aroused brain," Science **262**, 679–685 (1993).
[49]J. Lim and D. F. Dinges, "Sleep deprivation," Scholarpedia J. **2**, 2433 (2007).
[50]C. M. Morin and G. Belleville, "Insomnia," Scholarpedia J. **3**, 3314 (2008).
[51]S. Nishino, "Narcolepsy," Scholarpedia J. **2**, 2425 (2007).
[52]N. Hadjikhani, M. S. del Rio, O. Wu, W. D. Schwartz, D. Bakker, B. Fischi, K. K. Kwaong, F. M. Cutrer, B. R. Rosen, R. B. H. Tootell, A. G. Sorensen, and M. A. Moskowitz, "Mechanisms of migraine aura revealed by functional MRI in human visual cortex," Proc. Natl. Acad. Sci. U.S.A. **98**, 4687–4692 (2001).
[53]K. Lashley, "Patterns of cerebral integration indicated by scotomas migraine," Arch. Neurol. Psychiatr. **46**, 331–339 (1941).
[54]A. A. P. Leão, "Spreading depression of activity in the cerebral cortex," J. Neurophysiol. **7**, 359–390 (1944).
[55]S. Kodandaramaiah, G. Franzesi, B. Chow, E. Boyden, and C. Forest, "Automated whole-cell patch-clamp electrophysiology of neurons in vivo," Nat. Methods **9**, 585–587 (2012).
[56]J. Viventi, D.-H. Kim, L. Vigeland, E. S. Frechette, J. A. Blanco, Y.-S. Kim, A. E. Avrin, V. R. Tiruvadi, S.-W. Hwang, A. C. Vanleer, D. F. Wulsin, K. Davis, C. E. Gelber, L. Palmer, J. Van der Spiegel, J. Wu, J. Xiao, Y. Huang, D. Contreras, J. A. Rogers, and B. Litt, "Flexible, foldable, actively multiplexed, high-density electrode array for mapping brain activity in vivo," Nat. Neurosci. **14**, 1599–1605 (2011).
[57]B. M. Zamft, A. H. Marblestone, K. Kording, D. Schmidt, D. Martin-Alarcon, E. Tyo, E. S. Boyden, and G. Church, "Measuring cation dependent DNA polymerase fidelity landscapes by deep sequencing," PLoS ONE **7**, e43876 (2012).
[58]A. M. Lozano and N. Lipsman, "Probing and regulating dysfunctional circuits using deep brain stimulation," Neuron **77**, 406–424 (2013).
[59]R. D. Traub, D. Contreras, M. O. Cunningham, H. Murray, F. E. LeBeau, A. Roopun, A. Bibbig, W. B. Wilent, M. J. Higley, and M. A. Whittington, "Single-column thalamocortical network model exhibiting gamma oscillations, sleep spindles, and epileptogenic bursts," J. Neurophysiol. **93**, 2194–2232 (2005).
[60]M. W. Reimann, C. A. Anastassiou, R. Perin, S. Hill, H. Markram, and C. Koch, "A biophysically detailed model of neocortical local field potentials predicts the critical role of active membrane currents," Neuron **79**, 375–390 (2013).
[61]O. Yizhar, L. E. Fenno, T. J. Davidson, M. Mogri, and K. Deisseroth, "Optogenetics in neural systems," Neuron **71**, 9–34 (2011).
[62]E. N. Brown, R. E. Kaas, and P. P. Mitra, "Multiple neural spike train data analysis: State-of-the-art and future challenges," Nat. Neurosci. **7**, 456–461 (2004).
[63]R. M. Miura, H. Huang, and J. J. Wylie, "Mathematical approaches to modeling of cortical spreading depression," Chaos **23**, 046103 (2013).
[64]M. A. Dahlem, "Migraine generator network and spreading depression dynamics as neuromodulation targets in episodic migraine," Chaos **23**, 046101 (2013).
[65]A. Proddutur, J. Yu, F. S. Elgammal, and V. Santhakumar, "Seizure-induced alterations in fast-spiking basket cell gaba currents modulate frequency and coherence of gamma oscillation in network simulations," Chaos **23**, 046109 (2013).
[66]J. Cabral, H. M. Fernandes, T. Van Hartevelt, A. C. James, M. L. Kringelbach, and G. Deco, "Structural connectivity in schizophrenia and its impact on the dynamics of spontaneous functional networks," Chaos **23**, 046111 (2013).
[67]H. G. Rotstein, "Abrupt and gradual transitions between low and hyperexcited firing frequencies in neuronal models with fast synaptic excitation: A comparative study," Chaos **23**, 046104 (2013).
[68]S. Jalil, D. Allen, J. Youker, and A. Shilnikov, "Toward robust phase-locking in Melibe swim central pattern generator models," Chaos **23**, 046105 (2013).
[69]D. Terman, J. E. Rubin, and C. O. Diekman, "Irregular activity arises as a natural consequence of synaptic inhibition," Chaos **23**, 046110 (2013).
[70]X. Deng, E. N. Eskandar, and U. T. Eden, "A point process approach to identifying and tracking transitions in neural spiking dynamics in the subthalamic nucleus of Parkinson's patients," Chaos **23**, 046102 (2013).
[71]F. K. Skinner and K. A. Ferguson, "Modeling oscillatory dynamics in brain microcircuits as a way to help uncover neurological disease mechanisms: A proposal," Chaos **23**, 046108 (2013).
[72]H. Osinga and K. T. Tsaneva-Atanasova, "Geometric analysis of transient bursts," Chaos **23**, 046107 (2013).
[73]M. Desroches, T. J. Kaper, and M. Krupa, "Mixed-mode bursting oscillations: Dynamics created by a slow passage through spike-adding canard explosion in a square-wave burster," Chaos **23**, 046106 (2013).