A GRADUATE-LEVEL MULTI-PURPOSE EDUCATIONAL CASE STUDY ON MODELLING AND SIMULATION OF THE NEUROMUSCULAR SYSTEM

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Abstract

Case studies provide an excellent and well established way of linking theory and practice in advanced-level teaching. The biological control systems involved in the regulation of posture and the control of movement in mammals are complex and highly non-linear. This case study is concerned with the modelling of elements of these neuromuscular systems and with the application of simulation methods to investigate some of the properties of their control loops. The case study is designed to be used in more than one taught module, possibly within different degree programmes and is therefore aimed at groups of students with different backgrounds and different prior knowledge. It is believed that e-learning techniques offer an increased level of flexibility that can be used to overcome problems associated with bringing students in different areas to a common level of understanding. The preparation of e-learning material for a multi-purpose case study also ensures that gaps in the knowledge and understanding of individual students within each course are more readily dealt with. The paper provides an outline of the case study, discusses educational issues associated with preparation of the case-study material for use in an integrated simulation and e-learning environment and presents some results from project work and assignments.

Keywords: Education, E-learning, Neuromuscular system, Simulation.

Presenting Author's biography

David Murray-Smith is an Emeritus Professor of the University of Glasgow . Until October 2005 he was Professor of Engineering Systems and Control in the Department of Electronics and Electrical Engineering, where he is still actively involved in research. His current research interests are in system modeling and control techniques applied to a range of engineering and biomedical systems.

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1 Introduction

Case studies provide an excellent and well established way of linking theory and practice in advanced-level teaching within most subject areas. The choice of topics is inevitably linked to the subject of the taught module in question and the nature of the associated degree programme. Case studies that are intended to be used in more than one taught module, possibly within different degree programmes, are unusual since they are inevitably aimed at groups of students with different backgrounds and different prior knowledge. E-learning techniques offer an increased level of flexibility that may overcome the problems associated with bringing students in these different areas to a common level of understanding and can allow a single case study to be used across a number of different courses. This approach may even be used to encourage students in different programmes using the same case study to interact across the disciplinary divides.

The preparation of e-learning material for a multi-purpose case study should also help to ensure that gaps in the knowledge and understanding of individual students within each course are more readily dealt with. In any degree programme at graduate level the students joining the course have a variety of different educational histories and experience. Each student finds that, in a programme of this kind, they have some significant gaps in their knowledge and need to undertake additional individual study in order to deal with the course material and the associated assignments. E-learning should prove very helpful in such situations.

Since 2004 groups in four universities in the USA and four universities in Europe have been collaborating in a project named USE-eNET (US-Europe e-learning NETwork in Computer Science and Engineering). A list of the partner institutions and the relevant contact persons is provided in Appendix A. This work was funded by the European Commission through the Directorate General for Education and Culture and by the US Department of Education through the Fund for Improvement of Postsecondary Education (FIPSE). The work has been concerned primarily with the development of on-line resources for modelling and simulation to help create new opportunities for computer science and engineering graduate students to gain international experience. A second important objective for USE-eNET is that it should provide a basis for a generic environment suitable, more generally, for the development of multi-disciplinary courses within which modelling and simulation techniques can have an important role.

The approach adopted within USE-eNET involves the development of a general design framework for a combined e-learning and simulation environment that should meet the needs of a wide range of academic disciplines. Prototype course modules are being developed and these include case studies and material for international team projects. USE-eNET also places emphasis on the interdisciplinary nature of computer-based modelling by exposing students in selected subject areas to the use of continuous system and discrete event modelling and simulation techniques. One of these chosen areas is transportation and bio-medicine is a second. The eight partner institutions have been collaborating in the design of a generic e-learning and simulation environment that meets the needs of students in those fields as well as in mainstream areas of computer science and engineering.

The biological control systems involved in the regulation of posture and the control of movement in mammals are complex and highly non-linear. They have attracted the attention of researchers from a number of different fields, such as neurophysiology, engineering, computer science, physics and applied mathematics, for many years. This interest arises in part because of the potential clinical importance of improved understanding of this system but also because engineers and physical scientists find this to be a very interesting system which has features that could be valuable for engineering applications such as robotics.

The case study outlined in this paper is concerned with the modelling of some of the most important elements of neuromuscular systems (see, for example, [1,2]) and with the application of simulation methods to investigate some of the properties of neuromuscular control loops.

On an anatomical and functional basis the neuromuscular system may be divided into *peripheral* and *central* parts. The peripheral nervous system involves a sequence of repeating units within the spinal cord, which are known as *segmental levels*. The elements of the peripheral neuromuscular system at one segmental level of the spinal cord are shown in Figure 1. The muscular and skeletal subsystems and the associated sensory components (neural *receptors*) are elements within feedback pathways through the spinal cord that form the *stretch reflex* system. The higher levels of this hierarchical system involve the brain stem, cerebellum, motor cortex and other associated areas of the central nervous system. Neural communication pathways interconnect elements at these different levels.

The basic actuators are the load-bearing or *extrafusal* muscle fibres. A single anatomical muscle may contain many hundreds of active contractile elements, organised functionally into *motor units* that are connected in parallel to a common tendon. Each motor unit involves a single *motoneurone* and a group of about 250 extrafusal muscle fibres that can be activated simultaneously. Muscle fibres act as active nonlinear springs in which the forces developed depend upon both the neural input and the external loading. The fibres contain smaller elements (*fibrils*) and each of these contains many *microfilaments*. These microfilaments are of two types, thin filaments of *actin* and thick filaments of *myosin*. The active contractile properties of muscle depend upon the active sliding of one type of filament over the other.

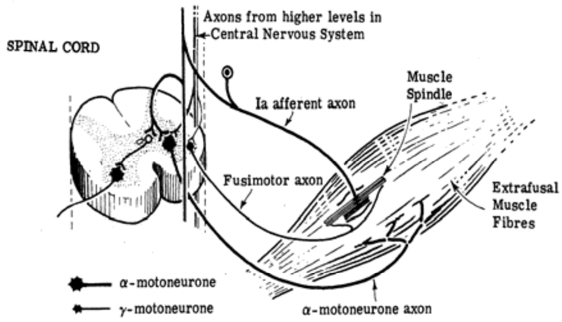

Figure 1: Highly simplified schematic diagram showing the neural and muscular elements of the stretch reflex system. (adapted from Figure 1 in [2])

Neuromuscular systems involve parts of the muscular system and nervous system that are used in the regulation of posture and in the control of limb movement as well as in some other physiological functions, such as the control of eye movement, the control of breathing and the operation of the heart. This case study has focused, initially, on the modelling of neuromuscular systems associated with skeletal muscle and thus with posture and movement control.

Better understanding of the properties of the main elements of neuromuscular systems and how they are used, in combination, to control posture and movement should assist in the treatment of neuromuscular diseases. It should also improve the prospects of patients following spinal cord injury or strokes. Such knowledge may also assist in research on how to apply the principles of biological systems in the development of better forms of prostheses for amputees.

The difficulty in applying control theory to improve our understanding of the relevant neurophysiology lies in the complexity of the system. It has a highly redundant structure, with many parallel neural pathways and many sense organs. However, mathematical modelling techniques and associated tools for experimental modelling based on system identification and parameter estimation methods have been applied extensively to the neuromuscular system and have undoubtedly led to an improvement in our understanding of some aspects of its behaviour (e.g. [1,2,3]). Computer simulation methods have allowed hypotheses about the system to be tested quantitatively, both under steady state and dynamic conditions and have thus provided important additional insight.

Knowledge of the principles of operation of neuromuscular systems has also proved to be of value to engineers working on biomimetics, which is a process of design that involves the deliberate mimicking of natural systems. Biomimetics has been particularly helpful in the area of biologically-inspired robots. Models of the human neuromuscular system have also been shown to be important in modelling human operators for situations where they have a critically important role, such as in the piloting of high-performance aircraft. Extensive use has been made of relatively simple neuromuscular system sub-models within the models of pilots that are used in the description of aircraft handling qualities in quantitative terms and for the development of aircraft flight control systems.

The neuromuscular system is also of special interest for those interested in system modelling and simulation methods in that it involves both discrete and continuous elements. The nerves that form the information pathways within the system are essentially discrete in terms of the signals that they transmit but other elements of the system, such as the muscles that form the actuators in the system and the muscle receptors that are the sensory elements, also involve continuous variables. This mixed discrete and continuous variable system is a challenging, but nevertheless rewarding, one to consider within courses dealing primarily with modelling and simulation methods. It is also potentially useful to use as an illustration of the benefits of applying modelling and simulation techniques within courses on control engineering or biomedical engineering.

One of the difficulties inherent in using an example of this kind as a modelling and simulation case study within a graduate-level teaching module is that few students are likely, initially, to have the background knowledge necessary to undertake the work. Most students of computer science and engineering have very limited knowledge of biology and require access to appropriate material at a basic level in order to understand even a simple description of each of the elements forming the neuromuscular system. E-learning techniques are ideal for this in that students can access on-line material and find references to other sources in a simple and straightforward fashion. Similarly, if a student with a background in the biological sciences were preparing to use the case study, e-learning materials could be put in place to guide them through the mathematical fundamentals and help them to understand the relationship between the model and the underlying biology.

2 The Case Study

Notes have been prepared on various aspects of the neuromuscular system and on modelling and simulation topics that are especially relevant to the case study. For the initial stage in the development of this case study the bulk of the background information provided to students was from these notes (normally made available to the students in electronic form) and information about a number of relevant web sites. The notes are structured in terms of a number of separate sections and associated appendices.

It is believed that through the use of e-learning methods students can access information at a number of different levels to suit their level of prior knowledge. Hence work is currently under way to further develop an e-learning version of the material that provides background information needed to undertake the work and to further integrate this with the simulation environment.

Within the notes and in the e-learning version the background information relating to the biology is divided into a number of separate sections. This division of the material has been made on a conventional basis using an accepted approach applied more generally in the teaching of systems physiology.

2.1 Section A: Introduction

This is an introduction to the case study and prepares students for the work that they are about to undertake. It emphasizes the fact that students have to seek the information that is needed in order to complete the various assignments and exercises that form an integral part of the study. This introductory section makes it clear that students cannot expect to deal with all aspects of the work simply by reading through the notes and using the software that is provided. They are expected to seek information themselves from other sources as well as making full use of the e-learning environment at all stages of the work.

2.2 Section B: Skeletal Muscle

This section describes the basic properties of the muscles used to regulate posture and control movement. Muscle fibres behave as active nonlinear springs in which the forces that are developed depend both upon the external forces and the neural input. This section of the notes provides students with the understanding necessary to start doing some practical modelling work using a simulation model of muscle that is provided as part of the simulation environment for their course. The notes suggest tests of the model that students should undertake themselves and links are provided to published papers where they should find relevant data relating to real experiments carried out on muscle. Comparison of model results and equivalent experimental findings are an essential part of the work (e.g. [2,3]).

2.3 Section C: Signal transmission pathways

Nerve fibres form the signal transmission paths within the system. Activity at any given point in a nerve fibre causes activity at adjacent points. The activity spreads into all the branches and this takes the form of voltage impulses known as *action potentials* or *spikes* and are separated by inactive periods, with information being transmitted through a form of pulse-frequency modulation.

The point of connection between one nerve cell and another is called a synapse. An impulse transmitted along one nerve fiber may not be sufficient to produce activation at a second cell on the other side of a synaptic junction and cumulative effects of many such impulses are more important. The synaptic connections are either facilitatory or inhibitory and may be viewed as equivalent to positive and negative inputs at a summing junction on an engineering system block diagram. A synaptic junction may therefore be regarded, in engineering terms, as a summing junction with additional properties involving attenuation and nonlinear effects such as a threshold. This is a topic that lends itself to modelling and simulation and use of these tools can assist students in gaining an understanding of how neural signals may be processed and interpreted. Similarities and differences between biological neural networks and artificial neural networks are discussed. Some relatively simple assignments using simple simulation models can be used to assist the learning process within this section.

2.4 Section D: Sensory Receptors

The main sensory receptors involved in the stretch reflex are the muscle spindle receptors and the Golgi tendon organ receptors (e.g. [1,2], [4]).

Functionally, muscle spindle receptors may be thought of as being like a strain gauge having a gauge factor that is under neural control. They provide neural output signals in response both to changes of length of the main muscle and to neural activation of their specialized muscle fibres through the fusimotor neurons.

The rate sensitivity of muscle spindles is thought to be important for neuromuscular control in the same way that velocity feedback is important within many engineering control systems.

Golgi tendon organs lie in series with the main load-bearing muscles and the neural output from this type of sensory receptor is directly related to the overall muscle tension. They are simpler than muscle spindle receptors in that they have no equivalent of the fusimotor innervation of muscle spindles and are essentially passive sense organs.

2.5 Section E: The stretch reflex and neuromuscular control

The alpha motoneuron provides the actuating input that produces contraction of extrafusal muscle. The level of alpha motoneuron activity is determined by feedback loops and by inputs from higher levels in the central nervous system. These feedback loops include pathways from muscle spindle receptors and Golgi tendon organs, together with other feedback signals from joint receptors and skin receptors. Local neural feedback pathways also exist at the spinal cord (involving the Renshaw cells), and these provide recurrent inhibition.

Many hypotheses have been put forward in attempting to explain the action of the neuromuscular control system. About fifty years ago, a servomechanism theory of neuromuscular control was postulated by Hammond, Marsden et al. [5,6] Subsequent research has suggested that the action of the stretch reflex system must be more complicated. It has also been pointed out that the controlled variables cannot be defined in a simple way because of the interactions taking place within the muscle spindle, which serves as the comparator element. Pure position control and pure tension control now appear unlikely to be capable of the tasks performed by skeletal muscle.

Students are encouraged to look critically at a number of different published models of the stretch reflex and of models relating more generally to neuromuscular control (e.g. [7,8]). They are also encouraged to investigate in detail one particular SIMULINK model published and made freely available by Prochazka et al.[9].

3 Assignments and Project Work

The topic of this case study allows a very large number of possible assignments to be devised. These can be tailored to suit the group undertaking the work and even to suit the background knowledge of individual students. Tasks can range from making use of a standard simulation model to carry out some simulation experiments and interpret the results to much more ambitious project work involving the testing hypotheses about the structure and function of the neuromuscular control system.

The nature of the assignments and project work appropriate for this case study depend on the nature of the course and degree programme within which it is being used. For example, within a course dealing with system modelling and simulation methodology, assignments and projects are most likely to be concerned with using the information provided in the accompanying notes or e-learning material to build up simulation models of a specific elements with the system (such as the muscle spindle) and carry out simulation experiments using those simulation models to try to answer physiologically meaningful questions. Within a course on control engineering, on the other hand, the emphasis is more likely to be on the use of a given simulation model of the neuromuscular system or some element of it (such as active skeletal muscle) in the context of a control engineering design problem. One example, that has actually been the subject of student project work, is the use of a simulation of active muscle to represent the load within a closed-loop actuator system that was being designed as a mechanical input device or “puller” for physiological experiments on the mechanical properties of skeletal muscle.

Figure 2 provides an example of the type of simulation-based investigation that can be carried out within practical work undertaken by students during this case study. The situation being considered relates to repetitive neural stimulation of skeletal muscle at different frequencies. The input in this case is essentially discrete, in the form of a series of events whereas the output involves continuous variables. The results show very clearly a summation of twitches, which is a well-known and highly nonlinear feature of muscle responses. The results also demonstrate the limiting condition known as *tetanus*. Tetanic conditions are obtained in the model for applied frequencies in excess of 11 pulses per second. The simulation results are broadly consistent with the behaviour of real muscle.

Because of the method of stimulation in the experiments carried out by Ritchie and Wilkie [10] which form the basis for the data used in the model, the muscle must be regarded as acting as a single motor unit. A typical muscle is made up of hundreds of motor units that are stimulated, under normal conditions, in an asynchronous fashion. A closer approximation to a representation for muscle operating under normal conditions could be obtained by a parallel arrangement of a number of models of the type described here, but with an asynchronous pattern of stimulation. This suggests further areas for investigation and could well provide a starting point for a more extensive project type of assignment.

4 Discussion

Many issues of interest arise in the investigation of elements of the neuromuscular system. The highly nonlinear characteristics of the elements of such systems are combined to produce stable and highly responsive control structures that can involve both negative and positive feedback pathways [9]. Although the overall neuromuscular system has very complex nonlinear and time-varying properties, relatively simple simulation models of elements of the system have been developed or adapted for use in this case study. Consideration of the limitations of these models and how the model imperfections may affect the interpretation of simulation experiments forms an important aspect of the case study.

The case study is multi-purpose in terms of its design. It is intended for use within a graduate-level teaching module on system modelling and control and also within graduate-level programs on computer-based modelling and simulation and biomedical engineering. Different aims and objectives apply in these different teaching applications but the adoption of e-learning techniques means that a single case study structure can be used. The flexibility that results from e-learning means that graduate students from different disciplines and with different levels of background knowledge reach the necessary common level of background understanding more quickly than otherwise and that they can then benefit from the multi-disciplinary experience that this case study offers.

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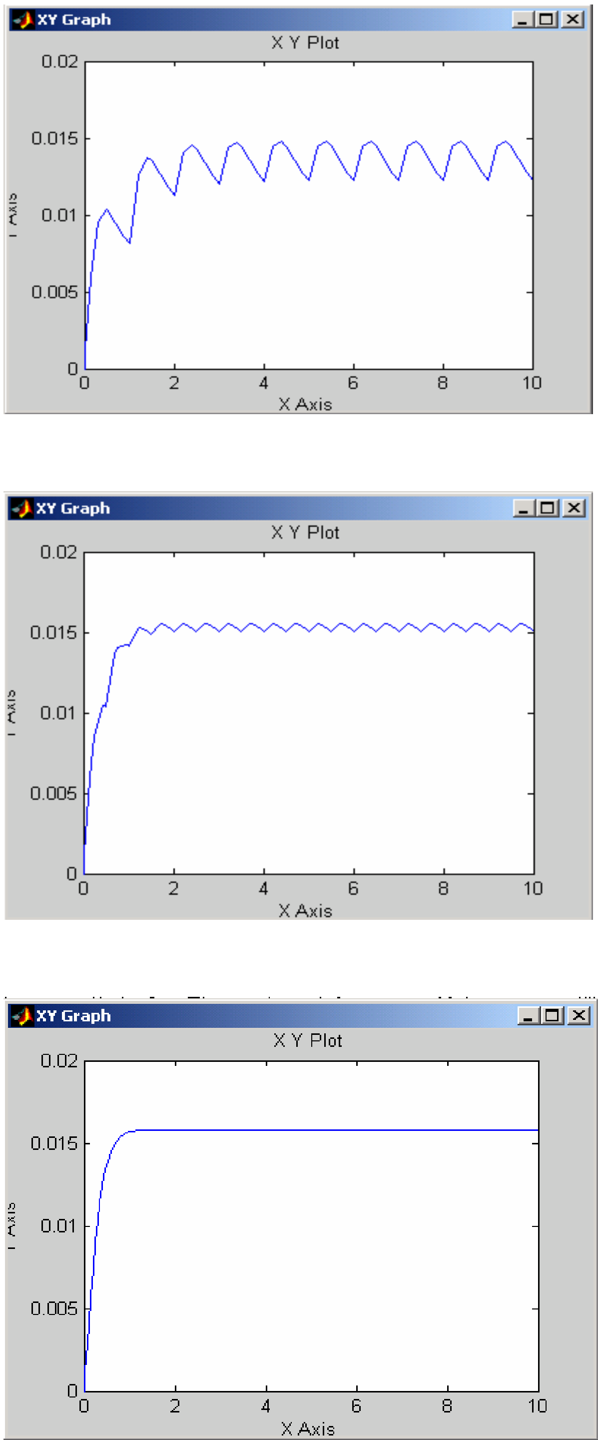

Figure 2: Responses of a SIMULINK simulation for a nonlinear muscle model under conditions of constant tension with repetitive neural stimulation at three different frequencies. The vertical axis in each case shows the length change (m) following the onset of neural stimulation. The model in this case is based on published data of Ritchie and Wilkie [10].

Appendix A

Institutions (and associated contact persons) involved in the USE-ME Project.

European Institutions

University of Hamburg, Department of Computer Science (Prof. Dr. Dietmar P.F. Möller).

University of Glasgow, Department of Electronics and Electrical Engineering (Prof. Dr. David J. Murray-Smith).

University of Aarhus, Section of Health Informatics (Prof. Dr. Jens Dørup).

Budapest University of Technology, Department of Information Management (Prof. Dr. András Jávor).

US Institutions

California State University - Chico, College of Engineering, Computer Science and Technology (Prof. Dr. Roy E. Crosbie).

University of Nebraska – Lincoln, College of Engineering and Technology (Prof. Dr. Hamid Vakilzadian).

University of Alabama, Huntsville, Office of Vice-President for Research (Prof. Dr. Bernard J. Schroer).

University of Louisville, Kentucky, Department of Anesthesia (Prof. Dr. Gary Loyd).

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