Unlike many areas of the cerebral cortex, the cerebellum is a structure whose exact function is very difficult to define. It is usually considered as part of the motor system, but has also been suggested to participate in sensory and even cognitive tasks (Bower, 1997; Ito, 2000, 2008). In contrast to its complex function, its anatomy and connectivity are strikingly simple. Therefore our understanding of cerebellar function relies heavily on our understanding of its circuit physiology. Indeed in many cerebellar theories it is the cerebellar network properties that are the basis for the suggested function (Braitenberg & Atwood, 1958; Marr, 1969; Albus, 1971).

During the last decades, the physiological properties of almost all neurons in this system were systematically studied. However, recent evidence suggest that some basic notions in the classical view of cerebellar physiology are in need for revision.

Here I describe two sets of observations that challenge the classical view of cerebellar function, demonstrating the need for a conceptual revision. The first deals with the spatio-temporal organization of cerebellar cortical responses to mossy fiber input, and the second deals with the biophysics of Purkinje cells and the way they respond to granule cell input.
The neuronal circuitry that comprises the cerebellar cortex is shown in figure 1. The most striking feature of this anatomical structure is the orthogonal arrangement of the iso-planar Purkinje cell dendrites (black) and their most numerous input, the parallel fibers (blue). The intuitive view emerging from this unusual arrangement is that mossy fibers that activate the parallel fiber system will activate Purkinje cells sequentially, thus generating propagating beams of Purkinje cell activity with accurate time intervals.

To test the “beam hypothesis”, we measured the responses to both parallel, and mossy fiber stimulation in an isolated cerebellum of a Guinea pig, using voltage sensitive dye imaging. This preparation preserves the 3D structure of the cerebellum, thus enabling measurement of the spatio-temporal properties of cerebellar cortex responses. We found that stimulation of mossy fibers simultaneously activates Purkinje cells that are organized in a radial patch of the cerebellar cortex (Figure 2A). Propagating beams of activity could only be recorded when parallel fibers were directly stimulated on the surface of the cerebellar cortex (Figure 2B). It should be noted that direct stimulation of parallel fibers is highly artificial as their only input in natural conditions is the mossy fiber system.

In another project we characterized some of the applications of the recently described bi-stability of Purkinje cells. As most neurons, Purkinje cells are classically described as having a resting potential from which deviation occur when synaptic input arrives. When these deviations exceed a certain threshold an action potential is generated. Thus, the simple spike output of Purkinje cells is considered to reflect the input from granule cells. The finding of Purkinje cell bi-stability has changed this view dramatically (Loewenstein et al., 2005). Purkinje cells were shown to be quiescent during the hyperpolarized (DOWN) state, and intrinsically active during the depolarized (UP) state. First we showed that synaptic input can induce transitions between the states.
Excitatory input from granule cells can induce a transition from a DOWN to an UP state, while inhibitory input from the molecular layer interneurons can induce transitions from an UP to a DOWN state (Figure 3).

Next we measured the effect of bi-stability on the 
$\text{Ca}^{++}$
dynamics in Purkinje cells. Using the 
$\text{Ca}^{++}$
indicator Oregon Green BAPTA1 we demonstrated that during an UP state there is a constant influx of 
$\text{Ca}^{++}$
into the soma. We also demonstrated that the 
$\text{Ca}^{++}$
influx that is associated with a complex spike is state dependent. In the soma 
$\text{Ca}^{++}$
transients were larger in the UP state, while in the dendrites 
$\text{Ca}^{++}$
transients were larger in the DOWN state (Figure 4). These results should affect 
$\text{Ca}^{++}$
dependent plasticity processes, as well as firing properties of Purkinje cells via 
$\text{Ca}^{++}$
activated 
$\text{K}^{+}$
currents.

The results presented here necessitate a revision in our view of cerebellar physiology and function. We have recently published a model of cerebellar function that incorporates these data (Jacobson et al., 2008). We proposed that the cerebellar system serves the function of timing by generating temporal patterns that can correctly time actions. These timing signals are based on the subthreshold oscillations that characterize neurons in the inferior olivary nucleus - the source for the climbing fiber input to Purkinje cells. Purkinje cell bi-stability serves to control olivary oscillations, and thus dictate the specific temporal pattern to be generated. The granule cell input in our model is viewed as a contextual input that controls the states of Purkinje cells and thus can be viewed as a request for a specific temporal pattern.

![Figure 4: State dependence of complex spike driven 
$\text{Ca}^{++}$
transients. A. superimposed traces showing bi-stability. Blue denotes DOWN state and red denotes UP state. Traces were aligned on climbing fiber stimulation. B. The complex spikes are shown in an enlarged scale. C, D, and E, The 
$\text{Ca}^{++}$
transients in the soma, primary dendrites, and fine dendrites.](image)
References


