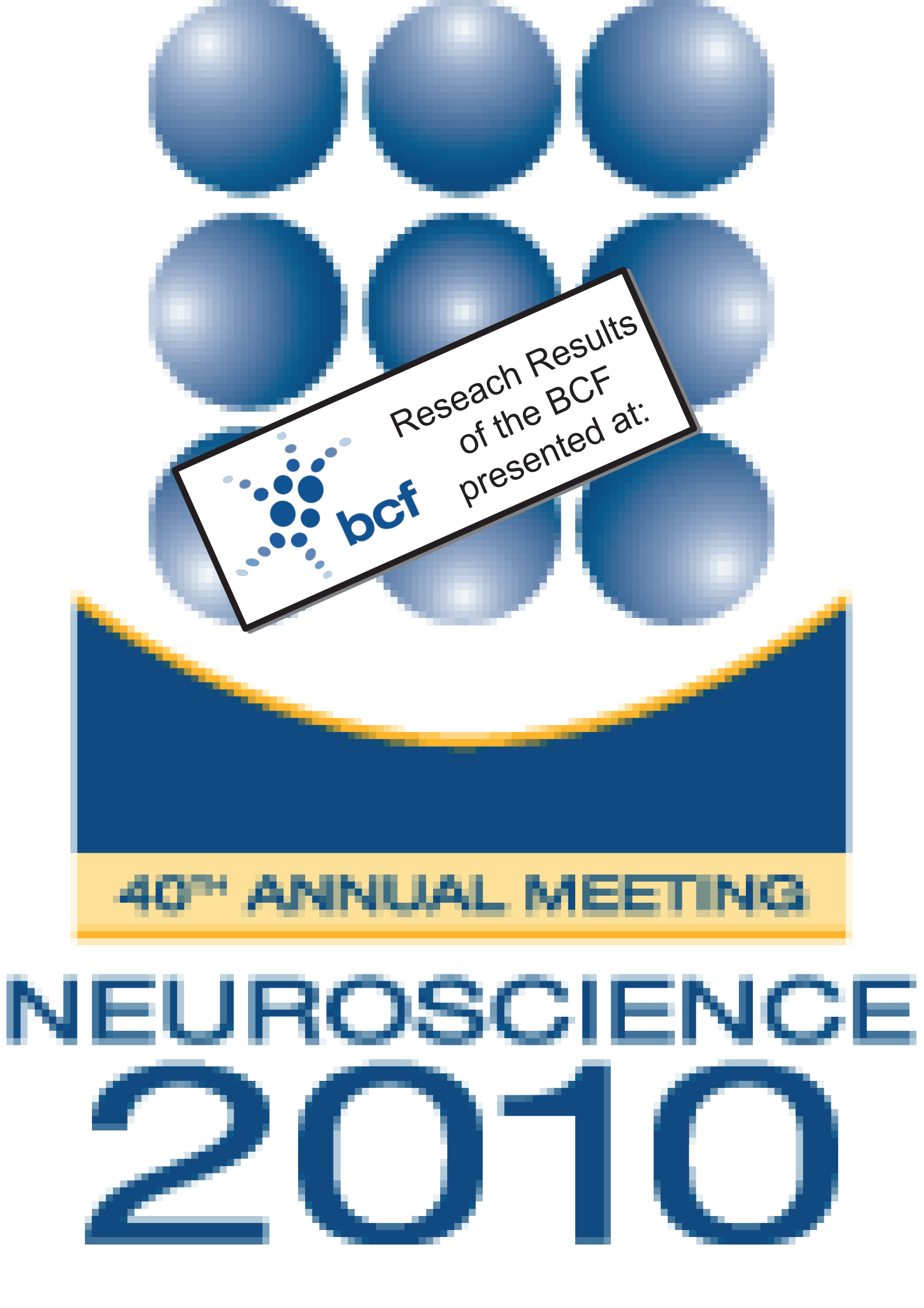
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Input resistance dependent switch in spiking dynamics of neocortical pyramidal cells

BOUCSEIN, J. AMMER, A. AERTSEN, J. BENDA

The temporal precision with which action potentials are generated strongly influences network activity dynamics and has far-reaching implications for coding schemes utilized in the brain. From their spiking dynamics, the majority of neurons can be assigned to one of two classes: fast spiking cells that precisely follow synaptic input and show properties of a resonator, and regular spiking cells which respond with much less temporal precision to incoming signals, but faithfully translate the integrated amount of input into a wide range of firing rates.

Here, we tested principal cells of the neocortex for their ability to respond precisely to slightly supra-threshold, transient inputs. In contrast to their counterparts in the hippocampus, neocortical pyramidal cells locked precisely to short current pulses, even though they are generally classified as regular spiking cells or integrators. Surprisingly, however, most neocorical pyramidal cells switched to temporally imprecise spiking dynamics when depolarized towards the spike threshold. Pharmacological blocking experiments and artificial changes of leak conductance via dynamic clamp revealed that this switch in spiking dynamics can be explained by a change in input resistance, rather than by properties of specific voltage gated channels. Simulations and phase-plane analysis of neuron models revealed that neocortical pyramidal cells are readily switched from resonators to integrators by membrane resistance changes well within the physiologically plausible range.

Taken together, our findings implicate that neocortical cells can operate in any one of two distinct working regimes, with qualitatively different spiking dynamics. A switch between these two regimes may occur through any slow modulatory mechanism that causes moderate changes in input resistance.

Consequences of delayed correlation between excitation and inhibition for signal propagation in spiking neural networks

J. KREMKOW, A. AERTSEN, A. KUMAR

Both ongoing and natural stimulus driven neuronal activity are dominated by transients. Selective gating of these transients is mandatory for proper brain function and may, in fact, form the basis of millisecond fast decision making and action selection.
Here we propose that neuronal networks may exploits timing differences between correlated excitation and inhibition (temporal gating) to control the propagation of spiking activity transients.
We studied the concept of temporal gating in a feedforward network (FFN, Fig. a) embedded in a large-scale recurrent cortical network model and stimulated the first group with different simple and complex stimuli. To assess the effectivity of temporal gating we systematically varied the latency (Δt) between direct excitation and feedforward inhibition (FFI) within the gate group of the FFN (Fig. a).
A state space analysis of the activity dynamics (Fig. b) indicates that altering the separatrix (blue line) by decreasing Δt (dotted gray line) can block the propagation of S1 type activity (gray line), which otherwise could propagate (green line). Likewise, propagation of activity S2 can be facilitated by increasing Δt (black line). Thus, small changes in Δt, within the range measured in vivo [1], can be used to selectively gate a host of neural signals composed of transients and tonic components.
As FFI is ubiquitous in the brain [2], temporal gating is likely to be a general mechanism which can affect network function and even influence animal behavior.

[1] Okun & Lampl, Nat Neurosci 2008 vol. 11(5) pp. 535-537
[2] Kremkow, Perrinet, Masson & Aertsen, J Comp Neurosci 2010 (in press)

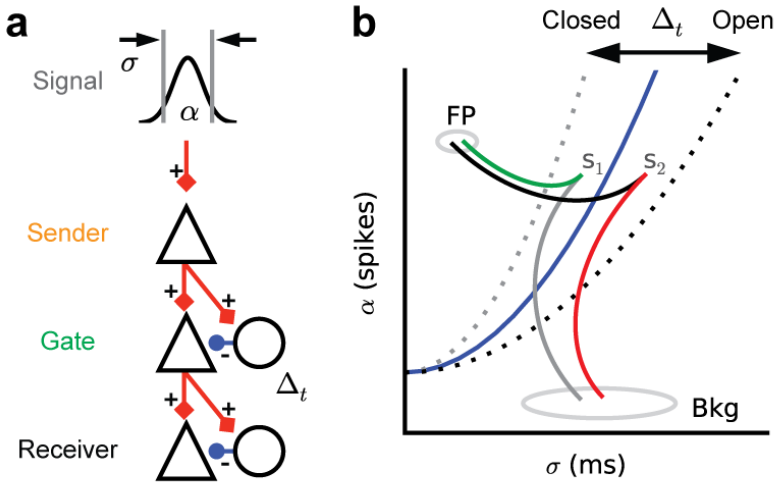

Figure. (a) Scheme of the FFN composed of sender, gate and receiver groups. (b) State space portrait of evolution of different types of neural activity in the FFN. The location of the separatrix (blue line) is controlled by Δt. The location of the activity relative to the separatrix determines whether it converges to the fixpoint (FP) or fades into the background (Bkg).

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Dual role of inhibition in unleashing and quenching oscillatory activity in the dopamine-depleted basal ganglia

A. KUMAR, A. AERTSEN, S. ROTTER, S. CARDANOBILE

Neural mechanisms underlying 4-30Hz oscillations and increased synchrony in the sub-thalamic nucleus (STN) and external globus pallidus external (GPe) in dopamine-depleted basal ganglia remain poorly understood. While the STN-GPe network has an inherent tendency to oscillate, it remains aperiodic and uncorrelated in the normal healthy state. Therefore, an understanding of what prevents this network from oscillating holds the key to understand STN-GPe oscillations in the dysfunctional state.

To this end we studied the dynamics of a large-scale spiking neuronal network model of STN-Gpe (see Fig). We found that increased striatal inhibition is a key parameter that may change aperiodic, uncorrelated activity of the STN-GPe network into periodic, correlated activity. Indeed, experiments have shown increased firing, not accompanied by correlations and oscillations, in the striatum of MPTP treated monkeys [1]. Next we explored what type of deep-brain-stimulation (DBS) should be most effective in quenching oscillations and synchrony. We found that DBS which inhibits the STN is most effective. However, even complete inhibition of only a fraction of STN neurons was not efficient in quenching the oscillations. By contrast, our model showed that weak, aperiodic (Poisson type) inhibitory input to all STN neurons was the most efficient in quenching STN-GPe oscillations. This type of stimulation is comparable to weak high-frequency stimulation of inhibition afferents in the STN [2].

In summary, we show that inhibition can both generate and prevent oscillations in the STN-GPe network. Increased inhibition to the GPe (from striatum) unleashes oscillations. By contrast, increased inhibition to the STN restrains the oscillatory modes of the STN-GPe network. Thus, we provide a unified explanation of the absence of oscillation in the normal state, of the origin of oscillations in dopamine-depleted state and of the efficacy of DBS in quenching oscillations.

1 Liang et al (2008) J Neurosci 28:7537-47.
2 Gradinaru et al (2009) Science 324:354-59.

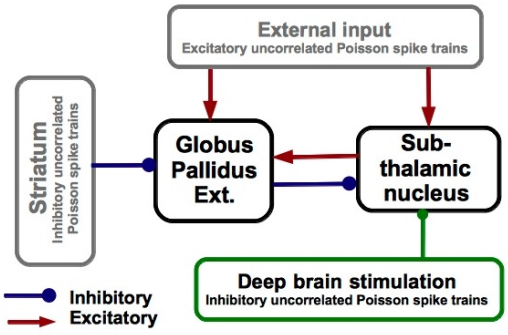

Figure: Schematic of STN-GPe network model

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Simulating neuronal networks at the brain scale on Blue Gene/P supercomputers with NEST

T. C. POTJANS, S. KUNKEL, A. MORRISON, H. E. PLESSER, M. DIESMANN

Neuronal networks exhibit a tremendously complex structure with a single neuron receiving on the order of 10,000 synapses (Braitenberg and Schuez, 1998). Over the last years, spiking network modeling focused on local cortical networks corresponding to one square millimeter of cortical surface and comprising some 100,000 neurons and 1 billion synapses. At this scale, the majority of the locally formed synapses can be represented and the activity dynamics and the functional input-output relations of the local cortical network can be investigated. However, the local connectivity accounts for only around 50% of all synapses (Stepanyants et al., 2009). In order to self-consistently represent the structure and activity of cortical networks, larger networks need to be considered that incorporate the missing long-range connections. Given that these connections originate in various cortical areas, a significant leap in network modeling from the local-network scale to the brain scale is required. Up to now, only few simulation technologies exist (e.g. Ananthanarayanan et al., 2009), but no community-wide available highly configurable simulation environment allows the investigation of networks at this scale.

NEST (Neural Simulation Tool) is a freely available (http://www.nest-initiative.org) simulation system for large networks of spiking neurons (Gewaltig and Diesmann, 2007). Local-network simulations with NEST scale up to hundreds of processes achieving close to real-time performance. Brain-scale simulations entail an increase in network and computer size by two or more orders of magnitude with the number of compute cores ultimately outnumbering the number of synapses per neuron, making connection infrastructure a dominant memory consumer.

We prepared NEST for brain-scale simulations by consequently reducing serial memory overheads for storing information about non-local neurons and network connectivity while sustaining the broad functionality of NEST. NEST scales excellently up to tens of thousands of processes on JUGENE, a petaflop Blue Gene/P system (http://www.fz-juelich.de/jsc/jugene). Our progress provides researchers with the opportunity to investigate the activity and behavior of brain-scale neural networks on leading-edge supercomputers.

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NEST 2: a parallel simulator for large scale neuronal simulations

M.-O. GEWALTIG, M. DIESMANN, J. M. EPPLER, M. HELIAS, A. MORRISON, *H. E. PLESSER

Progress in understanding brain function increasingly depends on simulation studies of large cortical networks. Simulating such networks poses several challenges: 1) The user interface must be clear and easy to understand and must allow users to quickly formulate even complex network models. 2) 10^9-10^12 connections must be stored and many spikes must be buffered until they are delivered to their target neurons. 3) Simulation results must be reproducible down to the level of membrane potentials and spike times. 4) Simulation results must be correct and testable.

In this contribution, we describe the second major release of the Neural Simulation Tool NEST [1] and how it addresses these issues. The Python based user interface PyNEST [2] eases the formulation and simulation of large-scale brain-like models. A hybrid parallel and distributed simulation kernel allows the simulation of large networks on architectures ranging from laptop computers to supercomputers [3]. An automated test-suite ensures that the NEST installation is working correctly [4].

Pre-releases of NEST 2 have already been used with great success at the European Advanced Courses in Computational Neuroscience in Arcachon and Freiburg, and the Okinawa Computational Neuroscience Courses 2008-2010.

NEST is developed by the NEST Initiative, a contract-based collaboration between HRI Europe and academic research institutes and is available under an open-source license. For more information and publications that used NEST, please visit www.nest-initiative.org.

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How do distinct neuronal subpopulations in the central amygdala shape the fear response? - A computational model

I. VLACHOS, S. CIOCCHI, C. HERRY, A. LÜTHI, A. AERTSEN, A. KUMAR

During a typical fear conditioning experiment a neutral stimulus is paired with a fearful one and after several trials the former acquires aversive properties. Such learning can be suppressed by repeated presentations of the initially neutral stimulus alone (fear extinction). The critical brain structures involved in these fear related processes are the lateral (LA), the basal (BA) and the central (CeA) nuclei of the amygdaloid complex. The CeA is a striatum-like structure containing almost exclusively GABAergic neurons [1]. It is known to be the major output nucleus of the amygdala and to control the fear response by its projections to the brainstem and hypothalamus.

To understand the interactions between the lateral (CeL) and medial (CeM) subdivisions of the CeA during fear conditioning and fear extinction, we built a spiking neuron network model of the CeA using the NEST simulator [2]. We modeled the CeA as a feedforward dis-inhibitory circuit, based on known anatomical and electrophysiological data. The input to the CeA was controlled by two distinct, fear and extinction specific neuronal subpopulations within the BA [3,4]. These inputs were crucial, as they altered the states of different subgroups within the CeA.

With our model we provide first insights about possible computations performed by the CeA. In particular, we show how CeL and CeM neurons might process fear and extinction related activity of the BA in order to shape the fear response.

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Functional compositionality realized in spiking neural networks by synfire chain competition

A. HANUSCHKIN, M. DIESMANN, A. MORRISON

It is commonly assumed that complex behaviour is constructed by combining primitives, a concept called compositionality. One theory how primitives can be stored in a network of spiking neurons is as feed-forward sub-networks, or synfire chains (SFC). Individual primitives can be represented by the stable synfire propagation along an individual SFC (Diesmann et al. 1999), and selection of primitives can be realized through competition between SFCs via synaptic inhibition (e.g. Chang et al. 2009). Here, we introduce two model examples that reproduce key behavioral findings in the generation of monkey scribbling and the production of birdsong, and derive experimental predictions.

The trajectory of free monkey scribbling is composed of parabolic movement primitives (Polyakov et al. 2009). We introduce a model of monkey scribbling, where each parabolic segment is encoded by an SFC (Hanuschkin et al. 2009); reliable switching is realized by unstructured mutual inhibition between chains. Unlike previous approaches (Chang et al. 2009), in the absence of synfire activity the network activity remains in the asynchronous irregular regime. The model generates random sequences of parabolic segments that fulfill the experimentally observed two-thirds power law (Lacquaniti et al. 1983), and predicts low frequency LFP oscillations.

The song syntax of the Bengalese finch can be reproduced by a network of competing SFCs (Jin 2009). We propose a reafferent model relying on auditory feedback (Hanuschkin et al. 2010). Each syllable is encoded by an SFC, motivated by the observed alignment of single neuron bursts to song onset (Hahnloser et al. 2002). We demonstrate that syntax may be coded by the auditory feedback provided to the HVC (high vocal center) via priming of the transition sites. If auditory feedback is suppressed, song syntax gradually deteriorates to random syllable sequences due to 'winner takes all' competition between chains. Restoration of hearing causes normal song syntax to be recovered, reproducing experimental findings (Woolley et al. 2002; Sakata et al. 2006). We characterize the changes to HVC activity and song syntax predicted by our model in response to specific feedback disturbances.

In conclusion, compositionality models based on SFC networks can reproduce experimentally observed behavior and enable us to make specific experimental predictions on the neural and behavior level.

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