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Review

From elementary synaptic circuits to information processing in primary auditory cortex

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ABSTRACT

A key for understanding how information is processed in the cortex is to unravel the dauntingly complex cortical neural circuitry. Recent technical innovations, in particular the *in vivo* whole-cell voltage-clamp recording techniques, make it possible to directly dissect the excitatory and inhibitory inputs underlying an individual cortical neuron's processing function. This method provides an essential complement to conventional approaches, with which the transfer functions of the neural system are derived by correlating neuronal spike outputs to sensory inputs. Here, we intend to introduce a potentially systematic strategy for resolving the structure of functional synaptic circuits. As complex circuits can be built upon elementary modules, the primary focus of this strategy is to identify elementary synaptic circuits and determine how these circuit units contribute to specific processing functions. This review will summarize recent studies on functional synaptic circuits in the primary auditory cortex, comment on existing experimental techniques for *in vivo* circuitry studies, and provide a perspective on immediate future directions.

Contents

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1. Introduction

Sound is a time-varying signal, specified by frequency and intensity distribution in a time domain. How cortical neurons represent these physical features of sound has been intensively investigated (e.g. Aitkin, 1990; Merzenich and Schreiner, 1992; Woolsey, 1960; Goldstein and Knight, 1980; Brugge and Reale, 1985; Clarey et al., 1992; Winer, 1992; de Ribaupierre, 1997; Rouiller, 1997). Neuronal functional properties in auditory cortex such as frequency tuning, intensity tuning and tonotopic organization are highly preserved among different species (mouse: Stiebler et al., 1997; Linden et al., 2003; Bandyopadhyay et al., 2010; Rothschild et al., 2010; rat: Horikawa et al., 1988; Polley et al., 2007; cat: Merzenich et al., 1975; Reale and Imig, 1980; monkey: Imig et al., 1977; Merzenich and Brugge, 1973; Kaas and Hackett, 2000; human: Formisano et al., 2003; Humphries et al., 2010), suggesting that the underlying neural circuits in different species are organized under common principles. In this review, we will focus on the primary auditory cortex (A1) of rats to discuss our current understanding on the synaptic circuitry basis for auditory cortical processing.

2. A reductive approach to unraveling neural circuitry

2.1. Realistic neuronal circuits

Cortical neurons are well organized into ensembles or circuits to process auditory information (Schreiner et al., 2000; Douglas and Martin, 2004; Read et al., 2002; Winer and Lee, 2007). Since neurons communicate with each other through synaptic connections, the ensemble of synaptic strengths can define the connectivity within a neural circuit (Fig. 1A). However, the neural circuitry in the brain is dauntingly complex. The human brain is estimated to contain about 10^{11} neurons (Azevedo et al., 2009). Each neuron makes thousands to tens of thousands of synaptic connections with other neurons, which brings the total number of synaptic connections to a level of 10^{15}. In addition, the intricately intermingled axonal and dendritic processes of neurons make it extremely difficult to trace individual connections. The diagnostic method used in dissecting electronic circuits by removing specific components cannot be easily applied to neural circuits. Finally, the heterogeneity of neuronal populations further adds to the complexity of neural circuits. To overcome these obstacles, a well-defined systematic approach has to be developed to reduce the complexity of neural circuits, which will facilitate our understanding of their function.

2.2. Cortical columnar and laminar organization

A prominent feature of the neocortex is its columnar and laminar organization, which provides a platform for parallel and serial processing, respectively (Schreiner et al., 2000; Winer et al., 2005). Within a cortical column, neurons are thought to exhibit similar functional properties, e.g. they are tuned to similar tonal frequencies. As other sensory cortices, the auditory cortex is stratified into six layers (Fig. 1B). Among them, layer 4 is the major recipient of inputs from the auditory thalamus, while layer 6 is weakly innervated by the thalamus (Cruikshank et al., 2002; Kimura et al., 2003; Romanski and LeDoux, 1993; Winer and Lee, 2007; Barbour and

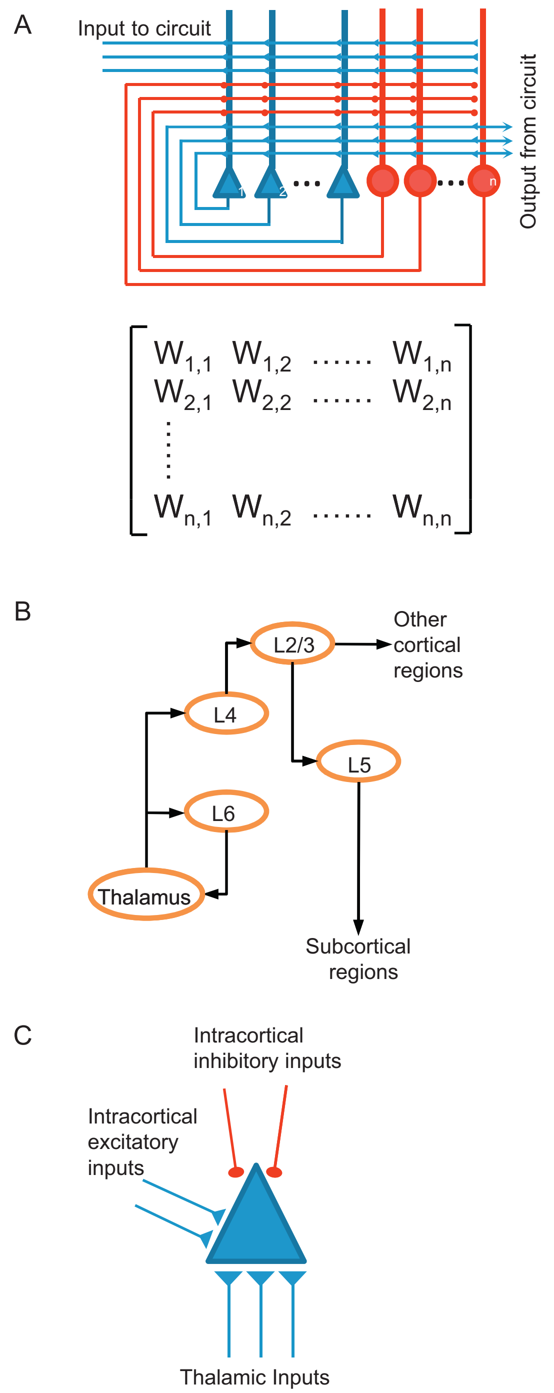

Fig. 1. . Schematic diagrams of cortical circuits. (A) Upper: a general neural network. Blue and triangle, principal cell; red and circle, inhibitory cell. Thin line, axon; thick line, dendrite; dot, synapse. Lower: the connectivity of this network can be described by a matrix with synaptic strength of synapses between each pair of neurons as individual elements. (B) Columnar and laminar processing in auditory cortex. Layer 4 (L4) and layer 6 (L6) are recipient layers of thalamic inputs. Layer 2/3 (L2/3) and layer 5 (L5) send outputs to other cortical regions and subcortical nuclei respectively. L6 sends corticothalamic feedback. (C) A simplified input circuit for a L4 neuron.