

New insights into olivo-cerebellar circuits for learning from a small training sample

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Artificial intelligence such as deep neural networks exhibited remarkable performance in simulated video games and ‘Go’. In contrast, most humanoid robots in the DARPA Robotics Challenge fell down to ground. The dramatic contrast in performance is mainly due to differences in the amount of training data, which is huge and small, respectively. Animals are not allowed with millions of the failed trials, which lead to injury and death. Humans fall only several thousand times before they balance and walk. We hypothesize that a unique closed-loop neural circuit formed by the Purkinje cells, the cerebellar deep nucleus and the inferior olive in and around the cerebellum and the highest density of gap junctions, which regulate synchronous activities of the inferior olive nucleus, are computational machinery for learning from a small sample. We discuss recent experimental and computational advances associated with this hypothesis.

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Current Opinion in Neurobiology 2017, 46:58–67

This review comes from a themed issue on **Computational neuroscience**

Edited by **Adrienne Fairhall** and **Christian Machens**

<http://dx.doi.org/10.1016/j.conb.2017.07.010>

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Introduction

Deep neural networks have been remarkably useful for image classification and phoneme recognition [1^{*}]. Combined with reinforcement learning algorithms, deep neural networks have outperformed human experts in simulated video games and the game ‘Go’ [2,3^{*}]. To achieve such successes, millions of images, hundreds of millions of phonemes, and tens of millions of records of game plays have been utilized as training data sets in the supervised learning or training trials in the reinforcement learning. Meanwhile, in the 2015 DARPA robotics challenge final

competition (2015 DARPA Robotics Challenge Finals; URL: <https://www.youtube.com/watch?v=dv9Wm20UrcU>), many humanoid robots fell while walking on sand, going up stairs, turning bulbs, or getting out of a car (DARPA Robotics Challenge; URL: <https://web.archive.org/web/20160428005028/http://www.darparoboticschallenge.org>). A small number of humanoids completed all the tasks, but they were extremely slower than humans. By age 5, human infants are able to execute all of the above tasks more quickly and reliably than humanoid robots developed by world premier researchers. What could be the reasons of this dramatic contrast between success and failure for simulated versus real-world tasks by artificial intelligence?

Challenges of motor learning in humanoid robots

In the simulated video games and ‘Go’, the world as a control target has relatively small degrees of freedom (DOF), it does not possess hidden variables, and its state transitions are simple with little noise. Thus, the computer simulations are exactly correct without errors. For the final reason, tens of millions of simulated games are generated by software players, and they can be used efficiently for DeepQ learning (a Q-learning algorithm of reinforcement learning combined with deep neural network learning) [2,3^{*}]. In contrast, a humanoid robot in the real world is a complicated nonlinear dynamical system with huge DOF. A humanoid with 100 joints, for instance, may have 300 DOF in total, assuming that each joint has 3 DOF (acceleration, velocity, position). If we digitize each DOF by only 10, the system has still 10 to the power of 300 possible states at least, while neglecting noise, hidden states, actuator dynamics, etc. On the other hand, ‘Go’ has only 3 (black, white, vacant) to the power of (19×19) possible states. Quantitative comparison yields that even a simple humanoid with 100 joints has the DOF 10 to the power of 128 times higher than those of ‘Go’, implying the curse of dimensionality in the learning of humanoids. If the DOF of a controlled system increases, the DOF of the corresponding learning system should be increased to deal with complexity of the control. Indeed, hidden states can be situated far above the measured sensory signals and far below the issued motor commands, causing a poor interface with the external world. Since many physical processes, including contact and friction, are difficult to model, quantitatively reliable simulations of humanoid robots in real-world environments are extremely difficult even if not impossible. Thus, reinforcement learning in humanoids designed to operate in the real world has been typically conducted

using real experimental trials. However, when humanoids fall, they are often damaged such that no further trials can be accumulated before painful, expensive and laborious repairs are made. In artificial intelligence, or more precisely, in neural networks learning and machine learning, it is well established that when a learning system with a fixed DOF n is utilized, approximately $10n$ training samples are necessary [4–6]. Note that the DOF n corresponds to the number of free parameters adjusted by the learning system, in most cases of neural networks, the number of neurons and the number of weight parameters. If it is possible to conduct tens of millions of learning trials, a large learning system, such as deep neural networks, can be utilized. For instance, under an extremely simplified condition such as 14 equivalent manipulators participating in a robotic grasping from monocular images, enough amount of training samples can be collected [7]. This is, however, a very rare situation for robotic learning, under which much fewer learning trials can be executed in general. If only 100 trials can be accumulated, only very simple learning systems with ten DOF should be utilized to avoid over-fitting problems in learning [8]. We postulate that these differences in the number of training samples and consequently resulting allowed DOF of the control systems readily explain the dramatic contrast between the success of the simulated learning and the failure of the real-world learning mentioned above.

Challenges of motor learning in animals and humans

Animal brains are confronted with sensorimotor problems that are much more challenging than those faced by humanoid robots. Animal bodies are flexible and possess an enormous number of muscles, sensors, and motor neurons. Neurons are slow-computing devices with a significant degree of noise. Thus, physical modeling of animal movements is very difficult, as there are many DOF, hidden variables, a high noise level, and a risk of injury or death in the case of failure. The human brain contains 10 to the 11th neurons and 10 to the 14th synapses. As a learning control system, it has enormous DOF. If we assume that the number of synapses correspond to the DOF of the learning system, and that a single reinforcement learning trial can be obtained within 100 seconds, then it follows that an animal brain will need 10 to the 15th training trials, and thus 10 to the 17th seconds for learning time to avoid over-fitting, which is about the age of the earth, and is much longer than an animal life. In contrast to this estimate, humans learn motor control very quickly. For example, humans can learn new dynamic environment within a few trials [9]. Human infants learn to walk after only several thousands falls [10*]. Even if we take into account other learning trials that were not counted as obvious falls in the infant playroom, the trial number should be much less than that of the deep neural networks. Moreover, some animals start to walk within few hours after birth [11]. Through computational neuroscience research of sensorimotor

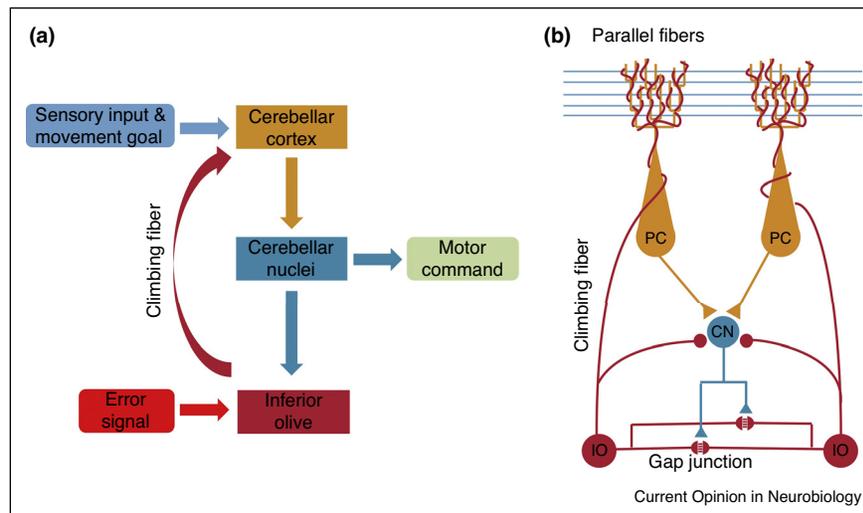
learning, we hope to understand a mystery to break the common sense in artificial intelligence: 10 to the 11th DOF learning system can learn to control an extremely complicated nonlinear dynamical system only after several thousands failures.

So far, several attempts have been made to elucidate the mechanism underlying such efficient motor learning. Kawato and Samejima [12] reviewed several computational schemes for enabling efficient reinforcement learning from small training samples. They include internal models [13,14], sparse estimation algorithms [15,16], multiple-paired forward and inverse models [17–19], and a hierarchical reinforcement learning algorithms [20,21]. Attention [22**], consciousness, metacognition [23], and episodic memory are important research topics in cognitive neuroscience, and have recently attracted the interests of artificial intelligence researchers with the hope that they could provide computational mechanisms to decrease high dimensionality of data in learning. They may play essential roles in constructing abstract concepts [24*], dimensions [25*], and attributes that are high-level representations necessary in the upper layers of hierarchical reinforcement learning. With respect to reducing the dimensionality of high-dimensional data, electrical synapses that transmit information via gap junctions are attractive elements in neuronal circuits because they tend to synchronize neurons and effectively reduce the DOF of the circuit.

Motor learning in the olivo-cerebellar system

Among various regions of the brain, we focus on the cerebellum as a potential region that may regulate the DOF of the neuronal circuit to realize an efficient learning. The cerebellum is important for motor control and motor learning and plays essential roles in fine adjustments of multi-joint movements such as reaching, walking, and balancing [26,27]. The inferior olivary (IO) nucleus sends climbing fiber inputs to Purkinje cell (PC), the only output of all motor coordination in the cerebellar cortex, and possesses the highest density of gap junctions in the mammalian brain (Figure 1A). As a good candidate for a neuronal system that plays a central role in motor learning and that may be useful in investigating the above-mentioned disparity between the large DOF of learning systems and conditions where only a small number of training trials are available, we focus on the olivo-cerebellar system [28,29,30,31**]. Of special interest is the network of IO neurons, which may control the DOF by adjusting their synchronous/asynchronous firing activities to provide an adaptive framework for the learning machinery [32**,33]. In the cerebellar motor learning, it has been known that the IO neurons transmit error signals to the PC [26,34,35], inducing plasticity at the parallel fiber-PC synapses [13,36] (Figure 1B). Recent investigations have also revealed multiple plasticity mechanisms [37–41] as well as evidence that parallel fiber-evoked

Figure 1



Neural computation and anatomy of the olivo-cerebellar circuit. **(a)** Schematic diagram of the neural computation in the cerebellum. Purkinje cell (PC) in the cerebellar cortex receives two types of inputs: (1) sensory input via many parallel fibers and (2) a teaching signal from the inferior olive (IO) via a sole climbing fiber. The cortex then sends motor commands to the peripheral system via cerebellar nuclei (CN), which inhibit IO neurons. **(b)** Circuit diagram of the PC-CN-IO triangle. When parallel fiber inputs and the climbing fiber input are conjointly activated at the PCs, plasticity is induced in the parallel fiber-PC synapses. The inhibitory signals from the CN are located very close to gap-junctions in the glomeruli, thus regulating the coupling strength between the IO neurons. Circles show excitatory synapses, and triangles inhibitory synapses. Horizontal lines show electrical gap junctions.

simple spikes to PCs contribute to cerebellum-dependent learning to some extent [42,43^{*}]. One dominant view over the last several decades suggests that complex spikes transmitted through the climbing fibers provide instructive signals to the PCs to drive learning [44,45^{*}].

To examine the functions of the IO, computational modeling has been one of the promising driving forces [46]. As the carrier of the teaching signals, the IO has been modeled to provide the climbing fiber inputs in the simulation studies of the cerebellar learning [13,47–51,52^{*},53]. To explore the IO dynamics in detail, a class of simplified conductance-based models has been developed to reproduce experimental observation of sub-threshold oscillations [54–58]. Further details of the electrophysiological properties of the IO neurons have been described by multiple compartment models [59], which have been applied to elucidate experimental observation of the sub-threshold activities [60], to examine the capability of their information transmission [61^{**}], and to estimate conductance levels of the IO network from experimental data [62^{*},63^{**}]. Owing to the advanced experimental methods as well as the rapid growth in computer power, the computational models have been nowadays utilized for quantitative understanding of the experimentally measured IO dynamics and furthermore for testing hypotheses regarding IO functions. Here, we review recent advances in the computational modeling of the olivo-cerebellar system.

Synchronized neuronal firings for regulating degrees of freedom and temporal resolution

One of the long-term questions on the role of the IO in the cerebellar learning has been the reason for the low firing rate of the IO neurons with at most a few spikes per second (typically one or two spikes per movement). This presents a severe limitation for the IO neuron in terms of precisely transmitting detailed error signals with a high temporal resolution. To resolve this issue, desynchronized firings of the IO neurons, which can be regulated by the electrical coupling, may play a crucial role [61^{**}]. The central point is that, as far as the IO neurons are active in a synchronous manner, an ensemble of IO neurons behaves as a single neuron, which does not improve the limited capability of the error transmission. However, if the IO neurons behave in an asynchronous manner, the spike timings of individual neurons will be scattered, and this will increase the temporal resolution of the population coding of the error signal.

Numerous studies have suggested that electrical coupling regulates the level of synchrony between IO neurons and thus plays a central role in the cerebellar learning [60,64–68]. On the basis of the compartment model [59], a network of IO neurons coupled by gap-junctions was constructed. The simulation study revealed that, with an intermediate strength of the coupling, irregular or even chaotic firings of the IO neurons were induced. The

chaotic dynamics effectively desynchronized the firing activities of the IO neurons and consequently improved the information transmission capability. The phenomena have been termed as ‘chaotic resonance’ [61**]. The chaotic resonance has been also reproduced in a large network of conductance-based IO models [69]. The feedback-error learning was further implemented in a network of IO neuron models, and electrical coupling was found to enhance the cerebellar learning of multi-joint arm control [70]. In these studies, the intermediate strength of the coupling, which optimized the error transmission as well as the learning procedure, corresponded to the coupling strength that provided the largest value of the first positive Lyapunov exponent, implying that chaotic dynamics was effective for desynchronizing the firing activities of the IO neurons.

To characterize the quantitative feature of the IO network dynamics in cerebellar learning, Onizuka et al. [62*] and Hoang et al. [63**] estimated the strength of the electric coupling from experimentally observed spike train data (Box 1). As a computational model of the IO network, the two-compartment model developed by Schweighofer et al. [59] was modified by adding spine compartments that form gap-junction connections to neighboring neurons (Figure 2A,B). Two types of conductance were estimated, namely, gap-junction conductance and inhibitory synaptic conductance, that are

Box 1 Estimating model parameters from experimental spike data

To date, various techniques have been developed to estimate the parameters of computational models from neuronal spike train data [97]. A simple yet popular approach is to define an error function, which measures the distance between the spike trains and the simulated data, and then to seek for the model parameters by minimizing the error using a variety of optimization techniques [56,97,98]. Nonlinear filtering and observer-based methods have been also developed [99–102]. In practical situations, however, these approaches are severely limited due to: (1) non-stationarity of the measured data and (2) huge difference in system complexity, i.e. hierarchy, granularity, and degrees-of-freedom, between the model and the brain. To address such mismatch problem, Onizuka et al. [62*] developed a segment-wise approach to minimize the modeling errors. The key assumption is that, in the non-stationary data, the parameter values may change from one time-segment to another. Accordingly, the spike data are divided into short time-segments, within which the data can be considered stationary. Multiple features, e.g., firing frequency, local variance, auto-correlograms and cross-correlograms were incorporated into the error function to bridge the mismatch between the model and the data [62*]. Hoang et al. [63**] further introduced a hierarchical Bayes framework, composed of two estimation steps, to the segment-wise approach. In the first step, the conductance parameters were estimated for each time-segment of the spike data by the Bayesian inference. In the second step, parameter values, which were separately estimated for individual time-segments in individual neurons, were merged into single ones using a neuronal constraint. This segment-wise approach relaxes the condition of the parameter search and, as a result, enables the model to capture complicated features of the experimental data.

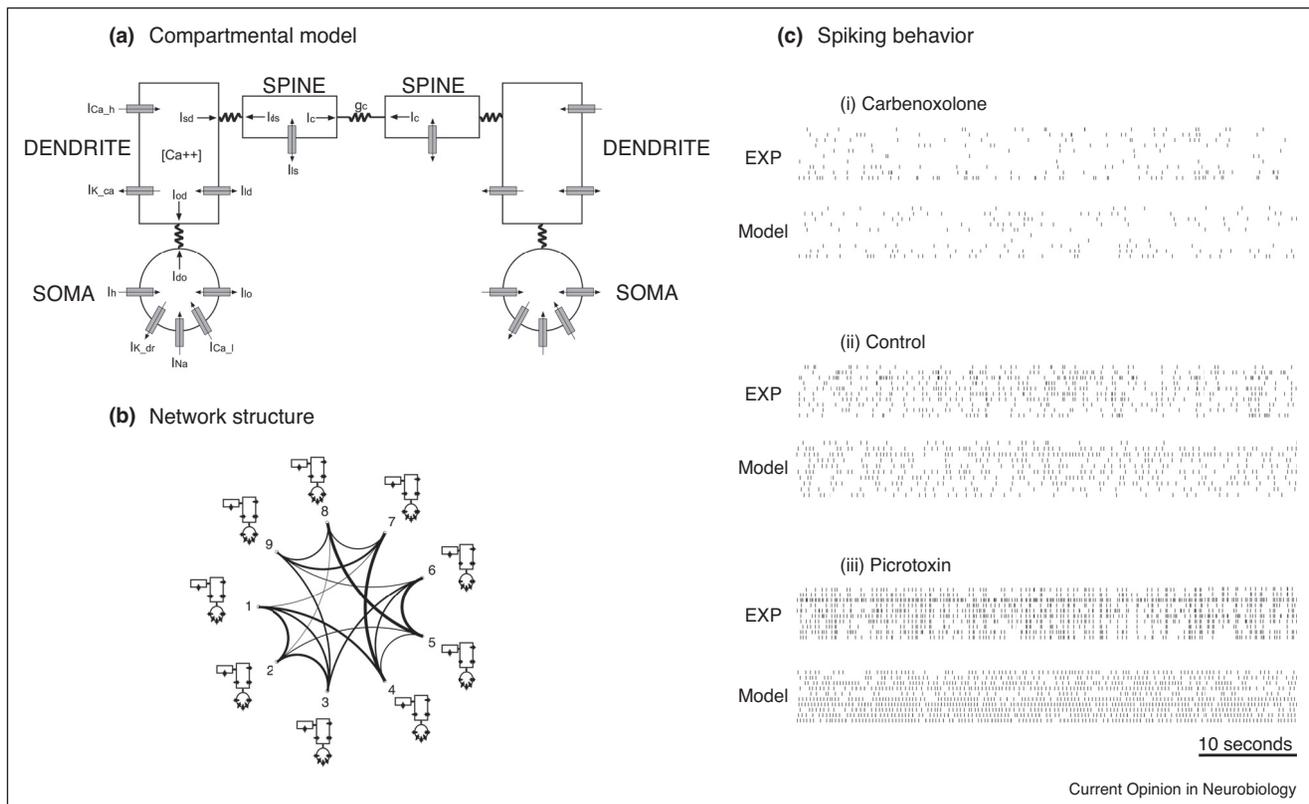
considered as the main regulators of the electrical coupling between the IO neurons [71–73]. Comparison of two pharmacological conditions (carbenoxolone, picrotoxin) with their control revealed a basic tendency that the control condition with an intermediate strength of the coupling gives rise to low level of neural synchrony and high level of complexity (Figure 2C) [74]. This implies that desynchronized chaotic firings are indeed present in the *in vivo* experiment (N. Schweighofer, personal communications).

Adaptive coupling during motor learning

The chaotic resonance hypothesis brings light to the question: what is the possible underlying mechanism that tunes the coupling strength between the IO neurons to an optimal level? The answer may come from the ‘micro-zone’ structure in the cerebellum, which is characterized by particular spatiotemporal patterns of cellular activities that occur in synchrony [75–79]. Anatomically, the micro-complex combines the PCs that discharge inhibitory inputs to the DCN, which in turn has inhibitory synapses on the dendritic spines that connect the IO neurons (Figure 1B). Recent studies have shown that the PC-DCN-IO triangle forms a closed loop of neural computation, which provides various functional modules in the cerebellum [80*,81*,82*]. In particular, highly synchronous complex spikes significantly decrease firing activity in the DCN [83*]. The inhibitory synapses from the DCN decrease the strength of the electrical coupling and consequently lower synchronous activities of the IO neurons [84*,85*,86,87]. The level of the IO synchrony determines the complex spike waveform injected to the PC [88*], which regulates synaptic plasticity in the cerebellar learning [89*].

Combining these pieces of evidence, Kawato et al. [32**] and Schweighofer et al. [33] proposed a scheme of adaptive electrical coupling of the IO network within the micro-zone. The cerebellar learning process is roughly described in two phases (Figure 3). In the early phase of the learning, the motor commands are strongly disturbed and do not closely resemble the desired commands. Then the amplitude of error signals is large, and the synaptic inputs to IO neurons are large. This leads to higher firing frequency of the IO and PCs. The PCs, which are in this way strongly modulated by motor commands, excessive sensory inputs, and large error signals, suppress the inhibitory effect of the DCN on the IO coupling. Thus the IO neurons are initially strongly coupled. Because of the limited temporal resolution of the synchronized neurons, the IO network may respond only to low-frequency component of the error signals, which may convey information on the gross feature of the motor behavior. Widespread synchrony among the IO neurons potentially leads to massive synaptic changes in the parallel fiber, resulting in a fast but crude learning in the cerebellar cortex. Here, the DOF in the cerebellum are low because the neurons

Figure 2

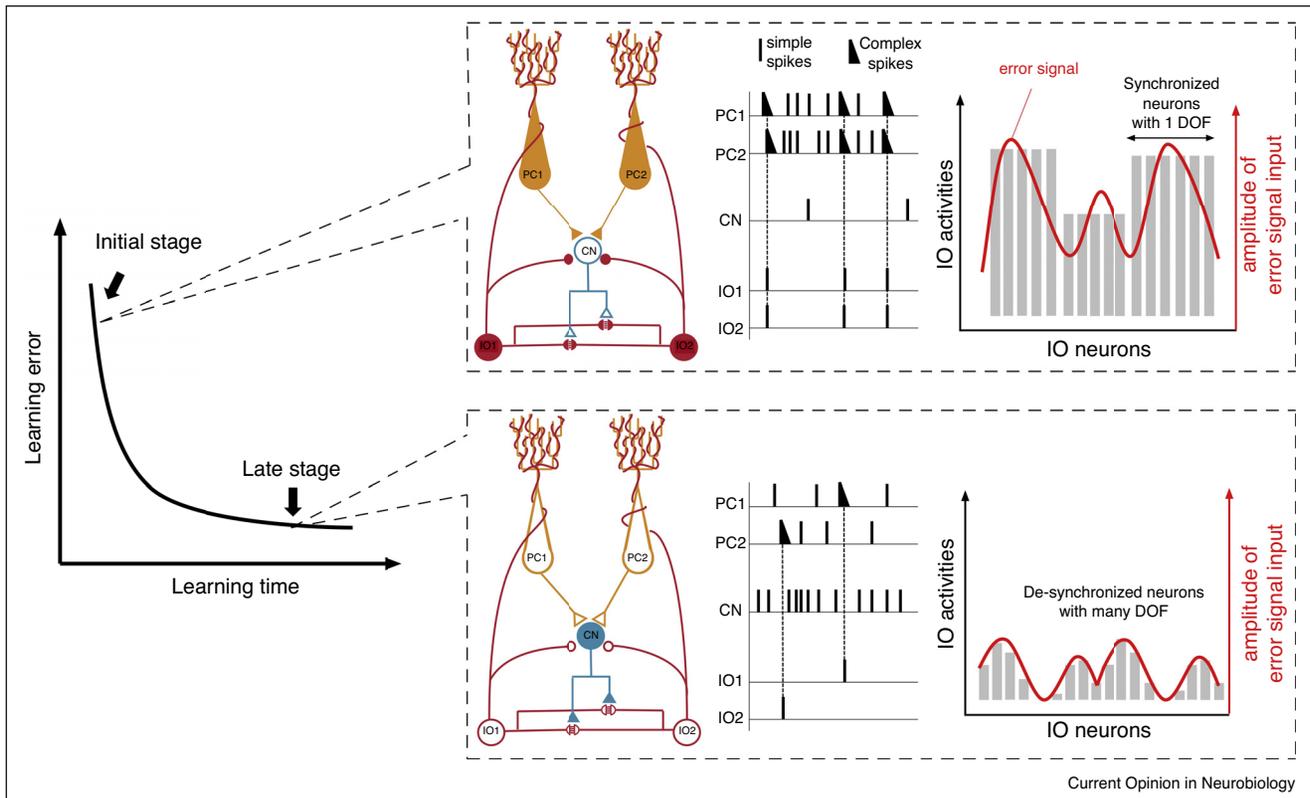


Computational modeling of the inferior olive (IO) neuronal network. **(a)** A conductance-based model of an IO neuron has three compartments: soma, dendrite, and spine. The somatic compartment contains ionic channel conductances for the inward sodium current (g_{Na}), the delayed rectifier outward potassium current ($g_{K_{dr}}$), the low-threshold calcium current (g_{Ca_l}), the anomalous inward rectifier current (g_h), and the leakage current (g_{lo}). The dendritic compartment includes ionic channel conductances for the high-threshold calcium current (g_{Ca_h}), the calcium-activated potassium current ($g_{K_{ca}}$), and the leakage current (g_{ld}). The spine compartment includes a conductance for a leakage current (g_{ls}). A neuron connects to its neighboring neurons via gap-junctions (conductance: g_c) through their spines. **(b)** 3×3 neurons are connected to the neighboring neurons. To take into account inhomogeneity in connectivity of the IO neurons, the coupling strengths (illustrated by the width of connecting lines) were uniformly distributed with maximum deviation set to 20% of the mean. **(c)** Spike trains of 10 representative IO neurons under three experimental conditions (upper panels) and those reproduced by the compartment model (lower panels). (i) Carbenoxolone condition (low frequency, periodic firings), (ii) control condition (irregular, asynchronous firings), (iii) picrotoxin condition (high frequency, synchronous firings).

in the olivo-cerebellar system behave in a synchronous manner. In the late phase of the learning, on the other side, as the motor error becomes smaller, the PCs are only weakly modulated and hardly inactivate the DCN cells. This, in turns, effectively suppresses the IO coupling. The IO neurons are desynchronized as a result of the weakened coupling and consequently transmit high fidelity error signals with high-frequency components, resulting in a sophisticated learning. The olivo-cerebellar neuronal activity is relatively low but occurs in an asynchronous mode that increases the DOF. Therefore, the hypothesis implies that, in the actual cerebellar learning, the coupling strength is adaptive and should decrease as the learning proceeds. Utilization of a large number of DOF only in the late stage could make the learning process fast and robust against the over-fitting difficulty at the beginning while sophisticated and complicated at the end.

The adaptive coupling scheme has been implemented in a network of IO neurons that learn two-joint arm movement [90^{••}]. For simplicity, the PC-DCN-IO triangle was not constructed but only the coupling strength of the IO network was monotonously reduced during the learning. Decreased coupling was indeed beneficial for the learning, because the optimal strength of the coupling was dependent upon the magnitude of the error signals. In the early phase of learning, the initially large error signals, which commonly drive the IO neurons, tend to induce synchronous IO activities. Under such circumstance, relatively large coupling with chaotic modulation was effective in lowering the synchronous IO dynamics so as to improve the error transmission rate. In the late phase of learning, the reduced error signals do not strongly drive the IO neurons to synchrony, and so a small coupling is sufficient to elicit desynchronized IO dynamics that enhance learning. By slowly reducing the coupling

Figure 3



Hypothesis regarding the two learning stages. It is hypothesized that the cerebellum controls the DOF of motor learning via the PC-CN-IO circuitry, which adaptively synchronizes or de-synchronizes the neural activities depending upon the stage of the learning. In the initial stage, since the real trajectories are far from the desired trajectories, the error signal is large and distributes broadly in the cerebellar cortex. The motor commands strongly drive the PCs and the activated PCs suppress CN cells. Since the inhibitory synaptic effect from the CN cells is also suppressed, the IO neurons are strongly coupled via the gap-junctions. As a consequence, the olivo-cerebellar neurons behave actively but in a synchronous mode to quickly reduce the error signal. The DOF is low. By contrast, in the late stage of the learning, since the movements become smooth and closely resemble the desired movements, the error signal is small and distributes in only a restricted region in the cerebellar cortex. The inputs to the PCs thus become weak. The weakly modulated PCs do not strongly inhibit the CN cells and, consequently, the coupling between the IO neurons is weakened due to the inhibitory synaptic effect from the activated CN. Because of the desynchronized neuronal activities, which should be effective for sophisticated learning, the DOF is high. The activated and deactivated neurons are shown by filled and unfilled shapes, respectively.

strength, the learning process of the arm movement was successfully accelerated [90**].

Conclusion

In this review, we discussed the network of IO neurons as one of the central coordinators of cerebellar learning. We revisited the chaotic resonance hypothesis to emphasize the importance of the effective coupling that efficiently regulates the cooperative behavior of the IO neurons to improve the error transmission rate and enhance learning. As an attempt to examine the chaotic resonance hypothesis, recent studies have been illustrated on how to estimate synaptic conductance, i.e., the determinants of the effective coupling, from experimental data. A self-organized mechanism that may adaptively tune the coupling strength to an optimal level has been discussed in terms of a neural computation carried out by the PC-DCN-IO triangle loop within the micro-zone.

In contrast to the deep learning neural networks, which recently draw immense attention, the olivo-cerebellar system learns complex motor tasks from only a small training sample. Considering the high-dimensional sensorimotor inputs coming from the real-world environment, this is a striking feature of the brain. To resolve the problem of ‘curse of dimensionality’, the DOF of the control system should be somehow adapted to the limited training sample. We postulate that the cerebellar circuitry embedded in the triangle close loop plays a key role of adjusting the DOF by regulating the synchronous firing activities of the IO neurons.

To further unveil the unknown functions of the IO network in the cerebellar learning, computational methods should be well combined with the advanced experimental technology. Of particular interest with respect to future research is the application of model-based data

analyses to the in vivo measurement of spatio-temporal spike data. For measurement of neuronal activities, a rapid progress has been made by two-photon imaging technique of the calcium (Ca^{2+}) status of cells, which enables whole-cell recording of behaving animals [91]. Climbing fiber inputs to PCs have been detected, even at the level of individual spines that receive parallel fiber inputs [92]. Additionally, synchronized activities of PC complex spikes have been observed within a functional unit [93]. Strengthening of the climbing fiber inputs to PCs has been observed during cerebellar development [94]. However, analysis of the complex spike dynamics is restricted by the relatively low temporal resolution of the two-photon recordings (typically, 10–30 Hz). Several attempts have been made to detect the spike timings at high temporal resolution from low-sampled Calcium response data ([95,96]; K. Toyama, M. Sato, O. Yamashita, and K. Kitamura, personal communications). When combined, the method for inferring computational models and the improved in vivo two-photon imaging of spike inputs to PCs may represent a new horizon for further examination of the learning hypothesis in the olivo-cerebellar system.

Conflict of interest

Nothing declared.

Acknowledgements

This work was supported by a contract with the National Institute of Information and Communications Technology entitled 'Development of Network Dynamics Modeling Methods for Human Brain Data Simulation Systems', and by 'Development of BMI Technologies for Clinical Application' of the Strategic Research Program for Brain Sciences supported by Japan Agency for Medical Research and Development (AMED), and also by Grant-in-Aid for Scientific Research (No. 16K00343, No. 16K06154, No. 26286086, No. 17H06313) from Japan Society for the Promotion of Science (JSPS).

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A consensus was built on functional roles of olivo-cerebellar system in both motor learning and motor control of the cerebellum. For distinctive characteristics such as low firing rates, synchronization, and variable complex spike waveforms, potential problems and benefits are discussed in the context of the multiple functions of the olivo-cerebellar system.

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The molecular basis of synaptic plasticity is reviewed with a special attention to supervised learning in the cerebellum. The level of synchronized firing of IO neurons, which controls the degrees of freedom of the cerebellar learning system, is discussed as the key component of the generalization capability that adjusts the resolution of supervised learning. The closed-loop triangle consisting of PCs, IO neurons, and DCN is proposed as a circuit that optimally controls the degrees of freedom in two stages in cerebellar learning.

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The authors propose a hypothesis, which states that simple spikes of PCs may encode error signals both as an internal prediction of motor commands and as the actual sensory feedback. From these dual representations, sensory prediction errors can be generated and used to update a forward internal model. This review supports the recent view that both simple spikes and complex spikes of PCs are the sources of error signaling in the cerebellar motor learning.

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Under cerebellum-dependent eyeblink experiment of mice, individual climbing fiber activities were recorded. Not only that the climbing fibers responded to instructive signal for the eyeblink conditioning but they also fired in response to stimuli from other sensory modalities if those stimuli were novel or if they predicted that the instructive signal was about to be presented. The observed activity patterns, which resemble those of dopamine neurons during reinforcement learning, suggest that temporal difference prediction error is encoded in the complex spikes from the climbing fibers.

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A computational model is presented to reproduce behavioral data as well as neural activity of wild type mice during experimental phase-reversal learning of the vestibulo-ocular reflex. Interestingly, the model is based on a closed loop comprising PC, DCN, and IO, which is capable of predicting simple spike modulation of PCs and concomitant behavioral learning in mutant mice.

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This electrophysiological study indicated that the firing activities of DCN neurons suppress the firing of IO cells and regulate the effective coupling between IO neurons. This is consistent with anatomical and *in vivo* studies suggesting that DCN to IO synapses control the synchronous firing of IO neurons by inhibiting IO coupling.

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The DOF control of the cerebellar learning system was examined in a network of simplified IO neuron models. To verify the two-stage learning hypothesis, the authors introduced adaptive coupling, in which the coupling was slowly weakened as the learning proceeded. Simulation of a human arm movement with the feedback-error-learning showed that

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