

## **Motor control schemes in the cerebellum and motor cortices**

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**Introduction:** The intricacies and complexities of the primate motor control system are simply mind-boggling. This is evident by looking at the magnitude of theories that are continuously being published, refined, and outright rejected on almost a weekly basis. Many times the problem comes down to the limited scope of the investigation. The primate motor control system is so incredibly multi-dimensional and non-linear that any engineer would tremble at the thought of characterizing such a juggernaut. But, no matter how complex the controller may be, it can be broken down into functional feedforward and feedback sensorimotor transformations. Almost any theory on motor control will define what roles one or both of these control schemes play [1-15]. A feedback control scheme uses state-related information (e.g. afferent signals) in the computation of the control signal. Feedforward control relies on an intrinsic model of the plant in its estimate of the control signal. While most researchers would attest to the fact that biological motor control systems inevitably take advantage of both control schemes, few provide any convincing physiological evidence on the sources of them in the brain. Since it is widely accepted that much of motor control in primates is distributed throughout the cerebellum and motor cortices of the cerebrum (e.g. primary, supplemental, premotor, and posterior parietal), the primary goal of this proposal is to answer the following: **What control schemes are used in the cerebellum and motor cortices?** The approach we will initially take is to classify each of the regions as primarily using feedback (using state information) or feedforward (prediction using intrinsic model). In route to addressing the proposal's primary goal, we will also put forward two related secondary goals that can be pursued in parallel to the primary goal and without adding too much complexity to the project. The secondary goals answer the following questions: 1) **What are the relative responsibilities of the cerebellum and motor cortices in primate motor control?** ; and 2) **How is state information encoded in these two brain structures?** (As an informal goal we'll either confirm or disprove the proposed control architecture illustrated in figure 1; the letters attached to each block will be used to refer to that block.).

These three questions are motivated by many active issues in the discipline of motor control. Studies on BMI typically record from the cerebrum (motor cortices) and develop control laws based on those correlations with motor activity. While it has been established that the cerebellum is an essential component of motor control, very little research has explored using the cerebellum in BMIs. The cerebellum has been proposed by many as using predictive control which is particularly useful in controlling high bandwidth motion [2, 3, 5, 10-17]. If BMIs hope to one day execute fast motions, then shouldn't it be advantageous to use the signals coming from the structure that renders the signals for such motion? While there have been many recent success stories in the BMI world [1, 6, 17-20], the motion tasks (used for both training and testing their model) are of low enough bandwidth that much of the control can be picked up by the feedback controllers distributed throughout the regions of the cerebrum that were recorded from. While exploring the relevant motor control signals from the cerebellum (in pursuit of the established goals), we could stumble upon an entirely undiscovered host of signals that would be beneficial to BMIs.

The ideal of recording from neurons in the cerebellum is a relatively new and difficult task, so by doing so we may be able to address a multitude of unanswered questions in route of pursuing our primary and secondary goals. An emerging theory in cortico-subcortical dependencies is the notion that cerebral cortices are individually regulated by loops through subcortical structures (e.g. cerebellum) [4, 5, 21, 22]. These loops allocate computational tasks via distributed processing modules (DPMs) in a manner similar to parallel processors on a digital computer. In route to addressing the two secondary goals, we could also broaden our understanding of the synergies and interplays between cerebellar and cerebral structures. This may even help us answer one of the fundamental questions in neuroscience: How is information encoded in the brain? In particular we'll explore the brain's intrinsic state space representation (Does the brain use local or global coordinates?... muscle, direction, or force?). By limiting ourselves to only the usual suspects of such coordinate systems such as muscle and direction, we would be neglecting the fact that the brain's intrinsic coordinates may use an entirely obscure representation that has no physical meaning (at least in the traditional way we think). There are simply too many questions to even list.

Many researchers have hypothesized that the cerebellum is able to compute the inverse dynamics for the muscular-skeletal system [6, 10-13, 15, 23]. This is yet another issue can be investigated by correlating various motion tasks with neural recordings from the cerebellum. To roboticists inverse dynamics has a well-defined meaning. But, in the context of biological motor control, the computation and representation of the inverse dynamics is ambiguous. It would be silly to propose that the cerebellum is capable of solving hundreds of non-linear partial differential equations in real-time for a particular movement. This would be the traditional engineering approach for controlling such a non-linear system with many degrees of freedom. It would be interesting to know how the cerebellum does indeed compute the inverse dynamics and how it represents this information.

The cerebellum has been linked to providing temporal adjustments in learned tasks [13, 15]. This essentially means the cerebellum uses a feedforward control scheme to cancel the effects of time delays in the system. In order to do this it needs an intrinsic model of the time delay in both the efferent path (CNS to muscle) and the afferent path (muscle to CNS). By manipulating the duration and absence of time delays in our experimental protocols, we can 'listen' to the cerebellum (neural recordings) to see how (if) it learns these delays.

Figure 1 is a block diagram of the model that will be investigated. The green boxes are abstract information transformation modules that are thought to be in cerebellum. Once the data from our experiments is analyzed, we hope to be able to prove or disprove the validity of this model. The A-B-C-D-E loop is a typical model of a feedback controller where block A is the controller, and forward the path of blocks B, C, D, and E is the plant. As in real motor control systems, noise and delays are present. It is these elements that truly make control a difficult task. The I-J path through the cerebellum is capable of predicting both of the following: 1) the resultant state of the of the muscular-skeletal system that is determined from the efferent copy; and 2) the expected sensory feedback that would result from that predicted state. The H block computes the inverse model. The result of the inverse model is integrated together with the output of the "feedback" controller that is said to be in the cerebrum (within the motor cortices).

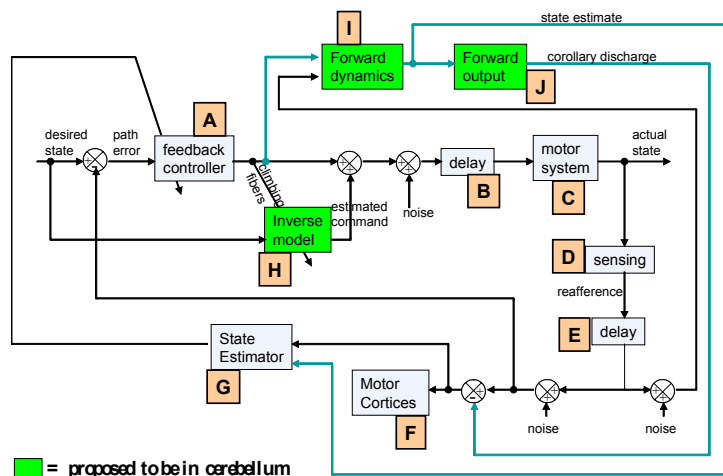


Figure 1. A block diagram of the proposed layout for a primate motor control system.

processing. The Todorov and Jordan model of optimal control relies on sensory feedback for the state estimation that is needed to determine the optimal corrective movement that will accomplish the task. This is illustrated as the A-B-C-D-E-F-G loop in figure 1. For a motor control system, feedback is an extremely powerful tool. But, if used improperly, it can cause catastrophic instabilities. Let's suppose that once the control signal is computed, block B (figure 1) induces a 50 msec transmission delay in the signal. The signal then recruits muscles that move the skeleton (block C). Afferent signals are encoded (block D), and block E induces another 50 msec to the signal. Upon arriving at the state estimator (block G), let's assume a small overhead computation time of only 25 msec. So, without even considering the phase lags (e.g. mechanical) induced by block C or the additional computation that would probably actually be needed by blocks G and A, there is pure delay of 125 msec (whether or not is an accurate estimate it will be used in this example). Let's say that a particular task to be performed requires a movement path that contains frequency components up to 4 Hz (a bandwidth of 4 Hz). By the time the 4 Hz component makes the A-B-C-D-E-F-G loop, it will have a 125 msec delay (just from blocks B, C, E, and G), which corresponds to a 180° phase lag. The system is now unstable. In reality, time delays can be longer, and phase lags (from muscular-skeletal mechanics) are finite and significant. This analysis would lead one to believe that any quick motion would cause the controller to go unstable and exhibit uncontrollable oscillations (using only feedback control). From a theoretical point of view, a controller can become more stable (larger range of stability) by taking advantage of an 'inverse dynamics' compensator (figure 1, block H) and a forward dynamics model (block I). A feedforward transformation is able to induce a phase lead that could cancel an anticipated phase lag. A forward dynamics transformation is able to predict the dynamics of the muscles from the state of the system and a copy of controller output. This means the CNS can predict the state variables and the errors without having to wait for the sensorimotor delay. The stability of such a system will strongly rely on the accuracy of the forward model and the ability to cancel the response from the remote system. It should be now evident that motor control systems need (at least) feedforward control.

A paper by Bhushan and Shadmehr [25] investigated a model of the human motor controller that utilized feedforward and a forward dynamics computation. The hand of a human subject was coupled to a robotic arm during some simple reaching tasks. The robotic arm was able to apply an arbitrary force field that could change the dynamics of the reaching task. After a series of experiments, they found that a control scheme that utilized an adaptive feedforward model (something like the H-B-C-D-E-F loop in figure 1) was pretty similar to the data observed in their subjects, but lacked some essential characteristics. It seemed that the controller was using descending commands to predict the dynamics of the plant (loop A-I-G). But, after constructing a controller architecture that incorporated an adaptive forward model, they found that this model didn't exactly match the data either. So, a third model was constructed that used the feedforward transformation in conjunction with the forward model computation (all blocks in figure 1), and they found that the resulting dynamics were remarkably similar to that observed in the experimental data. But, they were unable to verify the physiological origins for their control modules. What parts of brain were responsible for which aspects of the overall control? This is exactly what we propose to answer.

Of course Shadmehr isn't the first to speculate about feedforward models. Wolpert (and many others) have put forth many theories of the cerebellum computing inverse dynamics [10-13, 15], canceling predicted tactile stimulation [11, 16, 26, 27], and utilizing a Smith-predictor-type scheme to cancel time delays in the control loop [15]. These researchers have presented an abundance anecdotal and circumstantial evidence for the existence of such computational units in the cerebellum. But, they have fallen short of pinpointing the exact neural avenues and representations of these modules. With all of this potentially useful data being processed in the cerebellum, why have we neglected to do many recordings from it?

Barto, Houk, Strick, and others have approached the cerebellum's computational powers in a slightly different perspective [4, 5, 14, 21-23, 28, 29]. In the Barto-Houk model [14] by including realistic mossy fiber signals, as well as realistic conduction delays in afferent and efferent pathways, the model allowed the investigation of timing and predictive processes relevant to cerebellar involvement in the control of movement. Their model is much simpler (than Wolpert's) and without the need for explicit calculations. But, while their model is based on established properties of the various cerebellar neurons, they have not attempted to prove it by matching their model with actual neural recordings. Houk and Strick [4, 5, 22, 28, 29] have speculated about distributed processing modules (DPM) between the cerebrum and subcortical structures. Strick and Middleton have developed a new technique for tracing these circuits in the central nervous system of

**Background:** Does the motor control system really use both feedback and feedforward control schemes? If so, does it really need both? A somewhat recent paper by Todorov and Jordan [24] explained in their introduction that there is body of evidence that supports open loop (feedforward) control of planned trajectories. But Todorov et al chose a different path by proposing that the human CNS in fact uses an optimal feedback control scheme for motor coordination. Simulations were performed to explore the validity of such a theory. Their simulation used rigorous mathematics to define their feedback controller. For a modern PC the number of matrix multiplications, additions, and inversions needed in each sample for Kalman filtering (the type of calculations that they proposed to take place in motor control) isn't too overwhelming. But, to imply that the human CNS performs such calculations (in the same manner as an engineer would implement it) in real-time is simply absurd. While the paper does not explicitly state this conjecture, they offer no alternative explanation, let alone speculate on any neural mechanism that could perform such

primates: retrograde transneuronal transport of herpes simplex virus type 1 HSV1 [28]. They have been somewhat successful at mapping out complementary components of the DPMs. We will use these maps as a starting point when laying out our electrodes.

Perhaps the most relevant study found in the literature is an experiment by Lee Miller and colleagues [7]. In their paper they suggest that the cerebellum produces a predictive signal that is combined with a relatively crude cerebral signal in order to produce an appropriately refined descending command. The extreme relevance of this particular study is the fact that they derived this theory from actual recordings from the cerebellum. Their results led them to believe that during motor control, the Purkinje cell has basically two functions: 1) restrain the activity (via inhibition) in the premotor network to deter the use of muscles not associated with this task; and 2) amplify (via positive feedback) relevant motor commands. We have thus far presented ample evidence on just how important the cerebellum is during motor control. But, their (Miller, et al) conclusions from their experiments greatly diminish its importance. So, why should we continue with our experiments? There are many reasons! Their recordings failed to find any predictive (feedforward) capabilities of the PCs that they recorded from. But, this makes sense if you look at the nature of the movement tasks. The performed tasks of the monkeys were SLOW, which is the ideal scenario for feedback control. For these particular tasks, the feedback control units located in the cerebrum may have been sufficient (no feedforward needed). Recall, that we are speculating that the cerebellum uses predictive control to cancel phase lags and time delays... this is only necessary for fast movements. Also, it is fairly widely accepted that cerebellum plays a significant role in motor learning. Since the tasks are slow and learned, the cerebellum could have gone 'on vacation' because its primary capabilities were not needed. Consider the following scenario for the motor tasks in the Miller experiment: 1) Monkey learns task; cerebellum is used to train a neural network in M1 to perform this task. 2) Once task is learned, electrodes are hooked up to monkey's cerebellum and little activity is observed. The cerebellum could have aided in the learning of the novel task and then passed that on to the cerebrum (then there cerebellum is no longer needed).

**Research Design and Methods:** The experimental protocol calls for 3 monkeys, a heap of electrodes for the cerebrum and cerebellum, and a 2-D planar robot manipulandum. The robot would be similar to one used in the Shadmehr [25] study or to the one in the Mussa-Ivaldi-Patton lab. The robot will need to be able to measure force and position (velocity and acceleration) as well as providing arbitrary force fields and giving real-time visual feedback (via computer screen) to the subject. The monkeys first need to have electrodes strategically placed throughout their cerebrum and cerebellum. The idea is to use Strick's maps of the cerebral-cerebellar loops [28] in an attempt to get electrodes on both sides of the loop. In the cerebrum we'll place electrodes in the premotor, primary motor, and posterior parietal cortical areas, and then we'll attempt to place electrodes in the corresponding cerebellum locations. We realize the difficulty of placing electrodes so that they record from both sides of the cerebellar-cerebral loops, and our experiments are designed to deliver fruitful results even if we fail in this aspect.

The monkeys will sit in a chair and one of their hands will be controlling the manipulandum. The monkeys will not be able to see the actual motion of their hands, and will instead watch a monitor that displays the virtual motion of their hand (or what we want them to think is their hand). The experiments will take place in four phases where the first three phases are the same protocol but for different tasks, and the final phase requires "disabling" the cerebellum. The three tasks are: **phase 1**) move in straight line from a starting point to an ending point (reaching task); **phase 2**) movement of only the triceps; and **phase 3**) following an arbitrary path. During each phase (task) the monkey will be expected to perform the "same" task every time. For each of these phases the task will be subjected to five different variations, and for each of these variations there will be two distinct parts identified: **part 1**) while the monkey is learning the variation, and **part 2**) after it is learned. The **five variations** are: 1) normal: robot is not actuated (passive); 2) the monkey needs to produce the same force (in order to follow the desired path on the screen), but the actual manipulandum doesn't move; 3) monkey produces same force and motion as normal, but duration of motion is much shorter; 4) the perceived dynamical properties (e.g. mass, viscosity) of the monkey's arm are altered (by intelligent control of the manipulandum) while performing the normal movement; and 5) the monkey is subjected to spatially varying force fields while performing the task. The final phase (**phase 4**) is an extension and can be performed at the discretion of the researcher. Once neural signals from the cerebellum are correlated with cerebral signals and motor task, the region of the cerebellum that has been recorded from is 'disabled' (via local injection of neuronal 'disabling' agent). By using both recording and stimulating electrodes, we'll attempt to emulate the I/O of the cerebellum in real-time by using the correlations found previously. Alternatively, instead of emulating the cerebellum (this is a very difficult procedure), we could have the monkeys (attempt) to perform the same tasks and see how the cerebral output changes. And, we'll see if the monkeys are able to learn new tasks, and see if they are able to perform higher bandwidth tasks and other tasks that would typically need feedforward control.

The general idea with these experiments is to determine which parts of the brain are responsible for feedback control and which parts are responsible for feedforward control. Within the experiment just described we have made some of the scenarios for the monkey more indicative to feedforward control and others more indicative to feedback control. By monitoring different parts of the brain during different motor tasks, we should be able to tell where centers for feedback and feedforward control are located. Some of the tasks require a reference to an internal model, inverse dynamics, and/or predictor. We should be able to locate where these modules are located in the brain by correlating the neural signals with the computational requirements for that task. We will see how neural signals change as a task transitions from "being learned" to "learned". Phases 1 and 2 can show the difference between a pure direction task and a pure muscle task... how are they learned and stored? Phase 3 requires the monkey to use visual feedback control to keep its cursor on the moving dot during the learning phase. The exact motion path is kept constant so the monkey will eventually learn the path (then, won't need feedback). We expect the monkey to initially use feedback control to learn the task and develop an internal model. Then, it can use feedforward control (with its internal model). By changing the dynamic parameters of the monkey's arm, we are essentially changing the monkey's intrinsic model of its arm. This affects its forward and inverse dynamics model. It will eventually learn the new set of parameters. By having the monkey apply the same force (while it thinks it is performing the 'normal' movement) when it is not actually moving, we can see where force feedback goes to. If the monkey now does the 'normal' task with the same motion and force but in a shorter time, then we can look to see if feedforward takes over.

**Extensions:** If we were successful at mapping both sides of a cerebral-cerebellar loop (see [4, 5, 22, 28]), then we can run system identification algorithms to identify their input/output characteristics. If we have confidence in our I/O model of the cerebellar side, we can disable it and emulate it with recording and receiving electrodes. If we can do it in the cerebellum, then why not try the same in the basal ganglia? By artificially emulating the function of the basal ganglia, we may find a cure for Parkinson's disease.

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