Synaptic noise in motor output cells of the cerebellum

Many of the cells that provide the motor output of a specific structure are among the biggest cells of the central nervous system. Consider for example the alpha-motorneurons of the spinal cord, the layer V cells of the motor cortex, the output cells of the red nucleus and the vestibular nuclei, the reticulospinal cells and the Purkinje cells of the cerebellar cortex. As very large cells, they typically have huge dendritic trees and sample tremendous amounts of synaptic input. This fact may have a fundamental impact on how motor commands can be assembled, since huge amounts of synaptic input could mean a low impact of the single input. In addition, to the extent that all or most of the input may be expected to be activated during motor performance, the ensuing shunting effect on the membrane may fundamentally alter the computational state of these neurons compared to the environment in which neuronal synaptic integration is usually studied, i.e. *in vitro*. Therefore, *in vivo* intracellular studies of motor output cells may come with many surprises in terms of our knowledge of how these cells work.

In the cerebellum, the final output neuron is located in the deep cerebellar nuclei (DCN). These neurons have very large dendritic trees, which receive a dominant part of their innervation from the Purkinje cells of the cerebellar cortex. DCN neurons are from *in vitro* studies known to feature a dramatic postinhibitory, excitatory rebound response, which have heavily influenced some theories of cerebellar function in motor control. However, *in vivo*, the Purkinje cells fire spontaneously around 40 Hz, a background frequency which is modulated but not dramatically changed during behaviour. The DCN cells may sample 1000's of Purkinje cell inputs, which impose a big change on DCN neuron function. In order to understand the function DCN cells *in vivo*, we characterized the effects of inhibitory Purkinje cell (PC) inputs in whole cell recordings in the decerebrated cat. Despite a continuous, high-frequency bombardment of PC inputs, we found that the baseline membrane potential was surprisingly flat. This could be explained by a summation of a multitude of tiny PC-IPSPs, creating heavy tonic inhibition or background synaptic noise. We also found that even strong modulation of PC output consistently failed to trigger rebound excitation. However, synchronous climbing fiber activation of all PC inputs, which are known to lead to the induction of plasticity processes in the cerebellar cortex, leads to a massive IPSP and a strong rebound excitation. Hence, whereas DCN inhibitory responses under normal cortical processing appear too weak to induce rebound, rebound can be evoked during situations triggering cerebellar plasticity. The high conductance state of these neurons in vivo essentially eliminates the influence of single synaptic inputs and limits the full-blown expression of intrinsic membrane responses. However, the synaptic noise puts the neuron in a dynamic state in which the intrinsic membrane responses can fulfill other roles.