A Least-Action Model for Dyskinesias in Parkinson's Disease

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Abstract

A model of motor planning is proposed that relies on energy regulation. The system to be controlled is treated as a point mass, and its motion is governed in part by an artificial (or internal) potential. In this case, the energy to be regulated is also artificial, since it is the sum of real kinetic energy and artificial potential energy. Energy regulation is achieved by enforcing Hamilton's principle of least action to drive the motion. By regulating the energy of the point mass, straight-line reaches or circular orbits can be planned. An extension of a previous model for the striatum is summarized in terms of energy-based control. Finally, this extension is discussed in the context of hypokinetic symptoms seen in Parkinson's disease.

Introduction

A central issue in the control of articulated limbs is the specification of trajectories from one posture to another within constraints imposed by the task. The variety of objectives often motivates techniques that use models of the task to search for trajectories that meet task specifications (Rowe and Richbourg, 1990; Gupta and Guo, 1995; Chen, Huang, and Wen, 1993). However, these approaches are typically expensive and rely on the existence of complex models that are both complete and correct. Often, the underlying representation is sensitive to seemingly minor changes in geometrical constraints (Barraquand and Latombe, 1991). In general, this may lead to significant computational overhead (Canny, 1987). As a result, trajectory search may lead to brittle strategies that fail in ways that cannot be fully anticipated beforehand. The problem is further complicated in dynamical systems, where motion strategies must be feasible in light of the forces and inertias of the limb. This complication is especially relevant in periodic or orbital motion control, a very important class of motion control applications in both natural and robot systems. Smoothness of the trajectory is also desirable, since dynamic effects (overshoot, ringing) are prominent near discontinuities in the derivatives of the motion (e.g., sharp corners in the trajectory). A theory is required for motion control that incorporates generic constraints, is dynamically consistent with the articulated structure, and constitutes a feedback control policy for executing the motion.

Potential functions can be used to formulate a constant total energy motion-planning scheme that addresses the aforementioned issues. The use of a constant total energy constraint for control has been successfully exploited for hopping and juggling robots (Raibert, 1986; Koditschek and Bühler, 1991; Ostrowski and Burdick, 1993). In these cases, the total energy is the sum of kinetic energy and the potential energy that arises from gravity. Total energy is kept constant. The system's movement is driven by its inertia and the gradient of the potential (in this case, gravitational force). This results in a continual tradeoff between kinetic and potential energy, and such systems are said to obey Hamilton's *principle of least action* (Arnol'd, 1978). The system maintains its total energy at an approximately constant value. The treatment here, however, relies on an *artificial* potential function (in the same sense as in Koditschek (1991)). This is a potential function that is generated *internally* from the sensed positions of obstacles and goal points, rather than by some external field such as gravity.

A harmonic potential function is employed as the artificial potential. Harmonic potentials can be computed with resistive networks, and are *programmable*, in the sense that minimum and maximum values of the function can only occur at pre-specified locations. This means that goal points and orbit centers can be programmed into the potential with the guarantee that they will be the only such points in the potential. Obstacles or bounds on the motion are also programmed as maxima. This can be used to plan both goal-directed and repetitive motion for a manipulator. One important motivation for the use of harmonic functions is the utility of such functions as models of natural phenomena, such as resistive networks, stochastic processes and fluid flow.

Using constant-energy control with harmonic potentials results in *bounded* torques to the joints, and produces compliant, collision-free dynamic behavior. Harmonic potentials have previously been proposed to account for the role of the striatum in motor control (Connolly and Burns, 1993). This prior model, however, does not take into account the dynamics of limb movement, and was not able to explain certain features of basal ganglia diseases, e.g. Parkinson's disease.

The primary pathological feature of Parkinson's disease is the death of cells in the substantia nigra. These cells supply the striatum and prefrontal cortex with dopamine. This loss of dopamine is somehow connected with the motor dysfunctions found in Parkinson's disease. The potential-based striatal model can be extended by postulating that an "in-

ternal" potential generated by the striatum, and regulated by dopamine, could be part of a constant-energy control mechanism for generating movement. As a result, the extension of the model can also explain certain symptoms of Parkinson's disease, such as micrographia and rigidity.

Energy-Based Control of Motion

The technical details of energy-reference control have been described elsewhere (Connolly, Grupen, and Souccar, 1995; Rosenbaum and Collyer, 1997), and will be reviewed here. There are two basic components to this kind of control:

1. An internally-generated harmonic potential: Obstacles and goals are chosen (sensed), and mapped into a configuration space for the system. The harmonic potential function is computed by holding obstacles at one value (usually 1) and goals at another (usually 0). A relaxation step causes the remaining points to obey the mean-value property: Each point's value is the average of its neighbors' values (except at obstacles and goals).

2. An energy-regulating servo loop: In contrast to traditional servo loops, position and velocity are not directly regulated. The servo loop senses the system's current configuration and velocity, and uses these quantities to compute the total (kinetic + potential) energy for the system. The system's energy is then adjusted to match a pre-determined *desired* energy, by accelerating or decelerating the system. For the purposes of this paper, the desired energy is assumed to be constant. Normal motion and the symptoms of Parkinson's disease are treated solely by manipulating the potential energy function.

A mechanical system can be described in terms of its configuration (often denoted by q) and its momentum (p, mass times velocity). By configuration, we mean its position in some parameter space. For example, a mobile robot's configuration might include x, y in some cartesian coordinate system, along with orientation θ. The configuration of an arm can be represented by its joint angles. The space consisting of the configuration q and momentum p is the phase space for a system. The system can be thought of as a point moving through phase space.

The behavior of physical systems is often characterized by considering the system's trajectories in phase space. For example, the swinging of an idealized pendulum can be described as a closed orbit in its phase space (the pendulum angle θ plotted against its angular velocity $\dot{\theta}$, see Figure 1). In the case of a pendulum, gravity serves as the potential. Each phase-space orbit corresponds to a different constant energy level for the system. Such a system is said to be "conservative" or Hamiltonian,[1] and obeys Hamilton's *principle of least action.*

In robotic motion planning, an artificial potential can be used. Harmonic potentials (Connolly and Grupen, 1993)

[1] The total energy function is sometimes referred to as the Hamiltonian function for the system.

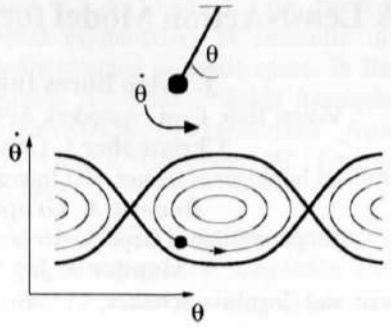

Figure 1: Swinging pendulum (top) traverses constant-energy surfaces in phase space (bottom).

are easy to compute (by repeated averaging, or resistive networks) and produce no local minima. The minimum and maximum points for harmonic potentials occur only where specified. By using such potentials, we can guarantee that the system will never get stuck orbiting (or reaching for) the wrong point. In order to treat a robotic arm as a point in a potential, it is reduced using a *configuration space mapping* (Udupa, 1977; Lozano-Pérez, 1981; Connolly and Grupen, 1993).

In energy-reference control, a servo loop is used to hold the total energy at a constant value for the system. The servo loop examines and regulates the total energy of the system:

$$E(p,q) = \frac{p^2}{2m} + \phi(q) \tag{1}$$

where the first term is the kinetic energy of the system (as measured by the servo loop) and the second term is the potential at the current configuration. If the total energy is greater than the desired energy, the servo loop applies the necessary torques or forces to "brake" the system, reducing its kinetic energy. Otherwise, torques are obtained from the gradient of the potential, as in a natural system. If the potential is well-behaved, then its gradient is always bounded.

Although the total energy is artificial, one component, kinetic energy, is real. The kinetic energy of the resulting motion never *exceeds* the desired constant energy. Because of this, positions and contact forces are bounded, and can be regulated by altering the desired energy, or by shaping the potential function. The resulting motion is compliant, and is constrained in both position and velocity.

Several useful features arise from such a control scheme: When the potential energy is held below the desired energy, the system orbits the minimum points of the potential, avoiding obstacles. Straight-line motion can be achieved by initially expressing goal points, then allowing these to decay toward the obstacle potential at an appropriate rate. The resulting time-varying potential function drives the system smoothly toward a goal state. Since torque is bounded, all motion is compliant, i.e., a sufficiently large external force can overcome the system. In summary, energy-reference con-

trol using harmonic potential functions can be used to plan motions that are:

- obstacle-avoiding (up to reaction times)
- goal-directed
- repetitive (orbiting)
- compliant

The performance of such motions in the environment is achieved by the human motor system in the presence or absence of obstacles. Aside from areas of the brain that are directly responsible for the execution of this motion (eg: motor cortex, spinal cord motor neurons) deeper subcortical structures also influence these motor plans. Abnormalities in these deeper structures are seen in numerous disease states resulting in abnormal motor performance. The basal ganglia comprise a collection of brain nuclei that fit this role. Although their role in motor control is unclear, we postulate that it is these structures that may utilize energy control mechanisms. A brief description of these structures, and their interconnections with a review of one prototypic disease, Parkinson's disease (PD), follows.

The Basal Ganglia

The neuroanatomical and neurochemical connections of the basal ganglia are beginning to be worked out (Gerfen, 1992). Comparatively, the neurophysiological basis of how these regions affect movement is unknown. Models to date have proven to be significantly incomplete, as they neither take into account features of normal function nor account for many of the symptoms of disease that affect the basal ganglia.

Anatomy and Histology of the Basal Ganglia

The basal ganglia comprise a group of interconnected deep-brain nuclei. These include (in primates) the striatum, the pallidum with external (GPe) and internal segments (GPi), the subthalamic nucleus (STN), and substantia nigra (SN) . Posteriorly, the internal capsule divides the striatum into the caudate nucleus (medially) and the putamen (laterally) while the two divisions join anteriorly to form the nucleus accumbens. On the basis of acetylcholinesterase staining, areas of low staining are termed striosomes while the remaining tissue with high staining is termed matrix. The striosomes and matrix form the two basic compartments of the striatum.

There are three types of striatal neurons, namely the giant aspiny (cholinergic), medium aspiny (GABAergic / somatostatin / neuropeptide Y) and medium spiny. The medium spiny neurons are the output neurons of the striatum and contain GABA. The striatum receives afferent input from almost the entire neocortex (excitatory; glutamatergic) with the exception of the primary visual cortex and perhaps the olfactory cortex, in addition to the centromedian (CM) and parafascicular(pf) nuclei of the thalamus and the amygdala.

Physiological studies have shown that a striatal projection neuron needs coherent activation of many of the approximately 20000 inputs that it receives to reach spiking threshold. Hence these neurons fire rarely. Despite significant axonal and dendritic arborization, medium spiny neurons have not been shown to have any inhibition of their neighbours. Local inhibition is possibly accomplished by the interneurons (Kita, Kosaka, and Heizmann, 1990). In sensorimotor behavioral learning settings, striatal interneurons[2] have been shown to develop synchronized pauses across several neurons (Aosaki, Kimura, and Graybiel, 1995). In addition, the dopaminergic input into the striatum has been linked to reward learning such that dopamine release increases in anticipation of reward (Schultz, *et al.*, 1995).

The primary output of the striatum (inhibitory; GABAergic) is to the globus pallidus (GPe and GPi) and the substantia nigra (SNPr). Pallidal neurons have a significant dendritic arborization and close to 100 striatal neurons synapse onto a single pallidal cell. Output from the pallidum is also inhibitory and GABAergic. The external segment projects to the subthalamic nucleus (STN) which in turn sends excitatory, glutametergic output to the SNPr and the GPi. The STN also receives direct excitatory glutamatergic input from the motor cortex. The GPi thus receives inhibitory output from the striatum and excitatory input from STN. The pallidal neurons have a high tonic rate of firing.

GPi and SNPr then send inhibitory, GABAergic output to the ventral anterior (VA) ventrolateral (VL) and dorsomedial (DM) nuclei of the thalamus. The SNPr also sends output to the superior colliculus. Excitatory, glutametergic output from the thalamus goes to motor, premotor and supplementary motor areas of the cortex. These complicated connections are summarized in Figure 2.

Aspects of Parkinson's Disease

Although neuronal death is natural process in aging, in degenerative diseases like Parkinson's disease, this cell loss becomes critical at an early stage (Brodal, 1981). Whether this is due to a smaller number of neurons from birth or from excessive cell death due to genetic or environmental causes, is unknown.

Nevertheless, the major site of cell loss in Parkinson's disease is the substantia nigra. The melanin-containing pigmented neurons in the SNPc undergo cell death thereby critically decreasing this input into the striatum. Autopsy specimens confirm this significant loss and it is estimated that a minimum of 70 percent of nigral neurons have to be destroyed prior to symptom manifestation. The striatum, pallidum and other structures are histologically normal, at least in the early stages. An important feature to note is that the disease is often pathologically and clinically asymmetric.

Symptoms and Signs

The cardinal symptoms are (Weiner and Lang, 1989):

[2] The TANs, or Tonically Active Neurons.

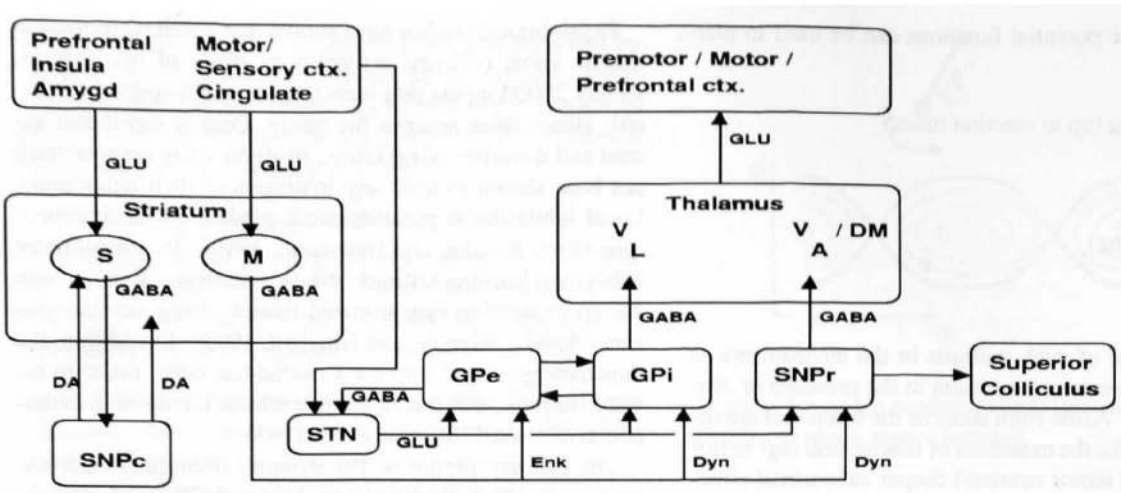

Figure 2: Basal ganglia anatomy, including cortical and thalamic projections; S=striosome, M=matrix. Neurotransmitters: GLU=glutamate; DA=dopamine; Enk=enkephalin; Dyn=dynorphin.

1. generalized slowness or decrease in movements (akinesia),
2. decrease in the speed with which a movement is performed (bradykinesia)
3. stiffness in the body brought out best with clinical examination (rigidity)
4. Rest tremor
5. Postural instability

Akinesia is seen and noticed as a generalized decrease in body movements. Automatic movements that we perform normally, such as minute changes in posture while sitting in a chair, intermittent crossing or uncrossing of legs, or number of eye blinks, are decreased. This gives rise to the characteristic "masked facies" of PD. In early stages, unilateral decrease in arm swing is perhaps the first sign of akinesia.

Bradykinesia is essentially a decrease in the amplitude, rhythm and range of the movements. Included is a sense of fatigue in the limbs with an additional difficulty in shifting from one motor act to another. The duration of the movement itself is therefore significantly prolonged as there is inability to alter the velocity of the task. There is also a gradual diminution in amplitude and rhythm in the task. This is classically manifested as micrographia during a writing task.

Rigidity is an abnormality in the tone that is elicited in the entire body, particularly in the limbs and neck. This is appreciated well if the patient's limb is slowly flexed and extended. The rigidity is velocity independent and bidirectional. The phenomenon of cogwheeling has been considered to be the underlying tremor, although the frequency of the cogwheeling is not the same and it can be elicited even when tremor is not otherwise clinically detectable.

Tremor is a prominent symptom in a majority of cases of PD. This involves the hands most often but feet can also be involved. In more severe cases the tremor can spread proximally. Although rest tremor with a frequency of 4-7 Hz, is most common, action tremor may also be seen in later stages of the disease. Stress and anxiety can worsen the tremor while action, concentration / attention on the tremor and sleep can eliminate it. Pathophysiologically, the tremor can be completely alleviated with a ventro lateral thalamotomy.

Postural stability is impaired, with an inability to perform rapid adjustments of posture when there is interference with body equilibrium. The patient thus continues to move along the trajectory imposed by shifting of the centre of gravity.

A Potential-Based Model for the Striatum

A prior model of the striatum (Connolly and Burns, 1993) proposed that the medium spiny neurons of the striatum "compute" a potential that can be used to control motion. Since the striatum receives widespread cortical afferents, it is in a position to integrate the necessary sensorimotor information for motor tasks. In this model, the cortex "programs" the striatum for motor tasks by a form of efferent copy of constraint information through the corticostriatal projection. Resistive coupling among medium spiny neurons (for which there is some evidence, see Onn and Grace (1994)) would be responsible for the formation of a potential, expressed by the membrane potentials of medium spiny neurons. Since many leakage currents are present across a neuron's membrane, the potential that results from resistive coupling will tend to sag toward the equilibrium potential for the cell. This has the effect of reducing the magnitude of the gradient near the goal point(s). Transmission of gradient information is achieved by striato-pallidal activity (Connolly and Burns, 1995).

Medium spiny neurons exhibit up and down states (Wilson and Kawaguchi, 1996) that are at least partially the result of cortico-striatal activity. We propose that the up and down states of medium spiny neurons correspond directly to the obstacle and goal boundary conditions for a potential. Without

loss of generality, we assume that the up state corresponds to an obstacle, while the down state represents goals.[3] Under this assumption, the cortex is able to constrain a potential in the striatum for use in the planning and execution of motor tasks. The up state is achieved by direct cortical excitation. We postulate that the down state is induced by cortical regulation of leakage currents that drive the cell to its equilibrium potential. In the context of this model, regulation of leakage currents must involve dopamine.

The control scheme discussed above provides a way of extending the potential-based striatum model described in Connolly, Grupen and Souccar (1995) to account for repetitive motion. In the revised model, the potential is used in conjunction with kinetic energy to regulate motion. The "desired energy" is assumed to be fixed. The resulting balance between kinetic and potential energy is maintained by either thalamic or cortical systems that are the targets of pallidal output from the striatum.

Energy-Reference Control

Energy-reference control can be used to describe some of the symptoms of PD. A General Electric P-50 robot arm was used to implement the control scheme described above. The implementation is described in more detail in (Connolly, Grupen, and Souccar, 1995). A potential is used with minimum and maximum values of 0 and 1, respectively. One goal (minimum) point was used, and the desired energy level was set at 0.5. At this energy, the robot exhibited a circulatory motion in the sagittal plane about the goal point. By varying the shape of the potential function, certain aspects of the aforementioned symptoms could be replicated, as follows:

- Bradykinesia: By progressively raising the minimum potential value from 0, the system executes orbits of progressively smaller radius. An effect analogous to micrographia can be obtained by allowing the potential to slowly decay upward, resulting in progressively tighter, but less energetic orbits (since the *desired* energy is not allowed to change, hence the kinetic energy must be reduced).

- Akinesia, rigidity: Akinesia can be modeled as a weak potential that does not permit the initiation of action. Rigidity can be described as a more acute version of this same condition. In the context of energy-based control, akinesia can be viewed as a flattening of the potential. The value of the potential function must be above the desired energy for the system, but beyond that, no other constraint is required. The degree of rigidity, however, is determined by *how far* the potential function has risen above the desired energy.

Note that akinesia and bradykinesia rely on a "weakening" of the goal potential. By raising or eliminating this potential (energy) relative to the desired energy, the kinetic energy is reduced or entirely suppressed over the entire configuration space.

As alluded to earlier, the model described here makes specific assumptions about the role of dopamine in maintaining a potential function. The concentration of Dopamine (DA) in the striatum appears to have multiple effects on ion conductance and hence polarization of striatal cell membranes. This is due in part to the presence of at least two distinct receptors (D1 and D2). However, in Mercuri, Calabresi and Bernardi (1989), several investigations were reviewed and it was concluded that the activation of the D2 type receptor in the striatum is perhaps the key factor in the pharmacological reversal of PD manifestations. There is strong evidence that activation of D2 receptors can increase K^+ conductance and hyperpolarization (Williams, MacVicar, and Pittman, 1989); an increase in K^+ conductance has also been observed in striatal cells (Fredman and Weight, 1988). If the artificial goal potential is taken to be a hyperpolarized state, then a large, permanent reduction in DA could mean a permanent raising and flattening of the artificial potential, i.e., an inability to maintain the goal potential. Thus, to the extent that the above observations on the D2 receptor role are correct, a reduction of DA would produce the effects of Bradykinesia and Akinesia according to our model.

Conclusion

A control scheme has been presented for planning repetitive and goal-directed motion. The scheme has also been applied to a potential-based theory of motor planning in the striatum, and discussed in the context of Parkinson's disease. Although preliminary, the control scheme described here raises the possibility that some symptoms of Parkinson's disease can be explained by considering the neural substrate of motor control as a "Hamiltonian" system, i.e., a dynamical system that relies on energy conservation (*least action*) to control movement.

It is still unclear whether the striatal network would be capable of maintaining a potential of sufficient gradation to be useful in generating movements. However, even taken as an abstraction, it may be useful to consider motion planning in terms of a potential function. Future work will attempt to explain a wider range of Parkinsonian symptoms, especially hyperkinetic symptoms such as chorea, ballism and tremor. Using the control scheme described here, simulations and experiments on robotic systems will be used to achieve this goal.

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[3] The polarity can be reversed; the result is still a harmonic potential, and the energy-reference control scheme can be derived by making an appropriate change in Equation 1.

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