

Rhythms of the Nervous System

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Nancy Kopell

Boston University, Charles River Campus

Rhythms of the nervous system have been linked to important behavioral and cognitive states, including attention, working memory, associative memory, bottom-up feature binding, object recognition, sensory motor integration, perception and language processing. Pathologies in the rhythms have been linked to schizophrenia and Alzheimer's disease. Although these rhythms have been detected both in vitro and in vivo, how they participate in cognition is still not understood. The general aim of this proposal is to make use of biophysical information about cells and synapses in modeling studies to understand the origin and mechanisms of coherence of the various rhythms displayed in nervous system. Some of this information exists from previous experiments. Other data will be gathered in experiments proposed here. The proposal focuses on three important rhythms: gamma (30-80 Hz), beta (12-30 Hz) and theta (4-11 Hz). A major goal of this work is to understand how the mechanisms that produce the rhythms influence the way the nervous system processes structured input. There are many experimental paradigms that produce different versions of rhythms with the same frequency range. These are analogues of different in vivo situations, and can have different reactions to pharmacological perturbations. In different versions of the same frequency rhythm, there are different synaptic conductances that are critical and there may be different classes of interneurons participating. The modeling aims to probe the roles of the different intrinsic and synaptic currents in producing the individual rhythms and the interactions among them, including nesting rhythms and the transitions among them that are associated with changes of behavioral state. Experiments, done in tandem, aim to reveal more details of the electrophysiological and pharmacological properties of the classes of interneurons, and roles of electrical synapses in producing rhythms. There will also be experiments aimed at teasing out different rhythms in different layers of the neocortex. Other experimental paradigms will probe effects of sensory stimuli, the importance of synaptic plasticity in the transformation among rhythms, and the conditions under which nesting of gamma and theta occur. We will also study, both experimentally and via modeling, separated networks that produce a coherent gamma rhythm, and networks distributed over space.

Publications

C Acker, N Kopell and J White, "Synchronization of strongly coupled excitatory neurons: relating network behavior to biophysics", *J. Comput. Neurosci.* (2003) 15: 71-90.

A Bibbig, RD Traub, and MA Whittington, "Characteristics of long-range synchronization of γ and β oscillations and the plasticity of excitatory and inhibitory synapses: a network model", *J. Neurophysiol.* (2002) 88: 1634-1654.

C. Borgers and N. Kopell, " Synchronization in network of excitatory and inhibitory neurons with sparse, random connectivity", *Neural Computation* 15 (2003) 509-538.

C Borgers and N Kopell, "Effects of noisy drive on rhythms in networks of excitatory and inhibitory neurons", *Neural Comput.* (2005), 17: 557-608.

MO Cunningham, CH Davies, EH Buhl, N Kopell, MA Whittington, "Gamma oscillations induced by kainate receptor activation in the entorhinal cortex in vitro", *J Neurosci.* (2003) 23(30): 9761-9.

MO Cunningham, DM Halliday, CH Davies, RD Traub, EH Buhl, and MA Whittington, "Coexistence of gamma and high-frequency oscillations in the medial entorhinal cortex in vitro" *J. Physiol.* (2004) 559: 347-353.

MO Cunningham, MA Whittington, A Bibbig, A Roopun, FEN LeBeau, A Vogt, H Monyer, EH Buhl, RD Traub, "A role for fast rhythmic bursting neurons in cortical gamma oscillations in vitro", *Proc. Natl. Acad. Sci.* (2004) 101: 7152-7157.

A Fisahn, A Contractor, RD Traub, EH Buhl, SF Heinemann, and CJ McBain, "Distinct roles for the kainate receptor subunits GluR5 and GluR6 in kainate-induced hippocampal gamma oscillations", *J. Neurosci.* (2004) 24: 9658-9668.

M Gillies, RD Traub, FEN LeBeau, CH Davies, T Gloveli, EH Buhl, and MA Whittington, "A model of atropine-resistant theta oscillations in hippocampal area CA1", *J. Physiol.* (2002) 543: 779-793.

T Gloveli, T Dugladze, S Saha, H Monyer, H Heinemann, RD Traub, MA Whittington, and EH Buhl, "Differential involvement of oriens/pyramidal interneurons in hippocampal network oscillations in vitro", *J. Physiol.* (2005), 562:131-47.

N Kopell, "Does it have to be so complicated?, Editorial Focus on "A single-column thalamocortical network model exhibiting gamma oscillations, spindles and epileptogenic bursts", *J. Neurophysiol.* (2005), 93: 1829-30.

N Kopell and GB Ermentrout, "Chemical and electrical synapses perform complementary roles in synchronization of neuronal networks", *Proc. Nat. Acad. Sci.* (2004) 101: 1542-1548.

S Kunec, M Hasselmo and N Kopell, "Encoding and retrieval in the CA3 region of the hippocampus: A model of theta phase separation", *J. Neurophysiol.* (2005), Feb. 23 (epub ahead of print).

FEN LeBeau, SK Towers, RD Traub, MA Whittington, and EH Buhl, "Fast network oscillations induced by potassium transients in the rat hippocampus in vitro", *J. Physiol.* (2002) 542: 167-179.

FEN LeBeau, RD Traub, H Monyer, MA Whittington, EH Buhl EH, "The role of electrical signaling via gap junctions in the generation of fast network oscillations", *Brain Res Bull.* (2003) 62(1): 3-13.

D McMillen and N Kopell, "Noise-stabilized synchronization in populations of model neurons", *J. Comput. Neurosci.* (2003) 15:143-57.

T Netoff, M Banks, A Dorval. C Acker, J Haas, N Kopell and J White, "Synchronization and phase locking in hybrid neuronal networks of the hippocampal formation", *J. Neurophysiol.* (2005), 93:1197-208.

M Olufsen, MA Whittington, M Camperi and N Kopell, "New functions for the gamma rhythm: population tuning and preprocessing", in *J. Comput. Neurosci.* (2003) 14: 35-54.

I Pais, SG Hormuzdi, H Monyer, R Traub, IC Wood, EH Buhl, MA Whittington, and FEN LeBeau, "Sharp wave-like activity in the hippocampus in vitro in mice lacking the gap junction protein connexin 36", *J. Neurophysiol* (2003). 89: 2046-2054.

D Pinto, S Jones, T Kaper and N Kopell, "Analysis of state-dependent transitions in frequency and long-distance coordination in a model oscillatory cortical circuit", *J. Comput. Neurosci.*, (2003) 15: 283- 98.

SK Towers, T Gloveli, RD Traub, JE Driver, D Engel, R Fradley, TW Rosahl, K Maubach, EH Buhl, and MA Whittington, "α5 subunit-containing GABAA receptors affect the dynamic range of hippocampal kainite-induced gamma frequency oscillations in vitro" *J. Physiol.* (2004) 559: 721-728.

SK Towers, FEN LeBeau, T Gloveli, RD Traub, MA Whittington, and EH Buhl, "Fast network oscillations in the rat dentate gyrus in vitro" *J. Neurophysiol.* (2002) 87: 1165-1168.

RD Traub, A Bibbig, FE LeBeau, EH Buhl, MA Whittington, "Cellular mechanisms of neuronal population oscillations in the hippocampus in vitro", *Ann. Rev Neurosci.* (2004) 27:247-278.

RD Traub, A Bibbig, FE LeBeau, MO Cunningham, MA Whittington, "Persistent gamma oscillations in superficial layers of rat auditory neocortex: experiment and model", *J Physiol.* (2004) [Epub ahead of print]

RD Traub, EH Buhl, T Gloveli, MA Whittington, "Fast rhythmic bursting can be induced in layer 2/3 cortical neurons by enhancing persistent Na⁺ conductance or by blocking BK channels", *J. Neurophysiol.*, (2003) 89: 909-921.

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Computational Neuroscience Workshop
Spring 2005 Principal Investigators' Meeting**

RD Traub, D Contreras, MO Cunningham, H Murray, FEN LeBeau, A Roopun, A Bibbig, WB Wilent, M Higley, and MA Whittington, "A single-column thalamocortical network model exhibiting gamma oscillations, sleep spindles and epileptogenic bursts" J. Neurophysiol., (2005), 93: 2194-232.

RD Traub, MO Cunningham, T Gloveli, FE LeBeau, A Bibbig, EH Buhl, MA Whittington, "GABA-enhanced collective behavior in neuronal axons underlies persistent gamma-frequency oscillations", Proc Natl Acad Sci , (2003) 100(19):11047-52.

RD Traub, I Pais, A Bibbig, FEN LeBeau, EH Buhl, SG Hormuzdi, H Monyer, MA Whittington, "Contrasting roles of axonal (pyramidal cell) and dendritic (interneuron) electrical coupling in the generation of gamma oscillations in the hippocampus in vitro", Proc. Natl.Acad. Sci. USA 100: (2003) 1370-1374.

MA Whittington, RD Traub, "Interneuron diversity series: inhibitory interneurons and network oscillations in vitro", Trends Neurosci. (2003), 12:676-82.

In Press:

O Jensen, P Goel, GB Ermentrout, M Pohja, R Hari and N Kopell, "On the human beta rhythm in the motor cortex: sources and modeling", Neuroimage.

HG Rotstein, MJ Gillies, CD Acker, JA White, EH Buhl, MA Whittington, and N Kopell, "Slow and fast inhibition and an h-current interact to create a theta rhythms in a model of CA1 interneuron network", J. Neurophysiol.

Submitted:

T Gloveli, T Dugladze, R Traub, N Kopell, U Heinemann, H Moneyr EH Buhl, MA Whittington, "Orthogonal arrangement of rhythm generating microcircuits in the hippocampus"