Alexay Kozhevnikov

Statement of Research Interests

My research focuses on the mechanisms of vocal learning and motor sequence generation in oscine birds. The song control system of oscine birds constitutes a remarkable example of how neural circuits learn to generate complex patterns of behavior. Songbirds represent one of a few groups of animals shown to exhibit vocal learning (the other ones are humans, cetaceans and, possibly, bats), and the birds' song control system is by far the most accessible to study the mechanisms of vocal learning. The process of song learning shows some intriguing similarities to speech acquisition in human infants (Doupe and Kuhl, 1999), and understanding the neural mechanisms of song generation and learning in birds may help better understanding the mechanisms of human speech production and learning.

The young bird first listens to his tutor's song, then begins to imitate it. By using auditory feedback to compare his vocal output to a memorized "template" of his tutor's song, the bird adjusts and improves his vocal performance until the song is highly stereotyped and often indistinguishable from his father's song. The neural circuits involved in song production have been largely identified (Nottebohm et al., 1976). The song control system consists of about a dozen brain nuclei that form two major pathways: a motor pathway necessary for song production and a basal-ganglia circuit crucial for song learning (Fig. 1). The fortuitous combination of a remarkably stereotypical, learned behavior and anatomically tractable neural circuits underlying this behavior makes the songbird an attractive system for studies of vocal learning, sequence generation, and motor learning in general.

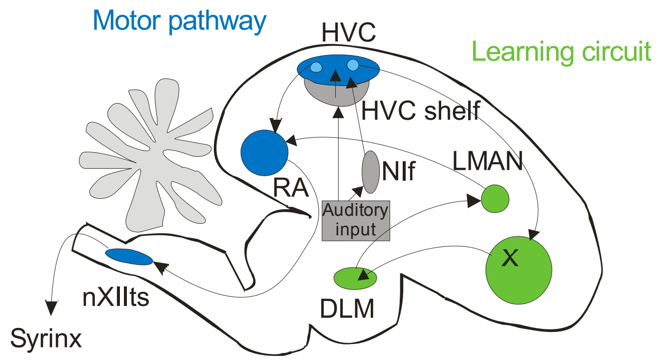

Fig. 1 - HVC provides inputs to two distinct pathways involved in song production and learning.

HVC projects to nucleus Robustus Archipallidum (RA). RA, in turn, projects to brain stem nucleus containing motoneurons innervating the syrinx. The anterior forebrain pathway (AFP) includes Area X, which is a homologue of mammalian basal ganglia, the thalamic nucleus DLM, and ultimately the Lateral Magnocellular Nucleus of the Nidopallium (LMAN).

Recent development of a

miniature motorized microdrive allows for recording from single neurons in a bird during singing (Fee and Leonardo, 2001, Fig. 2). This opens exciting horizons for studying neural activity in a functional neural circuit during the relevant behavior. Using the motorized microdrive, I have recorded from identified neurons in nucleus HVC and found that projection neurons in HVC burst sparsely during singing (Hahnloser et al., 2002; Kozhevnikov and Fee, 2004). Thus, HVC appears to transmit information about the timing in the premotor sequence. An unanswered question of much speculation is the mechanism of vocal learning. How does the bird evaluate the auditory feedback and how is the song-related auditory information processed to modify the motor program?

I intend to focus my future research on the studies of song learning and generation in a songbird with a particular emphasis on experiments in singing birds. These experiments are technically challenging and require both improvements in the currently available techniques and development of novel techniques for recording in behaving animals. I will work on perfecting the motorized microdrive technology in order to make it easier to use. I will also employ my experimental physics background to develop novel techniques for studies of neural activity. In the following sections, I detail my past experience and outline future directions of research.

Studies of the singing-related activity in the song control system

During my postdoctoral training with Michale Fee, I recorded neural activity from awake, singing birds using miniature motorized microdrives in both adult and juvenile zebra finches. We aimed to characterize singing-related activity in HVC in order to understand its role in premotor sequence generation.

Fig. 2 – Motorized microdrive implanted on a zebra finch.

I have recorded from antidromically identified neurons in nucleus HVC. Projection neurons in HVC burst sparsely during singing (Hahnloser et al., 2002; Kozhevnikov and Fee, 2004, Fig. 3), suggesting that HVC transmits information about the timing in the premotor sequence along premotor pathway and also to the basal ganglia circuit. Such sparse coding may speed up song learning: temporally sparse code enables correcting the motor sequence at any given time without affecting the motor output at any other times.

Until now, singing-related activity has been characterized in only a handful of nuclei in the song control system (HVC, RA, and, to a lesser degree, LMAN). Our knowledge about singing-related activity in brain areas upstream of HVC and in the basal-ganglia circuit is much more fragmented. Gaps in our knowledge about singing-related activity in the song control system need to be filled in order to understand the mechanisms of motor sequence generation. Using the motorized microdrive, I will record in the song control nuclei upstream from HVC in order to elucidate the mechanisms of sparse burst generation in HVC.

The currently hotly debated topic in the birdsong field is the mechanism of vocal learning. Songbirds rely on auditory feedback to learn their song. Deafening the bird or altering auditory feedback leads to song degradation. Lesion studies have shown that the anterior forebrain pathway (AFP) is crucial for song learning (Scharff and Nottebohm, 1991). Although a number of song learning mechanisms have been proposed (for a review, see (Margoliash, 2002), too little is known about neural activity in the song control system to discern among different possibilities.

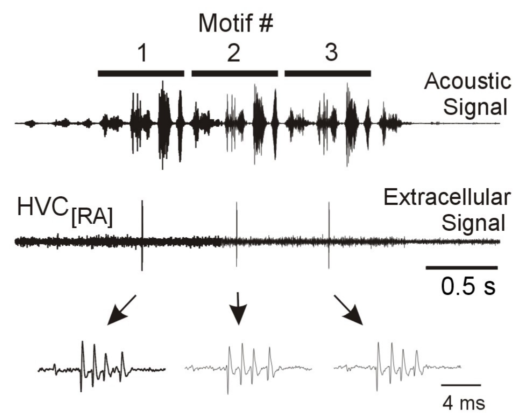

Fig. 3 Extracellular record of an RA-projecting HVC neuron during singing (middle), with the simultaneously recorded vocalization (top). The neuron generated a single burst during each of three song motif renditions. Bursts are highly stereotyped, as seen in the expanded timescale (bottom).

In order to find neural correlates of vocal error correction, it is necessary to both record neural activity of identified neurons during singing and to manipulate auditory feedback in order to dissect neural activity into auditory- and premotor-related components. I will record activity from key nuclei in the basal ganglia circuit while the bird is singing. Further, distortion of auditory feedback during singing will allow for analysis of error signals that may be involved in song evaluation. These experiments will address the questions about the neural mechanisms of singing-related vocal processing and vocal error correction.

Development of novel techniques for studying neural activity

Conducting experiments in singing birds is technically quite challenging. Improvements of currently available techniques and development of novel techniques are needed in order to answer fundamental questions about song generation and learning mechanisms.

One important avenue is making the motorized microdrive easier to use and less interfering with the animal's behavior. Ultimately, making the microdrive wireless and eliminating bird tethering would be a big step forward in recording techniques from freely behaving animals. Lightweight devices for wireless transmission of neural data have been demonstrated (for example, Nieder, 2000; Takeuchi and Shimoyama, 2004). I will develop a device for wireless neural data transmission by applying similar techniques and adapting them to fit the songbird. As a first step, such a device will be used for chronic multi-unit recordings in a songbird, for which motorized movement of electrodes is not necessary. Later on, in order to optimize the device for single-unit recordings, I plan to work on the development of a wireless device capable of motorized movement of electrodes, possibly using microfabrication and MEMS technology and collaborating with scientists specializing in MEMS and solid-state fabrication. During my Ph.D. work, I acquired a background in RF and microwave engineering and in micro- and nanofabrication which will be crucial for the work on wireless neural data acquisition system and development of the device for wireless electrode movement. These techniques will not be limited to the songbird - they can be applied to other neural systems and, possibly, to building neuroprosthetics and neuroregeneration devices.

Another direction is development of software and hardware for real-time acoustic processing, fast detection and recognition of the song syllables and generation of auditory feedback that is precisely time-locked to the bird's song. Generation of such acoustic feedback is necessary for the studies of auditory processing in the song control system. I have experience developing data acquisition and data processing systems using LabView and Matlab as well as electronics background necessary for building hardware for real-time acoustic analysis and feedback. Techniques for real-time acoustic processing can have applications for speech recognition and speech therapy.

In summary, I find the songbird to be an exciting system for studies of motor program generation and learning. Elucidating the mechanism behind song learning constitutes one of the most important avenues of research in this system. There are many pieces of the puzzle still missing, and many of the missing pieces relate to neural activity within the song generation and learning circuits during singing. Studying neural activity in behaving songbirds will bring us closer to understanding the fundamental mechanisms of vocal learning and, more generally, sensorimotor learning. Experiments in singing birds require development of novel experimental techniques, and I am going to utilize my experience in experimental physics in development of such techniques.

References

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Teaching Interests

Throughout my Ph.D. training at Yale University, I have been working as a teaching assistant to several undergraduate and graduate classes. I have also worked as an Acting Instructor for two classes: for the Undergraduate Physics Laboratory class and for the superconductivity section of the Graduate Laboratory Class. For over four years I was also a Math and Science Tutor in Trumbull College at Yale.

During the course of my education and training I have acquired background in diverse areas of physics and biological sciences. I believe that having been exposed to both physics and biology, I am a qualified candidate for teaching of the bioengineering curriculum, and I would like to participate in teaching core bioengineering courses. I consider teaching effort to be an important ingredient of an academic career and will be happy to contribute to the teaching curriculum of your department.