Biologically Inspired Neural Architectures of Voluntary Movement[1]

Vassilis Cutsuridis[1, 2]

[1]Computational Intelligence Laboratory, Institute of Informatics and Telecommunications, National Center for Scientific Research "Demokritos", Agia Paraskevi, Athens GR-15310
vcut@iit.demokritos.gr
[2]Department of Informatics and Telecommunications, National University of Athens, Panepistimiopolis, Ilissia, GR-15784

Abstract. Three novel brain-guided multi-modular neural network architectures are developed for the selection (decision making), generation and control of arm and ocular movements in normal and diseased brain states. The modules are developed using much of what is known about the human brain and its functional and modular decomposition. The models are: (1) Neural model of dopaminergic control of arm movements in Parkinson's disease bradykinesia, (2) Neural population model of decision making for the generation of ocular movements in the antisaccade task and (3) spiking neural model of decision making with variable climbing activity for the generation of ocular movements in the antisaccade task. All three computational neural models are consistent with pertinent constraints from primate and human neurobiology, and the related computer simulations reproduce key aspects of experimental observations regarding voluntary arm and ocular movements.

1 Introduction

Arguably one of the most difficult problems in science today is the brain-mind problem. Understanding the brain's principles of action would be of great value in many areas, such as in neuroscience, in understanding human diseases in medical science, as well as in applications to develop autonomous robot control systems. The "astonishing hypothesis" is that our minds can be explained by understanding the detailed behavior of neurons in the brain and their interactions with each other [27]. Brains are collections of billions of interconnected cells, each of them being an individual machinery, which receives, processes and transmits information. The human brain generates complex patterns of behavior at different scales of organization based on the large amount of neural components that interact simultaneously in a rich number of parallel ways. In order to understand the inherent complexity of such a system many complementary research strategies are usually employed.

[1] Supervising professor: N. Kaloupsidis, Ph.D

Nowadays scientists are oriented towards the test of mathematical models and the simulation of neurobiological details. This research direction has impelled the emergence of the computational neuroscience field, which is an evolving approach that draws on neurobiological data, but uses computational modeling and computer simulations to investigate the principles of operation governing neurons and networks of neurons. The domain is rapidly growing, involving researchers with backgrounds ranging from psychology and cellular biology to mathematics, physics and artificial intelligence.

The work presented in this doctoral dissertation lies at the intersection of three domains: neuroscience, artificial intelligence and robotics. This work makes use of computer simulations with networks of neuron-like elements in order to understand how cognitive phenomena of voluntary movement can be grounded at the neural level. In doing so, we employ simulations with biologically inspired neural models. The general aim is to explore the neural mechanisms that has been tested experimentally at multiple levels of complexity (cellular, neuronal and behavioral) and in different states of mind (normal and diseased) that underlie the selection of the appropriate motor command from a repertoire of other motor commands capable of generating and controlling arm and ocular movements in a given context that can at a latter time drive autonomous robotic control systems (not treated in this doctoral dissertation).

The innovative aspects of this doctoral dissertation are:

1. A neural model of neuromodulatory (dopamine) control of arm movements in Parkinson's disease (PD) bradykinesia is introduced [29, 9, 10, 11].
    - The model is multi-modular consisting of a basal ganglia module capable of selecting the most appropriate motor command in a given context, a cortical module for coordinating and executing the final motor commands, and a spino-musculo-skeletal module for guiding the arm to its final target and providing proprioceptive (feedback) input of the current state of the muscle and arm to higher cortical and lower spinal centers.
    - The neuromodulatory model is successful at offering an alternative explanation to what other models suggest about the causes of Parkinson's disease bradykinesia. More specifically, it focuses more on the effects of dopamine (DA) depletion in cortex and spinal cord and less on its effects in basal ganglia (as other models have done).
    - The neuromodulatory model provides a unified theoretical framework for PD bradykinesia and it is capable of producing a wealth of neuronal, electromyographic and behavioral movement empirical findings. From a mathematical point of view the model is an excellent one, since it can produce all these results with only six free parameters. The model's main prediction is that dopamine depletion in the cortex and spinal cord plays a significant role in the generation of voluntary movement in patients with Parkinson's disease. This

prediction is worth investigating more thoroughly by experimental brain scientists.

- The neuromodulatory model also offers functional roles for the reciprocal and bidirectional types of neurons observed experimentally in primary motor cortex [23]. The model suggests that both types of neurons correspond to two partly independent neuronal systems within the motor cortex [22]. The activity of reciprocal neurons is organized for the reciprocal activation of antagonist muscles, whereas the activity of bidirectional neurons is organized for the co-contraction of antagonist muscles. Whereas the reciprocal pattern of muscle activation serves to move the joint from an initial to a final position, the antagonist co-contraction serves to increase the apparent mechanical stiffness of the joint, thus fixing its posture or stabilizing its course of movement in the presence of external force perturbations.

- Furthermore, the model predicts that the origin of the repetitive triphasic pattern of muscle activation employed to bring the limb from a starting position to a final one originates from the oscillatory output of the basal ganglia structures [12]. This attempt is one of the few successful marriages of theory and experiment.

- Finally, the neuromodulatory model predicts that the movement variability observed in PD kinematic studies originates from variability in the levels of dopamine in BG, cortex and spinal cord and offers thought experiments that must be followed more thoroughly by experimentalists. This is one of the few attempts in the computational neuroscience field where theory leads and guides experiments.

2. A neural model of how decisions are formed in an antisaccade task is introduced [3, 7, 8].

   - The model is successful at explaining why the response times in the antisaccade task are so long and variable and at predicting accurately the shapes of correct and error RT distributions as well as the response probabilities of a large 2006 sample of subjects [1,2]. The wealth of simulated results makes the model unique in comparison to other models.

   - In the model, decisions are formed via stochastic accumulating processes and contrast enhancement of the decision signals. More specifically, two cortically independent and spatially separated decision signals representing the reactive and planned saccade signals, whose linearly rising phases are derived from two normal distributions with different means and standard deviations are integrated at opposite locations, where they compete against each other via lateral excitation and remote inhibition. An ocular movement is initiated when these decision processes, represented by the neuronal activity of subcortical neurons with nonlinear growth rates varying randomly from a normal distribution, gradually build up their activity until reaching a preset

criterion level. The crossing of the preset criterion level in turn releases the “brake” from the SC burst neurons and allows them to discharge resulting in the initiation of an ocular movement.

- The model predicts that there is no need for a top-down inhibitory signal that prevents the error prosaccade from being expressed, thus allowing the correct antisaccade to be released. This finding challenges the currently accepted view of saccade generation in the antisaccade task, which requires a top-down inhibitory signal to suppress the erroneous saccade after the correct saccade has been expressed.

3. A spiking neural model with variable climbing activity is introduced as an extension of the previous neural model of decision making in the antisaccade task [4, 6, 5].

    - In contrast to other models, which have addressed the problem of explaining the linearity of the climbing activity as well as providing a functional role of the climbing activity, the spiking model is an attempt of addressing the specific biophysical mechanisms underlying the generation of the slowly varying climbing temporal integrator-like activity of the decision signals in the previous neural population model of the antisaccade task.

    - The spiking model is a multi-modular neural network model consisting of two cortical modules that drive the neuronal population model to produce saccade reaction times (SRT) and response probabilities in the antisaccade task. The cortical neuronal firing rates of both cortical modules are derived from the interplay of a wealth of ionic and synaptic currents. Hodgkin-Huxley mathematical formulations are employed to model these currents. Symmetric and asymmetric types of neuronal connectivities as well as homogeneous and heterogeneous neuronal firings are tested.

    - The model predicts that only the I_{NaP}, I_{NMDA}, and I_{AMPA} currents can produce the observed variability in the climbing activities of cortical decision signals. The model also predicts the range of values of these currents’ conductances. The cortical decision signals can subsequently drive a well established SC antisaccade generation model and generate correct antisaccade and error prosaccade reaction time (RT) distributions as well as response probabilities of a large group of 2006 subjects.

2 Materials and Methods

2.1 Neural model of dopaminergic control of arm movements in Parkinson's disease bradykinesia

As a basal ganglio-cortical network, I chose the VITE (Vector Integration To-End point) model of [16], which I here extend. The original VITE model was chosen because (1) it is capable of generating single joint arm movements [16], and (2) it permits the functional interpretation and simulation of properties of many types of identified cortical neurons [20]. In my version of the VITE model, the types and properties of the cortically identified neurons are extended and the effects of dopamine depletion on key cortical cellular sites are studied. In the model, an arm movement difference vector (DV) is computed in parietal area 5 from a comparison of a target position vector (TPV) with a representation of the current position called perceived position vector (PPV). The DV signal then projects to area 4, where a desired velocity vector (DVV) and a non-specific co-contractive signal (P) [22] are formed. A voluntarily scalable GO signal multiplies (i.e. gates) the DV input to both the DVV and P in area 4, and thus volitional-sensitive velocity and non-specific co-contractive commands are generated, which activate the lower spinal centers. The DVV and P signals correspond to two partly independent neuronal systems with the motor cortex. DVV represents the activity of reciprocal neurons [23], and it is organized for the reciprocal activation of antagonist muscles. P represents the activity of bidirectional neurons (i.e. neurons whose activity decreases or increases for both directions of movement [23]), and it is organized for the co-contraction of antagonist muscles. Whereas the reciprocal pattern of muscle activation serves to move the joint from an initial to a final position, the antagonist co-contraction serves to increase the apparent mechanical stiffness of the joint, thus fixing its posture or stabilizing its course of movement in the presence of external force perturbations [15, 22].

The spinal recipient of my VITE variant model commands is the FLETE (Factorization of LEngth and Tension) model [15, 17, 18, 19]. Briefly, the FLETE model is an opponent processing muscle control model of how spinal circuits afford independent voluntary control of joint stiffness and joint position. It incorporates second-order dynamics, which play a large role in realistic limb movements. I extend the original FLETE model by incorporating the effect of the now cortically controlled co-contractive signal (in the original FLETE model, the co-contraction signal was simply a parameter) onto its spinal elements. Also, I study the effects that dopamine depletion on key spinal centers has on voluntary movements.

The complete mathematical formalism of this model can be found in section 5.2 of the dissertation manuscript.

2.2 Neural population model of decision making for the generation of ocular movements in the antisaccade task

The model is based on the competitive integration model of [24] (see section 8.2 of the dissertation) with LATER-like [25, 26] inputs (see section 8.1 of the dissertation).

In the model [3, 7, 8], the preparation of an antisaccadic eye movement consists of two independent and spatially separated decision signals representing the reactive and planned saccade plans. A movement is initiated when these decision processes, represented by the neuronal activity of SC buildup neurons with nonlinear growth rates varying randomly from a normal distribution, gradually build up their activity until reaching a preset criterion level. The crossing of the preset criterion level in turn releases the "brake" from the SC burst neurons and allows them to discharge resulting in the initiation of an eye movement. One of the key assumptions of the model is that in the superior colliculus, the two decision processes are integrated at opposite colliculi locations and they compete with each other via lateral excitation and remote inhibition. The growth rate in one decision process slows down when the other decision process is active at the same time.

The neural model proposes that (1) the competition between the SC buildup neurons encoding the decision signals and the randomly varying nonlinear growth rates of the decision processes are the underlying neural mechanisms needed to explain why the SRTs are so long, (2) the randomly varying nonlinear growth rates of the decision processes generate accurately the correct and error latencies as well as their shape distributions seen in the antisaccade task [1, 2], and (3) the interplay between the criterion level and the randomly varying growth rates of the decision processes can successfully simulate the error rates in the antisaccade task.

The complete mathematical formalism of this model can be found in section 9.2 of the dissertation manuscript.

2.3 Spiking neural model with variable climbing activity of decision making in the antisaccade task

Standard Hodgkin-Huxley modeling techniques were used to simulate networks of single compartmental models of cortical pyramidal neurons and cortical inhibitory interneurons (IN). The mathematical formalism of this model can be found in section 13.2 of the dissertation manuscript. Low spontaneous background activity in the network was simulated by delivering random noise to all pyramidal and GABAergic cells, generated from Poisson processes convolved with the AMPA, NMDA and GABA synaptic conductances. Because very little is known about the detailed connectivity of neurons and the associated synaptic strengths in the frontal cortices, we intentionally kept the network model as general as possible. Two networks of 10 pyramidal cells and 5 GABAergic interneurons each were simulated. In each network, I assumed that all pyramidal cells and GABAergic interneurons were fully connected. The output of each network was the average population activity of a homogenous population of neurons with identical connections. These outputs were then used as the input drives of the superior colliculus (SC) model presented in section 2.2 [3].

3 Results

3.1 Neural model of dopaminergic control of arm movements in Parkinson's disease bradykinesia

The present model is a model of voluntary movement and proprioception that offers an integrated interpretation of the functional roles of the diverse cell types in movement related areas of the primate cortex. The model is successful at providing an integrative perspective on cortico-spinal control of parkinsonian voluntary movement by studying the effects of dopamine depletion on the output of the basal ganglia, cortex and spinal cord. It can account for the many known empirical signatures of Parkinsonian willful action such as

- Increased cellular reaction time
- Prolonged behavior reaction time
- Increased duration of neuronal discharge in area 4 preceding and following onset of movement
- Reduction of firing intensity and firing rate of cells in primary motor cortex
- Abnormal oscillatory GPi response
- Disinhibition of reciprocally tuned cells
- Increases in baseline activity
- Repetitive bursts of muscle activation
- Prolongation of premotor and electromechanical delay times
- Reduction in the size and rate of development of the first agonist burst of EMG activity
- Asymmetric increase in the time-to-peak and deceleration time
- Decrease in the peak value of the velocity trace
- Increase in movement duration
- Substantial reduction in the size and rate of development of muscle production
- Movement variability

These findings provide enough evidence to support the main hypothesis of the model (see chapter 2 of the dissertation). Details of the simulation results can be found in chapter 5 of the dissertation.

3.2 Neural population model of decision making for the generation of ocular movements in the antisaccade task

The model presented herein offers an alternative view for saccadic eye movement generation that is supported by experimental evidence. The model is primarily concerned with what happens after the motor commands are formed, how the two processes of reflexive saccadic suppression and voluntary response generation are represented in the brain and how they are handicapped in the antisaccade task. In the model, the rising phases of the planned and reactive inputs were linear and they took

values from two normal distributions with different means and standard deviations. The model offers a functional rationale at the SC neuronal population level of why the antisaccadic reaction times are so long and variable and simulates accurately the correct antisaccade and error prosaccade latencies, the shape of RT distributions and the error probabilities. Details of the model's assumptions, simulation results and predictions can be found in chapter 9 of the dissertation.

3.3 Spiking neural model with variable climbing activity of decision making in the antisaccade task

The observed variability in the rising phases (slopes) of the reactive and planned inputs to the neural population antisaccade model (see section 3.2 of this paper) in the form of average firing rates of the pyramidal neurons was found to be due to noise in the conductances of the I_{NaP} and I_{NMDA} currents. Noise in the conductances of I_{Ks}, I_{DR}, I_C and I_{HVA} currents didn't produce any variability in the rising phase of the average firing rate. The slope of the climbing activity was carefully adjusted so that the simulated correct and error RT distributions and the error probabilities to approximate the experimental ones in an antisaccade task (see Table 9.3 of the dissertation). I estimated the slopes of the rising phases of the average firing rates of two cortical networks of neurons in each trial by fitting to them a straight line. I used these slope values as values of the slopes of the rising phases of the planned and reactive inputs of [3]. The slope values of the reactive and planned inputs were sorted in ascending order, so that the slope of the reactive input was always greater than the slope of the planned input. The threshold was adjusted, so that the simulated error rate closely matched the observed. Its value was set to a different value for each group, but it was kept fixed across trials for each group [3]. Details of the model's assumptions, simulation results and predictions can be found in chapter 13 of the dissertation.

4 Conclusion

Novel brain-guided multi-modular neural network architectures are developed for the selection (decision making), generation and control of arm and ocular movements in normal and diseased brain states. The modules are developed using much of what is known about the human brain and its functional and modular decomposition. All three computational neural models are consistent with pertinent constraints from primate and human neurobiology, and the related computer simulations reproduce key aspects of experimental observations regarding voluntary arm and ocular movements.

References

1. Evdokimidis, I., Smyrnis, N., Constantinidis, T. S., Stefanis, N. C., Avramopoulos, D., Paximadis, C., Theleritis, C., Efstratiadis, C., Kastrinakis, G., Stefanis, C. N.: The Antisaccade Task in a Sample of 2006 Young Men I. Normal Population Characteristics. Exp Brain Res. 147 (2002) 45-52
2. Smyrnis, N., Evdokimidis, I., Stefanis, N. C., Constantinidis, T. S., Avramopoulos, D., Theleritis, C., Paximadis, C., Efstratiadis, C., Kastrinakis, G., Stefanis, C. N.: The Antisaccade Task in a Sample of 2006 Young Males II. Effects of Task Parameters. Exp. Brain Res. 147 (2002) 53-63
3. Cutsuridis, V., Smyrnis, N., Evdokimidis, I., Perantonis, S.: A Neural Model of Decision Making by the Superior Colliculus in an Antisaccade Task. Neural Networks, under review.
4. Cutsuridis, V., Kahramanoglou, I., Smyrnis, N., Evdokimidis, I., Perantonis, S.: A Neural Variable Integrator Model of Decision Making in an Antisaccade Task. Neurocomputing, under review.
5. Cutsuridis, V., Kahramanoglou, I., Smyrnis, N., Evdokimidis, I., Perantonis, S.: Parametric Analysis of Ionic and Synaptic Current Conductances in a Neural Accumulator Model with Variable Climbing Activity. Proceedings of the 19th Conference of Hellenic Society for Neuroscience, Patra, Greece, September 30 - October 2, 2005.
6. Cutsuridis, V., Kahramanoglou, I., Perantonis, S., Evdokimidis, I., Smyrnis, N.: A Biophysical Neural Model of Decision Making in an Antisaccade Task Through Variable Climbing Activity. In: Artificial Neural Networks: Biological Inspirations - ICANN '05, Lecture Notes in Computer Science, LNCS 3696 (Springer-Verlag, Berlin, 2005) 205-210
7. Cutsuridis, V., Smyrnis, N., Evdokimidis, I., Kahramanoglou, I., Perantonis, S.: Neural network modeling of eye movement behavior in the antisaccade task: validation by comparison with data from 2006 normal individuals. Program No. 72.13. Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2003
8. Cutsuridis, V., Evdokimidis, I., Kahramanoglou, I., Perantonis, S., Smyrnis, N.: Neural network model of eye movement behavior in an antisaccade task. Proceedings of the 18th Conference of Hellenic Society for Neuroscience, Athens, Greece, October 17-19, 2003.
9. Cutsuridis, V.: A neural network model of normal and Parkinsonian EMG activity of fast arm movements. Proceedings of the 18th Conference of Hellenic Society for Neuroscience, Athens, Greece, October 17-19, 2003.
10. Cutsuridis, V., Bullock, D.: A Neural Circuit Model of the Effects of Cortical Dopamine Depletion on Task-Related Discharge Patterns of Cells in the Primary Motor Cortex. Rethymnon, Crete, Proceedings of the 17th Conference of Hellenic Society for Neuroscience, Poster 3, p. 39, October 4-6, 2002.
11. Cutsuridis, V., Bullock, D.: A Neural Circuit Model of the Effects of Cortical Dopamine Depletion on Task-Related Discharge Patterns of Cells in the Primary Motor Cortex. Poster Session II: Sensory-Motor Control and Robotics, p. xv, Proceedings of the 6th International Neural Network Conference, Boston, MA, May 30 - June 1, 2002.
12. Tremblay, L., Filion, M., Bedard, P. J.: Responses of pallidal neurons to striatal stimulation in monkeys with MPTP-induced parkinsonism. Brain Research. 498(1) (1989) 17–33.
13. Durstewitz, D.: Self-organizing neural integrator predicts interval times through climbing activity. J Neurosci. 23(12) (2003) 5342-5353
14. Durstewitz, D., Seamans, J. K., Sejnowski, T. J.: Dopamine-Mediated Stabilization of Delay-Period Activity in a Network Model of Prefrontal Cortex. J. Neurophys. 83 (2000) 1733-1750

15. Bullock, D., & Contreras-Vidal, J. L.: How spinal neural networks reduce discrepancies between motor intention and motor realization. In K. Newel, & D. Corcos (Eds.), Variability and motor control (pp. 183–221). Champaign, IL: Human Kinetics Press, 1993.
16. Bullock, D., Grossberg, S.: Neural dynamics of planned arm movements: Emergent invariants and speed-accuracy properties during trajectory formation. Psychological Review. 95 (1988) 49–90.
17. Bullock, D., Grossberg, S.: VITE and FLETE: Neural modules for trajectory formation and tension control. In W. Hershberger (Ed.), Volitional action (pp. 253–297). Amsterdam, The Netherlands: North-Holland, 1992.
18. Bullock, D., Grossberg, S.: Adaptive neural networks for control of movement trajectories invariant under speed and force rescaling. Human Movement Science. 10 (1991) 3–53.
19. Bullock, D., Grossberg, S.: Emergence of triphasic muscle activation from the nonlinear interactions of central and spinal neural networks circuits. Human Movement Science. 11 (1992) 157–167.
20. Bullock, D., Cisek, P., Grossberg, S.: Cortical networks for control of voluntary arm movements under variable force conditions. Cerebral Cortex. 8 (1998) 48–62.
21. Contreras-Vidal, J. L., Grossberg, S., Bullock, D.: A neural model of cerebellar learning for arm movement control: Cortico-spino-cerebellar dynamics. Learning and Memory. 3(6) (1997) 475–502.
22. Humphrey, D. R., & Reed, D. J.: Separate cortical systems for control of joint movement and joint stiffness: Reciprocal activation and coactivation of antagonist muscles. In J. E. Desmedt (Ed.), Motor control mechanisms in health and disease. New York: Raven Press, 1983.
23. Doudet, D. J., Gross, C., Arluison, M., Bioulac, B.: Modifications of precentral cortex discharge and EMG activity in monkeys with MPTP induced lesions of DA nigral lesions. Experimental Brain Research. 80 (1990) 177–188.
24. Trappenberg T.P., Dorris M.C., Munoz D.P., Klein R.M.: A model of saccade initiation based on the competitive integration of exogenous and endogenous signals in the superior colliculus. J Cogn Neurosci 13(2) (2001) 256-271.
25. Reddi, B.A.J., Carpenter, R.H.S.: The influence of urgency on decision time. Nat Neurosci 3 (2000) 827-831
26. Carpenter, R.H.S., Williams, M.L.L: Neural computation of log likelihood in the control of saccadic eye movements. Nature. 377 (1995) 59-62
27. Crick, F.: Astonishing hypothesis: the scientific search for the soul, Scribner, 1994.
28. Cutsuridis, V., Perantonis, S.: A Neural Model of Parkinson's Disease Bradykinesia. Neural Networks. (in press)