A New Striatal Model and its Relationship to Basal Ganglia Diseases *

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Abstract

A new model of the striatum has recently been proposed. This model suggests that the somatotopic regions of the striatum correspond to state spaces governing various aspects of organism behavior (e.g., reaching, egomotion, task planning). The model is reviewed, and shown to be applicable to sequencing tasks. The model is also discussed in the context of some basal ganglia diseases.

1 Introduction

In (Connolly and Burns, 1993), a model was proposed for the operation of the striatum, along with some speculation on the overall operation of the basal ganglia. The model was discussed mainly in terms of motor control. In this paper, we would like review the model, and to further motivate it by discussing it in the context of neurological disorders which appear to involve the basal ganglia.

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2 An overview of the model

The model proposed in (Connolly and Burns, 1993) suggests that the somatotopic regions found in the striatum are cellular representations of various state spaces. These state spaces are used to induce state changes for certain aspects of organism behavior (e.g., reaching movements, egomotion). Within each somatotopic region of the striatum, membrane potentials of primary neurons are varied under cortical control to "sculpt" a potential surface which describes the state changes necessary to reach a goal state. The proposed theory holds that undesirable states (groups of cells) are held to one fixed membrane potential while goal states are held to a different fixed potential. The remainder of primary neurons are "free", and are not held fixed to any particular potential.

From a mathematical standpoint, the system being controlled can be thought of as a point in a state space. For example, in the case of an arm, joint angles form an appropriate state space. Movement of the current-state point in this state space results in changes to the arm's configuration. The model proposed in (Connolly and Burns, 1993) suggests, for instance, that the arm-related somatotopic regions of the putamen form state spaces for the arms, within which the membrane potentials of primary neurons are manipulated to direct the arm to a goal configuration, while avoiding undesirable states (e.g., solid obstacles).

Passive computation within a somatotopic region results in a smooth progression of membrane potentials between the undesirable states and the goal states. Specifically, the model proposes that the membrane potentials of "free" neurons converge to the average of their neighbors' potentials. This computation could be carried out directly by resistive coupling via gap junctions (Cepeda, et al. 1989). Such a passive computation would also explain the relatively quiet nature of striatal primary neurons. The tonic cholinergic activity of giant aspiny cells serves to suppress inappropriate striatal activity, until a state change is to be effected (Kimura, et al. 1984). In concert with presynaptic cortical modulation (Leviel, et al. 1990; Krebs, et al. 1991), dopaminergic terminals in the striatum could be acting as a thresholding mechanism, to select those cells which correspond to the current state (e.g., arm position). Dopamine also appears to regulate gap junction permeability (Grace and Bunney 1983), and hence may be responsible for preventing undesirable state transitions by decreasing gap junction permeability.

State transitions, such as arm movement, are accomplished by a form of gradient descent (or possibly ascent) to the goal state. The system is driven in the direction of the goal potential via the globus pallidus, resulting in a smooth transition from the current state to the goal state. The model proposes that the globus pallidus is responsible for sampling the local shape of this potential surface to determine the appropriate state change at any moment.

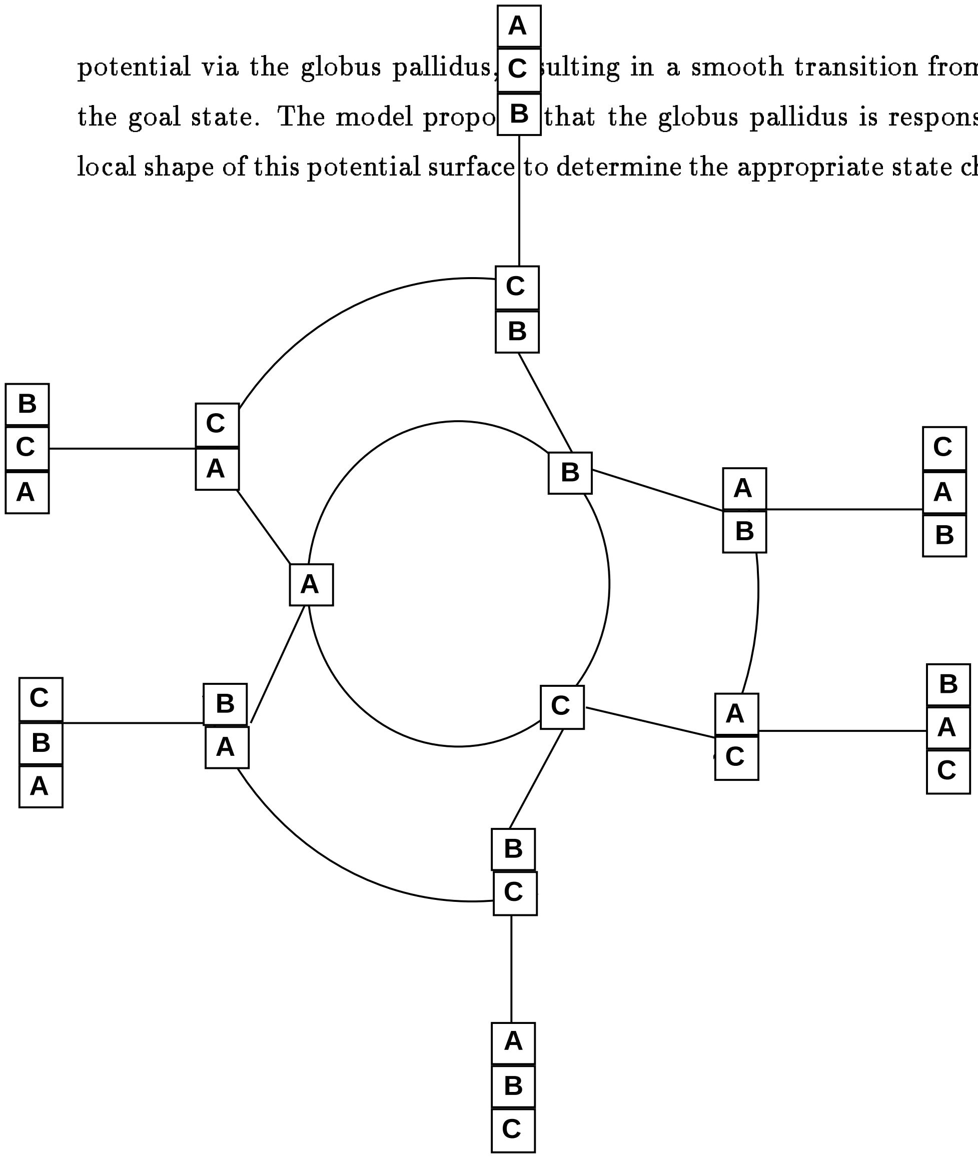

Figure 1: Possible block states and transitions.

3 Sequencing Tasks

The model described in (Connolly and Burns, 1993) can be applied to sequencing tasks, which Parkinson's patients have difficulty performing. The model posits that each somatotopic striatal region corresponds to a state space. For the case of an arm, such a state space would be some deformation of a coordinate system consisting of three joint angles, or perhaps three Cartesian coordinates (X, Y, Z). In general, however, such a state space need only describe all relevant states and transitions between those states. It is possible to cast sequencing problems in such a framework, and to use a resistive network (as the model proposes) to solve such problems.

For example, consider a block-stacking problem: Given three blocks labelled A, B, and C, the blocks must be stacked vertically in a particular order. We can then detail the possible states of the blocks, and then describe the legal transitions between those states. Figure 1 illustrates such a description of states and transitions. To solve this problem with a resistive network, one can replace each arc in Figure 1 with a resistive connection. Then, by holding the current state at a high potential, and the goal state at a low potential, a correct sequence of transitions can be obtained by following the steepest potential changes in the network. Each transition in this sequencing network can be made to trigger goals within a separate motor-control network. For example, the transition from state "BC" to state "ABC" triggers a sequence of motor plans that moves the arm to block "A", grasps it, and places it atop block "B".

We believe that this sort of picture is consistent with the view that the basal ganglia are involved in multiple parallel loops (cortex, striatum, pallidum, thalamus), which interact to govern certain aspects of organism behavior (Alexander, et al. 1990). The sequencing network just described should be considered only as a schematic. It is doubtful that a strict one-to-one correspondence between striatal cells and "states" exists, although the relation could be many-to-one.

4 Basal Ganglia Diseases

In an attempt to motivate the model and provide some means for determining its plausibility, we would like to review some basal ganglia diseases and describe some of their symptoms in terms of the model.

4.1 Parkinson's Disease

Victims of Parkinson's Disease (PD) often display akinesia, festination, rest tremor, and deficits in map-following and sequencing tasks. Parkinsonism is characterized by cell death within the substantia nigra (SN) and thus a loss of dopamine within the striatum.

In the context of the model, dopamine loss has consequences which vary with the degree to which cell death occurs in the SN. In the most severe cases, striatal dopamine levels are extremely reduced. Primary striatal neurons appear to be most active when dopamine (DA) is at levels above 100 nM and below 1000 nM extracellular DA (Williams and Millar 1990).

Below these levels, striatal cells are silent, and incapable of modulating pallidal activity. This is consistent with the severe akinesia noted in some patients. Intermediate DA levels cause primary neurons to fire. We speculate that inappropriate firing of primary neurons at this level of DA concentration gives rise to the rest tremor. Both low and intermediate levels of DA will adversely affect the ability of a sequencing network (such as that described in Section 3) to function properly. In the case of extremely low DA concentrations, such a network would cease to function simply because no information can be extracted (since the cells within the network would not fire). When DA concentrations are at intermediate levels, many of the cells in such a network would fire inappropriately, adversely altering the potentials within the network. It would therefore become much more difficult to see such a sequencing task to its proper conclusion.

The results from testing PD patients on various sequencing tasks indicate possible deficits in this area (Brown and Marsden 1990, Morris et al. 1988). Although the results are not considered by some to be conclusive (Brown and Marsden 1990), some experiments do show a strong connection. In one experiment (Brown and Marsden 1990) subjects were asked to arrange pictures in an order that tells a sensible story. The patients with PD were significantly impared in this task.

Morris et al, tested subjects on their ability to plan a sequence of operations that logically led to a goal state, using a bead-moving game similar to the tower of Hanoi (called Tower of London). It was found that the PD patients generated plans with the same number of moves as the normal subjects, but they took significantly longer to form their plans.

This result could be consistent with our model given that reduced dopamine levels in the striatum can lower gap junction resistance. In our previous paper (Connolly and Burns 1993), we suggested that a significantly lower resistance might flatten the potential surface by over-taxing the ion pumps maintaining the membrane potentials. Rather than completely flattening the surface, the reduced resistance might have the effect of slowing down the process of creating the surface. Thus, it would take longer to produce potential gradients of large enough magnitude to trigger the execution phase (ball rolling). Alternately, the flattened nature of the surface might result in a reduced gradient or state change. This in turn could slow the system down.

4.2 Huntington's and Sydenham's Choreas

Huntington's Disease is a genetic disorder resulting in progressive striatal cell death (Barbeau, et al. 1972). Sydenham's Chorea is believed to be the result of childhood rheumatic fever, and is also characterized by a loss of striatal cells, but is not progressive. These disorders exhibit similar deficits (e.g., choreic movement). In (Connolly and Burns 1993), we speculated that the depletion of primary neurons in the striatum in Huntington's disease would result in a coarser representation of state space in the striatum. Choreic movement could be a result of such a coarse representation, in that the state space for movement would be under-represented. This, in turn, can lead to deviations from a smooth trajectory. One can view this in the following way: regions of cell death will tend to act as obstacles to the intended movement; although no obstacles are actually present, the postulated resistive network in the striatum has been damaged to the point where permanent "obstacles" (dead zones) appear in the striatum.

In light of the aforementioned sequencing experiments on Parkinson's patients, and the framework described in Section 3, we would expect that, whereas Parkinson's patients are merely slower than normals in solving these problems, Huntington's patients should experience difficulty in execution of the tasks, perhaps making redundant or inefficient steps. Consider the effect of removing some of the arcs (resistive connections) in Figure 1. The path length from any start state to a goal state can be increased, resulting in redundant or inefficient placement of the blocks. In severe cases, it would be impossible to reach perfectly legal goal states. We emphasize that this is merely a schematic view of what could be happening in the striatum, but we hope it can stimulate further discussion.

4.3 Obsessive-Compulsive Disorder

Obsessive-Compulsive Disorder is a disease whose victims suffer from a need to pursue certain rituals, sometimes to a life-threatening extent. In general, it appears that OCD patients are unable to suppress the repeated execution of certain activities. Chemical therapy for OCD relies on serotonin reuptake blockers such as clomipramine. A general review of OCD appears in (Rapoport 1989). In particular, Rapoport and Wise in that volume suggest a link between OCD and the basal ganglia. Some studies also suggest shrinkage of the head of the caudate nucleus in OCD patients (Rapoport 1989).

In the context of the model described above, it is possible to view OCD as a failure of the striatal-prefrontal system to recognize completion of a goal. For example, in the block sequencing task described in Section 3, once the goal state is achieved, cortical maintenance of the goal state should cease. In OCD, such a goal-directed process appears to persist, as if the original goal state is maintained (i.e., its potential fixed at goal levels) even after it has been achieved. If this is the case, then even after subsequent state changes, the system will tend to drift back to the prior goal state, perhaps orbiting around this state indefinitely. The computational analogue to OCD in the block-stacking example would manifest itself as an "obsession" to stack the blocks in a particular order, regardless of the true desired state. Physiological changes in the striatum of some OCD patients may place this state change mechanism in the head of the caudate nucleus.

5 Conclusion

We have reviewed our model of striatal function, which basically states that somatotopic regions of the striatum are representations of state spaces which are used to control various aspects of organism function. The model posits that the gradient of membrane potentials of groups of striatal primary neurons are used to drive state changes. These potentials are "sculpted" within each somatotopic region by cortical afferents. This cortical control fixes membrane potentials for goal states and undesirable states for the given system (e.g., arm, egomotion). All other cells (states) are "free" in the sense that they converge to intermediate potentials. It is possible that this is achieved by resistive coupling between striatal primary neurons.

We have also demonstrated one possible way in which such a network can be used to execute sequencing tasks, in more abstract state spaces. This allows us to use the model to describe deficits encountered in basal ganglia diseases, including the sequencing difficulties seen in victims of Parkinson's disease. We have also suggested ways in which victims of Huntington's disease could be affected in the execution of sequencing tasks, namely, that Parkinson's disease results in a slowing of the execution of such tasks, while Huntington's disease should in some cases result in superfluous or inefficient steps in performing such tasks. We have also suggested a way in which Obsessive-Compulsive disorder can be described in the context of the model: as inappropriate cortical maintenance of a goal state.

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