Role of the Olivo-cerebellar Complex in Motor Learning and Control

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Abstract:

How is the cerebellum capable of efficient motor learning and control despite very low firing of the inferior olive inputs, which are postulated to carry errors needed for learning and contribute to on-line motor control? Inferior olive neurons form the largest electrically coupled network in the adult human brain. Here, we discuss how intermediate coupling strengths can lead to chaotic resonance and increase information transmission of the error signal despite the very low inferior olive firing rate. This increased information transmission can then lead to more efficient learning than with weak or strong coupling. In addition, we argue that a dynamic modulation of inferior olive electrical coupling via the Purkinje cell-deep cerebellar neurons — inferior olive triangle could speed up learning and improve on-line control. Initially strong coupling would allow transmission of large errors to multiple functionally related Purkinje cells, resulting in fast but coarse learning as well as significant effects on deep cerebellar nucleus and on-line motor control. In the late phase of learning decreased coupling would allow de-synchronized IO firing, allowing high-fidelity transmission of error, resulting in slower but fine learning, and little on-line motor control effects.

Keywords: Cerebellum, motor learning, inferior olive, electrical coupling, Purkinje cells, deep cerebellar nucleus, complex spikes, synchrony.
1 Efficient cerebellar learning and control despite sporadic IO spiking

The Purkinje cell receives two distinct types of excitatory input. The climbing fibers, which are the terminal portions of the axons of the inferior olive neurons, form a powerful input to the Purkinje cells of the cerebellar cortex. Although each Purkinje cell is innervated by only a single climbing fiber, this one fiber makes hundreds of synapses onto its Purkinje cell, and is thus so powerful that it always triggers a response in the form of a “complex spike”. Complex spikes are relatively sporadic, however, with a mean firing rate of 1-2 spikes per second in behaving animals. Mossy fibers, via granule cells, provide the second excitatory input to Purkinje cells. In contrast to the climbing fiber input, Purkinje cells are innervated by at most a few synapses from each of the ~200,000 parallel fibers and ascending granule cell axons. These inputs help modulate the Purkinje cell “simple spike” firing rate over a range of 0 to ~200 Hz.

According to the motor learning theory of the cerebellum (Marr, 1969; Albus, 1971; Ito, 1982), these two classes of Purkinje cell inputs are those required by a supervised learning machine, i.e. a machine that learns to improve performance by minimizing errors. Specifically, Purkinje cells learn the weighting of granule cell inputs to minimize the error signals conveyed by climbing fibers (Gilbert and Thach, 1977; Kitazawa et al., 1998), via plasticity in Purkinje cell synapses (Ito, 2001). In this way, the cerebellum can learn inverse models to refine motor commands from desired states (Kawato and Gomi, 1992; Shidara et al., 1993; Schweighofer et al., 1998) or forward models to predict the consequences of movements from motor commands (Kawato et al.; Wolpert and Miall, 1996; Miall et al., 2007; Tseng et al., 2007), or both.

The cerebellum has many features that appear to match those found in effective and efficient artificial learning machines that can learn inverse or forward models from errors, such as the Cerebellar Model Articulation Controller (CMAC (Albus, 1975)). Like the cerebellum, these “supervised learning” machines recode multiple inputs into high dimensional patterns (the mossy fibers to granule projections), have modifiable synapses from the high dimension layer to the output (the granule cells to Purkinje cells synapses), and use a learning rule to minimize the errors in outputs (error signals carried via climbing fibers). Differences exist, however. One that is bound to affect the learning performance of the cerebellum negatively is that the firing rates of IO neurons are very low, with typically just a single or two spikes per movement. Such low firing rates significantly decrease the error transmission rate and thus the learning efficiency compared to an artificial machine that is capable of high frequency transmission of errors (as needed for instance to learn forward or inverse dynamics models for the control of fast arm movements).

To overcome this poor error transmission efficiency, the IO firing rate cannot simply be increased while maintaining good functioning of the cerebellum. One reason is that climbing fiber inputs are carried downstream by the Purkinje cells in the form of complex spikes, and increases in complex spike firing rates would decrease the signal to noise ratio in the Purkinje cell output, interfering with the information being conveyed by simple spikes (assuming simple spikes are the only relevant output of the Purkinje cell). In contrast, in artificial machines, because the error signal is only propagated to the level at which it is used to cause synaptic plasticity, and is not carried further downstream, it can carry any high frequency signals needed to minimize errors.

In addition to its role in motor learning, however, the olivo-cerebellar system may contribute
directly to the ongoing motor commands issued by the cerebellum. It has been known for a long time that abnormally high or low levels of complex spike activity can cause motor coordination problems and tremors (de Montigny and Lamarre, 1973; Llinás et al., 1975).

More convincing evidence for a direct contribution is the fact that changes in complex spike activity are associated with performance of well-learned movements. In particular, increases in complex spike synchrony levels were first demonstrated in relation to conditioned tongue licking movements (Welsh et al., 1995). Subsequent studies have confirmed that complex spike synchrony increases during motor acts (Mukamel et al., 2009; Ozden et al., 2012).

Moreover, several studies have recently shown that complex spikes cause a significant inhibition of DCN activity, and that the strength of this inhibition is correlated with the level of synchrony (Bengtsson et al., 2011; Blenkinsop and Lang, 2011; Lang and Blenkinsop, 2011).

How can the olivo-cerebellar system thus solve the problem of contributing both to on-line motor control and to motor learning given the constraint of low firing rate? Here, we propose that the ability of this system to modulate the level of synchronization is central to answering this question. We address this question as follows. First, we review the anatomical and physiological organization of the olivo-cerebellar system, with emphasis on the electrical coupling between inferior olive cells via gap junctions. Second, we discuss how electrical coupling in the IO network can create a chaotic resonance, which by increasing the information transmitted despite low firing, can allow and even speed up learning without causing unwanted motor acts. Third, we concentrate on the possible function of the closed triangle circuit formed by the IO-Purkinje cell- deep cerebellar nucleus (DCN), in dynamic modulation of the coupling strength, and suggest how this can modulate the transmission of errors at different stages of learning. Finally, in the discussion, we speculate how a partial dissociation of the two roles of the Purkinje cell- DCN -IO circuit in both learning and control could be made possible by their differential dependence on synchrony levels, which are controlled by feedback from the cerebellum.

2 Inferior olive network anatomy and physiology

IO neurons likely form the strongest gap-junction coupled neuronal network in the adult human brain (De Zeeuw et al., 1995; Condorelli et al., 1998; Belluardo et al., 2000). The gap junctions mainly occur between the dendritic spines of neighboring neurons within complex structures known as glomeruli (Llinás et al., 1974; Sotelo et al., 1974). Within these glomeruli, and in close proximity to the gap junctions, are chemical synapses: inhibitory GABAergic synapses from deep cerebellar nuclear neurons (for most IO regions) and excitatory synapses from a variety of brainstem and spinal cord regions (De Zeeuw et al., 1989; Nelson and Mognaini, 1989; Fredette and Mognaini, 1991). These chemical synapses are thought to control the effective coupling between specific pairs of IO neurons (Llinás et al., 1974; Lang et al., 1996; Lang, 2001; 2002; Leznik et al., 2002). In addition to intraglomerular synapses, excitatory and inhibitory synapses occur on the main dendrites and somata of IO neurons, and likely exert a more global control over the excitability of each IO neuron. Thus, the activity of IO neurons is modulated by excitatory inputs (such as those carrying errors), gap junctions between other IO neurons, and inhibitory inputs from cerebellar nuclear neurons (Lang, 2003).

The electrical coupling of IO neurons by the gap junctions allow these cells to fire synchronously, leading to synchronous complex spike activity (Llinás et al., 1974; Llinás and
The synchronized and oscillatory firing characteristics of the olivo-cerebellar system have been investigated in vivo primarily using multi-electrode recording of Purkinje cell complex spike activity. These studies have shown that despite the extensive gap junction coupling of IO neurons, the spatial distribution of synchronous complex spike activity is rather restricted, with synchronous activity occurring mainly among Purkinje cells located in narrow cortical bands that are oriented parallel to the transverse axis of the folium in which they are located (Sasaki et al., 1989; Lang et al., 1999). This banding pattern, however, is dynamic, and appears to reflect the control of effective IO coupling by chemical synapses. For example, intra-IO injection of picrotoxin (PIX), a GABA-A antagonist, induces higher firing rates, and more rhythmic, regular, and widespread synchronized complex spike activity, whereas block of glutamatergic activity produces lower firing rates and smaller, more discrete groups of Purkinje cells with synchronized activity (Lang et al., 1996; Lang, 2001; 2002).

That the cerebellar nuclei are a major afferent source to the IO suggests that the cerebellum can shape its own input. Indeed, the topography of the connections between the IO and cerebellum allow functionally related Purkinje cells, deep cerebellar nuclear cells, and IO cells to be grouped into "microcomplexes" or modules (Ito, 1984b; Schweighofer, 1998; Apps and Hawkes, 2009). That is, the connections between the IO and cerebellum are precisely aligned so that anatomically closed loops are formed between corresponding regions of the IO, cerebellar cortex and nuclei (Voogd and Bigaré, 1980; Sugihara and Shinoda, 2004; Apps and Hawkes, 2009; Sugihara et al., 2009; Ruigrok, 2010). Thus, the cerebellar cortex can be subdivided into numerous longitudinal zones, and Purkinje cells from any one zone will target a specific region of the cerebellar (or in a few cases, the vestibular) nuclei, exerting an inhibitory influence on those neurons. In turn, about 30-50% of the cerebellar nuclear neurons from each region send inhibitory projections to a particular IO region (De Zeeuw et al., 1989; Nelson and Mugnaini, 1989; Fredette and Mugnaini, 1991). Thus, a double-inhibitory feedback circuit from Purkinje cells to the inferior olive via the deep cerebellar nuclei exists, and enables each cerebellar cortical region to influence the activity of its own projection from the IO. Consistent with this anatomical arrangement, complex spike synchrony bands appear to follow this modular organization (Sugihara et al., 2007), and the simple spike activity of each cortical region, via this feedback circuit, can regulate its own complex spike synchrony levels (Marshall and Lang, 2009).

Thus, it seems clear that synchrony is likely to be a physiologically important parameter of olivo-cerebellar function. However, there is less consensus on what its function or functions may be. This lack of consensus is certainly due to several factors, but here we will focus on the problems related to motor learning and specifically how electrical coupling of IO neurons can allow learning processes to occur at complex spike firing rates and synchrony levels that do not interfere with on-line motor coordination.
Chaotic resonance enhances learning by increasing information transmission

3.1. Intermediate coupling leads to chaotic resonance and increase information transmission

Coupled IO cells do not necessarily synchronize their firing, and indeed, although the system has the capability of generating widespread synchrony, it normally does not do so. Several results suggest that in addition to underlying synchronous activity electrical coupling among IO neurons may allow other patterns of activity. In coupled oscillatory cell IO models, depending on coupling strength, the neurons can fire in phase or anti-phase (Schweighofer et al., 1999), and antiphase firing of IO neurons has, in fact, been observed experimentally under in vitro conditions (Llinás and Yarom, 1986). In networks of IO cells, coupling can induce chaos in subthreshold oscillations (Makarenko and Llinas, 1998). Moreover, in models of IO neurons a maximum chaotic regime for spiking activity was observed for intermediate levels of gap junction conductance (Schweighofer et al., 2004), whereas lower and higher coupling strengths induced more regular firing. Note that these results are robust to cell parameters and complexity and do not depend on the specificity of the cell model (Tokuda et al., 2010a). In our original chaotic IO model, we used a rather complicated compartment model (Schweighofer et al., 1999), and many physiological parameters were chosen rather arbitrarily, casting doubt on the generalizability of our results. In Tokuda et al. 2010, however, we showed that a simple model of IO neurons also exhibits chaotic resonance for intermediate coupling.

These models also indicate that such chaotic behavior can enhance information transfer in these neurons. Specifically, in the chaotic regime, the increase in information transmission in IO neurons is achieved via distributing-frequency components of the error inputs over the sporadic, irregular, and non-phase-locked spikes (Schweighofer et al., 2004). Desynchronization is indeed necessary for scattering the spike timings of each neuron to increase the time resolution of the population rate coding (Masuda and Aihara, 2002). Then the complete error signal can be reconstructed by spatio-temporal integration across Purkinje cells and IO cells within a microcomplex.

3.2. Increased information transmission leads to more efficient learning

We tested the prediction that efficient learning is realized with an intermediate coupling strength using a feedback error learning scheme to control a multi-joint arm (Tokuda et al., 2010a). In these simulations, the IO neurons provide error signals to an idealized model of the cerebellar cortex that learns, via feedback error learning (Kawato et al., 1987; Kawato and Gomi, 1992), to control a simplified model of the human arm in rapid reaching movements. As predicted, intermediate coupling levels, which allow chaotic resonance and increased information transfer of the error signals, accelerated motor learning for multi-joint arm models, despite the low IO firing rate (Tokuda et al., 2010a).

Experimental support for this role of electric coupling in cerebellar learning comes from mice mutants lacking electrotonic coupling between IO cells. These mice have no prominent general motor deficits, but they do exhibit deficits in learning-dependent motor tasks such as locomotor or eye-blink conditioning (Van Der Giessen et al., 2008). Similarly, humans with reduced or no IO coupling exhibit no general motor deficits but show motor learning impairments (van Essen et al., 2010).
4 Dynamic Modulation of IO electrical coupling during learning

4.1 Modulation of coupling via inhibition from nuclear cells

In recent simulation work, we investigated whether inhibitory modulation of electrical coupling is indeed a major determinant of the IO firing dynamics. We (Onizuka et al., 2012) aimed at reproducing the IO firing dynamics of the picrotoxin and carbenoxolone experimental studies (Lang, 2002; Blenkinsop and Lang, 2006). Here, the original model by Schweighofer et al. (1999) was modified by adding a model of the glomerulus comprised of dendritic spine necks that accommodate gap junctions and inhibitory synapses.

In this model, under simplifying assumptions, the effective coupling conductance \( g_{\text{effective}} \) between connected IO cells is computed from the gap junction conductance \( g_{\text{junction}} \) and the conductance of inhibitory synapses \( g_{\text{inhibitory}} \) and from the spine neck conductance \( g_{\text{spine}} \) as follows (Katori et al., 2010):

\[
g_{\text{effective}} = \frac{(g_{\text{junction}} \cdot g_{\text{spine}})}{(2 \cdot g_{\text{junction}} + g_{\text{spine}} + g_{\text{inhibitory}})}
\]

Thus, if the inhibitory synaptic conductance is large, the effective coupling conductance decreases because of shunting inhibition.

In Onizuka et al. (2012), we determined the gap junction conductance \( g_{\text{junction}} \) and the conductance of inhibitory synapses \( g_{\text{inhibitory}} \) that minimize the fitting error between simulated IO firing from the model and actual IO data in the three conditions of PIC, carbenoxolone (CBX), and control. We found that the inhibitory \( g_{\text{inhibitory}} \) and gap junction \( g_{\text{junction}} \) conductances roughly halved under the PIX and CBX conditions, respectively, supporting the role of a direct modulation of coupling strength via inhibitory inputs. Thus, because the inhibitory neurons controlling the strength of coupling between inferior olive cells are located in the deep cerebellar nuclei, the strength of effective coupling, and thus the level of chaotic behavior, presumably depends on the modulation of the deep cerebellar neurons via plastic processes in the cerebellar cortex and nuclei.

Experimental support for a functional role of the inhibition near gap junctions was previously reported (Shaikh et al., 2010). It was argued that oculopalatal tremor may be due to the removal of inhibition near the electronic gap junctions in the inferior olive. Interestingly, such patients with oculopalatal tremor show slower motor learning. This could be explained by the fact that only poorer error information can be transmitted when IO cells are strongly coupled and oscillate in-phase (Schweighofer et al., 2004).

4.2 Dynamic Modulation of IO electrical coupling via the Purkinje cell-deep cerebellar neurons – IO triangle

The Purkinje cell-DCN-IO triangle may act as a circuit to satisfy the motor learning requirements of the cerebellar learning system (Kawato et al., 2011). That is, in the early phase of motor learning, when motor acts are clumsy and far from the desired ones and the executed movement trajectories are perturbed, the motor plans and commands both need to be grossly modulated. Conversely, in the late phase of the learning, when the motor acts become skillful and the movement trajectories are smooth and close to the desired ones, the
motor plans and commands need only fine tuning.

The mosaic structures of the cerebellar system where the IO-Purkinje cell-CN loop is
topographically organized in “micro-complexes” (Ito, 1984a; Marshall and Lang, 2009) may
help such modulation of motor learning. The neural events to meet these motor learning
requirements would be massive climbing- and mossy- fiber inputs to the Purkinje cells in the
early phase of motor learning (leading to low DCN activity), and small mossy- and climbing-
fiber inputs in the late phase. In the early phase of learning, highly effective coupling across
the IO neurons due to low DCN activity would allow widespread synchronized IO firing in
response to error signals, which could potentially lead to synaptic weight changes in many
Purkinje cells. Cerebellar learning would be fast but coarse. Conversely, in the late phase of
learning, if IO neuronal firing becomes less synchronized, synaptic changes would occur
among more restricted Purkinje cell groups, which would allow more subtle modifications in
the final learning stages.

In Tokuda et al. (Tokuda et al., 2012), we conducted simulations to examine the advantage of
the adaptive coupling strength over fixed coupling strength during motor learning. IO
neurons transmitted error signals in a feedback-error learning scheme to learn the inverse
dynamics of a 2 D arm. In the adaptive coupling condition, the coupling strength between the
IO neurons was slowly decreased as learning proceeded. The error signals were large early in
learning because movements were mainly under feedback control, which was poor because of
large feedback delay and forced low gain. As learning of the internal inverse model
proceeded, the movements became straighter and the error signals became smaller. Since the
small error signals provided only a weak influence on the IO neurons, weak coupling was
needed to maintain the desynchronized neural activities. Results showed that adaptive
coupling led to a more efficient learning process than with a fixed coupling strength.

In addition to synchronized IO activity in the early phase of learning, learning can further be
accelerated by IO neurons firing in bursts (Eccles et al., 1966; Crill and Kennedy, 1967). The
nature of this burst varies with the state of the IO, and in addition, the spike bursts enhance
long-term depression in Purkinje cells proportionally to the number of spikes in the burst
(Mathy et al., 2009). Thus in response to large errors early in learning, both the spatial
characteristics of the network, with high number of IO cells discharging simultaneously, and
the temporal characteristic of each cell, with several complex spikes being transmitted, would
speed up initial learning.

5 Discussion

We have reviewed experimental and computer simulations studies suggesting that the
Purkinje cell- DCN -IO circuit may act as a self-regulating circuit that potentially has two
functional roles, one in motor learning and one in on-line motor control. That is, the control
of synchrony between IO complex spikes via modulation of electrical coupling could
enhance cerebellar learning and on-line motor control. Here, we first discuss one possible
challenge to this view: besides coupling, noise can also desynchronize neurons. We then
discuss how a partial dissociation of the two roles of the Purkinje cell- DCN -IO circuit in
both learning and control could be made possible by their differential dependence on inferior
olive neurons synchrony levels, which are controlled by feedback from the cerebellum.
5.1. Is coupling necessary to enhance learning – what about noise-induced desynchronization?

Noise is ubiquitous in the nervous system. In previous simulation work (Tokuda et al., 2010b), we showed that the effects of noise and coupling are similar in enhancing learning. Thus, is there an advantage of chaos-induced de-synchronization learning over noise-induced de-synchronization of IO neurons? We showed that coupling induced desynchronization is indeed preferable in three ways. First, from an energetics point of view, coupling generated chaos is a cheaper way of destroying the synchrony between cells, because noise in the nervous system is thought to arise mainly from synaptic noise (Hubbard et al., 1967). On the other hand, electrical coupling itself does not require energy expenditure. Second, although coupling could be modulated during learning by inhibitory inputs from the cerebellar nucleus, it is unclear how noise could be modulated during learning. In addition, we showed that noise and coupling are complementary and reinforce each other. In particular, the interplay between coupling and noise enlarged the parameter ranges of both coupling strength and noise intensity that provide efficient learning.

5.2. Control of climbing fiber synchrony for efficient motor control and learning

If the olivo-cerebellar system has two functional roles, then ideally it would best if the performance of each function was controlled independently. Modulation of the effective electrical coupling of IO neurons, and thereby the levels of complex spike synchrony, may allow at least semi-independent control. Specifically, we suggest that the olivo-cerebellar system contributes to motor commands primarily when it is operating in a relatively synchronized state. Synchronization, coupled with the convergence of the PC to DCN pathway, would allow complex spikes to be distinguished from ongoing simple spike activity, and therefore they could alter the activity of DCN neurons in distinct ways from the latter signals. Thus, synchronous complex discharges would make a contribution to outgoing cerebellar motor commands distinct from that made by simple spike activity.

Such high synchrony states may be due to increased effective coupling levels among IO cells via low activity in the subset of DCN neurons that project to the IO. In this case, simple spikes would, via their action on the DCN, help in determining whether or not olivo-cerebellar activity will contribute to the upcoming motor command. Alternatively, large, highly synchronized volleys in excitatory afferent IO pathways could lead to synchronous complex spikes, which could also trigger a motor response. Thus, the olivo-cerebellar system may switch into an on-line motor control state for causes internal or external with respect to the cerebellum.

In contrast, when complex spike activity is desynchronized it may not contribute significantly to motor commands, because in this state complex spikes may be less distinguishable from simple spike activity. It is possible that the burst nature of the complex spike may still allow the DCN neurons to distinguish them from simple spikes; however, the extent to which the secondary spikes of each complex spike are propagated is debated ((Ito and Simpson, 1971; Campbell and Hesslow, 1986; Khaliq and Raman, 2005; Monsivais et al., 2005)). Nevertheless, based simply on the firing rate superiority of simple spikes, it seems plausible that asynchronous complex spike activity would generally make a less significant direct contribution to shaping DCN activity.

Unlike their ability to influence the DCN cells, the ability of complex spikes to modulate
synaptic plasticity at a single cell level should not be affected by synchrony levels: processes
intrinsic to any one Purkinje cell caused by its firing a complex spike would be expected to
be independent of the number of other Purkinje cells generating complex spikes at the same
time. Thus, the potential for triggering synaptic plasticity exists regardless of synchrony
level. Moreover, as described earlier, there is more efficient transmission of certain aspects
of the error signals in the desynchronized state, which would facilitate the learning process in
the later stages of learning. Thus, by modulating the effective coupling among IO cells, the
DCN may control the characteristics of error signals sent to the cerebellum, once again acting
in a self-regulating manner.

The above implies that by limiting synchrony levels, feedback from the cerebellum would
enable the olivo-cerebellar system to allow modification of synaptic weights without causing
movements. However, the separation of function is not complete, because synchronous
complex spike activity could cause both generation of movements and synaptic plasticity.
This implies that each time complex spikes contribute to movement generation, the circuitry
generating the movement is altered, and thus the mapping of brain activity to movement is
modified. This is in some ways analogous to the proposal that the process of retrieval may
modify the memory trace itself (Sara, 2000). Indeed, it may partly explain the fact that even
in highly skilled athletes and musicians the performance of highly practiced motor acts still
retains some variability (e.g., the highest average season free throw percentage of an NBA
basketball player is only 90.4 %
http://www.nba.com/statistics/default_all_time_leaders/AllTimeLeadersFTPQuery.html?top)
Conversely, subtle modification of cerebellar circuits could underlie the efficacy of taking
practice swings before hitting in baseball or similar warm up routines.

Finally, it is worth considering, in the context of the motor learning process, cases where
truly high synchrony levels may occur. In the early phase of motor learning the motor plans
and commands both need to be grossly modulated. Motor acts are clumsy and far from the
desired ones and the executed movement trajectories are likely to be perturbed as a result.
Consistent with this hypothesis, in motor learning of arm reaching under novel force fields,
changes in motor commands are large for the first few trials, much more than the level of
trajectory errors (Franklin et al., 2008). Such perturbations, if they resulted in a synchronous
afferent volley to the IO, would be a way to elicit widespread synchronous complex spike
activity, and thus possibly elicit corrective movements, and perhaps more importantly to
allow large-scale changes in synaptic connectivity. As the learning process continues, the
motor acts become skillful and the movement trajectories become smooth and close to the
desired ones. In this case, there is less likely to be major perturbations with highly
synchronized complex spike activity resulting. Instead, motor plans and commands need
only fine-tuning and the olivo-cerebellar system may generate relatively desynchronized
activity that would drive such fine-tuning.

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References


