THE ROLE OF THE CEREBELLUM IN OPTIMAL MOTOR CONTROL

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Content

A natural moving robot?

A popular field of research these days is robotics. A lot of engineers developing these robots try to make the robot walk like a human and although this work has been improved much over the last decades, there is still a very profound discrepancy between the walking robot and the walking human. Walking can't be considered to be the most complex human movement, but still it cannot be programmed into the robots blue print. To be able to mimic the smooth movements humans are able to make, much effort is done to understand the processes which are used while moving. Already in 1954 Fitts et al. published a paper in which he described regularities in movement planning, Also lesions in certain neurological structures showed profound movement alterations indicating that a basic architecture is governing the movements and thus can be translated to programs deducting the movements of robots.

The search now points at elucidating the normative laws which govern the distinct processes in movements. Much insight in the functional architecture of motor control comes from lesion studies, which address the contribution of a certain neurological structure to the motor control. Due to this research the cerebellum has been remarked to have a very important role in motor control. Lesions in this structure will not result in a total disruption of movements, but rather show a subtle consequent impairment in movement. It is thus a very interesting study object.

Considering the role of the cerebellum in motor control there is still a lot of controversy as will be addressed in this paper. Research of the cerebellar function in motor control is done from different angles. As mentioned, lesions studies have shown insight in the cerebellar function. Other research fields that have contributed to understanding its function are neurologic imaging studies, cell research and research focusing on the algorithmic functions underlying motor control. It is however important to remember that results of each of the research field should be in concordance with results found in other fields. Algorithms thought to underlie movements should be implemented in the neurological networks according to the cellular mechanisms found.

In this paper insight in the role of the cerebellum in motor control will be presented considering knowledge from the different research angles.

A historical overview of cerebellar functioning

The role of the cerebellum in the process of motor movements is largely conducted from studies researching the effect of cerebellar damage, e.g. cerebellar lesions. Already since the 18th century physiologist reported that patients with cerebellar damage showed problems with motor coordination and movement. In the 19th century cerebellar research focussed on lesion studies in animals. Cerebellar lesions became known to cause strange movements, awkward gait and muscular weakness. These studies stated the importance of the cerebellum in motor control. The classical lesion studies in patients with cerebellar damage, as done by Dow and Moruzzi (1958) introduced the view that the cerebellum is an important structure for learning new motor skills and carrying out smooth movements (Dow et al. 1958). The basic functions nowadays linked to the cerebellum are: integration of sensory perception, coordination and motor control.

Recent research shows that the cerebellum also has a role in a number of key cognitive functions, including attention and the processing of language, music, and other sensory temporal stimuli. These functions will however not be mentioned further throughout this paper as they are not relevant to the motor control function of the cerebellum.

Much of the current believes in the functioning of the cerebellum in the learning of new motor skills and making smooth movements is based on theories developed by Mar, Albus and Ito. The theory they proposed is based on findings into the neurological architecture of the cerebellum and cellular processes found in the cerebellum. First a short description of the neurological network will be given.

The cerebellar cortex structure is unique, because of its uniformity throughout the whole structure (Fig 1). The only output of the cerebellum are the Purkinje cells (PC), these neurons receive two excitatory inputs from climbing and parallel fibers. Climbing fibers (CF) have their origin in the inferior olive, the CF neurons have a one-on-one contact with Purkinje cells. The signals of the CF evoke a powerful voltage gated Ca^{2+} spike in the dendrite called the complex spike (CS). Purkinje cells also receive input from the parallel fibers (PF). These PF lie in a plane rectangular to the Purkinje cells. This geographic spacing enables the formation of 150,000 to 200,000 parallel fiber synapses with a single Purkinje cell. The parallel fibers originate from granule cells which are innervated by mossy fibers originating from precerebellar nuclei.
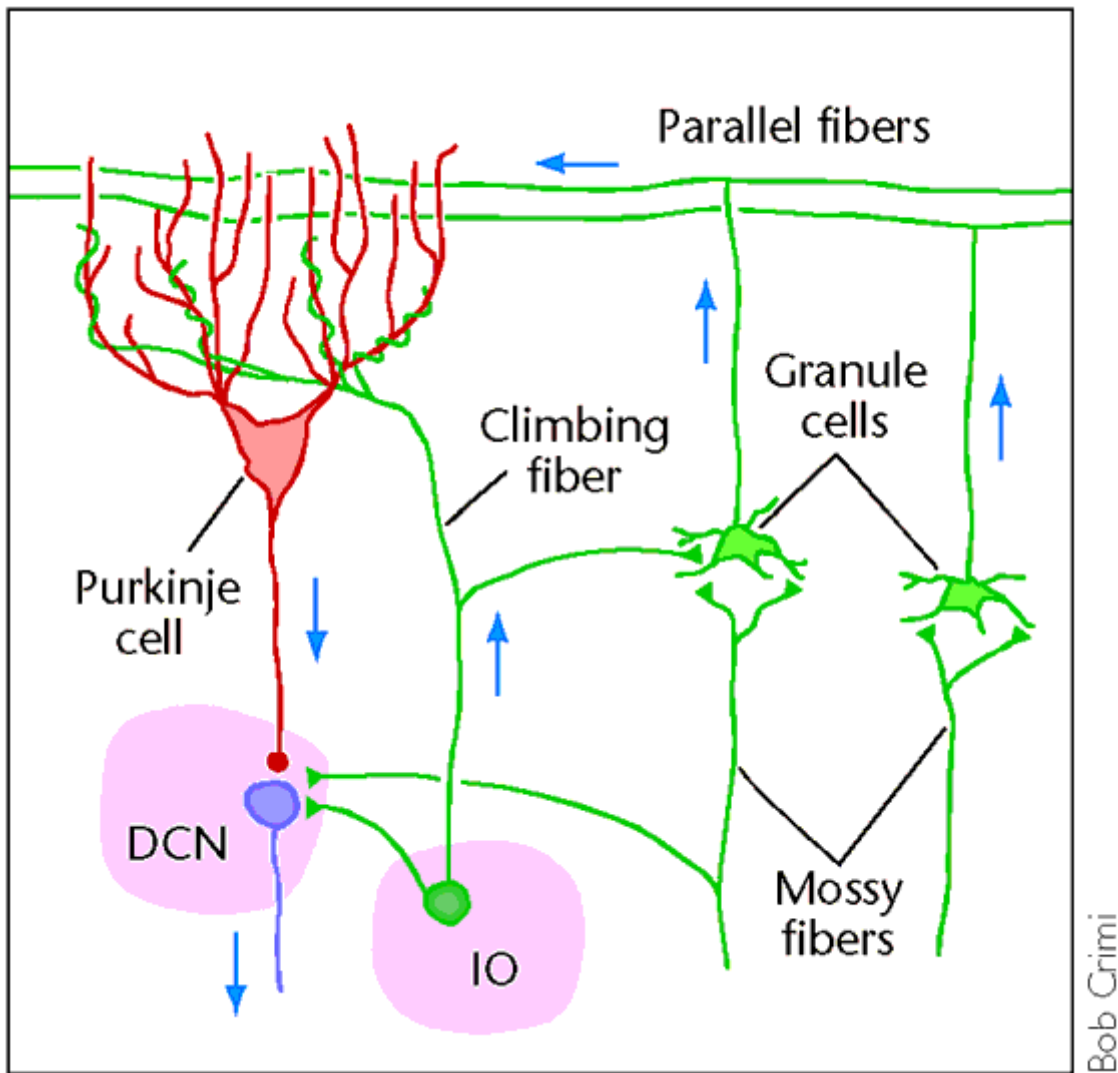
Fig 1. Schematic overview of the most important cells in the cerebellum. The output of the cerebellum is generated by Purkinje cells and goes through the Deep cerebellar nuclei (DCN), Climbing fibers (CF) are innervated through the Inferior olive (IO).

Before motor learning capabilities had been recognised as a capability of the cerebellum, they already had been linked to synaptic modification, based on pre- and post-synaptic activity, by Hebb (1949). The first connection between motor learning and the cerebellar cortex was proposed by Marr in 1969. Marr's theory stated that the Purkinje fiber (PF) synapses within the cerebellum were facilitated trough simultational firing of the climbing fibers and the parallel fibers. The olivary nucleus was believed to signal in case of correct motor performances through the climbing fibers on the Purkinje cell, this neuronal `correct` signal would be stored as facilitated PF synapses.

Albus refined this theory in 1971, his theory stated that the cerebellum has a layered structure in which different layers have complex neuronal connection allowing complex motor behaviour. Moreover he stated that the complex spike represents the unconditioned stimulus and the mossy fiber input represents the conditioned stimulus. Albus studied the conditioning of reflexes according to Pavlonian learning in the eye blink process, an unconditioned stimulus is for example an air puff in the eye which elucidates automatically the blinking of the eye. The conditioned stimulus can only trigger an eye blink after training; the stimulus is for example a specific sound. An important change he proposed was that the CS input was an error signal that

subsequently weakened the PF synapses with the Purkinje cell. This was in a time Long term depression (LTD) was still unknown. The theory is extended by Ito in 1984, who stated that climbing fibers from the inferior olive provided a teacher signal. This signal could adjust the synapse strength of the Purkinje cell with certain parallel fibers.

The exclusive right of motor learning for the cerebellum as proposed by the Marr-Albus-Ito theory is now being criticised. LTD knockout mice still have learning properties in the eye blink process (Thompson et al. 1986). Also the vestibule-ocular-reflex (VOR) adaptation showed contradicting linkage with Purkinje cell simple spike activity (Ito, 1984, Lisberger S.G and Krauzlis R.J, 1994)

Current theories state that the cerebellum has a controlling function in generating motor commands, in which it has a predicting role. To make preferred movements a state estimation should be made of the body and the environment, in these processes the cerebellum is important. The importance of prediction is clear in for example controlling saccades, in which the eyes have to move very quickly from one position to another. These movements are too fast for visual sensory information to control the eye movements. Moreover it has been found (Thiele et al. 2002) that the brain even suppresses the visual processing during saccades to reduce the perception of motion. The control of the movement is thus based on predicting the state, position, of the eye with efferent copies of motor commands.

Cellular mechanisms underlying motor learning

A first glimpse into cerebellar function originates from neuro-anatomical insight of the cerebellum and the cellular processes within this structure. In this paper a couple of models will be proposed that possibly underlie the cerebellar function. In respect to these models it should not be ignored that these have to be in concordance with the cellular processes found in the cerebellum. In this chapter some important cellular neuronal mechanisms found in the cerebellum will be addressed.

The basis of learning and memory in the brain is long term plasticity, which is a modification of synaptic strength (Bliss et al. 1993, 2003, Malenka 1999). In the cerebellum the best known mechanism of plasticity is LTD, which occurs at the parallel fiber-Purkinje cell synapse (Ito et al. 1982). This plasticity is the elementary cellular process of supervised motor learning in the cerebellum (Marr 1969, Ito 1984) A strong indication that LTD is responsible for associative motor learning comes from a study performed by de Zeeuw et al. (1998). Inactivation of this cellular mechanism by inhibition of protein kinase C in the purkinje cells of a transgenic mouse prevents motor learning in the vestibule ocular reflex (VOR). More recently a second cellular plasticity mechanism, long term potentiation (LTP), has been revealed. LTP was first described in acute splice preparates of granule cell layers of the rats cerebellum (D'Angelo 1999). Work done by Roggeri et al. (2008) showed LTP also in rats in vivo. LTP also works in the parallel fiber-Purkinje cell synapse and can be thought as the counterpart of LTD. (Boyden and Raymond 2003). (LTP appears to be in more sites of the cerebellum.) Because LTD is postsynaptic LTP can only completely reverse the working of LTD if it works on the same side, LTP has long been found to occur only at the pre-synapse, more recently it has also been found at the post synapse (Lev Ram et al. 2002).

Whether LTP or LTD is induced in the parallel fiber-Purkinje cell synapse depends on the local excitatory/inhibitory balance. A repeated high-frequency mossy fiber bursts, thetaburst, induces LTP when synaptic inhibition is weak, whereas the same patterns induce LTD when synaptic inhibition is strong (Mapelli and d'Angelo 2007). The molecular mechanisms behind this differentiation has been studied intensively and has been revealed for a great deal (Gall et al 2005). LTP and LTD have influence on intrinsic excitability and release probability, and thus control the delay and discharge frequency of granule cells responses to mossy fiber bursts (Nieus et al. 2006).

Much insight in LTP and LTD functioning comes from research to the cerebellar function within the VOR. This reflex pathway is relatively short and is thus thought to have a limited number of possible neuronal mechanisms which makes it a more simple circuit to study. The basic goal of the reflex is to generate eye movements that stabilize the gaze generated by head motions. For example if one turns its head to the right and fixates on a certain fixed point in space. The reflex should thus be capable of increasing and decreasing the eye movement along an axis to compensate for the head movement and obtain a good visual input. In terms of synaptic strength it has been a well accepted thought that the cerebellum, which guides the VOR, has two different mechanisms which can either strengthen or weaken the purkinje cell synapses.

In VOR research it has been seen that whether the eye velocity has to be highered or lowered to stabilize the gaze depends on different mechanisms. The time course of returning to normal gaze, is different for an experiment in which the gain of the eye velocity had to be highered compared to one in which the gain was lowered, (Miles and Eighmy 1980, Boyden and Raymond 2003) There is also molecular evidence for the existence of two different plasticity mechanisms in the cerebellar circuit Li et al. (1995) found that the intercellular messenger nitric oxide is required for gain increases in the VOR but not for gain decreases, the same finding was found for an metabotropic and N methyl D aspartate NMDA type glutamate receptor in the cerebellar cortex (McElligot and Spencer 2000).

This mechanism could well regulate the spatiotemporal characteristics of neuron transmission in the mossy fiber pathway and thus determine whether spikes will emerge within appropriate time windows (Mapelli and d'Angelo 2007, Nieus et al. 2006). Which is important in the plasticity of the cerebellum.

Although these biological processes are fundamental in the processing of cerebellar information, they will likely not elucidate functioning of the cerebellum on their own. This is part because of the possible feedback loops and input from other brain structures into the cerebellum. These factors difficulty the possibility to place the knowledge obtained from the biological processes in a functional model. Moreover cerebellar function has been concentrated mainly on plasticity of the Purkinje cell parallel fiber synapse. However, it has been shown that plasticity is present in other sites such as the connection between the Purkinje cell and its postsynaptic target (Hansel et al 2001).

Cerebellar damage shows internal model prediction

Much of the knowledge of cerebellar function in the motor system is based on motor behaviour changes seen in cerebellar patients. These patients don't show loss of motion, but show more subtle problems within motor coordination. Profound characteristics in their deficits are; tremors, a lack of coordination, e.g. people who cannot touch their nose with their fingertips having their eyes closed, increased variability in movements, as seen in drunk walk and poor accuracy. In this chapter the above mentioned deficits will be analysed in more detail.

A remarkable characteristic that cerebellar patients show is that they have problems with anticipation on movements and show difficulties with this movement. However when making a movement they can react to external factors as well as healthy people, as observed in experiments done by Nowak et al (36). In this experiment the researcher dropped a ball and subjects were asked to catch the ball in a force transducer with a basket which they held in their right hand. When the ball hits the basket it will exert a downward force, the subject will try to hold the basket steady by compensating the downward force with a counteracting force upwards. The force and timing of the counterforce could be measured with the force transducer. Because there is a delay in sensing the impact of the ball and the upward reaction, the response will follow with a mean delay of 100ms after the ball's impact. After testing the response in healthy patients Nowak et al tested a cerebellar patient, HK, who does not have a cerebellum due to a rare developmental problem. Both groups of subjects showed a similar response in the delay and force. However, when the researcher asked the subjects to drop the ball themselves and again catch the ball in the force transducer, the cerebellar patient and healthy patients showed differences in their response. Healthy subjects made predictions of the impact of the ball and had a profound shortening of the reaction time. Subject HK, however did not seem to make anticipations and had similar response delays as in the first situation in which the experimenter dropped the ball. To be able to smoothly catch the ball one should make an internal representation of the arm in which you have the ball. This representation is able to accurately represent the physical characteristics of the ball and to make a prediction of upcoming states, the impact of the ball.

A second example of a characteristic deficit in cerebellar patients is seen in a treadmill test done by Morton and Bastian (2006). In this test subjects are placed on a split treadmill. While the treadmill is turning, one wheel is suddenly set twice the speed. Both healthy and cerebellar subjects show fast reactive changes towards this speed difference by holding the slow moving feet longer on the treadmill than the one on the faster side. But where cerebellar patients have identical corrections each single step, healthy patients are gradually evolving a new coordination of their walking movements in which the interlimb relation is more effective. A striking difference between healthy subjects and cerebellar patients is seen when both treadmill wheels return to the same speed. Cerebellar patients will walk normally instantly, while healthy subjects show a decaying changing movement. This also indicates that healthy subjects have evolved a more adjusted walking movement while cerebellar patients still rely on a hard wired walking movement. If one of the treadmills is suddenly set at a faster speed, only the healthy subjects can rapidly use the new walking movement to cope for the speed increase.

Also postural responses can be influenced by cerebellar damage. Horak and Diener (1994) asked subjects to stand stable on a floor which could be moved. If movements were in a predictable order, healthy subjects could well predict the amplitude of their counteracting movements to stay steady. Cerebellar patients showed comparable results with healthy patients for random floor movements, but not for the predictable pattern movements (Horak and Diener, 1994).

To have optimal motor control, we make state estimations of the environment and the body. This state estimation is based on sensory information and from prediction (Kording and Wolpert 2004, Vaziri et al. 2006). As seen in the above mentioned examples the cerebellum seems to be a crucial site to make these estimations.

It has also been found that cerebellar lesions inflict great difficulties in learning to use new tools (Maschke et al. 2004, Smith et al. 2005). Some of these profound deficits in learning new tools are seen in tests in which subjects are asked to move a handle of a robot to a certain goal. The handle of the robot can be perturbed in different ways, like mirroring the direction of the movement. Subjects show a learning process and will successfully reach the goal; cerebellar patients however show difficulties in evolving in the learning process (Maschke et al. 2004, Smith et al. 2005).

As can be concluded from different results, for example the floor test by Horak and Diener (1994), damage to the cerebellum causes greater impairments in movements that require predictive control, than those requiring reactive control. Predictive control clearly is crucial when making fast and ballistic movements. It is also important when new motor skills are learned. One may assume that in life new motor skills are getting less often newly acquired. But to have optimal control of the body movements, we constantly have to adjust our movement control with the changing state of the body. Having fatigued muscles, getting older or holding objects in a hand will alter the state of the body; thus movement control will need adjustments of internal predictions to make accurate state estimations.

A nice example of the predicting nature of the cerebellum has been visualized by an experiment using transcranial magnetic stimulation (TMS) to disrupt the lateral cerebellum in human subjects. In contrary to the lesion studies this is a good way to disrupt the cerebellum in a non-invasive way. While cerebellar function was blocked the experimenters observed the subjects arm movements while they were preparing for a fast reaching movement Miall (2007). The reaching errors observed, due to TMS, suggested that the movements had been made on an estimated hand position 140ms in the past. This indicates that the cerebellum updates the state of the arm, but due to its disruption the state estimation wasn't updated.

If the cerebellum is mainly involved in predictive motor control, this would suggest that patients with damage in this area have to rely more on feedback mechanisms. These mechanisms are slow and corrections are always based on a moment in the past. As a result of which it is not a perfect control mechanism. According to this theory it is seen that if cerebellar patient move at their own ease in grabbing tasks, they are able to make more accurate and smooth movements, indicating that their feedback mechanism is more reliable in these situations. Patients can also move more smoothly if they close their eyes and try to grab something. This suggests that cerebellar patients are constantly adjusting their movements through online feedback corrections, which is fed by visual information. By inhibiting constant visual feedback, online correction cannot be based on the sensory information and will thus result in less online feedback and more smooth movements.

As mentioned earlier, a large number of studies trying to resolve the cerebellar function are based on cerebellar lesion research. A disadvantage of these studies is that processes in motor command forming might try to compensate for the loss of the cerebellar components. The compensational machinery might possibly give a distinctive characteristic to motor movements which might be falsely attributed as a cerebellar function. This once more states the importance to approach the search for cerebellar function from different research fields.
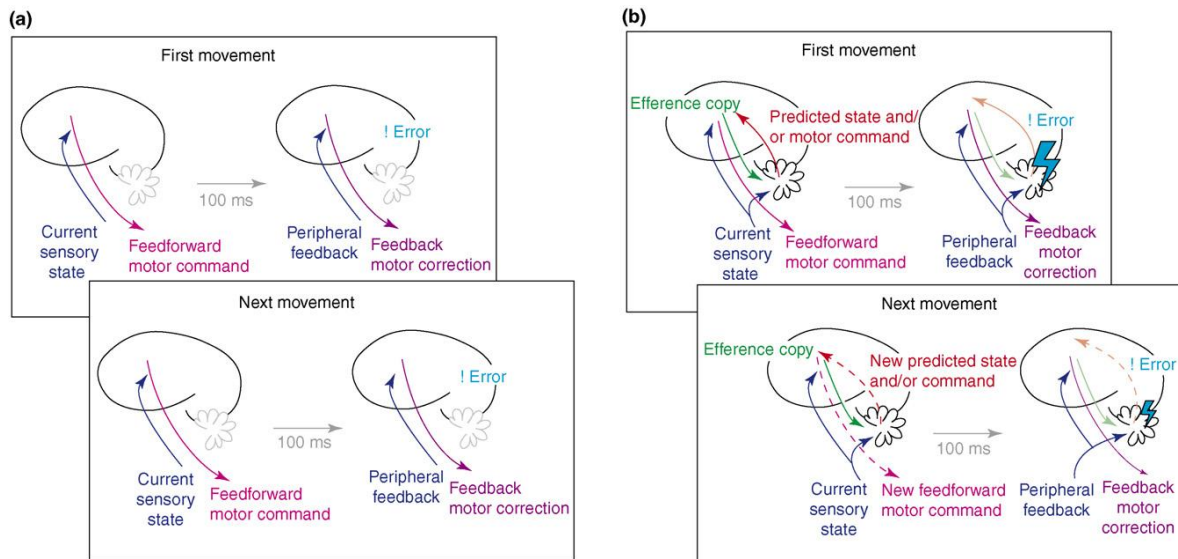
Fig 2. Differences in motor correction mechanisms. On the left side reactive motor control is stated. Errors detected through sensory feedback will result in a motor reaction which compensates for the detected error. This mechanism can operate without a cerebellum and there is no learning involved. In the next movement the motor command will harbor the same motor error and thus requires the same motor correction feedback.

In the feedforward control, for which the cerebellum is required, the sensed error will result in an adjustment of the feedforward motor command. Through this learning process the error in the feedforward command will be reduced. The feedforward mechanism requires a cerebellum which gets sensory input as well as efferent motor commands.

Figure of Amy J Bastian (2006) Learning to predict the future: the cerebellum adapts feedforward movement control.

The cerebellum as predictive element

A general conclusion of the cerebellar damage studies is that the cerebellum is important in predictive control. Based on upcoming states it can plan accurate movements in advance and it is important for fast movements in which feedback correction would be processed too slow to contribute to appropriate movements. However the predictive function of the cerebellum is well acknowledged in literature, there is no consensus about what specific predictive information is computed in the cerebellum. In literature basically two cerebellar prediction models are mentioned which explain the cerebellar function in optimal motor control. Either the cerebellum predicts the future state of the body or it could predict the optimal motor command. In the first model, the forward model, the cerebellum predicts the future state of the body, which is either the upcoming state of the body, position and body dynamics, or the upcoming sensory input as result of an intended movement. The second model, the inverse model, computes the ideal motor commands which will result in the intended movement.

The state prediction model theory

In this chapter the prediction model will be issued, this model uses predictions of upcoming sensory states or of the future body state, this encompasses the body's dynamics. The dynamics are the parameters that define physical characteristics of the body. The predictions of the result of motor movement will influence the computation of the next movements. For example during an eye saccade (rapid eye movements that move the eyes to a new location) the processing of sensory feedback would be to slow to effectively guide the eye to a new location. It has even been found that visual sensory information processing is suppressed during these saccades (Thiele et al. 2002). Predictions of the future state of the eye should thus be used to compute an accurate motor command to guide the eyesight to a new location. To compute state predictions, efferent copies of an intended movement command are used in a forward model to compute the future state.

An example of the elements that contribute to a simple state prediction will first be given, thus without adjusting the next motor command. Wolpert et al. (1995) designed a model that described the results of an experiment in which subjects were asked to predict their arm position in the dark after they made a movement. The prediction of the position is a combined estimation of two different paths, the sensory information and a forward motor model prediction. The forward model prediction starts with a state estimation of the motor system, joint angels and velocity, and uses efferent motor command copies to compute a prediction of the state after the movement. Because the subjects couldn´t see their arm, the sensory information describing the position of the arm is based on proprioception. The combined estimation model, called the sensorimotor integration model, is depicted in fig. 3. The difference between prediction and actual position had a profound profile, in which the prediction error increased fast during the beginning of the movement and stayed at a set value thereafter. Since the state estimation of the arm before the movement is precisely known, it can be assumed that during the first part of the movement the position prediction is mainly based on computations by the forward model using efferent copies of the motor command. The reason for this is that sensory information describing the position is much more unreliable in the beginning of the movement then the internal prediction. But as the movement evolves the error in the internal prediction would be multiplied because the error in the state estimation would again be used to compute the new position through efferent copies. During the first second the prediction based on proprioception will get more important and after the first second it is the most important mechanism of the prediction.
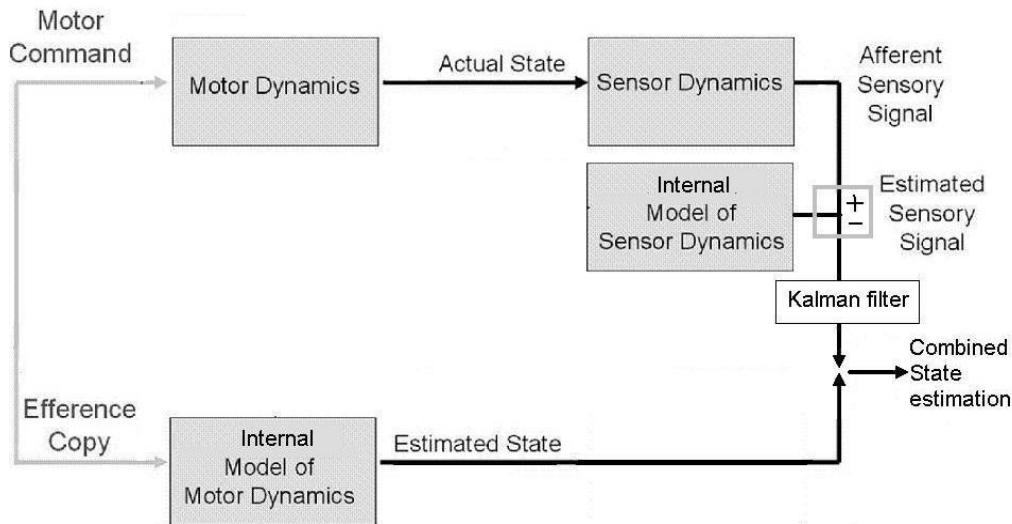
Fig 3. State estimation model as proposed by Wolpert et al. (1995). A prediction of the state of the arm, such as position, is made based on internal model predictions and sensory information. The position estimation in the upper half is based on sensory information. An internal model predicts the sensory information and corrects the sensory input estimation. In the bottom half of the figure the position prediction is based on an internal model of motor dynamics using efference copies. A kalman filter regulates the weight of both prediction pathways.

Two different paths thus predict the arm's state, in this example the state is represented as only the arm's position. The weight of both estimations is set by a Kalman filter, which in this example gives the 'sensory path' gradually more weight during the first second. To accurately control the ratio of the two pathways for the combined state estimation the Kalman filter must "know" which path is the most accurate. This is done by comparing the predicted sensory input, based on the internal model prediction, with the actual sensory information. The error between these two is used by the Kalman filter to adjust the weight of the sensory path to the internal model prediction (Kalman et al. 1961).

The state prediction through sensorimotor integration as depicted in fig. 3, is an important element in optimal motor control. In this process, in which the cerebellum plays a key role, the cerebellum adjusts upcoming motor commands, for which it will use the state estimations. A model describing the adjustments of upcoming motor commands based on the future state prediction is depicted in fig. 4. Efferent copies of motor commands coming from the motor cortex or brain stem are input to the forward computation, which computes the body state after the movement. The predicted state will, together with the desired state, control the computation of motor commands. Because the dynamics and kinematics of a movement are heavily changeable the internal model prediction should be constantly updated. The computed prediction states are compared to the resulting states. The error between these two is used to adjust the internal motor and sensor dynamics and will thus adjust the command computed in the motor cortex.

In normal day to day movements Slijper et al. (2009) showed that the contribution of optimal motor control to appropriate scaling of executing movements will get more successful during the movement. This in concordance with the findings of error development shown in the state estimation model of Wolpert et al. (1995). At the onset there is great uncertainty of the kinematics and dynamics of the motor apparatus (Flash and Sejnowski, 2001). During the movement the sensory information will add to the experience of the movement and update the internal model in a Bayesion fashion (Kording and Wolpert, 2006). This will result in improvement of the prediction as seen in Wolpert et al (1995) and decline of the movement error (Slijper et al. 2009).
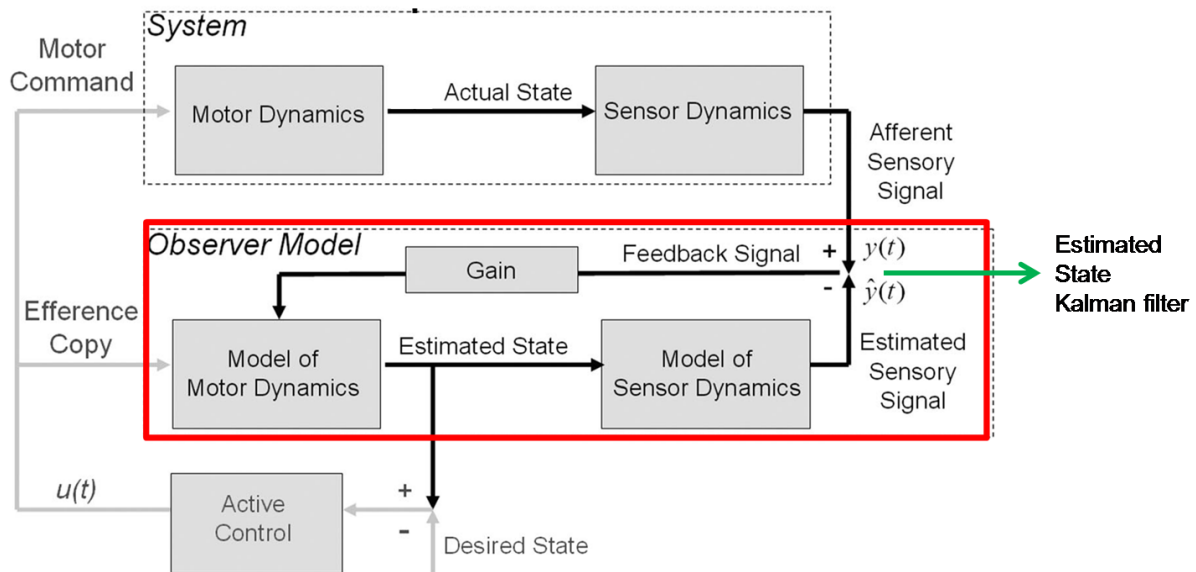
fig. 4 Sensorimotor-integration. Forward models are used to help each other making an accurate prediction of the state of a body after a movement. In the scheme the controlled body is the arm. In the red box the processes which are believed to be computed in the cerebellum are stated. The forward model combines the state of the arm with the efference copies of the motor commands to predict the next state (position) of the arm. This state estimation will also be translated in the estimated sensory input. In the real world, denoted system, the motor command is executed according to the motor dynamics. The sensory feedback will be compared to the predicted sensory feedback, this will as in fig 3. be combined through a Kalman filter to a state estimation. But also the difference between predicted and real sensory input is used to adjust the internal motor dynamic model. Adjustments in the motor model dynamics will result in adjustments of computation of desired movements into motor commands.

Evidence has been found in neurological image studies for the state prediction mechanism in the cerebellum as proposed in the forward model. In a study by Miall and Jenkinson (2005) subjects were asked to complete a task in which either the hand had to follow a trajectory lead by the eyes or the eyes had to follow the hand. Neuro-imaging of the cerebellum showed that distinct structures known to be related with the hand or the eyes were active. In case the hand was leading, the regions known to represent the hand were active and vice versa. This indicates that the cerebellum computes the future state of the controlled body. A practical example of the internal predictive sensory models can also be demonstrated easily. When one inflicts tickling to itself it will not cause the tickling sensation, because it is predicted and subsequently cancelled centrally in the CNS. (3)

Inverse model

In this chapter the process underlying the computation of a desired movement into a motor command will be issued. The necessary computation for this transformation process, referred to as the inverse function, is considered to be carried out in the cerebellum. To explain this model we will first discuss the translation of a desired movement into a motor command, schematically represented in fig. 5. Motor commands are sent through motor-neurons which then will result in a force exerted by the activated muscles. The translation of the motor command information into a movement depends on the dynamics of the muscles that get signaled. The strength, length and fitness of the muscle as well as the combination of muscles will influence the resulting movement. These parameters are denoted as the motor dynamics which are stated as H in fig. 5. To execute a desired movement, an appropriate neuronal message has to be send to the muscles which is in respect to the parameters in function H, the body's dynamics. To compute an appropriate signal in respect to function H a motor command should be computed through the inverse function of H, H^{-1}. Important to remember is that the cerebellum is not the only structure involved in computing motor movements, as the commands are still originating from the motor cortex. The cerebellum in the inverse model is believed to produce correcting motor commands in a feedforward fashion as will be discussed later in the VOR loop chapter. The output of the motor cortex or brainstem is augmented with cerebellar output to produce optimal motor commands.

Although the inverse model is sometimes mentioned as an opposite model compared to the forward model it has been shown that they are interconnected. The differences between the models are more subtle then their name would indicate. The difference between the two models is that the cerebellum has a more prominent role in computing motor commands in the inverse model, while it has a more guiding role through state representation in the forward model.
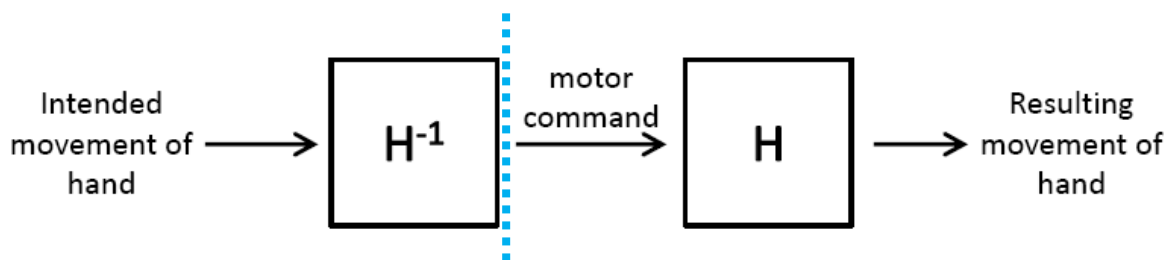

Fig. 5. In the inverse model the cerebellum is believed to compute an optimal motor command. In this schematic model a hand motor task is used as example to discuss the translation of intended movements into appropriate motor commands. Right of the bleu dotted line a motor command has been formed through the CNS and is translated into a movement according to the motor dynamics, H. The square with H thus represents the state of the arm moving the hand. To compute appropriate muscle commands, which result in the resulting movement becoming equal to the intended movement, the intended movement should be translated into motor commands through the inverse function of H, denoted H^{-1}.

To discuss the functions of the cerebellum in the reverse motor model we will use a motor task, picking up an apple, as example. The inverse model states that the input to the cerebellum is a desired movement signal, this signal can be interpreted as an intended velocity with direction of an end effector, in this example the hand. In the motor cortex a signal must be present describing the position of the hand and of the apple in respect to the hand to calculate a desired movement. The computation of the desired movement is also depending on the kinematics of the task, e.g. we should change the desired movement if the apple is rolling away. Although the cerebellum seems to play a role in adjusting for kinematic variables as well and kinematic variables cannot be processed equal to dynamical adjustments (A Haith and S Vijayakumar 2009), we will not address theme in this chapter.

To elucidate the computation of the appropriate motor commands we will first look at the different steps that translate a motor command into a movement. The motor area's in the central nervous system produce motor commands and will send these through α neurons to innervate separate muscles. As mentioned translation of a motor command into a muscle action depends on the state of the plant being controlled by the muscles. E.g. the moment of the arm, the muscle strength, as well as external factors such, as the weight carried by the arm. These biophysical dynamics are described by a function denoted g. See fig. 6. Subsequently different forces exerted by the separate muscles will all act on the arm. The total combinations of muscle forces (F^A) will combine according to physical characteristics of the total arm, denoted G, to result in a velocity with a certain direction, $\Theta^{\bullet A}$.
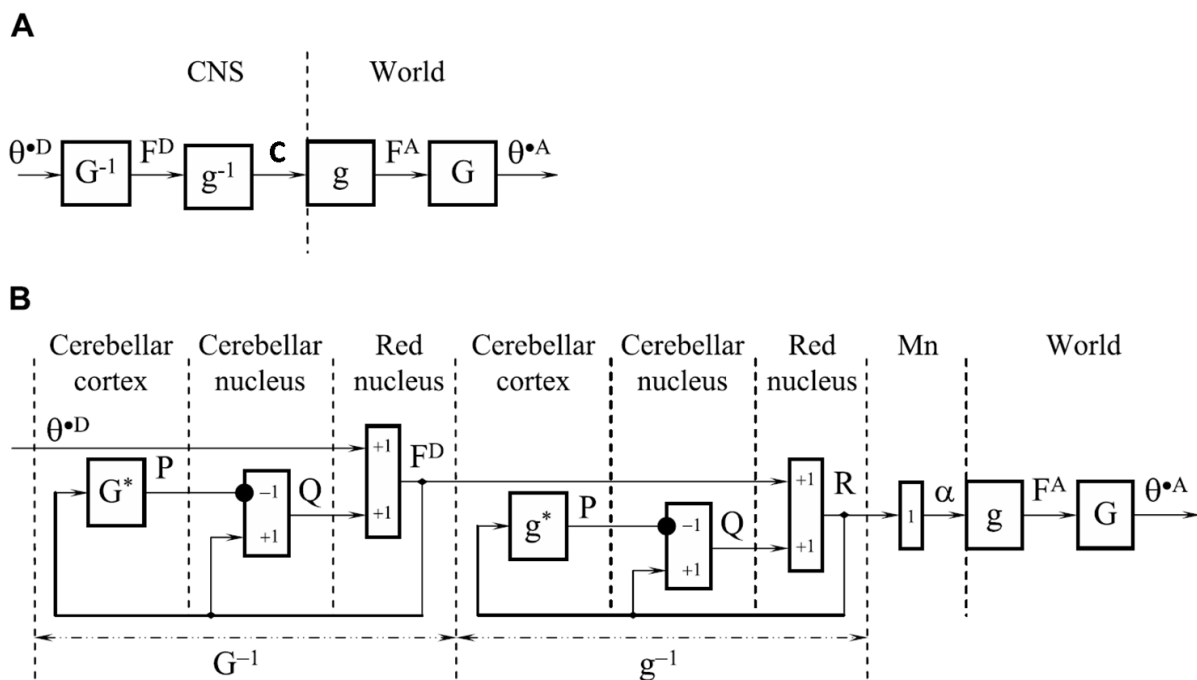

Fig. 6A The computation of appropriate motor commands is based on constraints of the muscle and the limb. A motor command (C) is generated in the central nervous system and will be translated by muscles into a force (F^A). The forces will be integrated in the limb segment, G, resulting in a resulting velocity with direction. Because these two functions are processed in successive orders it is believed that the motor command is computed as well in this successive order through the inverse functions of g and G. 6

Fig. 6B This model shows how the inverse functions, G-1 and g-1, translate the desired movement into appropriate motor neuron signals. The two inverse functions consist of two feedback loops containing a direct function, G and g*, computing the expected outcome of the signals produced by the inverse function circuit. The outcome of the direct function sends an inhibitory signal to cells in the cerebellar nucleus, line with circle. This is comparable to the inhibitory Purkinje cells projecting to neurons in the cerebellar nuclei. The signal P is believed to be the simple spike activity of Purkinje cells. Q denotes the activity of the cerebellar nuclei neurons. FD and R are the output signals computed by the G-1 and g-1 inverse functions. The anatomical representation is based on rodent models and monkey models. Fig. from Ebadzadeh 2005.*

The described processes are both in the real world, meaning that they are outputs of the CNS and act according to physical laws. To compute accurate movements, there must be an internal model which can compute the appropriate neuronal innervations which considers the functions g and G. The internal model computing appropriate motor commands should thus be the inverse functions of g and G, referred to as g-1 and G-1. Because both processes are in series in the 'real world' it can be assumed that the inverse functions of both are

also in series. As depicted in the model, figure 6A, the input is the desired velocity and direction of the end effector, the hand. This signal is generated through the inverse kinematics discussed above. First the inverse function of G-1 will compute the forces which should be exerted by the separate muscles to result in the desired movement of the hand. Subsequently the g-1 box will translate the desired force in a motor signal send to the separate muscles.

Mathematically the difficult part of the theory is to generate approximate inverse function of g-1 and G-1. In figure 6B, a model is proposed describing how the inverse functions G-1 and g-1 are generated. This model bypasses the mathematical inverse problem through a feedback loop. A more detailed model is given by Ebadzadeh et al. (2005). In this chapter we will briefly discuss the network that in total will act as an inverse function. This model states that an approximate inverse function is formed trough a predicting element able to anticipate the effect of a motor order in a feedback fashion, this model is according to mathematical and physical models. (Darlot et al, 1996; Eskiizmirliler et al ,2002; Ebadzadeh et Darlot, 2003). The inverse function G-1 seen in figure 6B consists of an input which encodes the desired movement ($\Theta^{\bullet D}$). The desired movement will reach a summing element, the output of this element is sent to a predictive element G* containing an intern forward model that predicts the outcome. The predictive element containing a feed forward loop is comparable to the feed forward model described in the previous chapter.

By comparing the desired state and the state formed by the internal predictive model a feedback loop is formed which will update the commands generated by the inverse model. The positive loop, coming from the summing square, ensures short memory by storing the current premotor order. The predictor G* is constantly updated by errors detected in the 'real world'. The same principle accounts for the predictive element g* in the inverse function g-1. The pathway that updates the predictive elements is not shown in fig. 6 for clarity. The inferior olive is believed to be the crucial site in sensing errors and adjusting the predictive element. Anny changes in the g* or G* will adjust the computed motor command R which is ultimately send to the muscles.

The model proposed in figure 6B has been successfully tested in computer simulations (Ebadzadeh et al 2005). An important aspect of the model is the feedback loop with a forward function that can predict errors and correct for these. A comparable feedback-error learning model has also been proposed by M. Kawato (2008),this model contains an inverse model which first transforms a desired trajectory into a feed forward command to update the inverse model in a feedback loop. Stability and convergence of the feedback-error-learning algorithm has been mathematically proven by Nakanashi and Schaal (2004) as well as successfully applied to several robotic demonstrations by Miyamoto et al. (1988).

The model proposed by Ebadzadeh et al. (2005) has been constructed considering the anatomical pathways seen in the cerebellum of rodents and monkeys. Although some cell types are not represented as Basket cells and stellate cells, the model is thought to represent a model capable of producing the simplest forms of movement. The model states that the desired premotor order arrives in the red nucleus. The predictive computations G* and g* are both formed in the cerebellar cortex, their projections are comparable to the inhibiting projections from PCs in the cerebellar cortex to the cerebellar nucleus, signal P therefore is believed to be the simple spike activity by the PCs. Positive signals from the red nucleus will be transported via excitatory mossy fibers to area´s in the cerebellar cortex and the cerebellar nucleus. The red nucleus also receives descending afferent connections from the cerebellar nuclei and the cerebral motor cortex (Padel 1993, Keifer and Houk 1994).

Cerebellar input

The previous chapter the focused on what the cerebellum computes, prediction or optimal motor command. In this chapter the cerebellar function will be discussed in light of the information the cerebellum receives to make accurate commands. To elucidate the cerebellar function it is useful to look at the vestibule-oculo-motor reflex (VOR). This reflex pathway, in which the cerebellum contributes to optimal motor control as seen with more difficult movements, is relatively simple and thus ideal for research. Also the eye movement and the error, the retinal slip, can be easily used in experiments. That's why a lot of research has been done into this reflex pathway.

Although a variety of brainstem circuitry contributes to the VOR, the basic reflex is mediated by a fast free synapse pathway in the brainstem (Boyden et al 2004). This brainstem pathway is augmented by an adaptive pathway through the cerebellum. It is known that among its many inputs, the region of the cerebellum involved in the VOR receives a variety of parallel-fibre inputs including vestibular-related signals and efferent copies of outgoing oculomotor commands (Hirata and Highstein 2001)

The efference motor commands reaching the cerebellum are most likely projected from the premotor cortex through the cortico-ponto cerebellar pathway (Ramnani N, et al. 2006). In the VOR the efferent motor command copies are believed to be sent from the nucleus prepositus hypoglossi.
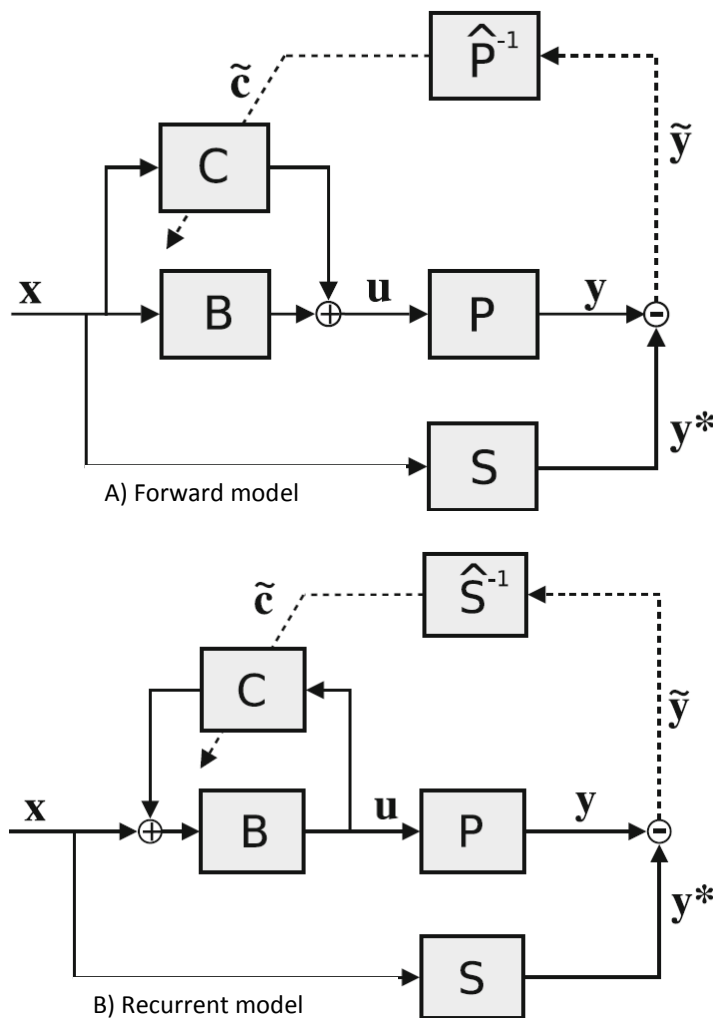

A) Forward model

B) Recurrent model

Fig 7. Two models of the vestibular oculo-motor reflex (VOR), Both models act to stabilize gaze during head rotations (x) by counter rotating the eyes (y). The difference between these two is given as retinal slip (ŷ).

A In this model the cerebellum receives vestibular feed forward input, representing head velocity (x), the motor command generated from the brainstem (B) and the cerebellum (C) added together makes up the motor command (u). The error, retinal slip, is translated through an inverse function of the plant motor dynamics(P^{-1}). The cerebellar error (Č) is sent as a learning signal to the cerebellum.

B The cerebellum receives only efferent copy input (u) from the brainstem (B). The retinal slip is translated into an cerebellar error through the inverse function of the kinematics of the task and sent to the cerebellum as learning signal.

C = cerebellum, B = brainstem, P = oculomotor dynamics, S = Task kinematic, u = motor commands, y = eye velocity. X = head velocity. Y= desired eye velocity. Č = the error in cerebellar output.*

Fig. from A. Haith & S. Vijayakumar (2009).

The VOR thus has been shown to have both vestibular input and efferent motor command input. The output of the reflex network in mammals is to stabilize gaze during head rotation by counter-rotating the eyes. In some cases this will mean that the velocity of the eyes should be the exact opposite of the head velocity, $y^* = -X$. In many more cases we must be able to change our eye velocity to changing kinematics and dynamics of the task as in experiments using prisms or lenses.

Two models have been proposed that lead to gaze stabilization, the forward model and the recurrent model. These terms should not be confused with the models mentioned earlier, the forward and inverse model. In short the difference between the two is that the cerebellum in the forward model uses only vestibular information to perform it's task (Shibata and Schaal 2001), while the cerebellum in the recurrent network uses the efferent motor commands (Porill et al. 2004), Fig. 7. Both models have been tested successfully (A Haith & S Vijayakumar 2009).

Both the forward model and recurrent model start with a head motion that will give rise to vestibular signal input. In the two models proposed the kinematic variable is represented as S. The vestibular input will, according to the kinematics of the task, result in a desired eye velocity that should lead to gaze stabilization. The motor command produced will be translated in an eye velocity depending on the ocular muscular dynamics, denoted P. In both models the difference between desired eye velocity and the real eye velocity will result in retinal slip denoted as $\hat{y}$.

In the feedforward model the cerebellar receives the vestibular information and its output contributes directly to the outgoing motor command. The motor command generated is a sum of the command generated by the brainstem circuitry, B, and the cerebellar circuitry, C. To contribute correctly to the motor command the cerebellum must learn an inverse model of the motor apparatus.

In the recurrent model the cerebellum receives efferent motor commands coming from the brainstem circuitry. The output of the cerebellum contributes to the vestibular signal that is received by the brainstem. In this model the cerebellum can only function properly if it contains an inverse function of the kinematics of the task.

The error signal which should adjust the cerebellar contribution should be translated into a signal representing cerebellar error. Due to the models connection architecture and also stated by mathematical proof (Adrian Haith and Sethy Vijayakumar 2009) the retinal slip is translated through different inverse functions for each of the models. In the forward model the retinal slip is translated by an inverse function of the dynamics of the oculomotor plant, in the recurrent function the inverse function is represented as the kinematics of the task.

Error signaling and internal model adjustments

One element that is essential in all previous mentioned motor control models is an accurate state prediction. This prediction is based on the state of the plant that is operated, because the state is changeable the internal models should be constantly updated. The adjustments of the models are based on the sensed prediction errors, as also seen in fig. 4, which is thus important in predictive control executed by the cerebellum. (Diedrichsen et al. 2005, Suminski et al. 2007)

The cerebellum seems to be an important structure in sensing errors and adjusting the internal model. Some evidence for this comes from neurological image studies in which a strong correlation was found between error signaling and cerebellar cortex activation. Moreover the magnitude of the sensed error and the magnitude of the motor correction showed correlation with the rate of activity seen in the cerebellar cortex. Activation in the cerebellum is highest during difficult movements, when interplay between muscles is required (Seidler and Noll 2008). The location of possible error processing was seen in zones corresponding with the functional output related to the tasks requirement (Diedrichsen et al. 2005, Grafton et al 2008).

Sensed errors are also used for in flight corrections, both mechanisms, in flight corrections and adjusting internal models through error signaling, work at the same time. The error signaling will however not contribute to the both systems equally over time (Smith et al. 2006, Grafton et al. 2008).

Although there is a strong link found between cerebellar activity and error signalling, it is not known exactly how error signalling is processed and classified. When errors contribute to adjustments of an internal motor model and when is it used to correct in flight movements is not fully understood. To answer these, first the differences in sensed errors will be considered. Sensing errors in motor movement is by for example trough proprioception and visual feedback. The errors can be of very different origin, errors could be generated for example by intrinsic or external factors, fatigued muscles or computer guided point tasks. The errors can also be in a regular fashion, arise random or arise due to kinematic or dynamic alterations. The difference between errors can be of influence in the feedback exerted by the cerebellum. The difference in error processing has been described by Diedrichsen et al. (2005) who introduced errors in reaching movements. Subjects were asked to reach a target while or the hand was perturbed during flight or the cursor representing the hand was visually perturbed (e.g. mirrored) or the target itself was moved during flight. The first two errors introduced are considered to originate from the movement itself, while the latter is believed to originate from external factors only. Correction of the movement was seen in all three errors, but in repeating trials only the first two showed adapted feedback, feed forward cerebellar learning, which indicates that external errors are not interpreted the same. Surprisingly neuroimaging showed that all the different experiments showed the same areas being activated in the cerebellum.

Whether the sensed errors contribute to learning new motor skills or were solely used to correct in flight movements didn't alter the activation observed in the cerebellum. As seen in previous neuroimaging reports visuomotor tracking tasks (Diedrichsen et al. 2005, Grafton et al 2008) requiring eye-hand coordination also showed correlation between cerebellar cortex activation and the magnitude of perceived error. (Miall et al. 2000, 2001, 2005)

In an experiment by Tseng et al. (2006) subjects were asked to adapt their reaching in a rotated visual environment (Tseng et al. 2006). Two different experimental setups were tested. In the first experiment subjects were allowed to make feedback corrections, while in the second the same reaching tasks was given, but this time the subjects were not allowed to make corrections. Both conditions resulted in adaption of the movement and thus showed adjustments of the predictive model. Adjustments of the internal model can thus take place without motor reaction on sensed errors and thus indicate that sensing errors is enough.

Error signals are believed to be signaled through the inferior olive. Processed sensory signals and desired sensory signals come together in the inferior olive which will calculate the differences. The inferior olive as

detection mechanism of differences between desired and actual state is described in various reports. For example: when passive proprioceptive stimuli are induced in trained animals, their inferior olive shows activation in contrast when similar stimuli arise from active movements (Frens et al. 2001, Horn et al. 1996). The differences detected in position, velocity etc. will be send as a teaching signal to the cerebellum, via pathways representing the climbing fibers. It is believed that the teaching signal results in LTD induced in the dendritic spines of the purkinje cells and in this way can adjust internal model prediction.

Internal models not stored in the cerebellum

So far the internal models and the adjustment of internal models through error detection are considered to be solely a cerebellar mechanism. But while there is strong evidence that the cerebellum is an essential component in adapting to changes of kinematic or dynamics in movements, it has not been associated convincible been associated to storage of new acquired motor programs.

The side of motor movement storage has been a topic of debate because of conflicting results. In goldfish and monkeys the flocculus was inactivated by use of lidocaine. (McElligot et al. 1998, Nagao and Kitazawa 2003) This led to a total abolishing of the learned motor performance a few hours before. However inactivation of the lateral vestibule cerebellum has also been found to have no effect on the adjusted VOR gain. (Luebke and Robinson 1994). The contradicting results could be explained by the transfer hypothesis, which states that short term changes take place in the cerebellum which subsequently sends signals to the brainstem to drive long term memory.

Neuroimaging studies by Grafton et al. (2008) also questioned the storage site of internal models. Through neuoimaging techniques the area's which are active in feed forward and feedback control were studied. Through a visuomotor task the activity of different areas was visualized during feed forward motor control. The cerebellum showed no change of activity when feed forward learning was observed in the task. This indicates that the internal storage is not in the cerebellum. Moreover cerebellar damage doesn't result in loss of executing complex movements as riding a bike, but instead leads to difficulties in movements when dynamics or kinematics of a movements are altered. Functional studies also show strong activation of the cerebellum when executing movements in which these parameters are altered, (Grafton et al. 2008). The storage of complex motor programs have been suggested to be stored cortically and adjusted or modified via cerebellar modulation (Smith M.A. and Shadmehr R., 2005)

The recurrent VOR model, (Haith A. and Vijayakumar S. 2009), discussed earlier showed some instability in its motor adaption performance. These instabilities were observed for dynamic changes as well as kinematic changes introduced. It has been suggested that this instability in the network could be rectified through the transfer of the internal model system to the brainstem (Porill and Dean (2007).

State estimation through sensory input and efferent motor commands

The function of the cerebellum in optimal motor control is related to prediction of either future sensory information or the future motor command necessary to fulfill an action. Both predictions depend on having an accurate and update internal model which reflects the state of the body. This chapter discusses the mechanism by which internal model predictions and sensory information are combined to give a sound representation of the body state. Although this will not directly explain the mechanism that computes optimal motor commands, it will show neurological network characteristics that can give insight of the cerebellar mechanism as a whole.

To explain the neuronal mechanisms acting in the state estimation process, a simple motor coordination tasks will be used; grabbing an apple. To make an accurate movement with the hand towards an apple, we should first make an estimation of the location of both the arm and the apple. We will begin with localizing the apple, this to simplify the example because it's estimation is solely based on visual input and not on proprioception for example. The focus will be on the electrophysiological characteristics of the neurological network used to determine the apple's location. This neurological network is very likely used for tasks that are much more complex.

Neurons reacting to visual input can be used to localize the apple because they are represented within a visual topographic map. The individual neurons within the neurological network will be able to respond differently towards a variable such as position. Each individual neuron will have a strongest electrical reaction to visual input from a particular position, position R, which is its preferred position. As the distance between the visual input location and the neurons preferred visual location gets bigger, the magnitude of the neuron's reaction will decrease. The tuning curve describing a neurons reaction along an axis with the distance from its preferred visual location is bell-shaped as shown in fig. 8.
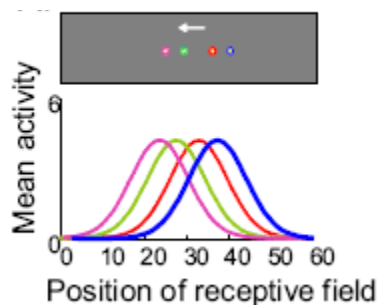

Fig. 8. The mean activity curves of four neurons, indicated by different colors, towards visual input from different positions. As every neuron has its preferred activity position the hill of the mean activity is centered at four different positions. The curve of each activity curve is bell shaped. Figure from Deneve et al. 2007

The individual neurons will make up a topographical map because they lie in planar structure according to their preferred position to which they have the strongest reaction. Considering the visual input from the apple location this will result in a population code from multiple neurons, within a so-called retinotopic map of neurons. (To have a simplified example, pretend that the location is one-dimensional and has only a variable along one axis.) At any given time the individual neurons will react to the hand position according to their preferred position. If this reaction would be noiseless the summed neural activity, a combination of overlapping bell curves, for visual input from one location would follow the bell shaped curve as seen in fig. 9A with the strongest activity, the center of the hill, representing the hand position. Unfortunately neurons have a noisy reaction pattern, with the noise following a near Poisson distribution (Vogels et al. 1989), the population code will be less regular, as seen in Fig. 9 B.
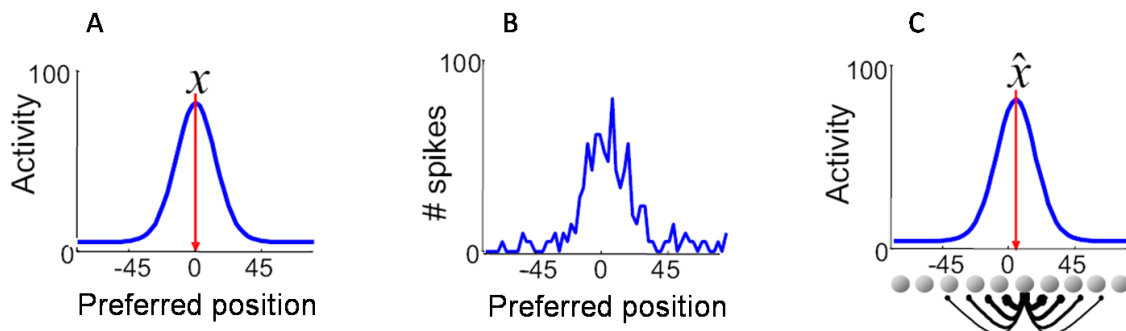
Fig. 9. Neural activation curves. A) Average activity of a population sensory cells when presented with visual input from position 0. B) Example of population activity for a given trial. C) Through iterations and appropriate tuning of the lateral connections between neurons the noise, as seen in B, is filtered and the peak activity x is within 5 % of the true peak. Figure adjusted form Deneve et al (2007)

To have an accurate visual estimation of the apple, the noise in the sensory information should be filtered. This can theoretically be done by computing the mean activity of a big number of repeating inputs of the same visual arm position. This would result in a perfect Gaussian curve with the top of the hill at the position of the hand, in case there is no bias in the noise

The network described in this chapter will indeed filter the noisy which is inherent to sensory information by iterating the signal as discussed by Denève et al (2007). The neurological system Deneve et al. brought up is a so called "attractor network" in which neural signaling is encoded within iterative signals. The general idea is that neurons are interconnected to each other, with the connections between neurons being stronger when they lie closer together. This implies that the neurons having a preferred reaction for visual input from location R will be stronger connected to neurons at R + d then R + 2d. When such a network has an iterative signal a smooth hill as seen in fig. 9C will be formed as seen in computer models. A bell shaped curve will develop, the hill of the top will represent the variable, in this case location R, which is estimated from the noisy hill input. This network has been shown to be a sound network since the estimate is not biased, meaning that it is equal to the true value of direction on average.

If we now consider for a moment that the apple we want to grab is rolling from a table this will enlarge the difficulty too filter out the noise in the visual input. The recurrent network needs a couple of iterations to be able to filter out noise and thus also has a minimal amount of time that enables filtering. The visual input of a rolling apple will result in neuronal iterations of the apple position at time t(x) which will interfere with iterative signals of the new visual apple position at time t(x+1). Because these are different positions, the network representing the visual location cannot stabilize onto smooth hills and thus cannot compute an accurate position of the apple.

To overcome this problem an internal model prediction should be implemented within the recurrent network (Deneve et al. 2007). The internal model prediction that should be incorporated in this example would only have to compute the position estimation of the apple. When considering the movement of the apple as a simple movement with speed A along one axis we can formulate the internal model predictions of the apple's position as.

$\hat{x}_a (T+\delta T) = \hat{x}_a (T) + A.$

In which the x^ a(pple) denotes the position of the apple on T=0 and A is the velocity of the apple.

Implementation of a prediction into the network is based on interneural connection strength within the iterative network. The connection strength between neurons in the layer can be rearranged by which the

pattern of activity predicts the future state at t+δt. If the predicted position of the apple can be described as X (t+δt) = xi (T) + A. The neurons in the network will be interconnected in line with this prediction, meaning that neurons responding to their preferred position Xi will be most strongly connected to neurons with position Xi+A. Neurons triggered to position X will thus have a strong connection to the neuron which would be triggered if the trajectory of the apple would unchanged follow the internal prediction.

The Internal system thus predicts the position of the apple, based on the sensory information received in the past. However due to sudden changes in the speed of the apple or inaccurate estimation of sensory input the internal prediction could get an error. To cope with these discrepancies the internal system should be updated constantly and thus the network combines the estimates with on-line feedback control. Visual input from the apple will tell if the predicted trajectory is still followed. Visual input and internal model estimates are combined to give the most optimal prediction and also to update the internal model. The ratio of weight given to both the internal prediction and the visual input is thought to be set by a Kalman filter. This network is also described in more basic terms in the chapter 'the prediction model theory', fig. 3.

State estimation using an internal model

The previous chapter introduced some of the principles of an iterative network. In the next chapter a comparable iterative network will be discussed in a motor task example which is more relevant in respect to optimal control. Prior to grabbing an apple it is not only necessary to know the location of the apple but also of the state of the arm. This involves determination of the position, the velocity and the forces exerted by the muscles. Because of the use of continuous visual feedback for online control during a movement as reported by Saunders et al. (2005), it is also necessary to make continuous state estimations of the hand during its flight to the apple.

As in the 'apple location example' an prediction of the upcoming state of the arm should be implemented into the network . This prediction is computed with efferent motor commands. The network should thus cope with a combination of sensory information, visual input, proprioception and efferent motor commands, which will be used to calculate a state estimation. Although the previous network described comprises only one sensory variable, the same principles can be used to combine multiple variables and compute the state of the arm, variables however must be functionally related to each other (Deneve 2001, 2004, Pouget et al 2002).

To have an optimal state prediction the neurological network should have a Kalman filter equation implemented. This filter can effectively integrate different variables, sensory information and internal model predictions, and gives each variable a weight in the summation according to its reliability. Motor movement studies reporting accuracy of trajectories followed using visual feedback have indeed shown that motor movements follow a Kalman filter prediction (Wolpert et al. 1995, Saunders and Knill 2005).

To be able to integrate the increased variety of sensory inputs a 3D-model of neurons is used. This 3D-network model implements the variables; velocity, position and efferent motor commands. Fig. 6. Along the axis the neurons are positioned topographically, with their preferred response for the different variables. Three different input layers for each of the variables will provide the input for the 3D-neuronal network, the sensorimotor network, fig. 6. One input layer will receive visual sensory information encoding position. A second input layer will receive velocity information, a third input layer will receive efferent motor command information. The neurons within this input layer each have their unique preference state for each of the variables. These neurons connect a single neuron in the network; as a result each neuron in the network has a preferred state for each of the three variables. The state of the arm will trigger the neurons in the map that represent this state with respect to the variables for velocity, position and motor command. The internal model prediction is incorporated into the network through the preferred lateral neural connections.

The sensorimotor map receives noisy input from the online sensory feedback each iteration. The weight of the sensory information is for each sensory variable thought to be set by the Kalman filter. More formerly the gain is computed iteratively on the variance of the sensory feedback estimate (the Cramer-Rao bound) and the variance of the unpredictable fluctuations $\epsilon(t)$. The internal model estimate will gain modulate the neural activity. The network is iterated and a three-dimensional activity profile develops from which the activity location tells something about the state of the arm

To elucidate the neuronal connections implementing the internal model prediction it is useful to look at the formula describing the state of the arm in the movement.

$$X(t+dt)=Mx(t)+Bc+\epsilon(t)$$

$X(t)$ denotes the state of the arm for the two sensory variables, position and velocity. M and B are matrices describing the sensorimotor dynamics. $C(t)$ is the motor command at time t and reflects the force put upon the arm. ϵ is the noise produced by the arm motor commands.

However arm dynamics are normally not linear. In general the formula is a common approximation when working in small spaces. (Wolpert et al 1995, Todorev et al. 2000). The internal model is implemented by adjusting the interneural connection strength. Neurons with preferred arm state xi and efferent motor command i have a preferred connection to neurons with a preferred arm state close to $Mx_i + c_i$. The strength of these connections follow a function considering their position following a Gaussian profile centered on $Mx_i + c_i$. Fig 6B shows a hypothetical connection from neuron with a preferred state X_i to a neuron with a preferred state $MX_i + c_i$. The connectivity might be based on spike timing-dependent plasticity (Abbott et al 1996). The neural connectivity thus predicts the future state, according to the internal model matrices.
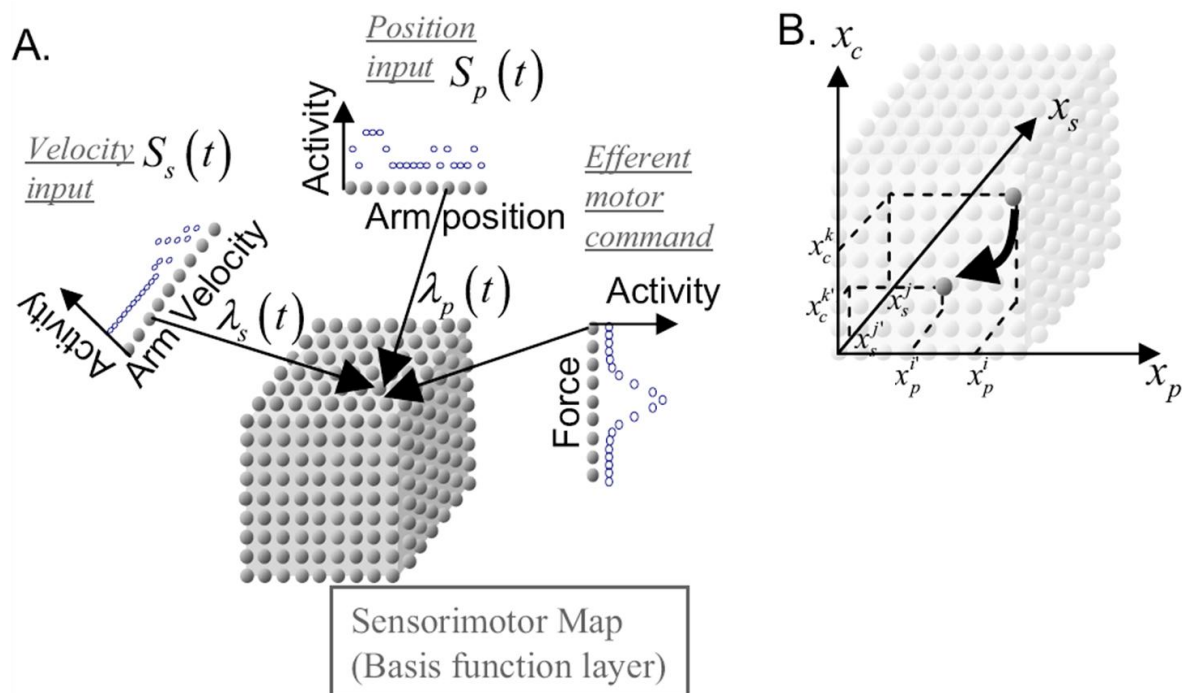

Fig. 10. The cube represents schematically the recurrent neurological network where the arm position is computed through sensory information and the internal model. The 3D structure follows three axis which are velocity, position and efferent motor command. Three input layers provide the input and because single neurons from the input layers have specific connections with the 3D network the neurons in this network each have their specific preference combination of these three parameters. In B the internal model prediction is stated. Neurons with preferred state Xi and a certain force are connected strongest to neurons with preferred states $Mx_i + c_i$. . Adjusted from Deneve et al.(2007).

The network described in the previous sections is not so much based on biological findings but more on computational models following a mathematical framework. The mathematical laws of the model will be addressed in the next section. The mathematical framework of the model has been tested in computer simulations by Deneve et al. (2007). These results showed that the model is unbiased and can accurately predict the position of the arm after a certain amount of time. Moreover they found that the strength of the connectivity between the neurons representing the internal model can vary in a limit of 10% of the optimal value without affecting the performance of the network, which makes the model more likely to fit with biological mechanisms.

Mathematical framework

The sensorimotor map network, fig. 10, gets its input from input layers, which encode either sensory or motor input. The single neurons within the neurological networks each have their preferred state variable, which evokes the highest electrical activity. The mean activity of a single neuron with preferred value X_i^d for a certain sensory observation X^d can be described by the formula

$F X_i^d(t) = 3 [\exp(2)\cos(X^d(t)- X_i^d)-1))+0,01]$

This formula will give rise to the bell shaped curves seen in fig. 9C.

As stated before, the iterative network can filter out the noise of visual and proprioceptive sensory information, which has a Gaussian noise distribution. The motor commands that are input to the sensori-network however are noiseless since they are directly incorporated into the system.

The input layers are connected to the 3d sensorimotor map, so that each unit in the 3d map has a preference for each of input layer variables it connects. The sensorimotor map of the hand position gets sensory input from proprioception and visual sensory input. This input can be described in terms as velocity and position, which are described by the input layers. The motor commands are also incorporated into the sensorimap. Each unit in the sensorimotor map is thus characterized by a set of preferred sensory and motor states $[C_i, X_i^d]$based on their connection to neurons from the input layers The combination of the different variables covers the total of possible body states.

Each neuron within the sensorimotor map is updated through input from the sensory input layers and by the internal model. The gain of each is determined by a Kalman filter. Each unit in this layer, the basis function layer, is characterized by a set of preferred sensory and motor states. The activity of the basis function units at time t+1 is updated according to the following formula.

$Ai (t+1) = [h (A(t))]^l fi(t) + \sum \lambda^d(t)S_i^d(t)$

S_i^d stands in this formula for the sensory input from the input layer; the weight of this input is set by $\lambda^{d.}$. Which is set by a Kalman filter equation. The input generated from the internal model is set by the motor commands: fi(t). The activity in the input unit due to the motor command is regulated by the internal model set by h. In short h represents the connection strength between different neurons which, as seen in the example before, can implement a prediction.

In the previous formula the sensory input was shown to be set by the sensory gain λ^d. This gain is set by a Kalman filter equation which considers the reliability of sensory input and internal input.

$\Lambda_d (t) = \sum_{dd} / q_{dd}$

Q_{dd} is the variance of the sensory estimates and $\sum_{dd}$ is derived from the Kalman filter equation representing the internal input reliability. The internal input harbors the predictive element. The Kalman filter will give the most weight to the most reliable variable. Movement studies have indeed shown that the on-line control of reaching movements by visual/proprioceptive feedback can be accurately predicted by Kalman filter equations as are used in the described sensory network.(33,34, 35)

The internal model thus influences the activity of single neurons. As stated before, the internal model prediction of the state of the hand is implemented into the sensorinetwork through the connection strength between lateral neurons. These lateral connections strength between neurons I and j in the network is regulated is described by the function.

$W_{ij} = \exp (K_w(\sum \cos ([Lx_i]^d - x_i^d) - D))$

The most important feature of this formula is the matrix L which describes the combined effect of sensory and motor input. These sensorimotor dynamics have been mentioned before in the formula that describes the future state estimation based on motor command input.

$X(t+dt)=Mx(t)+Bc+e(t)$

The matrix L from the previous function combines both matrices M and C and thus represents the state of the controlled arm. It is the component that sets the parameters of the internal model prediction. Neuron unit I will be most strongly connected to a unit with preferred state Mx_i by which an internal model prediction is incorporated within the sensorinetwork.

Kw stands for the width of the weight and can be set arbitrary in computer simulation. In the cerebellum this physical characteristics will be depended on the biological processes in the neurologic network.

Optimal motor control

Computing motor commands through optimal motor control depends on having an exact representation of the state of the body. The neurological system described above is involved in computing the state of the body, but the network does not explain generation of optimal motor commands. It can however be used to aid optimal motor control. In this chapter a possible mechanism to compute motor commands using the described sensory network will be presented.

In the previous example, grabbing an apple, the appropriate motor commands should be based on the state estimation of the arm. Moreover this estimation should be accurate for the moment in time at which the planned motor command reaches the arm. The sensorimotor network described generates a state estimation of the arm based on sensory information and internal model prediction. Sensory information however represents a state in the past due to the time it needs to get processed and travel to the integration network. This would suggest that the sensorimotor network as described in the previous chapter cannot be used directly to compute optimal motor commands.

A time accurate state estimation should be given by a network that bases state estimation on internal model prediction and not on sensory information, because of the inherent delay of sensory input. The internal model prediction is based on the sensorimotor dynamics as described in the previous section, these sensorimotor dynamics should however be computed in networks having sensory input.

Considering the coupling of state estimations and time accuracy, we should note that different sensory information is not processed with equal delay. Therefore different sensory information cannot be summed together into one sensorimotor network to come up with a time accurate state estimation. Sensory

information can be considered to be processed either slow or fast. Both types of feedback should be integrated into different iterative sensorimotor networks. Because sensory information that needs more time to get processed will at the time it reaches the sensorimotor network represent a state of the body that is more in the past than sensory information with shorter delays. To have time accurate state representations, different networks should exist that represent different time points. Again Kalman filters integrate the predictions of the internal model with the sensory feedback to have state estimations for the two neural networks.

The different time-point networks are believed to run simultaneously, with one receiving sensory input with a long delay and the other receiving sensory input with a short delay. For example the 'long delay' network, receiving visual sensory input, computes the state estimate of the arm 100 ms ago**.** While at the same time the 'short delay' network, receiving proprioceptive information, computes the state estimation of the body state 50 ms ago. The longer-delay network integrates an internal model prediction of efferent commands issued 100 ms ago, while the network with shorter delay integrates the motor copies issued 50 ms ago. See fig. 10. As seen before, the network implements an internal prediction through the lateral neuron connection strengths. The internal model prediction-parameters of the state estimation network 100 ms can be used to serve as internal model for the network giving an estimation 50 ms in the past. The internal model thus gets transferred from a state 100 ms in the past to predict movement outcome in a network 50 ms in the past. Subsequently the internal model of 50 ms can then be used to predict the future state which would be accurate in real time. Logically this network would not receive sensory input since there is none, because is in process at that very moment. This state assumption can be used to compute accurate motor commands.

Through connections between the different networks it is possible to have insight in the effect of a motor command on the body state. The difference between two state estimations, as given by different networks, can be attributed to the efferent motor command.

$X(t) + C = X(t+1)$.

The formula can be visualized as neural networks, the neuronal activity of one represents the body state at time t=0 and the other activity profile represents the body state at t=1, see fig. 11. Due to the motor command input there is direct insight into the effect of the motor command. For there are two networks running simultaneously representing two different time points; the difference between the two states is caused by the motor command input. These networks and motor command information could also be used the other way around. Through connections from the cerebellum to the motor cortexes, a pathway arises capable of using the desired future body state, X(t+1) and the current body state X(t=0) to compute appropriate motor commands through optimal motor control. This model however requires neural connections to the motor cortexes. Loops found between motor cortical areas and the cerebellum suggest the existence of this inverse model (Padel 1993, Keifer and Houk 1994). The existence of different temporal networks signaling each other as proposed above has been suggested by data found in M1 neurological structures. (Paninski et al. 2004).
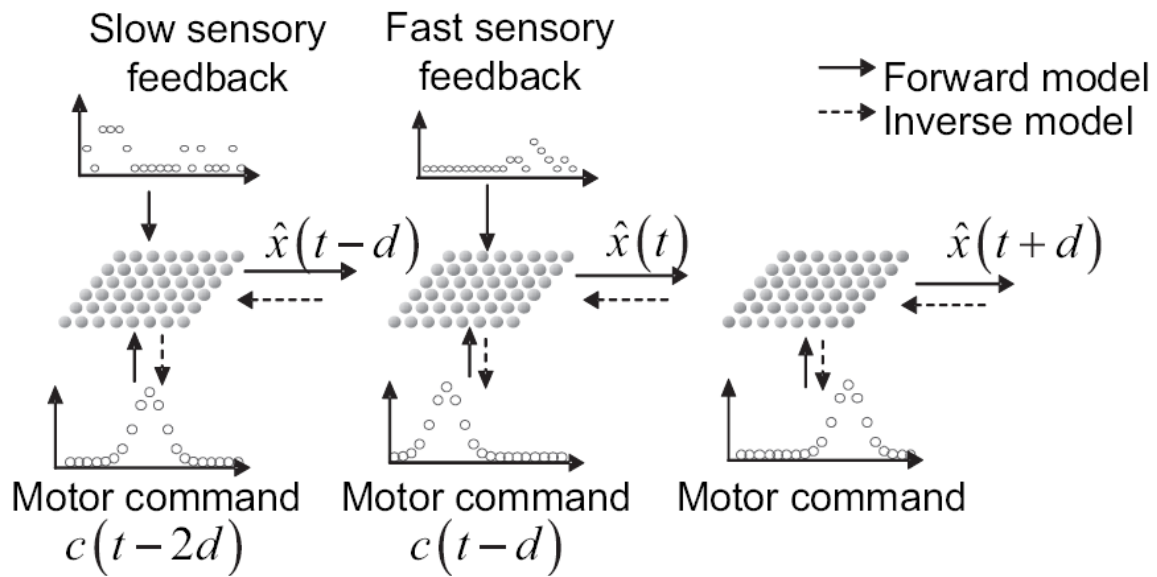
Fig. 11. Because of the delay in sensory feedback compared to the corresponding motor command, multiple delayed networks are supposed to cope with this problem. Slow and fast sensory feedback both provide sensory input for different delayed recurrent networks. Each network will give an estimate of the arms state (velocity, position, end-force) for the specific moment at that time. The two networks giving the state estimate of the hand in the past are interconnected. The network receiving 'slow' sensory feedback will serve to give input to the network receiving 'fast' sensory feedback. The input will encode a prediction and thus implements an internal model. Connections, in which the network with shorter delays act as input for the networks with longer delay, implement an inverse model. Through the connections with the motor cortex the inverse model can compute accurate motor commands. Fig. from Deneve et al. (2009). Note that the forward and inverse model are not the same models as mentioned in previous chapters.

Summary and discussion

Increasing numbers of research reports that try to reveal the basic processes underlying optimal motor control have been presented. The whole process is a combined effort of different neurological structures, reaching from the motor cortex to the cerebellum (Shadmehr and Wise 2005, Shadmehr R and Krakauer J W 2008). An interesting neurological element in optimal motor control is the cerebellum. Its contribution to optimal motor control has been first recognized in cerebellar lesion studies focusing on the problems and irregularities seen in motor movements (Dow and Moruzzi 1958).

Much of the current believes in the functioning of the cerebellum in the learning of new motor skills and making smooth movements is based on theories developed by Mar, Albus and Ito. They combined functional studies with the known neuro-anatomical pathways seen in the cerebellum to elucidate the cerebellar function. An important observation has been the correlation found between the facilitation of Purkinje cell synapses and motor performance. This mechanism was believed to act as a teaching signal in the optimal motor control model (Marr 1969, Ito 1984).

In this paper the cerebellar function will be discussed considering different research fields with the main focus on computational models. But first the cerebellar function will be presented in light of cerebellar lesion studies. These have considerably contributed to the knowledge of the functioning of the cerebellum in optimal motor control. An important observation made is that the cerebellum functions in feed forward control rather than in feedback control (Horak and Diener 1994, Bastian 2006). Functional studies in cerebellar patients have shown that the cerebellum is necessary to predict upcoming states of the body, which are necessary to compute accurate upcoming motor movements (Morton and Bastian 2006). However, the extend of usable information considering cerebellar function extracted from lesion studies is limited. This is because the optimal motor control is an interplay between a lot of neurological networks e.g. the premotor cortex, motor cortex, parietal cortex and basal ganglia (R Shadmehr J. W. Krakauer 2008), which makes it hard to interpret the deficits observed. Other structures in the optimal motor network could try to compensate for the loss of function in the cerebellum and in this way cause error patterns in movements, which would falsely be connected to the cerebellar function.

A more recent research field which could be helpful in elucidating the cerebellar function, is the quantitative and computational characterization of motor systems. This research field has become popular due to robotics for which motor movement programs are developed that should result in execution of smooth movements. The proposed computational models could be together with functional studies inform each other. It is however important not to forget the biological framework in which the models have to fit; e.g. connectivity with other neurological structures and neuronal cell mechanisms as LTD and LTP.

A couple of cerebellar models have been proposed in this paper. They are not necessary complete different to each other, they merely try to show different aspects of the model. The first model proposed, the state predictive model, shows the cerebellar function in light of its state prediction. Internal models of motor dynamics and sensory dynamics use efferent copies of motor commands to predict the sensory outcome. The state prediction is used to adjust the translation of a desired movement into a motor command. Sensory outcome computed by the internal model is compared to resulting sensory outcome to adjust the internal model.

The inverse model takes over characteristics of the prediction model but here the cerebellum has a more prominent role in computing the future motor command. The mathematical characteristic of the model is the motor command computation through an inverse function of the arms dynamics. A neurological model capable implementing an inverse function has been presented, the inverse motor model proposed by Ebadzadeh et al. (2005). The model also contains elements that compare sensory feedback with estimated feedback to adjust

the internal predictive models. To underline the difference between the two models the main focus in the inverse model has been put on the neurological architecture capable of implementing an inverse function.

Cerebellar models have also been presented in light of the input information they receive and which they use to translate a desired movements in an appropriate motor commands (A. Haith and S. Vijayakumar 2009). These models are based on the vestibule-ocular motor reflex pathway, which is a useful pathway to study because the network is relative simple and is not interconnected with too many other networks. The model has a clear goal; stabilization of gaze through eye velocity motor commands. The information, used by the cerebellum to fulfill the desired goal, could be vestibular input and efferent motor commands. To elucidate the differences, the two models are proposed having only one form of the input, both models have been tested in computer simulations and seem to work.

If we consider the feed forward VOR pathway we see that the cerebellum contributes directly to the motor command going to the ocular motor apparatus. In this pathway the cerebellum is supposed to translate vestibular information (head motion information) into motor commands. This translation depends on an inverse motor command function, as was discussed in the inverse model (Ebadzadeh et al. 2005). Where the inverse model has focused on how an inverse function can be neuroanatomical implemented in the cerebellum, the VOR feed forward model focuses on the kind of information used for computation of appropriate movements. The inverse model however differs from the feed forward model because it does not explicitly uses vestibular information only, but also efferent motor commands.

The second model, the recurrent VOR pathway, does not compute motor commands directly, but contributes to the computation of motor commands made through the brainstem. The model uses solely efferent motor commands to predict motor movement outcome and to adjust the motor commands computed by the brainstem. In this model the cerebellum thus should be able to predict the state outcome using efferent motor commands. A network capable of this computation is the iterative sensorimotor network.

One of the major differences between the two VOR models is seen in the adjustments of the internal cerebellar models. Computer simulations of the models showed that the effectivity of the cerebellum to adjust for motor errors depends on whether the motor error is either a result of kinematic changes in the task or dynamical changes of the body (A Haith and S. Vijayakumar 2009). Functional studies in healthy subjects show that humans are capable of adjusting to both kinds of errors, implicating that possible both VOR models operate in the cerebellum at the same time.

Adjusting the optimal motor model to changed parameters is based on sensing differences between expected outcome and resulting outcome, the error. Because this is a very important characteristic in optimal motor control the diversity and the processing of these are mentioned in this paper. Only errors attributable to the plant controlled can result in feed forward adjustments (Diedrichsen et al. 2005).

Neuroimaging studies showed that the magnitude of perceived motor errors (Miall et al. 2000, 2001, 2005) was correlated with the observed activity in the cerebellum and there was no correlation with the contribution to feed forward or feedback motor control. (Diedrichsen et al. 2005, Grafton 2008) An important cerebellar component in error perception is the inferior olive, activation in these structures have been specifically linked to movement errors (Horn et al. 1996).

Not only should the cerebellum detect and signal motor errors, it should also result in storage of newly acquired motor movements. An important cellular mechanism in this process has been recognized to be long term plasticity (Bliss et al. 1993, 2003, Malenka 1999). In the cerebellum the best known mechanism of plasticity is Long term depression (LTD), which occurs at the parallel fiber-Purkinje cell synapse. (Ito et al. 1982) This plasticity is the elementary cellular process of supervised motor learning in the cerebellum (Marr 1969, Ito 1982). LTP has been recognized more recently to have a role in motor learning and motor memory, but

increasing numbers of evidence accounts LTD and LTP to have an opposite role in the cerebellum (Boyden and Raymond 2003).

The cerebellum as site of motor programs has been a subject of debate. Inactivation of the cerebellum led to disappearance of recently learned new motor skills, while motor programs learned longer ago were not abolished (McElligot et al. 1998, Nagao and Kitazawa 2003). It has been proposed that complex motor programs are stored cortically and adjusted or modified via cerebellar modulation (M.A. Smith and R. Shadmehr 2005).

The cerebellar function as proposed in the models mainly considers a more abstract functioning of the structure, trying to describe the processes underlying the cerebellar function. In the iterative sensorimotor network the neuronal at cellular level will be more analyzed. The sensorimotor network describes the integration of sensory input and internal model prediction in an iterative network (Deneve et al. 2009). The state estimation as described in this network has also been discussed in the chapter 'the cerebellum as predictive element' and is more or less the model of state estimation proposed by Wolpert et al. (1995). The main goal has been to show the working of the network which gets on with the neuronal signal characteristics; e.g. the poison noise which should be filtered, to get accurate estimations. The model considers sensory information processing and internal model implementation, through lateral connections, in the sensorimotor network.

Subsequently the mathematical laws governing this model have been mentioned to get more insight in the working of the system. The mathematical framework guiding the sensorimotor network, as it has been tested in computer simulations, is quite extensive but in this paper has been discussed only partly for the sake of clarity. An important process that has been described in mathematical terms is the integration of sensory and internal model signals. Because the resulting estimate is a combination of these two factors set by a Kalman filter (Wolpert et al. 1995, Saunders and Knill 2005), the mathematical rules followed by the filter are also discussed. The formula that defines the interneuronal connection strength to implement the internal model prediction has been addressed as well.

The sensorimotor integration network discussed has one important disadvantage in respect to optimal motor control and that is the time representation of the state estimation. As seen in eye saccades motor commands are computed in advance (Thiele et al. 2002). Computation of these upcoming motor commands should therefore be based on upcoming states. The state estimation based on the sensorimotor network represents, due to delay in processing of signals, a state in the past. A possible solution to this time conflict is to have several sensorimotor networks for different time points. As different networks have state estimations of different time points and the motor command that has caused this change is known we have a possible model that could compute optimal motor commands. Connections that have been found from the cerebellum to the motor cortex support this hypothesis (Padel 1993, Keifer and Houk 1994).

The cerebellar models described in this paper all are based on a computational framework, only for the sensorimotor network insight has been given in these computations. This paper presents insight in the cerebellar functions, for which different cerebellar models have been proposed. To highlight different models it was not necessary to give full insight in the formulas governing the models. However, the computation framework is important for testing a proposed network. E.g. the inverse model proposed by Ebadzadeh et al. (2005) has been shown to successfully control a pneumatic McKibben muscle machine which was representing a simplified arm. The computation framework might also be used for analyzing functional study results. Through using detailed image techniques or by inferring in the motor system the validity of the proposed motor models could be tested. Until now there is still a lot of controversy about the cerebellar function, even in the more simple reflex pathways as the vestibulo oculo-motor reflex. Developing naturally moving robots still seems to be far away.

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