ON PATTERN GENERATORS FOR LOCOMOTION IN MAMMALS

by

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ON PATTERN GENERATORS FOR LOCOMOTION IN MAMMALS

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ABSTRACT

Neurophysiological research has established the presence of central pattern generators that can produce motor patterns during locomotion. Attempts to model these pattern generators have been restricted to studying small networks that provide alternating activation of two groups of motoneurones. It is not clear how the complex motor pattern observed during locomotion can be produced by such oscillators. It has been shown that a limb is controlled as a single unit and in this thesis an alternate analytical approach to modelling limb pattern generators is presented.

The model generator is considered to have a tonic input and six outputs, one each for flexion and extension for the three joints of the limb. The model suggests that the limb pattern generator consists of a labile sine/cosine relaxation oscillator that produces the fundamental frequency oscillation of the output in response to a tonic signal. The output of this oscillator is then fed into modules for each muscle used in the study, to produce the output pattern that we observe during locomotion. Each module contains two nonlinear functions 'g' and 'h' that depend on the amplitude of the cosine function. The model was tested using the data obtained from two series of

experiments using : a) an acute post-mammillary cat preparation and b) kinematic studies on human subjects. Besides these experiments, EMG data for humans was obtained from a research report.

For the cat data, the model is able to account for speed and phase changes in locomotion with a relatively smooth change of system parameters. Model simulation results on interlimb coordination are in concurrence with the experimental observations found in the literature. A simple neural network implementation of the model has been suggested. An intrinsic property of the model is that the functions g and h are amplitude and not time dependant.

There is a reasonable body of evidence to suggest that a similar model may be applicable to humans. The model in the case of humans is able to accomodate different rhythmic movements of the lower limb such as walking, cycling and climbing stairs. This was shown from EMG and kinematic recordings.

To

my parents

Ruby and Esoof

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CHAPTER I

INTRODUCTION

1.1 Introduction

Locomotion involves movement of the body from one point to another, relative to its environment. It is understood that three basic mechanisms are utilised for locomotion : amoeboid, ciliary and muscle action. Amoeboid movements are as a result of changes in the cell shape by flow of cytoplasm and pseudopodal activity. Ciliary movements, occuring in an aqueous medium, are produced by wave like motion of fine hairs known as cilia. In the majority of animals however, movements are accomplished by the use of the skeletal muscles. These effector organs are driven by the animal's neural machinery. They act on the skeletal frame structure to produce movements. Though the principle is the same for all animals, the resulting forms of locomotion are quite different. The differences are mainly due to the various types of skeletal structures and the environment in which these movements are performed.

Locomotion has been studied by various individuals for some hundreds of years. The sustained interest in the study of this repetitive behaviour is understandable. Man's desire to fly for instance, led to the study of naturally occuring solutions of similar movements with some attempts at imitation. Though detailed understanding of how birds fly contributed little to the development of the airplane, it did lead to some improvements in its design. Besides the human desire to improve mobility, the study of locomotion has other implications that are discussed next.

Animals exhibit a variety of rhythmic behaviours such as walking, swimming, scratching, breathing and chewing. All these behaviours, in which all or part of the animal's body moves in a repetitive manner, are generated by the nervous system. As pointed out by Delcomyn (1), the study of these behaviours has helped establish a general principle of integration in the nervous system. There are general principles in neurobiology at the cellular level such as the physiological basis of an action potential. But, the neural basis of locomotion in animals addresses organisation at a multicellular level where are there are few universally accepted principles. The study of locomotor movements may help in gaining insights into storage and control of learned movements in general.

Aside from the fundamental nature of its inquiry, the study of locomotion has some useful applications. It is generally recognised that animals, including man, possess off-road mobility characteristics far superior to those of conventional wheeled or tracked vehicles. The principle of legged locomotion should, in theory, allow for efficient and mobile legged vehicles. But the actual effective realisation of such robots is in its infancy (2).

A major concern in the treatment of physical disabilities in humans is dealing with various degrees of functional loss of the lower limbs. Diagnosis of the problem, and effective design and utilisation of various orthoses and prostheses used in treatment, necessitates understanding normal and pathological gait. This has led to a renewed interest in the study of gait characteristics guided in part by biomechanical considerations (3,4). Biofeedback training has been used to improve the gait of the patient (5). Also, studies in muscle stimulation hold out hope for rehabilitation of paraplegic patients (6,7).

1.2 General Objectives of the Thesis

Neurophysiological studies have established that there are pattern generators in the nervous system of animals that produce locomotory movements (1). This thesis addresses the problem of understanding the nature of these pattern generators.

The main objective of this thesis is to model the periodic innervation of the muscles of the lower limbs during locomotion as the output generated by a multioscillator community. It is hypothesised that a population of oscillators that produces the desired output, can be an adequate representation of the actual system controlling the movements.

It is intended therefore to:

a) determine a mathematical model for such an oscillator community,

b) determine the model parameters from experimental data, and

c) try to ascertain the neurophysiological correlates to the model.

A mathematical model for the limb pattern generator is derived. The model parameters are determined from electromyographic data obtained from the cat muscles. The applicability of this model to human locomotion is discussed. Electromyographic and kinematic data from human subjects is used to study the model's behaviour under different types of rhythmic movements of the lower limb.

It is hoped that the study will enhance our understanding about the generation and control of movements in general and locomotion in particular. Before we can discuss the details of the proposed work, it is essential to get a perspective on some general aspects of motor control.

1.3 An Overview on Neural Control of Movement

In this section the general principles of motor organisation during voluntary movements are discussed. This is followed by a review of the neural control of locomotion.

1.3.1 General Principles of Motor Control

The control of movements in general has been a major concern of neurophysiology. For coordinated movements the skeletal muscles have to be activated in an appropriate spatial, temporal and quantitative manner. How this requirement is met is discussed next.

a) What is the Output ?

It is known that the motoneurone pool channels the output of the nervous system to the skeletal muscle. But with which parameters of the muscle output these motoneurones are programmed is not clear. As noted by Stein (8), the controlled variables may be force, velocity or length. It can be argued that given the initial conditions, the specification of the forces at any instant can, through Newtonian mechanics, determine the other variables. For concentric contractions Patla et al (9) have suggested that the power output of the muscle is programmed in the firing rate of the motoneurone pool.

b) How is the Output Generated ?

For coordinated movements to take place, it is clear that the system must progress through the folowing stages.

i) General Decision to Act

How the decision to act is made is not known. But, the study of EEG recordings prior to voluntary movements has shown a depression of the Rolandic Alpha rhythm. This was termed by various researchers as the 'E - wave' (expectation wave) or the 'Readiness Potential' (10). It is most clearly expressed in the associative region of the cortex and occurs 1-1.5 seconds prior to any myoelectric activity. The readiness potential is shown to be dependant on a variety of factors such as attention, reaction time and instruction.

This readiness potential is followed by another change in EEG recordings termed as 'Premotor Potential'. These changes in potential seem to signal the nervous system's decision to act.

ii) Preparation and Movement Execution

It is realised that movements are not generated by a simple stream of instructions in a 'top-down' sequence of brain structures, but rather by multiple feedback and feedforward interactions (11).

The pyramidal tract neurons (PTN) which are the output neurons of the motor cortex, were shown to be active prior to the onset of movement by Evarts(12). Thus, a temporal relationship between the initiation of a movement and the activity of the motor cortex was established. But the substantial delay (100 msec) between this activity and the onset of movements led researchers to consider that these neurons may have an indirect motor function and may play a role in the recruitment of subcortical structures.

The role of basal ganglia and the cerebellum in the initiation and control of movements has also been studied by various researchers (13,14). These functional groups of nuclei have connections, separated by several synapses, to the motoneurone pool. Besides their direct involvement in the initiation and control of movements, these structures have rich interconnections with the cortex and the brainstem. Figure 1 (15) shows a very simplified information flow diagram in the central nervous system. It has been suggested (16) that these structures play a vital role in 'tuning' the movement prior to its occurence.

Besides the efferent system preparation, it is known that the afferent system is also readied prior to the onset of the movement (10). The somatosensory cortex which has efferent connections to the PTNs, receives input from subcortical structures like the cerebellum. The afferent pathways are also under central control. Thus the system is readied for receiving and interpreting feedback relevant to the movement.

Thus all the components of the motor system seem to play an aggregate role in the organisation and control of movements.

iii) Error Corrections Based on the Feedback Received

Movements are accomplished by means of active muscular forces (internal) as well as inertial and reactive (external) forces. It is clearly impossible to calculate a

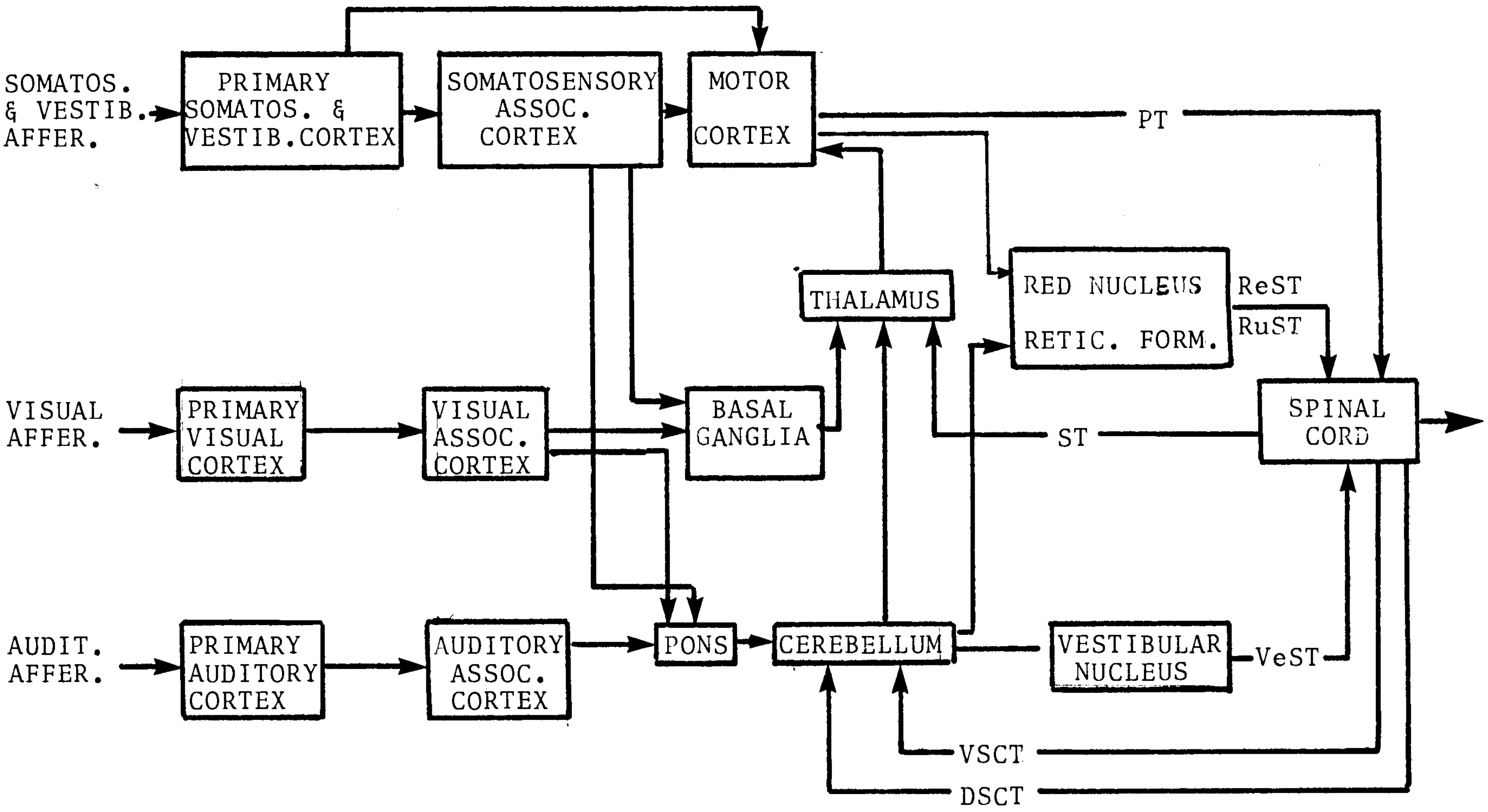

Figure 1. Information Flow Diagram in the Mammalian Nervous System from Kornhuber (15).

priori, the effects of the numerous factors involved. Thus corrections are made based on the feedback received. These corrections, listed in order of the response time, are mediated by:

Spinal Reflexes :

Muscle spindle afferents have direct monosynaptic connections to the alpha motoneurone. They monitor the length of the muscle and form a negative feedback loop. This prompted researchers to view the muscle as a servomechanism (17). Studies showing alpha-gamma coactivation (18) led to the formation of a servo assisted hypothesis (19). Since the gain of this negative feedback loop is low the compensation it can provide is low (20).

Besides length feedback, the Golgi tendon organs which respond to tension have disynaptic connections to the alpha motoneurone. Initially, it was thought that this negative feedback loop was active only at very high level of force production to protect the muscle from damage. Subsequent studies have shown that it is active at low levels of force generation (21). This led Nichols and Houk (22) to suggest that the muscle stiffness (ratio of force to change in length) is controlled rather than force and length individually. The reflexes compensate for the nonlinear properties of the muscle and make it more linear, and hence a simpler element to control (23).

Long Loop Reflexes :

The response of a limb to muscle stretch can also involve long-loop reflex pathways, probably mediated by the fast pathway to the somatosensory cortex and then to the motor cortex and/or the red nucleus (8,24). These pathways contain many synapses and hence posess greater flexibility in responding to perturbations. Miles and Evarts (25) point out that the cortex receives convergent inputs from various modalities and hence the long-loop reflex response may be dependant upon the interactions of these various inputs.

Corrections Mediated by the Central Structures :

Aside from the fast reflex responses, ongoing corrections are mediated by the central structures which modify their output based on the feedback received. As seen in figure 1, all the central structures receive feedback, peripheral as well as internal (efference copy or corollary discharge). They alter their output appropriately and smooth coordinated control of movements is achieved.

1.3.2 Neural Control of Locomotion

Locomotion is an unique subset of the full range of movements an animal is capable of performing. The range, of course, is dependant upon the animal's position on the phylogenetic scale. To explain the generation of locomotory movements, two main hypotheses have been put forward. The first hypothesis, peripheral control, maintains that afferent feedback cues are used to generate the motor patterns observed during locomotion. Early experiments as mentioned by Delcomyn (1), did support this hypothesis, but subsequent studies proved them to be incorrect. Having shown that feedback is not needed for the generation of the rhythmic patterns, efforts were directed towards understanding the intrinsic properties of the central nervous system that regulates these movements. The idea that the central nervous system is capable of generating the movements without the help of the afferent feedback, constitutes the second hypothesis.

a) Evidence for a Central Pattern Generator

Numerous isolation (all or part of the nervous system is physically removed from the animal), deafferentation (all or some of the sensory nerves are cut) and paralysis (using a paralytic agent like curare all movements and hence phasic feedback is eliminated) experiments have shown that the basic movements during locomotion can be generated by the central nervous system. In his paper, Delcomyn (1) lists the studies done on a variety of animals. In mammals various authors (26,27,28,29,30) have shown that a central pattern generator is responsible for the locomotory movements.

b) Where are these Central Pattern Generators ?

To determine the minimal neural substrate capable of producing the desired movements, researchers have transected the neuraxis at various levels (from the cortex to the spinal cord) and studied the animal's locomotor behaviour. The locomotor behaviour in different preparations is described below.

i) Decorticate Preparation (26,27)

Removal of the cortex has no apparent effect on the locomotion of the animal. It can move around spontaneously and avoid obstacles properly.

ii) Acute Thalamic Prepartion (26,27)

Stimulation of the subthalamic region, the nucleus subthalamicus can elicit rhythmic locomotor-like activity (see figure 2, preparation I). Bilateral lesion of the subthalamic locomotor region (SLR) eliminates only voluntary locomotion. From studies on the mesencephalic preparation, it seems likely that the SLR is responsible for initiation of locomotion as a part of goal directed behaviour. Thus the function of the SLR cannot be described in motor terms.

iii) Mesencephalic Preparation (26,27)

The brainstem is transected such that the entire mesencephalon is intact (see figure 2, preparation II). Under such conditions the animal cannot walk, but when a circumscribed region below the inferior colliculus is stimulated repetitively (30-60 Hz) the animal starts to walk. Increasing the strength of stimulation results in increased speed and altered mode of locomotion (walk-trot-gallop). The SLR effects could still be elicited after the destruction of the mesencephalic locomotor region (MLR). Thus it appears that MLR is not a common center for locomotion in the brainstem over which all the effects are relayed. It seems to be one of the several structures from which locomotion can be elicited and these effects are exerted over several brainstem descending systems.

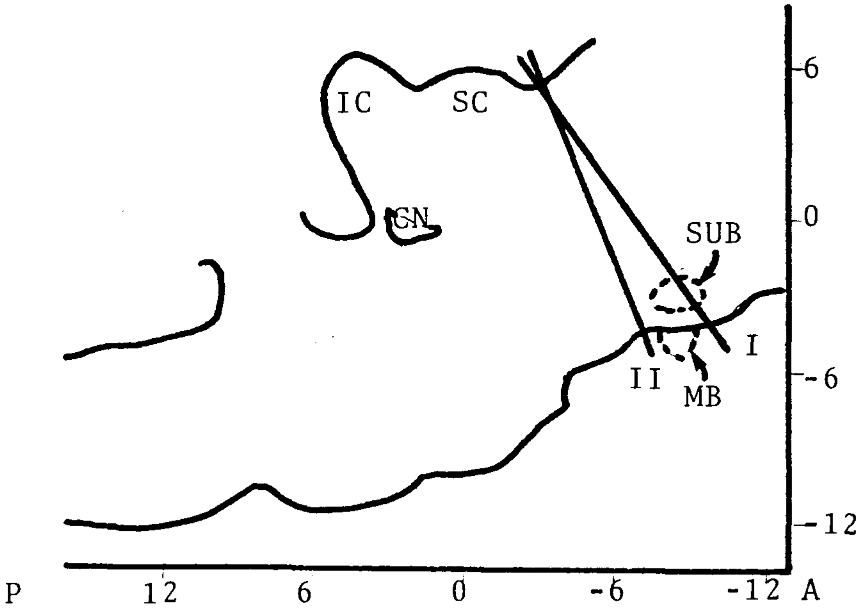

Figure 2. A schematic diagram of the brainstem of a cat on the L4 parasagittal plane showing acute thalamic preparation (I) and post-mammillary preparation (II). Abbreviations include : IC, inferior colliculus, SC, superior colliculus, CN, cuneiform nucleus, SUB, subthalamic nucleus (SLR), and MB, mammillary body.

(Adapted from Mori et al, J.Neurophys,1977)

iv) Spinal Preparations (29,30)

If the spinal preparations, where the neuraxis is transected at the lumbar level, are kept for a longer period of time, locomotor movements can be elicited. This could not be due to plastic changes in the neuronal circuits because the acute spinal cat can perform stepping movements after injection of DOPA (a noradrenergic precursor).

All of this evidence make a strong case for central pattern generators at the spinal level. This does not preclude the involvement of the higher centers and peripheral feedback in the control of the locomotor movements.

c) How are the Pattern Generators Triggered ?

It is clear that the pattern generators responsible for locomotion unlike those for breathing for instance, are not continously active and need to be initiated. The evidence from the midbrain stimulation and the effects of DOPA in the spinal preparation suggests that the noradrenergic system is involved in initiating and maintaining the locomotor movements (26,27). The arguments for this hypothesis are as follows. The circumscribed MLR region is close to noradrenergic cell bodies and thus could stimulate the noradrenergic system. Furthermore, by blocking the noradrenergic receptors, locomotion is prevented in the mesencephalic cat. Also there are no interspinal neurones containing noradrenaline. The involvement of other descending systems is not discounted.

d) How is the Output of the Pattern Generators Modified ?

Though the basic motor patterns during locomotion require only tonic excitation from the higher centers, this pattern can be modified by other descending pathways and the peripheral feedback.

i) Effects of Fast Descending Pathways

The tonic command system can trigger the locomotor movements but the rapid adaptation to the environment requires the fast descending pathways to act, at least in part, on the motoneurones and the last order inhibitory neurones. The fast rubro- and reticulo-spinal neurones are active during the flexion phase of the step cycle, whereas the vestibulo-spinal neurones are active during the extension phase of the step cycle (31,32). Their activity does not seem to be necessary for the generation of locomotion nor is there evidence that these pathways are part of the intrinsic generator network itself. Rather, they may be useful in providing phasic corrections acting at the generator output level. This phasic activity is dependant upon an intact cerebellum.

ii) Effects of Peripheral Feedback

Though peripheral afferent input is not necessary for generation of the locomotor pattern, it can interact with and hence influence the pattern generator. The various effects the peripheral input can have are (33):

1) tonic excitation of the nervous system as in the case of the locust's flight system.
2) phasic reinforcement of alpha motoneurone activity as in the case of lobster swimmeret.

In the case of mammals there are two types of input that can interact with the pattern generator (26). They are:

1) Hip Input

   Since the duration of the stance phase in spinal cats varies with the speed of the treadmill, it is apparent that peripheral signals must be influencing this part of the step cycle. It is observed that afferent signals from the hip can trigger the switch from extensor to flexor activity. Since the central program can generate the switch, it seems that this input directly interacts with the generator and could block the switch under abnormal circumstances such as when the movement is slowed down.

2) Nonspecific Excitation

In a spinal preparation it is observed that nonspecific stimulation such as squeezing the tail results in faster and more forceful locomotion (26). This potentiating effect seems to be a general feature. The precise action of this stimulus is unknown.

There is also evidence of phasic control of the reflex arcs (34,35,36,37). For example, electrical or mechanical stimulation of the dorsum of the foot produces responses which depend on the phase of the step cycle. Stimulation in the swing phase produces flexion of the limb whereas stimulation in the stance phase produces extension of the limb. Thus the animal can respond appropriately to unpredictable disturbances of the step cycle.

e) Summary of Known Facts

The following is a summary of the evidence accumulated by various researchers through numerous experiments:

1) there are generators at the spinal level which on activation by the higher centers produce the stepping movements.

2) there are generators for each limb and these are coupled during locomotion.
3) peripheral feedback is not necessary for the sequencing of the limb movements during locomotion.
4) feedback from the hip when present, has influence on the duration of the swing phase.
5) specific cutaneous inputs from the dorsum of the foot elicit different responses in different phases of the step cycle.
6) the descending pathways, the corticospinal tract, the reticulospinal tract, the vestibulospinal tract and the rubrospinal tract modulate the activity of the stepping generator in different phases of locomotion.

Figure 3 is a schematic representation of the controlling system.

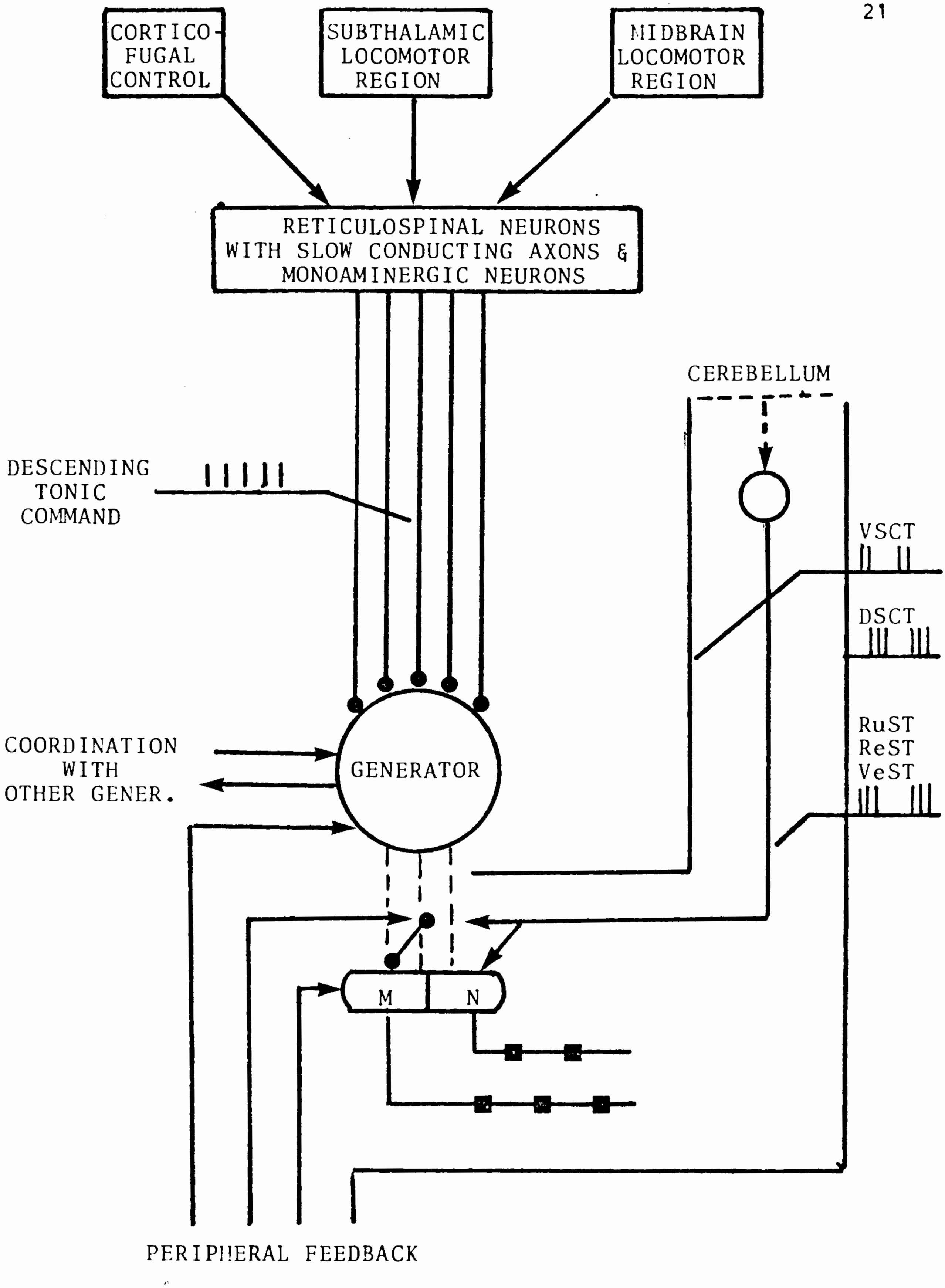

Figure 3. A schematic diagram of the neural control system for locomotion from Grillner (26) & Shik (27).

CHAPTER II

PROBLEM DEFINITION

2.1 Introduction

Through the efforts of many reseachers over the span of a few decades, the concept of a central pattern generator that can produce the motor patterns during locomotion has been established. Though by no means a trivial accomplishment, the real mystery lies in unravelling the structure of such a pattern generator. Herein, nature has provided us with a way to understand how the nervous system stores motor programs and how it interacts with information from the periphery as well as the higher centers. We can certainly entertain the hope that someday, through improved experimental techniques, we may be able to explain the structure adequately. But for the present, we have to rely on deducing at least the principle, if not the structure, of the operation of this network from the available data. This is the premise of this thesis.

To understand the principle of operation of such pattern generators, it is desirable to model them. Two options are available to us. These are:

a) to find a mathematical model which produces the desired input output characteristics, or

b) to study the motor pattern generation through simulation of hard wired networks.

Traditionally, neural modelling has followed the second approach and for good reasons. For biological systems in general and neural networks in particular, it has been difficult to identify the state variables. Even if in some instances they are identified, measurement of those variables is always a difficult task. Besides, nonlinear modelling techniques which can be applied to analysis of such networks have only recently been developed. The simulation of neurons and small networks using hard wired systems on the other hand, was available. Based on the Cartesian notion that understanding of the so called 'atoms' or 'building blocks' would lead to understanding of large masses of neural tissue, there has been extensive use of neuromimes in nervous system modelling. This approach led to better understanding of the neuron and small networks. But how this method could be used to deduce the structure of the central pattern generator for instance, is not clear.

In this thesis the mathematical modelling approach, a kind of a neuromime, will be adopted. It is hoped that this will help to elucidate the conceptual principles of organisation of such generators and to suggest possible hard wired implementations of the network.

2.2 Review of Existing Models

Neural modelling has been used for general studies of networks which produce rhythmic behaviour. In this section general neural networks for rhythmic behaviour are reviewed first followed by a discussion of specific networks for locomotion in animals.

2.2.1 Neural Networks for Rhythmic Behaviour

Rhythmic motor patterns can be generated by the endogenous oscillatory property of individual neurons or by a network of interconnected, endogenously stable, neurons. These two modes are discussed next.

i) Endogenous Rhythm Generation

There are neurons for example in the molluscan nervous system, which are capable of producing rhythmic bursts of impulses in the absence of any rhythmic synaptic input(38,39). These rhythmic bursts have an ionic basis and involve changes in membrane conduction that are slow compared to the time course of a single action potential. Figure 4 shows a schematic diagram of how these rhythms are generated. As pointed out by Freisen and Stent (38), it is possible to control the period of the rhythm by setting the tonic inhibitory or excitatory input to the cell. It can also produce multiphasic rhythmic movement by an ensemble of endogenous oscillator cells. These endogenous bursters generate chronic rather than episodic rhythms, such as in the heart and stomach movements of the lobster and the leech (39).

ii) Network Rhythm Generation

Episodic rhythms like walking or swimming are believed to be produced by network oscillators. The rhythmic output of such an oscillator does not depend upon any endogenous oscillator neuron in its network, but rather on the pattern of interconnections. It is useful to classify such networks in terms of the nature of their neuronal interconnections : excitatory, inhibitory or a combination of the two.

Networks with Excitatory Connections :

In networks with excitatory connections, rhythm is generated through positive feedback which forces the cells to fire at succesively higher frequencies. To oscillate, a restorative feature has to be included so that the cells

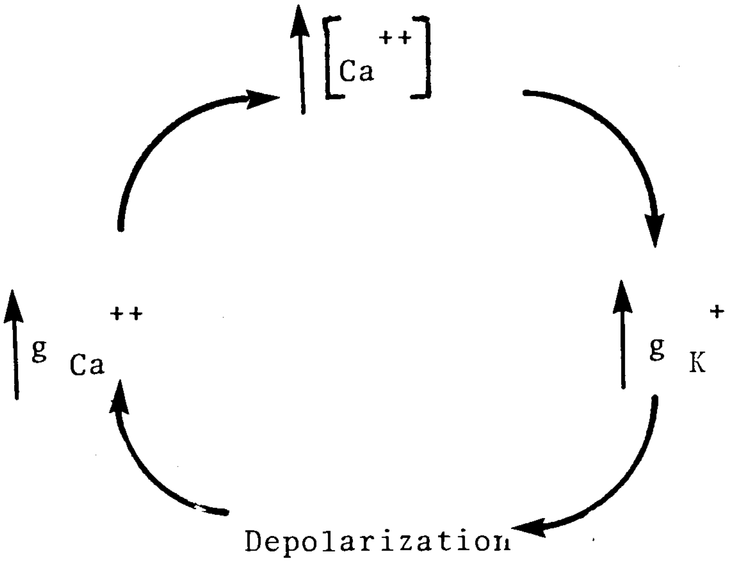

Figure 4. The process responsible for the generation of endogenous rhythm bursts (38).

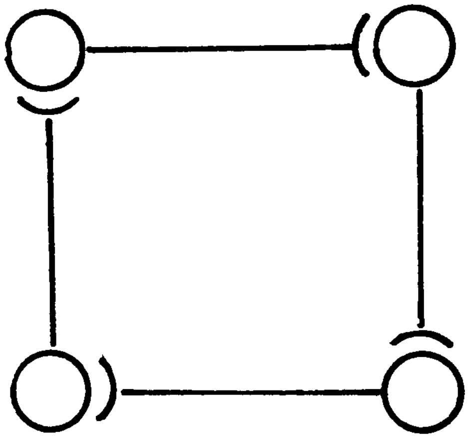

Figure 5. A schematic diagram of a neural network with excitatory inter-connections.

could start afresh. One suggestion has been adaptation which would increase the threshold of firing. Figure 5 shows a schematic diagram of such a network. These networks of two or more neurons generate concurrent bursts of impulses. To produce stable oscillatory patterns requires a delicate balance of the system parameters (39). No actual case of a oscillatory network based on this configuration is known so far.

Networks with Inhibitory Connections :

Networks with inhibitory connections and tonic excitatory drive (intrinsic or extrinsic) can produce stable rhythmic output patterns provided they have certain interconnection patterns. The first such network consisting of two neurons with tonic excitation and inhibiting each other (Figure 6) was proposed by McDougall (39). For stable oscillatory output a restorative process such as fatigue, adaptation or post-inhibitory rebound has to be present. Various neuromimes incorporating adaptation and post-inhibitory rebound have been proposed (39). These simulations show that the maximum range of periods obtained is about two-fold. This network is also limited to producing biphasic rhythms.

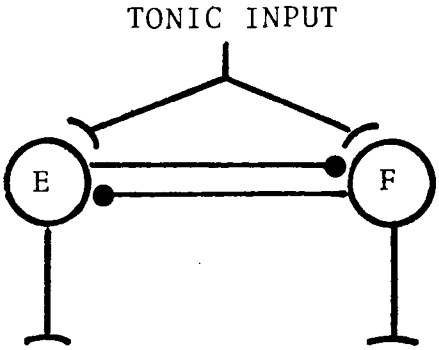

Figure 6. McDougall's two neuron inhibitory network.

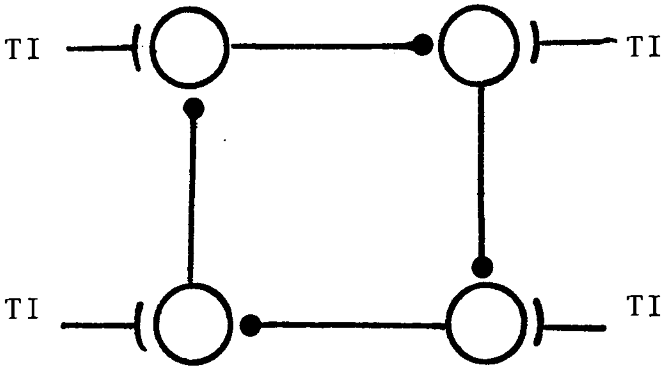

Figure 7. Recurrent Cyclic Inhibitory Network with more than two neurons.

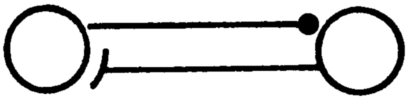

Figure 8. Neural network with inhibitory and excitatory interconnections.

When the number of neurons in such a network is greater than two (Figure 7), the production of rhythmic bursts becomes independant of the time varying properties of a neuron. Only the pattern of connections determines the output. These networks have been studied extensively (38,39,40) and can produce stable multiphasic output patterns. This network configuration has been suggested as a basis for the mammalian electroencephalogram.

Networks with Inhibitory and Excitatory Connections :

Theoretically networks with mixed connections should have a statistical advantage over the other two. Despite this very few examples have been found to support its candidacy. The schematic diagram of Figure 8 shows the operation of such a network. This mechanism had been suggested as the pattern generator for mammalian respiration (38), but has not found universal acceptance (41).

2.2.2 Neural Networks for Locomotion

Studies on mammalian locomotor behaviour have shown that the limb behaves as a single unit (26,27). Thus the models that were suggested were for a single limb. The spinal generator can coactivate alpha and gamma motor-neurones to the same muscle and can alternately excite and inhibit alpha motorneurones and exert this inhibition at least partly via the same interneuron that mediates the reciprocal inhibition from Ia afferents. It is apparent that there is reciprocal organisation at the output stage, but the intrinsic organisation of the generator itself is still not clear. Various hypotheses have been put forward and these are discussed below.

i) Brown's Half Center Hypothesis

Brown first proposed the half center hypothesis to explain the limb movements in cats (42). This is equivalent to McDougall's model as shown in Figure 6. This model is founded basically on two groups of neurons which inhibit each other and in addition have high enough excitability to discharge when not inhibited. Such a system can be made to oscillate if fatigue is introduced as a crucial factor. The fatigue could operate as an accumulating afterhyperpolarization in the discharging neurons or by successively decreasing transmitter release in the inhibitory synapse possibly combined with postinhibitory rebound. Such a network has not been shown to generate locomotor movements. Though it is conceptually consistent, the idea of fatigue playing a crucial role in generation of such complicated movements does not seem right. Besides this is a symmetric model producing biphasic rhythms. Locomotor rhythms are multiphasic and asymmetric.

ii) Shik's Ring Model

Secondly, we consider a ring model due to Shik et al (27). This is shown in the schematic diagram of Figure 9. The model consists of a closed chain of neurons and flexor and extensor motorneurons are connected to different parts of the chain. In this way it is easy to generate rhythmic coordinated activity in different motor-neuronal groups and also model efferent activity with cocontraction of different muscle groups. The asymmetry in extensors and flexors with speed is explained by differnt cross-sectional areas in the ring. Though the behaviour is explained conceptually, neither the actual structure of the network nor the principle of operation is clear.

iii) Scott and Miller Model

The third model, proposed by Miller and Scott (43), is unique since it is the first attempt to model the generator using known neuronal connections at the spinal level. They have used alpha motorneurones, the Renshaw cells and the Ia inhibitory interneuron to form an oscillator network. It demonstrates reciprocal activation of the flexor and extensor motorneurons and by varying the tonic input to the alpha motorneuron and the Ia inhibitory interneuron , coactivation of the flexors and extensors is achieved. The objections to this model (c.fig 10) are (44) :

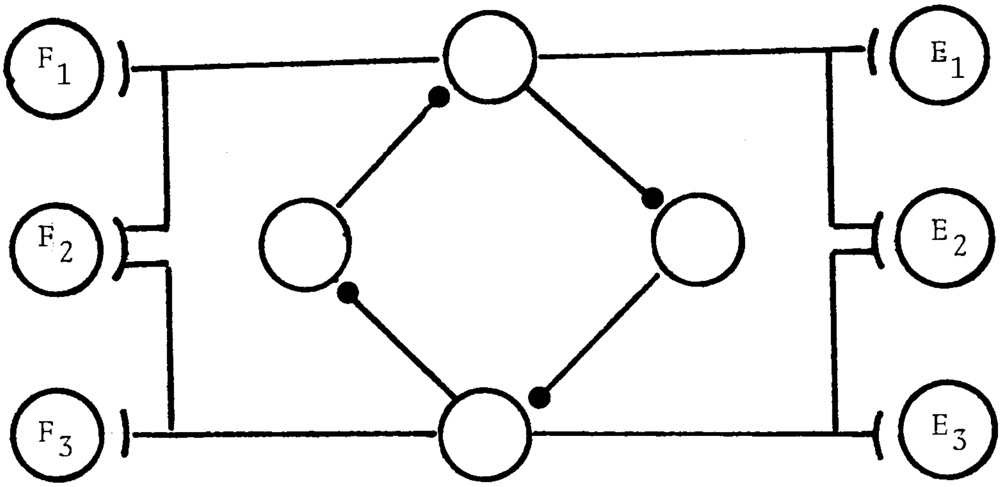

Figure 9. Shik's ring model for the pattern generator for locomotion in mammals.

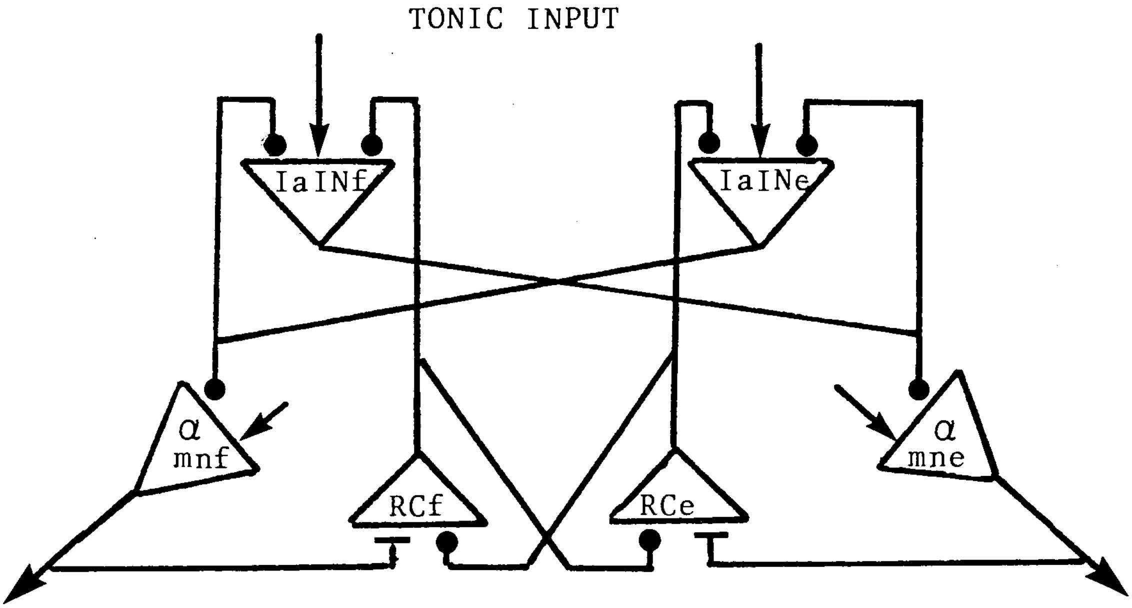

Figure 10. Miller & Scott model of the pattern generator for locomotion in mammals. Abbreviations include : IaIN, Ia inhibitory interneuron, RC, renshaw cells, α mn, alpha motoneurone and 'e' and 'f' stand for extensors and flexors.

1) only very few neurons are used in the oscillator network.
2) the network is symmetric
3) the Renshaw cell inhibition of the alpha motoneuron is not considered, and
4) only the reciprocal organisation at the output stage is modelled. The intrinsic organisation of the generator itself is not tackled.

Despite these objections it does represent a genuine attempt at modelling the pattern generator using known neuronal connections.

iv) Willis's Model

Willis (45) used a mathematically tractable model of activity in a neural population. The neural network used (Figure 11) was basically similar to Scott and Miller's. Though the modelling approach is attractive, the output has no physiological basis. One could argue that any harmonics and hence any waveform could in principle, be generated. Though nature is not always parsimonious (46), this seems to be a cumbersome way of generating the motor patterns during locomotion.

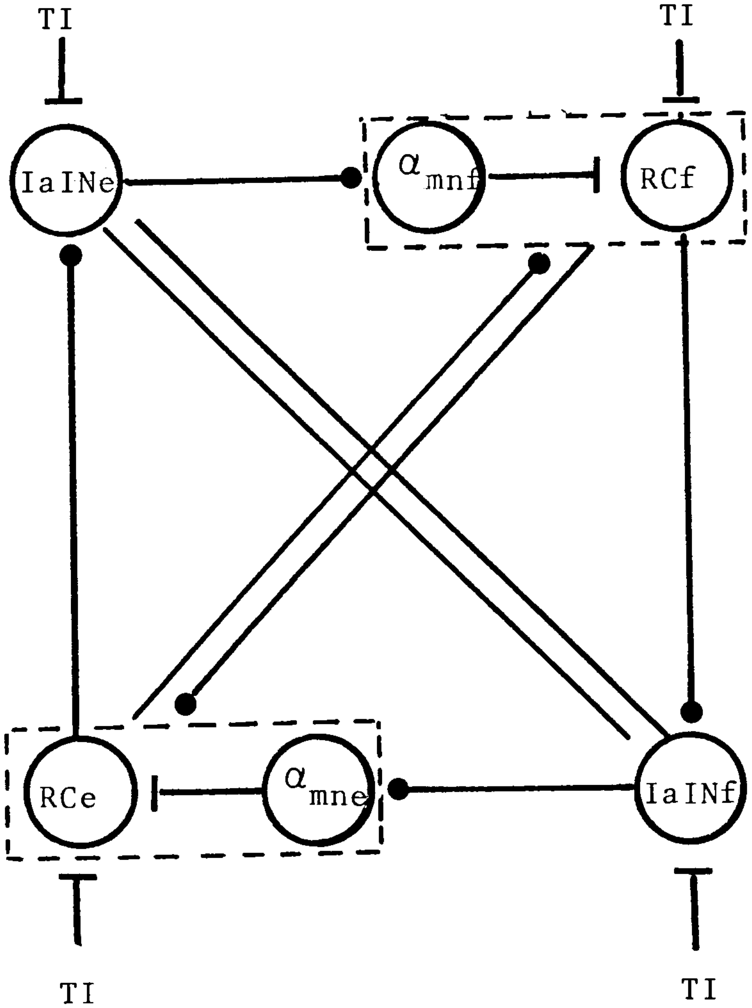

Figure 11. Willis's adaptation of the Miller & Scott model for mathematical analysis.

2.2.3 Interlimb Control

In mammals there is a definite phasic relationship between the limbs for different modes of locomotion. A study by Halbertsma et al (47) shows the phase relation between limbs in cat locomotion. The changes in the phase relationship for different modes of locomotion are observed to be abrupt. In contrast to animals like fish, there is no evidence of coordinating neurons in cats. Various suggestions have been made (26,27), including the hypothesis that information from the VSCT or the vestibular apparatus could be used for interlimb control. This can be questioned since interlimb control is possible in spinal cats (48). Frossberg et al (48) suggest that reciprocal inhibition between congruent parts (both flexor for example) of the individual limb generator may provide alternate coupling as in walk, whereas mutual excitation may provide synchronous coupling as in gallop. This hypothesis needs to be tested.

2.3 Limitations of the Existing Models for Locomotion

A majority of the models discussed above are conceptual in nature. It is realised that in mammals the locomotor behaviour is due to an emergent property of a network of neurons. Thus, these efforts are aimed at studying a 'unit' network that exhibits alternate bursts in two groups of motoneurones. It is always argued that this could be a building block for generating any complex waveform that may be required. From an analytical point of view this is clearly possible. But, whether it is probable is a matter of conjecture.

The application of the philosophy of reductionism has helped us understand the behaviour of simple networks. But it has not been able to explain the principle of generation of the complex firing pattern of muscles measured during many kinds of rhythmic behaviour. Thus, instead of trying to find the appropriate 'unit' network it may be helpful to channel the efforts into understanding the principle of generation of a complex pattern.

2.4 Limb Pattern Generator Input/Output Characteristics

It has been shown that a limb is controlled as a single unit (26,27,48), and in this thesis an analytical model of a limb pattern generator is presented. Before proceeding further, it is necessary to list the known inputs and the outputs of the limb pattern generator, define the nature of these signals and determine how they can be estimated.

2.4.1 Inputs to the Generator

The inputs to the pattern generator are listed below. Their effects on the generator output have been reviewed in the previous chapter.

i) Tonic input from the higher centers

This input is necessary for locomotion to occur. It can be represented by a signal level. For a mesencephalic preparation the strength of the stimulation can be an estimate of this input.

ii) Feedback signals from the periphery

It is known that these are not essential for producing the basic stepping movements. The nature of the feedback signals is difficult to estimate. One can deduce their effects through studying the patterns in a deafferentated animal.

iii) Inputs from fast descending tracts
(ReST,VeST,RuST)

The inputs from these tracts are not necessary for the generation of locomotor rhythms. The nature of these signals is difficult to estimate.

iv) Coupling signal

It has been speculated that a coupling signal takes care of the interlimb coordination. What form, if any, this signal takes is a matter of conjecture.

2.4.2 Output of the Generator

Since lower limb motion is a direct result of motion of the joints of the lower limb, it is obvious that the motion of the joints is periodic. The motion of the joints is produced by a group of muscles. The generator output is the activation of these muscles via the alpha and the gamma motorneurones. This activation can be defined in terms of the instantaneous firing rate of the motorneurone pool termed α.

To estimate this parameter 'α', recordings can be made from the nerve trunks that innervate the muscles. Though theoretically possible, there are problems since the signal thus obtained is a composite of motor and sensory signals. Stein et al (49) have shown an elegant way of separating these two signals. The method requires signals from two sets of electrodes placed apart on the same nerve trunk. Long nerve trunks are not easily available to meet this demand especially for the hip muscles. Besides, the additional surgery involved increases the trauma to the animal and reduces the chance for a succesful experiment. Thus an indirect way of estimating this parameter is required.

Models of myoelectric signal generation (50,51,52) have shown that the parameter 'α' can be estimated. For constant force output, time average of the rectified myoelectric signal gives a reasonable estimate of 'α' (50,51). But in the case of time varying force output observed during movement, the myoelectric signal is nonstationary. Hence instead of time averaging we need to do ensemble averaging (51,52).

Thus, at least in principle, estimating the output of the generators should be simple. But there are practical problems. Groups of muscles are involved and they are activated in a definite pattern since, for example, some muscles act on two joints. Various hypotheses have been forwarded to explain the activation pattern. Several attempts have used energy minimisation as the principle behind the activation of these muscles (53,54). It is not the task of this thesis to answer this problem, and to circumvent the problem a representative muscle is used for each joint. This approximation is reasonable, since our interest lies mainly in the temporal aspect of the generator output. Besides it is known that there are problems with combining EMG's from different muscles to give a composite signal (9).

2.5 Problem Definition

The inputs and the outputs of the limb generator are summarised in the schematic diagram of Figure 12. The problem then is to determine the nature of the limb generator. The questions that need to be answered are :

a) Is the limb generator a collection of interacting oscillators ?

b) How many oscillators are there ?

c) What is the form of a mathematical equation that can represent the oscillators ?

d) How does the model reproduce changes observed in the pattern during speed changes ?

e) Can it predict the phasic reversal of the reflex arc ?

f) Can it reproduce the coupling between the limbs ?

g) If a similar model is accepted for human locomotion, how does the model reproduce the different types of rhythmic movements of the lower limb such as cycling, and climbing stairs ?

h) Can these equations suggest a possible 'hard wired' implementation ?

i) Is this implementation neurophysiologically feasable ?

These questions will be addressed in the subsequent chapters.

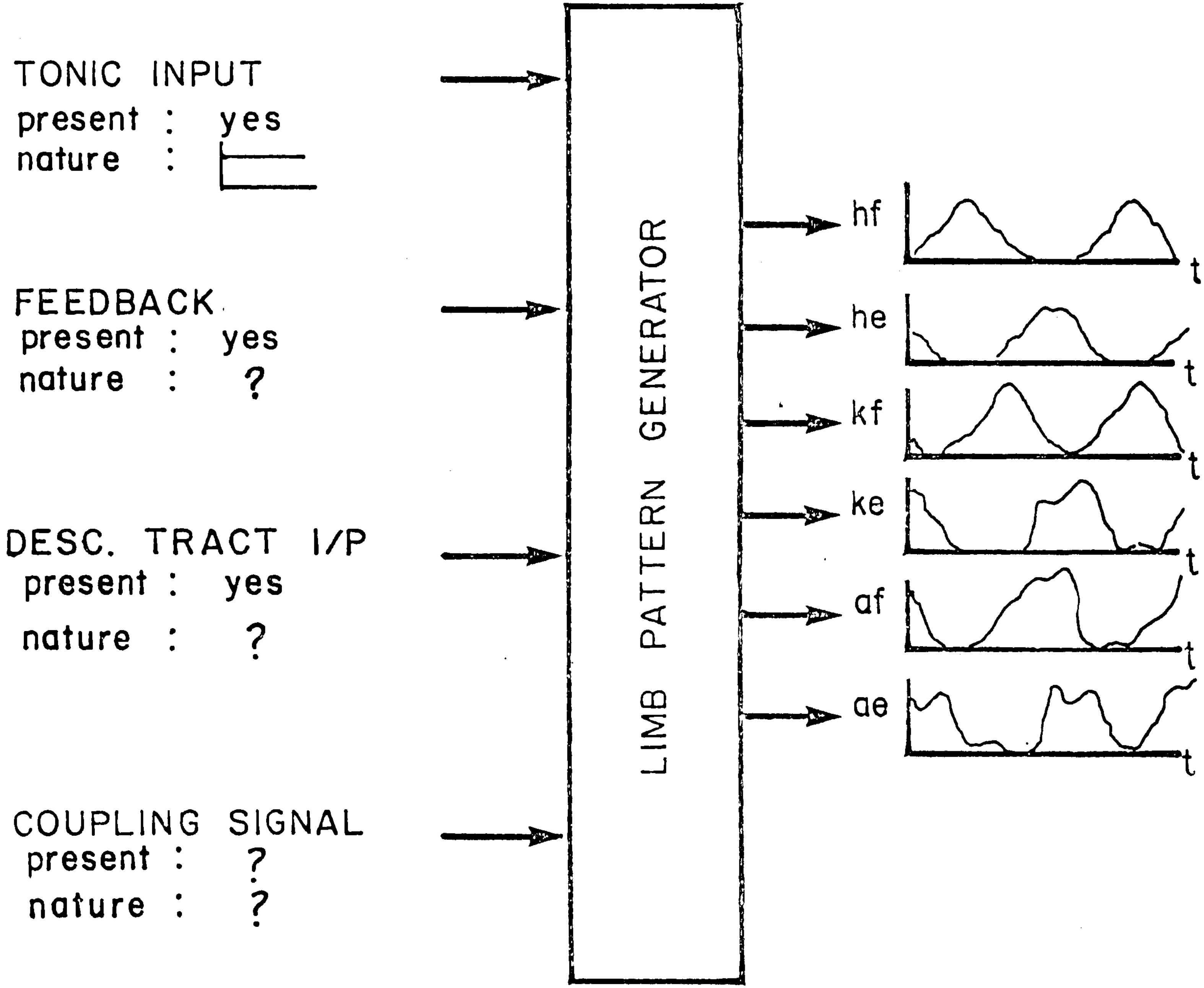

Figure 12. A block diagram of the limb pattern generator in mammals

CHAPTER III

THEORETICAL MODEL OF A LIMB PATTERN GENERATOR

In this chapter a mathematical model for the limb pattern generator (c.fig 12) is derived. Only the tonic input, treated as a constant signal level, is considered. Since peripheral feedback and phasic descending tracts inputs are not necessary for the generation of the output, they are not explicitly incorporated into the model. The outputs of the generator are assumed to be general periodic waveforms.

3.1 Proposed Model

For a given speed the tonic input is constant, but the outputs of the generator are periodic. Thus the generator is not a linear filter, but functions as an oscillator community which alters its output in response to input. The periodic outputs are due to the intrinsic properties of the generator. There are six outputs as shown in Figure 12. The nature of the outputs determine the number of oscillators that constitute the limb pattern generator. For instance if all the outputs were identical, a single oscillator would suffice.

The problem of determining the minimum number of oscillators required can be viewed as determining the minimum number of orthogonal basis functions required to represent a set of time functions. The Karhunen-Loeve technique of representing a set of time functions as a linear sum of basis functions is appropriate for the problem at hand (55,56). This technique minimises the mean square error in estimation of the given functions.

Let $o_i(t)$ $[i = 1,6]$, be the outputs of the generator. These time functions can be expressed as a linear sum of basis functions $u_j(t)$ $[j = 1,n \quad n \leqslant 6]$, as shown below

$$o_i(t) = \sum_{j=1}^{n} c_{ij} \cdot u_j(t) \quad \dots\dots\dots\dots\dots\dots \quad (3.1)$$

where c_{ij} is a constant given by

$$c_{ij} = \int_0^T o_i(t) \cdot u_j(t) \; dt \quad \dots\dots\dots\dots \quad (3.2)$$

The derivation of this expansion is given in Appendix A. The number of basis functions required is dictated by the mean square error in estimation of the given time functions. The allowable minimum mean square error is determined by the noise level in the data.

Since the time functions, o_i (t) [i = 1,6], are periodic, the basis functions, u_j (t) [j = 1,n n < 6], are also periodic. Thus the pattern generator consists of 'n' independant oscillators. There are rich connections between the agonist and the antagonist and between the muscles of different joints (57), and this suggests that the oscillators are coupled. The precise function and nature of these interactions between oscillators is unknown. It may provide phase locking of the waveforms. Therefore the limb pattern generator can be represented by a population of interacting oscillators. Figure 13 summarises the proposed model.

3.2 Model for an Individual Oscillator

To study the behaviour of the population of oscillators in Figure 13, we need to model an isolated oscillator as depicted in Figure 14. To find an equation for such an oscillator, we need to determine the order of the differential equation. Using the state space approach, it is clear that the state variables 'u_1', the instantaneous value of the output and 'u_2', the first derivative of u_1 with respect to time, define the system completely. Thus we have a system with one degree of freedom and it can be

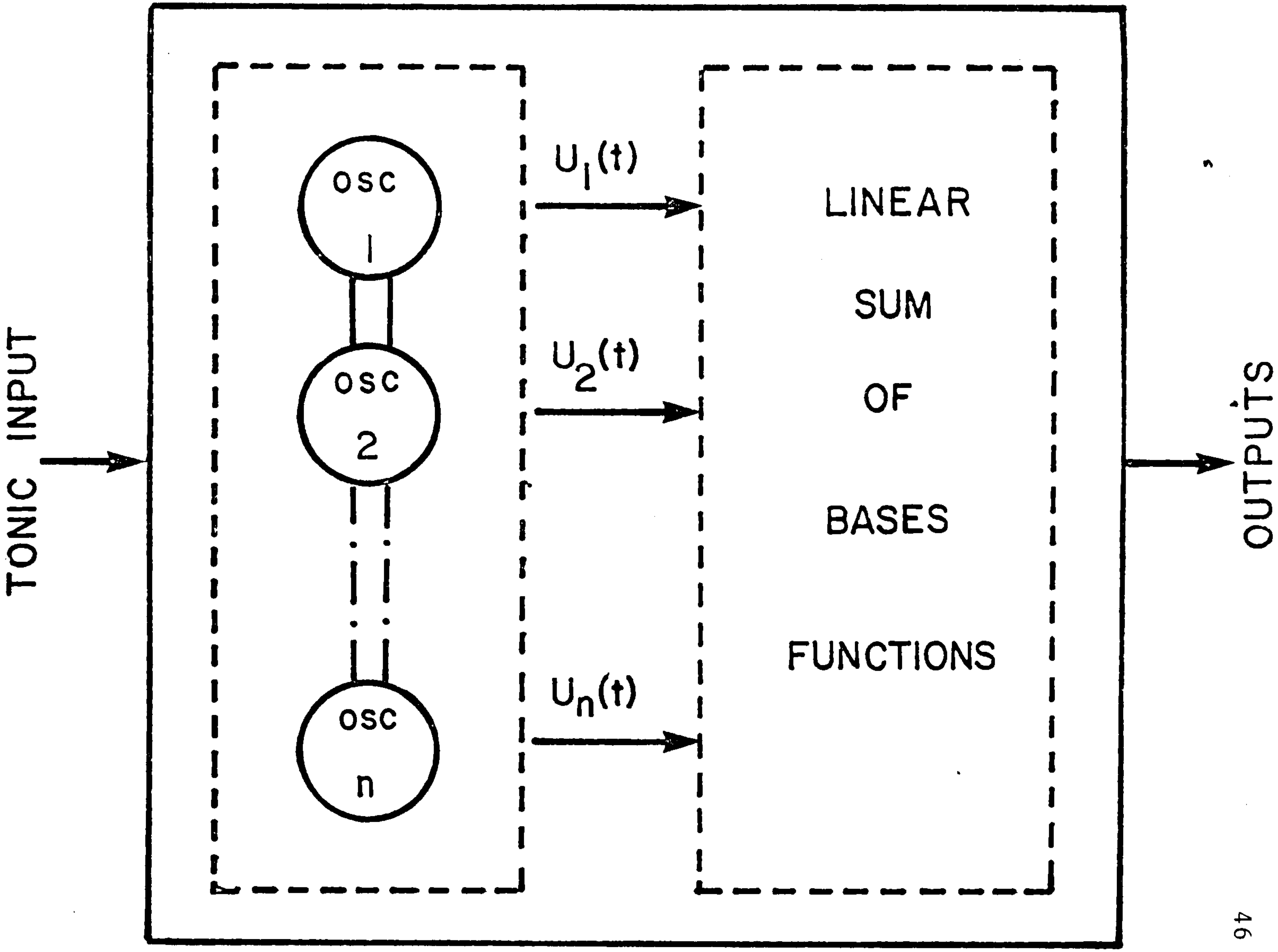

Figure 13. A block diagram of the limb pattern generator modelled in this thesis.

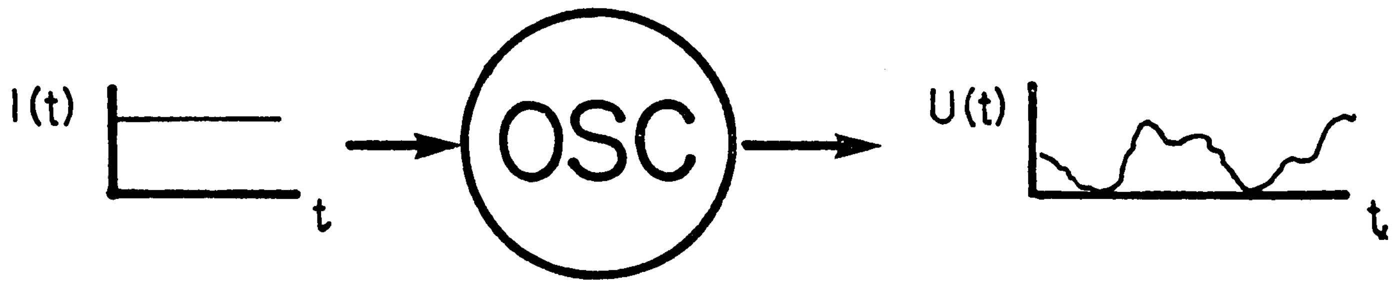

Figure 14. A schematic diagram of an oscillator in the limb pattern generator of Figure 13.

represented by the following generic pair of differential equations :

$$u_1 = f_1 (u_1 , u_2) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (3.3)$$

$$u_2 = f_2 (u_1 , u_2) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (3.4)$$

where f_1 and f_2 are functions of the two state variables.

The nonlinear output of the oscillator necessitates the examination of the two classes of nonlinear differential equations : nonlinear conservative systems and nonlinear nonconservative systems. These two classes of nonlinear differential equations are discussed next.

3.2.1 Nonlinear Conservative Systems

A nonlinear conservative oscillator can be defined by the following equation :

$$\ddot{u} + p (u) = 0 \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (3.5)$$

where u is the output of the oscillator and

p is a nonlinear monotonic functions.

Integrating equation 3.5 we have,

$$(1/2)\ (\ddot{u})^2 + P(u) = T \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (3.6)$$

where $P(u) = \int p(u)\,du$

and T is the integration constant.

It is known that the period of the output is a function of the value of T. Thus 'T' can be thought of as representing the tonic input to the oscillator. Though the ouput from such an oscillator is nonlinear, from equation 3.6 it is apparent that it is symmetric about the peak value. Thus the oscillator is not suitable for our model (58).

3.2.2 Nonlinear Nonconservative Oscillator

It is known that for endogenous (within the system) oscillations to occur the nonlinear nonconservative system must have a limit cycle. Many biological rhythms like the mammalian heart and the gastrointestinal signal, have been modelled using variants of the well known Vander Pol equation (59,60). The Vander Pol equation produces rhythmic output once a signal pushes it into the limit cycle. Once it is in the limit cycle no input is required to sustain the oscillations. Thus it cannot be used in modelling the locomotor rhythm. Besides the oscillator cannot faithfully reproduce the frequency content of the innervation pattern measured during locomotion.

Chua and Green (61) and subsequently Bass (62) and Bardakjian et al (63) have suggested ways of synthesising a relaxation oscillator to produce any given periodic waveform. In this thesis their general approach is adopted. The derivation of a synthesised relaxation oscillator is discussed next.

It is a well known fact that any periodic stable waveform can be represented by a finite Fourier series (64). Thus the output of the oscillator, u(t), can be represented by the following series

$$u(t) = a_0 + \sum_{k=1}^{m} (a_k \cdot \cos(k\omega t) + b_k \cdot \sin(k\omega t)) \quad \ldots \quad (3.7)$$

where a_0 represents the d.c. value of the waveform

a_k is the cosine coefficient

b_k is the sine coefficient and

ω is the fundamental frequency.

The series in equation 3.7 is a linear sum of the harmonics. Using the Chebyshev polynomials of the first and the second kind, T_k and U_k, any harmonic can be represented as a function of the fundamental frequency 'ω' as shown below (65):

$$\cos(k\omega t) = T_k(\cos(\omega t)) \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (3.8)$$

and

$$\sin(k\omega t) = \sin(\omega t) * U_{k-1}(\cos(\omega t)) \quad \ldots\ldots \quad (3.9)$$

Substituting equations 3.8 and 3.9 in 3.7 we have

$$u(t) = a_0 + \sum_{K=1}^{m} (a_K \cdot T_K(\cos(\omega t)) + b_K \cdot \sin(\omega t) \cdot U_{K-1}(\cos(\omega t))) \quad \ldots\ldots\ldots\ldots \quad (3.10)$$

The series defined by equation 3.10 is a nonlinear sum of functions of sinusoids of the fundamental frequency. Let us define two functions 'g' and 'h' as follows

$$g(x_2) = a_0 + \sum_{K=1}^{m} a_K \cdot T_K(x_2) \quad \ldots\ldots \quad (3.11)$$

$$h(x_2) = \sum_{K=1}^{m} b_K \cdot U_{K-1}(x_2) \quad \ldots\ldots\ldots \quad (3.12)$$

where $x_2 = \cos(\omega t)$.

Thus the equation 3.10 can be rewritten as

$$u(t) = g(x_2) + x_1 \cdot h(x_2) \quad \ldots\ldots \quad (3.13)$$

where $x_1 = \sin(\omega t)$.

The equation 3.11 suggests ways of generating any waveform using a sine/cosine fundamental frequency generator and the two nonlinear functions 'g' and 'h'.

To produce a set of equations that will generate the waveform of equation 3.7, we need to generate the sine and cosine waveforms from another set of equations. The derivation of a second order system that can produce these functions has been shown by Sansone & Conti (66). This system is defined by the following set of equations

$$\dot{x}_1 = \omega \cdot [\; x_2 + x_1 (1 - x_1^2 - x_2^2)\;] \quad \ldots \quad (3.14)$$

$$\dot{x}_2 = \omega \cdot [\; - x_1 + x_2 (1 - x_1^2 - x_2^2)\;] \quad \ldots \quad (3.15)$$

where $\dot{x}_1$ is the first derivative of x_1 w.r.t time and
$\dot{x}_2$ is the first derivative of x_2 w.r.t time.

It can be easily shown (Appendix B) that the system defined by the equations 3.14 & 3.15 has unique nonperiodic solutions given by

$$x_1 = \sin(\omega t + \theta) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (3.16)$$

$$x_2 = \cos(\omega t + \theta) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (3.17)$$

Choosing appropriate initial time t_0 we can set $\theta = 0$.

To embed the nonlinearities 'g' and 'h' we have from 3.13

$$\dot{u} = [\, \dot{g}(x_2) \cdot \dot{x}_2 + \dot{h}(x_2) \cdot \dot{x}_2 \cdot x_1 + h(x_2) \cdot \dot{x}_1 \,] \ldots\ldots \quad (3.18)$$

where $\dot{u}$ is the first derivative of u w.r.t. time

$\dot{g}$ is the first derivative of g w.r.t. x_2

and $\dot{h}$ is the first derivative of h w.r.t. x_2

Substituting for $\dot{x}_1$ and $\dot{x}_2$ from 3.14 and 3.15 we have

$$\dot{u} = \omega \cdot [\, (\dot{g}(x_2) + \dot{h}(x_2) \cdot x_1) \cdot (-x_1 + x_2(1 - x_1^2 - x_2^2)) + h(x_2) \cdot (x_2 + x_1(1 - x_1^2 - x_2^2)) \,]$$

$$\dot{x}_2 = \omega \cdot [- x_1 + x_2 (1 - x_1^2 - x_2^2)] \qquad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (3.19)$$

The transformation of equation 3.13 establishes a one to one mapping between the state space points of system defined by equations 3.14 & 3.15 and those of system given by equation 3.19 provided $h (x_2) = 0$ (for all x_2). Therefore the system defined by equation 3.19 inherits a number of properties from the system given by equations 3.14 & 3.15 (61,62,63). Among them is the existence of a single stable limit cycle generating

$$u(t) = a_0 + \sum_{k=1}^{m} (a_k \cdot \cos(k\omega t) + b_k \cdot \sin(k\omega t))$$

and

$$x_2 = \cos (\omega t)$$

3.2.3 Oscillator Model Used

The synthesised relaxation oscillator defined by equation 3.19 is an autonomous oscillator. Bardakjian et al (67) have shown how this can easily be transformed into a labile relaxation oscillator. For the second order system generating the sine and cosine oscillator the transformation is as shown below

$$\dot{x}_1 = \omega \cdot [\quad x_2 + x_1 (st - x_1^2 - x_2^2)] \quad .. (3.20)$$

$$\dot{x}_2 = \omega \cdot [- x_1 + x_2 (st - x_1^2 - x_2^2)] \quad .. (3.21)$$

where st = (Ti - Th)

Ti = tonic input

Th = excitation threshold

Figure 15 is the plot for a labile relaxation oscillator which was simulated using the CSMP simulation program on a computer.

3.4 Summary

A set of equations has been formulated to describe the oscillator in the limb generator. There are 'n' such oscillators where 'n' is less than or equal to six. Each one of these oscillators is described by 'ω', the fundamental frequency and two nonlinear functions 'g' and 'h'. Since they are coupled, the output of each oscillator affects the output of the others. The coupling may provide phase locking of the waveforms.

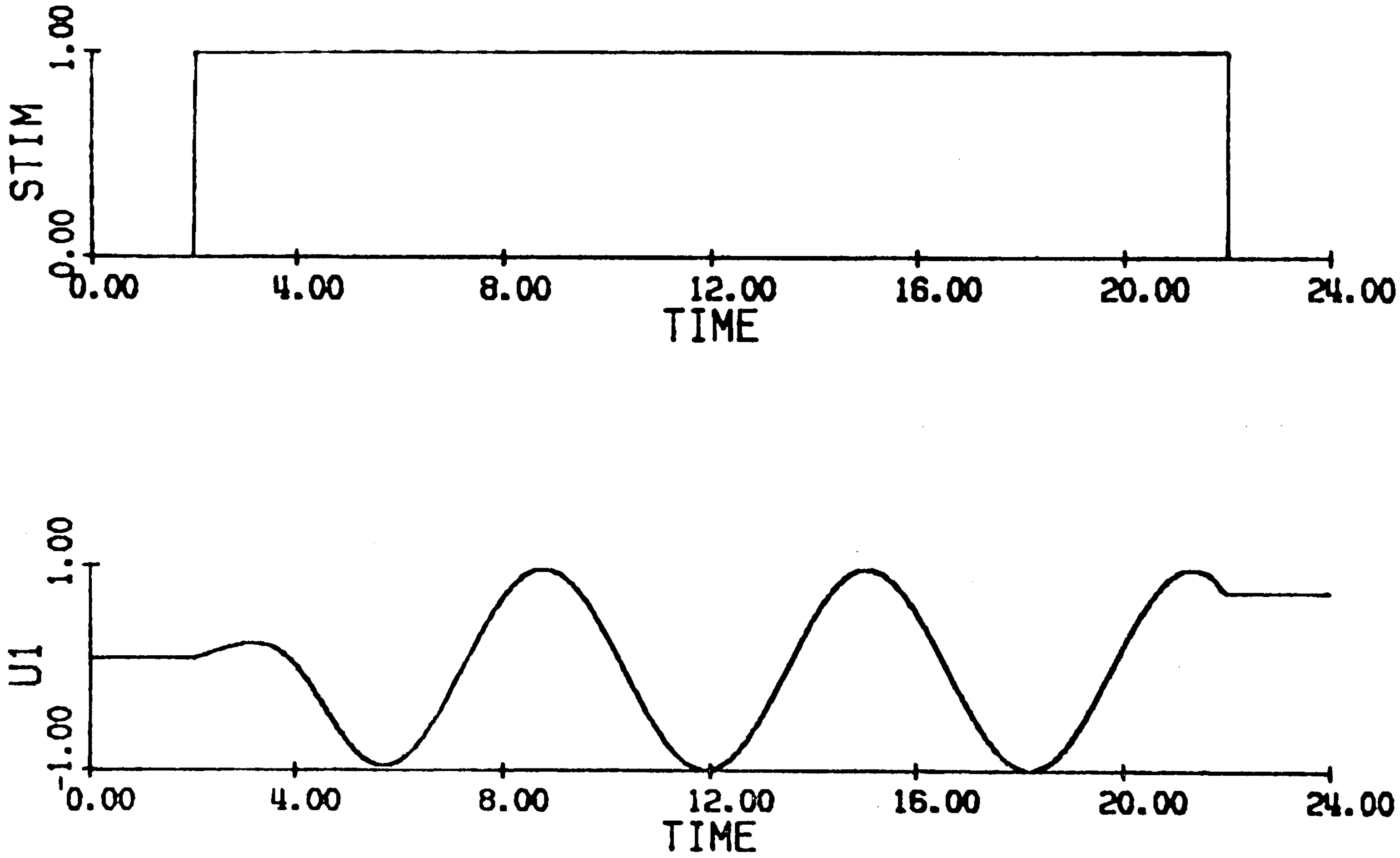

Figure 15. CSMP simulation result of a labile sine/cosine relaxation oscillator (stim - input, u1 - output).

CHAPTER IV

EXPERIMENTAL DETERMINATION OF SYSTEM PARAMETERS

In the previous chapter a theoretical model for the limb pattern generator was derived. To study how the model behaves, we need to record the outputs of the generator under varying input conditions. From these recordings the system parameters are determined. The output data was obtained from two series of experiments using : a) acute post-mammillary cat preparations and b) kinematic studies on human subjects. Besides these experiments, EMG data for humans from a research report by the Berkeley group (68) was also used. In this chapter the experimental procedures are described.

4.1 Background on Cat Experiment

In order to determine the oscillator characteristics under different input conditions, it is necessary to control these inputs. Specifically the tonic input must be controlled and thus we cannot record from an intact animal. A spinal preparation is most appropriate to minimise the effects of other descending inputs. However, although acute adult spinal cats can walk, they usually take few steps or present disturbed movements in some joints (69). Therefore this preparation is not useful for our purpose. A chronic spinal cat with peripheral feedback can walk remarkably well (70), but the time involved in the experimentation limits its usefulness.

An acute mesencephalic preparation without the mammillary bodies is an useful experimental preparation which meets our requirements. This preparation was used in the experiments carried out in the laboratory of Dr. R.B. Stein in the Department of Physiology at the University of Alberta. In these experiments generator output data from a cat was recorded for various inputs under two different condition : a) with peripheral feedback present and b) with the dorsal roots cut. The procedures used in this experiment are now described.

4.2 Experiment on Cat Preparation

4.2.1 General Procedure

Twelve adult cats weighing 2-4 Kg were used in this study. The cats were anesthetised with a humidified mixture of 95% O_2, 5% CO_2 and 4% Halothane. The halothane concentration was reduced to 2% after about half an hour.

Halothane was used because it is volatile and its effects wear off quickly. In preparation for this experiment the cats' hind limbs were shaved to facilitate later insertion of the electrodes . Under anaesthetic the two superior carotid arteries were ligated and one was catheterised to monitor the blood pressure. A second catheter, placed in the jugular vein, was used to inject a volume expander in case of execessive blood pressure drop. A tracheal cannula was also inserted to artificially ventilate the cat in case of a respiration problem.

The right hind limb was used to record the myoelectric signals. The following muscles were monitored :

Hip flexor - Iliopsoas
extensor - Biceps Femoris
Knee flexor - Semitendinosus
extensor - Vastus Lateralis
Ankle flexor - Tibialis Anterior
extensor - Soleus .

These muscles have been used by many researchers to monitor locomotor rhythms (29,30,71,72). As part of a study unrelated to this thesis the left hind limb was used to study the modulation of the stretch reflex during the locomotor cycle. This involved extensive surgery and allowed identification of the appropriate muscles for electrode placement on the contralateral limb. The photographic plates from a cat anatomy book (73) also helped in locating the muscles. All muscles except the Iliopsoas, were accessed through the skin. To get at the Iliopsoas a small incision was made on the medial side of the hip joint and the muscle was identified. Xylocaine jelly was applied around the incision before it was closed to reduce any noxious stimuli that may inhibit walking. Figure 16 shows a schematic diagram of the anatomy of muscles used in this experiment.

The electrodes used in the experiment were 9 stranded 200 micron teflon coated steel wires from Bergen Rope Co., N.J. About one centimeter of the tip was bared on both ends and the wire was threaded through a 22 gauge hypodermic needle. The bare end around the needle was bent to form a hook. Once the electrodes were inserted into the appropriate muscles, the needle was removed. The hook assured that the electrode stayed in the muscle. Three pairs of electrodes were inserted into the belly of each muscle used.

After this procedure the cat was taken to the treadmill. The cat's head was placed in a sterotaxic frame and the cat itself was supported at the hip with the help of

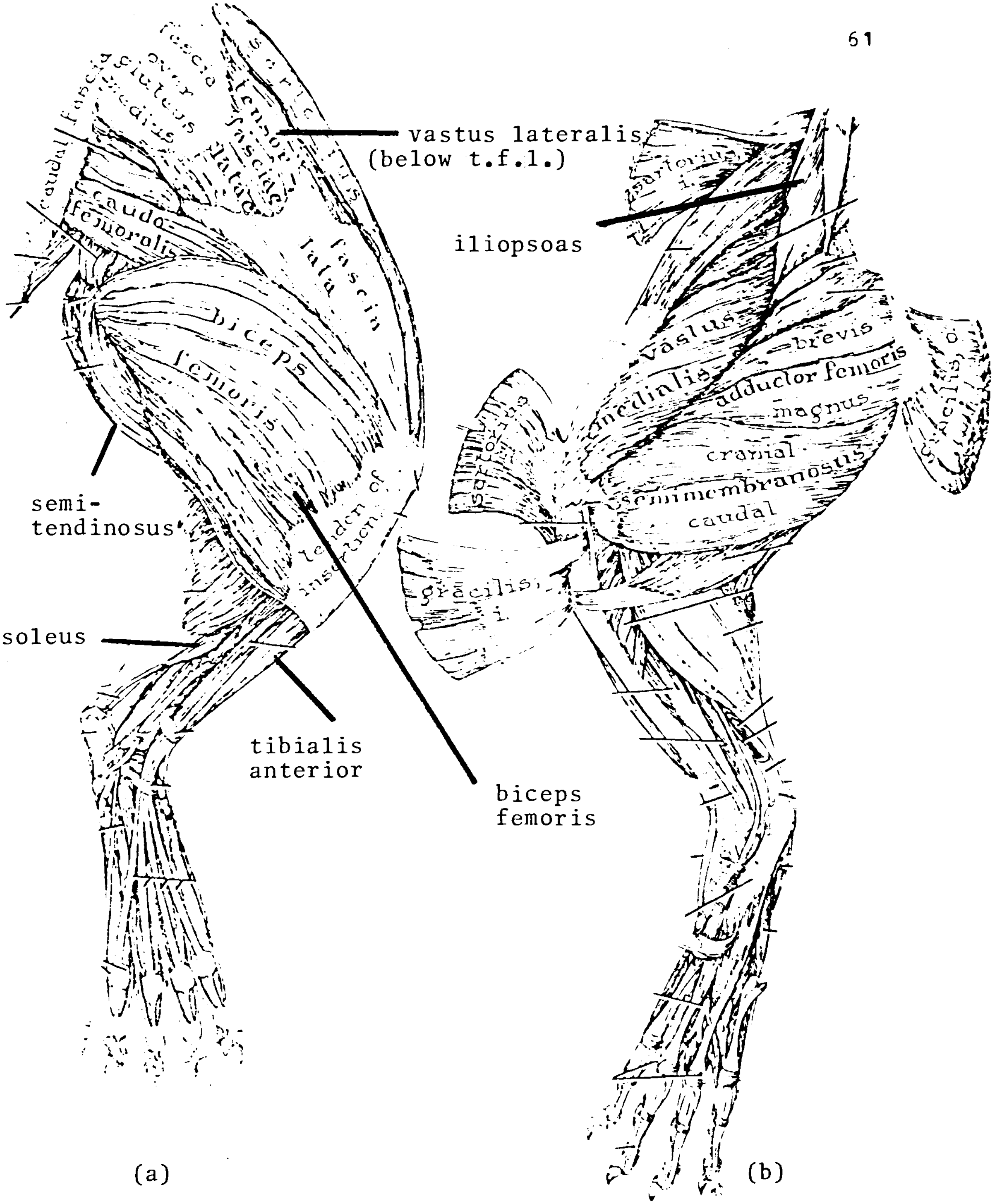

Figure 16. A schematic diagram of the anatomy of the muscles used in the cat experiment (a, lateral view and b is the medial view of the hindlimb).

bars inserted below the iliac crest. The hip bars are necessary since a mesencephalic cat has no sense of balance. The areas around the hip bar were injected with novacaine to lessen the noxious inputs. To fix the head properly in the sterotaxic frame, bars were carefully inserted into the ear canal. The head should rotate in the sagittal plane freely if this is done correctly. Next the head is fixed with the L shaped bars. One of the bars is placed on the bony orbit of the eyes and the other is inserted into the mouth and clamped on the hard palate. These bars secure the head tightly for the decerebration procedure. A rectal probe was used to monitor the cat's body temperature, and the cat was heated by a heat lamp. This is necessary because the temperature regulation is often poor in such a preparation, probably due to some damage to the hypothalamus. Once these procedures are complete, the decerebration procedure begins.

A large incision was made on the head from front to back and the skin was parted. The underlying tissue was then cleared to expose the skull. A hole was drilled and with a blunt spatula the cerebrum was carefully lifted out. To prevent bleeding bone wax was applied to the cut end of the bones. With the help of fine gauze any blood pool in the cavity was removed. Next a incision was made that extended from the rostral border of the superior colliculus dorsally to the caudal border of the mammillary bodies ventrally. The anesthetic was removed after the cat was decerbrated. The cat was breathing on its own and the effects of the anesthetic wore off quickly.

Locomotion was induced by stimulating the mesencephalic locomotor region with a monopolar stimulating electrode. The electrode was positioned 4 mm. lateral to the midline and 1.0-1.5 mm caudal to the rostral border of the inferior colliculus and lowered 4 - 7 mm. until a depth was reached at which consistent locomotion was produced. The stimulus used was a square wave constant current pulse of 0.5 msec duration, 100 - 200 microamp amplitude and at a repitition rate of 30 Hz. Figure 17 shows a schematic diagram of the experimental set up.

4.2.2 EMG Recording Procedures

The wire electrodes were numbered starting from 1 for the ankle extensor to 6 for the hip flexor. Once the cat was secured over the treadmill, these wires were attached to spring loaded connector placed near the limb. From this connector a shielded cable carried the signals to the instrumentation panel. The signals were passed through preamplifiers and high pass filters and recorded on a 8

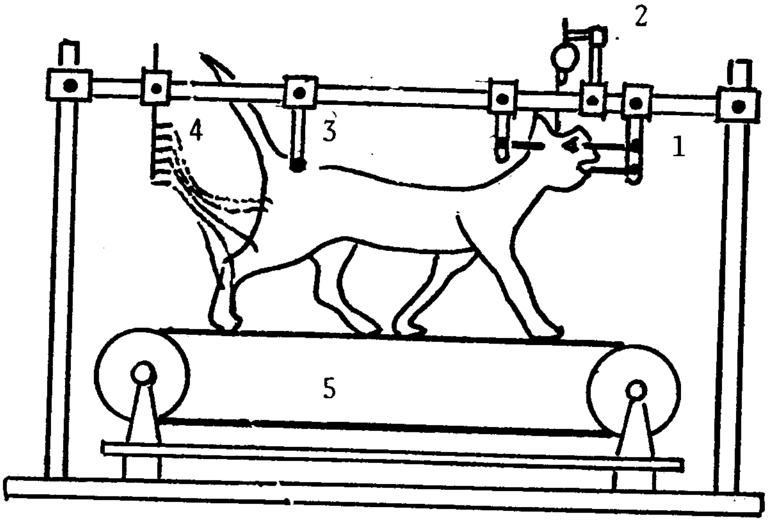

Figure 17. A schematic diagram of the experimental setup. The layout of the apparatus is as follows : 1, stereotaxic head holder, 2, electrode holder, 3, hip bar holder, 4, EMG electrode holder and 5, treadmill.

channel 1/2 inch Honeywell tape recorder. The schematic diagram of connections is shown in Figure 18. The signals recorded on the tape were monitored on an oscilloscope and signals from four channels were rectified and passed through a 30Hz low pass Paynter filter and recorded on a four channel chart recorder. On the tape a voice channel provided a record of the experiment. The treadmill used was motor driven and by manually changing the gear ratio, a range of speeds could be obtained.

4.2.3 Part A - Mesencephalic Preparation with Peripheral Feedback

The purpose of this part of the experiment was to record myoelectric signals in the presence of peripheral feedback(i.e. with dorsal roots intact). By varying the amplitude of the stimulus and increasing the speed of the treadmill, a two fold range of speeds was obtained for two cats out of the total of twelve used in the study. In the majority of the preparations, the range obtained was limited.

4.2.4 Part B - Deafferented Mesencephalic Preparation

For the second part of the experiment peripheral feedback was eliminated by cutting the dorsal roots in order

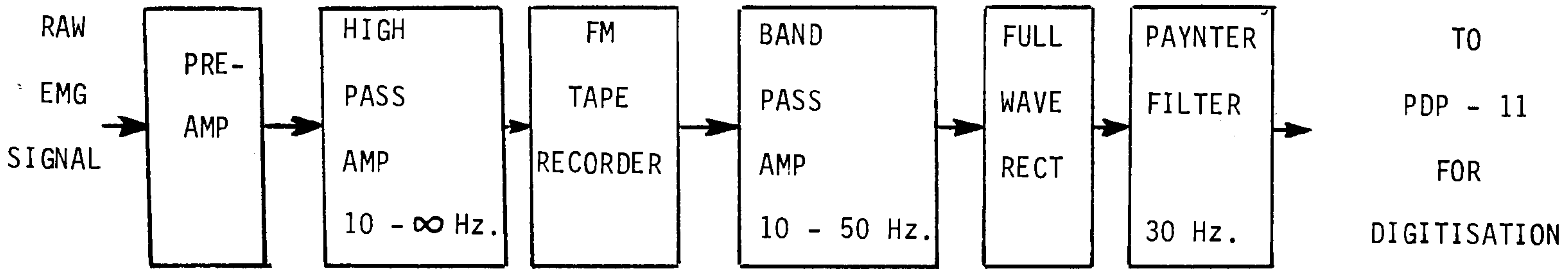

Figure 18. A schematic diagram of the data recording and analysis procedure.

to study the effects of peripheral feedback on the outputs of the pattern generator.

The laminectomy procedure to cut the dorsal roots involved making a large incision over the spinal cord from front to back. The skin was parted and the muscles and tissue were removed. The notch between the lumbar and the sacral cord was used to start cutting the bone with a bone cutter. The spinal cord was exposed from L3 - L7. Bone wax was applied to stop bleeding from the bones. A gauze pad bathed in saline was put over the cord and the skin closed with the help of clips. This procedure was carried out prior to transporting the cat to the treadmill.

After the data on the preparation with feedback had been recorded, the cord was exposed. The dura was cut very carefully and with the aid of a magnifying glass and a glass hook, the dorsal root inputs to the cord were traced and cut. This procedure is possible in mammals since there is a clear division between the motor and sensory fibers at the entry point to the cord. Some researchers have cut the dorsal roots outside the dura to reduce the trauma to the animals (74), but there is a danger of damaging the ventral roots in this process. By removing the dorsal roots from L3 - L7 on the right side, all the peripheral feedback from that limb is eliminated. There are some unmyelinated afferent fibers in the ventral root (75), but these are mainly from the viscera and do not provide any relevant phasic information.

Once the dorsal roots were cut, the animal was allowed to recover from the spinal shock for about half an hour. Locomotion was induced by stimulating the MLR and the myoelectric signals were recorded from the same muscles under various stimulus amplitudes. This part of the experiment was carried out on two cats.

4.2.5 Data Extraction from EMG Recordings

In both parts A and B of the experiment high pass filtered (10 Hz cutoff) EMG signals (to eliminate movement artifacts) were recorded on the tape. To extract relevant information, these recordings were processed as follows :

a) The high pass filtered signal was passed through a band pass filter (10 - 50 Hz) and a 30 Hz Paynter low pass filter in cascade.

b) Four channels of Paynter filtered data were sampled at 125 Hz and the digitised data stored on a disk on a PDP-11 minicomputer. This sampled data contained a number of step cycles of walking.

c) A block of data in each channel was averaged over the recorded run to give an ensemble average for more than one step cycle. The flow chart of Figure 19 shows the ensemble average program used.

d) The steps a to c were repeated for four more channels of data, two of which were channels from the previous set. Thus the same ankle extensor channel was used for triggering in the ensemble average program. This channel had a fast rise and hence was chosen for that part of the program.

e) Each averaged data channel was normalised to its maximum value.

Figure 20 is a plot of a typical processed data set ; the example shown is for cat #1 at 1.85 c/s with peripheral feedback intact.

4.3 Introduction to Human Experiments

In this thesis it is assumed that the general conclusions derived from cat experiments are applicable to man. The validity of this assumption is discussed in the next chapter. To see how the limb pattern generator model accomodates rhythmic movements such as walking, cycling and

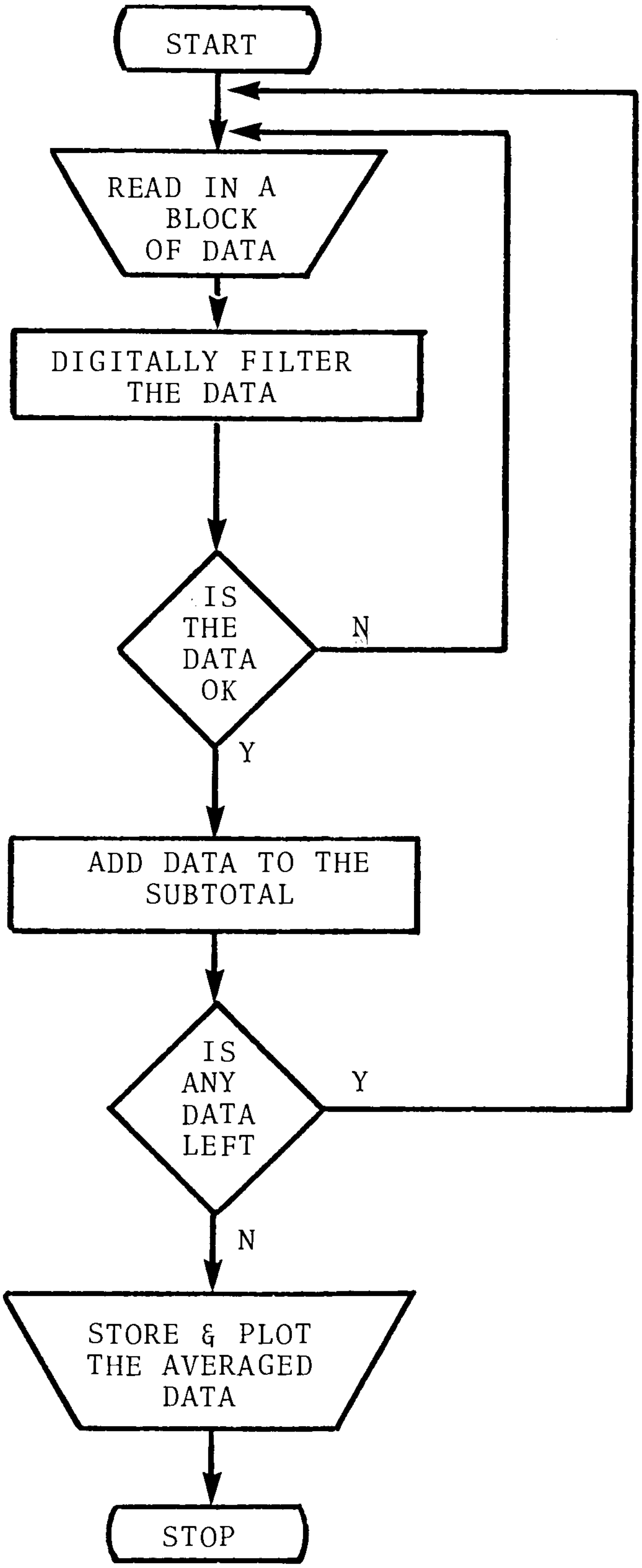

Figure 19. Flowchart of the ensemble averaging program.

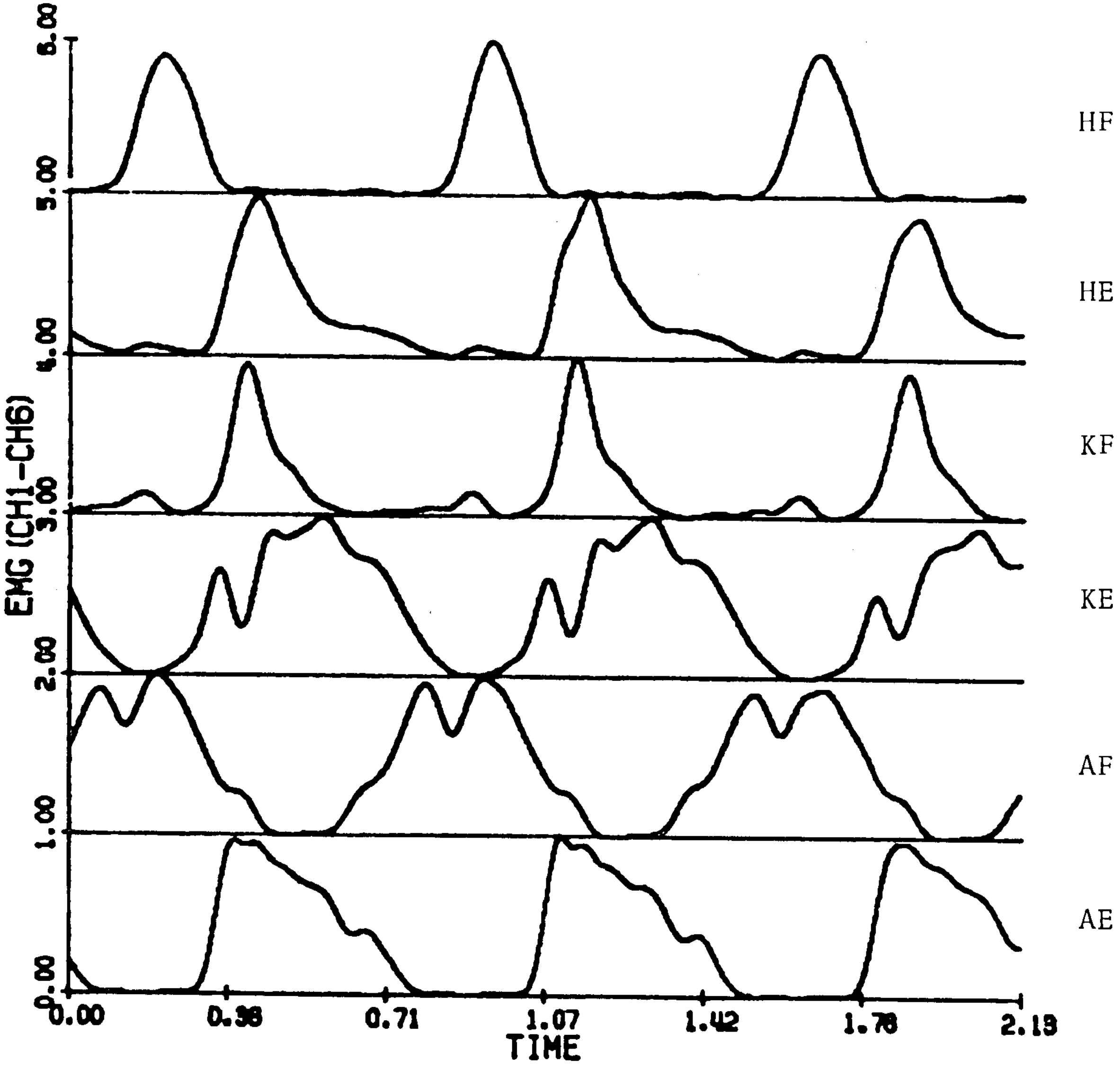

Figure 20. Plot of typical processed data with peripheral feedback intact for cat #1.

climbing stairs, two steps were taken :

a) EMG data for humans from a research report were used to study the model, and

b) Kinematic data for human subjects were measured to examine the model.

These two different ways of testing the model are described next.

4.4 Human EMG Data

It is theoretically possible to record EMG signals from the lower limb muscles during locomotion and to estimate the limb generator output, but in practice, multiple EMG recordings are at best difficult. Until recently, EMG recordings from the muscles of the lower limb during a rhythmic activity were done one at a time. Kinematic data was then used to align the recordings from all the muscles. Recent advances in small telemetry transmitter units will facilitate this procedure (76). For this thesis EMG recordings made by the Prosthetic Research Group at Berkeley (68) were used. They studied the following rhythmic activities :

a) normal level walking

b) fast level walking

c) climbing stairs

d) going downstairs

e) walking up a ramp, and

f) walking down a ramp.

EMG data were collected for thirty lower limb muscles for six normal subjects. The EMG signals were recorded using wire electrodes and were appropriately amplified, low pass filtered and averaged over the subjects. From this set data for six muscles were hand digitised and analysed. The following muscles were chosen as representative of the flexor and extensor groups across the three joints :

hip flexor - iliacus
    extensor - biceps femoris long head
knee flexor - semitendinosus
    extensor - vastus lateralis
ankle flexor - tibialis anterior
    extensor - soleus .

Figure 21 shows a sample data set for a normal level walk.

This was the only study found by the author that contained usable recordings from a number of lower limb muscles for a variety of rhythmic activities. Wherever possible, the data was checked for concurrence with other studies (77).

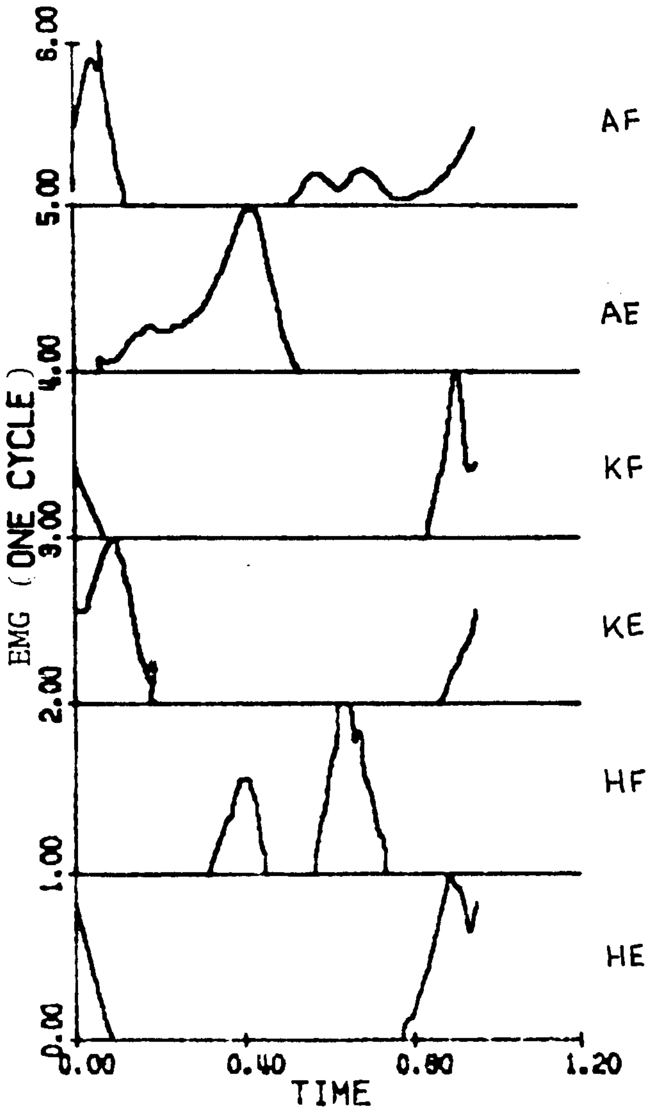

Figure 21. A sample human EMG data set for normal level walking (68).

4.5 Kinematic Measurements on Human Subjects

The outputs of the limb pattern generator are the firing rates of the pool of motoneurones. This output activates the muscles, which in turn generate appropriate torques at the joints and cause the limbs to move. The kinematic data describe these movements and hence are indirect measurements of the generator output. One can think of the kinematic data as generator outputs that have been through a transfer function. Figure 22 is the schematic diagram of this transformation. At least for the present the transfer function is very difficult to determine because of many unknowns in the process. Despite these problems, it is an easy, accessible way of studying locomotion and was used in this thesis.

4.5.1 Experimental Protocol

The CARS - UBC electrogoniometer was used in this study. This electrogoniometer records the joint angles with the help of three potentiometers placed orthogonal to each other at each joint. The double parallelogram arrangement and the sliding telescopic bar absorbs the linear translations (78) and allows the recording of the relative angular displacements.

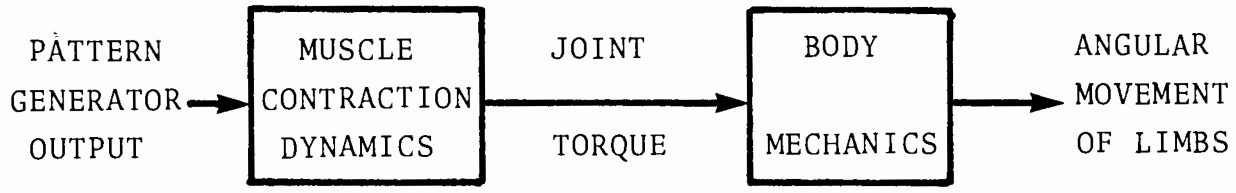

Figure 22. Block diagram of the transformation of the generator output to the angular movements of the limbs.

The subject, a male University student, was fitted with the goniometer. The outputs of the goniometer were fed directly into the PDP-11 minicomputer via a 16 channel multiplexer unit. Data were recorded for both limbs but the ankle rotations were not measured in this study. Figure 23 is a schematic diagram of the experimental setup. Kinematic data were recorded for the following activities :

a) Three speeds of walking
   The subject was asked to walk along a straight line at subnormal, normal and fast walking speeds. This self pacing minimises any disturbance of the step cycle. Actual period of the step cycle were in the range of 1.0 sec to 2.0 sec.

b) Cycling
   A bicycle ergometer was used for the study. The seat was adjusted such that the leg was fully extended when the pedal was at the lowest position. Three different loads, 1,3,5 kp were used. The subject was asked to produce the maximal effort each time. Thus with increasing load the frequency of pedalling decreased.

c) Hopping
   The subject was asked to hop on the spot at subnormal, normal and fast rate. The period of hopping ranged from 1.0 sec. to 2.0 sec.

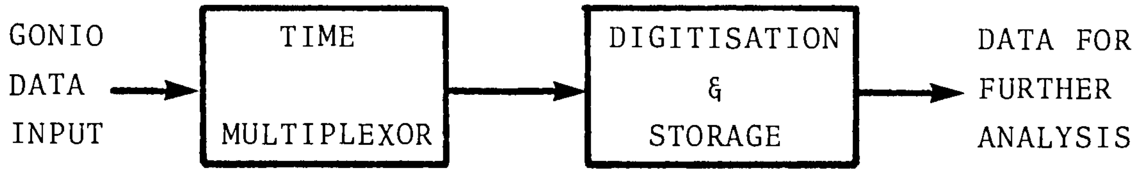

Figure 23. A schematic diagram for recording kinematic data for human subjects.

d) Stair Climbing

The subject was asked to go up and down a flight of stairs near the laboratory. The long umbilical cord allowed freedom of movement.

All these recordings were repeated atleast three times. Figure 23 is a sample data set for level walking at 0.94c/s.

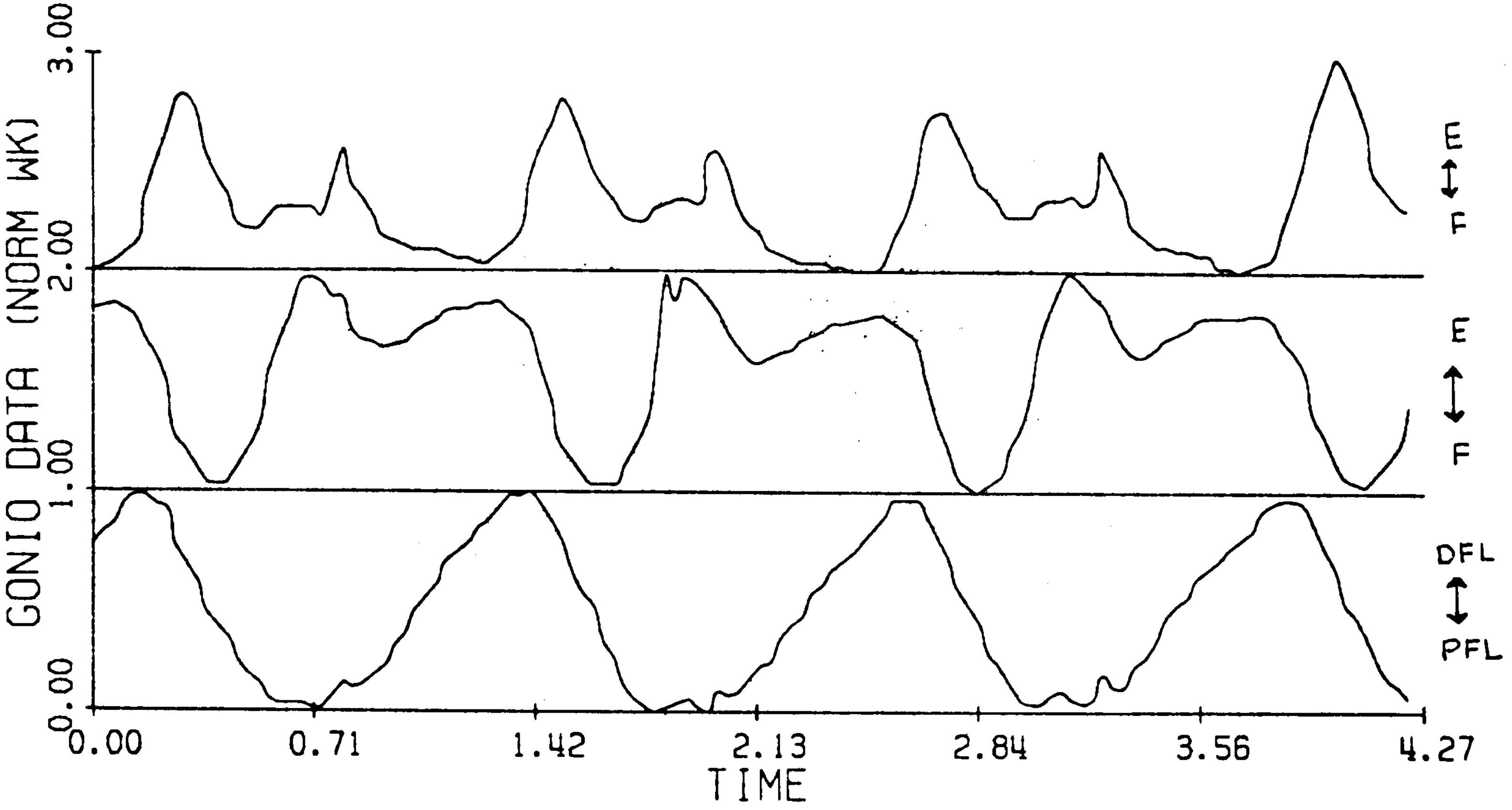

Figure 24. A sample kinematic data set for normal level walking at 0.94 c/s.

CHAPTER V

RESULTS, ANALYSES AND DISCUSSION

5.1 Data Analysis

The data obtained from the experiments described in Chapter IV are analysed to study the model. As shown in Chapter III, the first step in data analysis is to determine the minimum number of basis functions required to represent a given set of data. Subsequent analysis deals with the calculation of the oscillator parameters. These two stages of analysis are described below.

5.1.1 Calculation of Basis Functions

The theoretical analysis for determining the basis functions is shown in Appendix A. A computer program implementation of this procedure is summarised in the flow chart diagram of Figure 25. The EMG data from the hindlimb muscles of the cat were processed and a typical result for normal walking (1.25 c/s) for cat #1 is shown in Figure 26.

The mean square error [ϵ^2] in estimating the data is given by the linear summation of the eigenvalues whose eigenvectors (basis functions) are not selected to

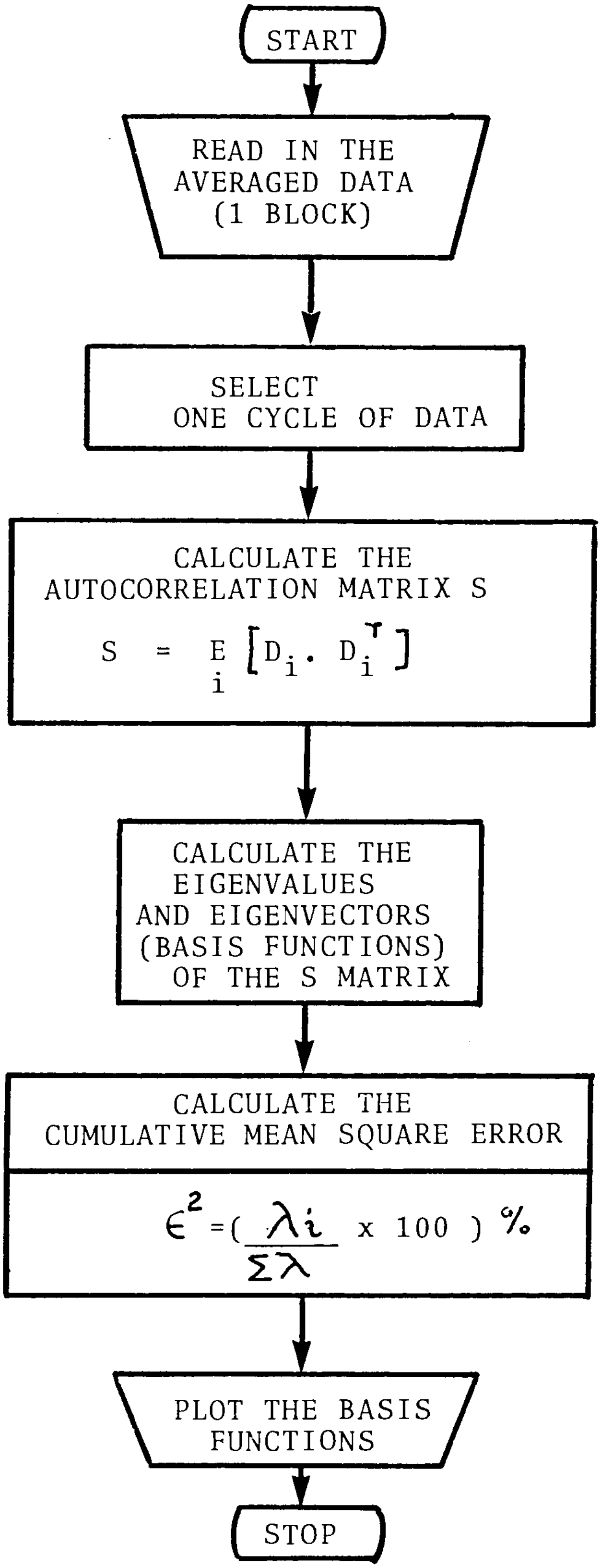

Figure 25. Flow chart of the basis function program

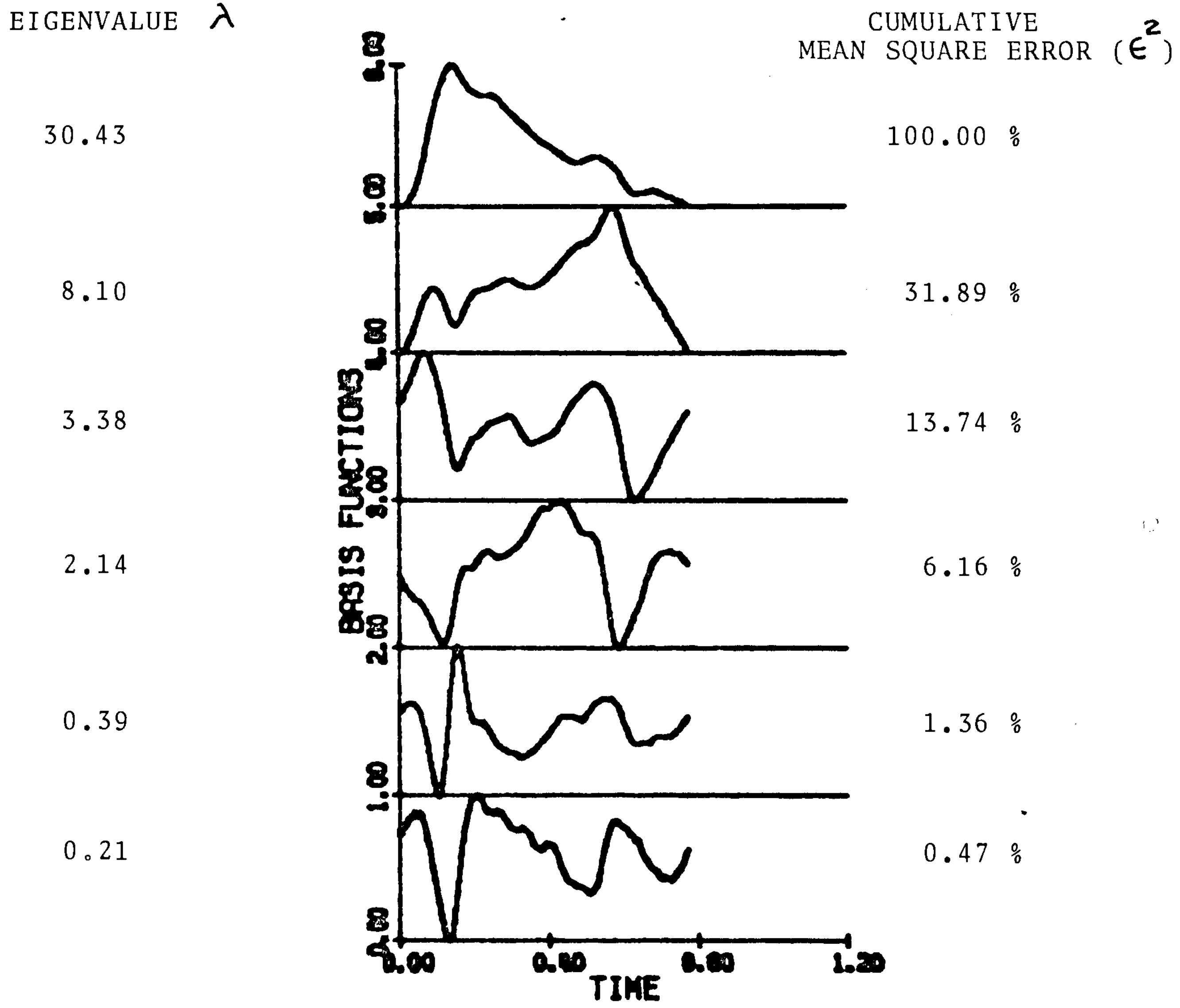

Figure 26. A typical result showing the six basis functions for data from cat #3 for walking at 1.25c/s. The eigenvalues and the cumulative mean square error are also shown.

approximate the data. Thus the basis functions can be selected in order of eigenvalues until ϵ^2 becomes smaller than the noise level in the data. Noise, from various sources, can be introduced into the data at each stage of signal recording and analysis. To estimate the noise level in the data, each potential source of contaminant is examined in some detail.

Stainless steel wire electrodes produce the least tissue reaction and are easy to make. They were used to record the myoelectric signal. These electrodes with only their tip exposed, pickup signals from a small region and hence minimise noise due to crosstalk. But the small area of the electrode offers high impedance and can cause signal distortion due to loading (79). Besides crosstalk, the biological noise in the source itself (for example neural noise) contaminates the signal (79).

Electrical interference from sources such as fluorescent lights, and electric motor of the treadmill can distort the signal. Short wire electrode leads, shielded cable, single ground, charge preamplifiers and differential amplification of the signal helped minimise the outside electrical noise. Besides the external interference, electrical components of the amplifier can generate noise. An example of the internal noise would be the thermal noise generated by the passive resistive elements in the circuit (80).

Since the data processing could not be done in real time, the signals were stored on a tape recorder. Beyond the limitations in magnetization-reproduce and modulation-demodulation operations, there are other problems in tape recording that need to be considered. The Frequency Modulated recording has high signal to noise ratio (49 db. for the tape recorder used) ,but is sensitive to tape speed. The time base errors associated with variation in speed (flutter) can be on the order of 0.25 % , noise amplitude level (81).

The raw data collected from the experiments was digitised and processed. Digitisation involves two distinct operations a) sampling and b) quantization. Each of these operations can introduce error in the data. The raw signals from the tape recorder were filtered (30 Hz. low pass Paynter filter) and sampled at 125 samples/sec. This sampling rate is well above the Nyquist frequency for the data and hence the problem of aliasing is minimised. Quantization error is inversely proportional to the number of bits used to represent the data in numerical form. For example the ten bit analog to digital converter used would have a signal to noise ratio of about 70 db . The range of analog data was set to occupy as much of the available quantizing range as possible to minimise error.

Thus it is evident that despite careful instrumentation, the myoelectric signal recording is contaminated by noise. An estimate of 0.1 % noise power level in the data seems reasonable. For a sample data set, the cumulative mean square error in estimation when the corresponding eigenvectors are not chosen to approximate the data, is shown along with the eigenvalues in Figure 25. From this figure it is clear that for $\epsilon^2 < 0.1$ %, the number of basis functions required to estimate the data is six. This decision does not take into account the inter-step variability in the myoelectric signal. If this variability is considered to be equivalent to a noise power of 5 %, one can estimate the data using four basis functions. But this would necessitate determining four constants for each of the six channels of data and also taking into account their variability with speed of locomotion. Besides, unlike two (one each for flexion and extension) or three (one each for the hip, knee and ankle joint) basis functions, there is no physiological correlate for four or five basis functions. Therefore, although the decision is somewhat arbitrary, for the purpose of this thesis six independant oscillators were used to produce the six channels of output. It is recognised that the actual physiological situation may be different.

5.1.2 Calculation of 'ω' and 'g' & 'h' Functions

Each of the six oscillators in the limb pattern generator is defined by the fundamental frequency 'ω' and two nonlinear functions 'g' and 'h'. These parameters were calculated for each of the six channels in a given data set. Figure 27 shows the flow chart diagram for the computer program used to calculate these parameters. The functions 'g' and 'h' for the ankle extensor channel for cat #1 are shown in Figure 28.

5.2 Revised Model of the Limb Pattern Generator

From the data analysis it is clear that for any given data set, the fundamental frequency for each of the six channels is identical. Therefore only one sine/cosine oscillator is needed to generate the fundamental frequency of the oscillation. The output of this oscillator can then be fed into the two nonlinear functions for each of the six muscles to produce the observed pattern generator output. Figure 29 is a schematic representation of the revised limb pattern generator model.

The model of Figure 29 is a parsimonious realization of the observed signal generating property of the limb pattern

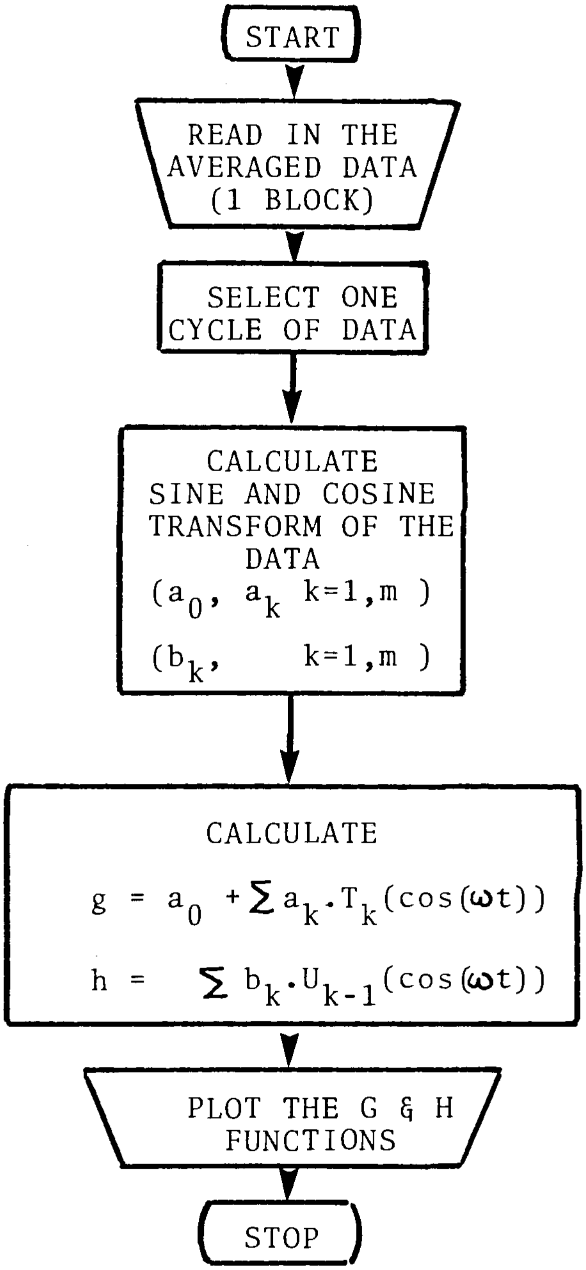

Figure 27. Flow chart of the program for calculating the 'g' and 'h' functions.

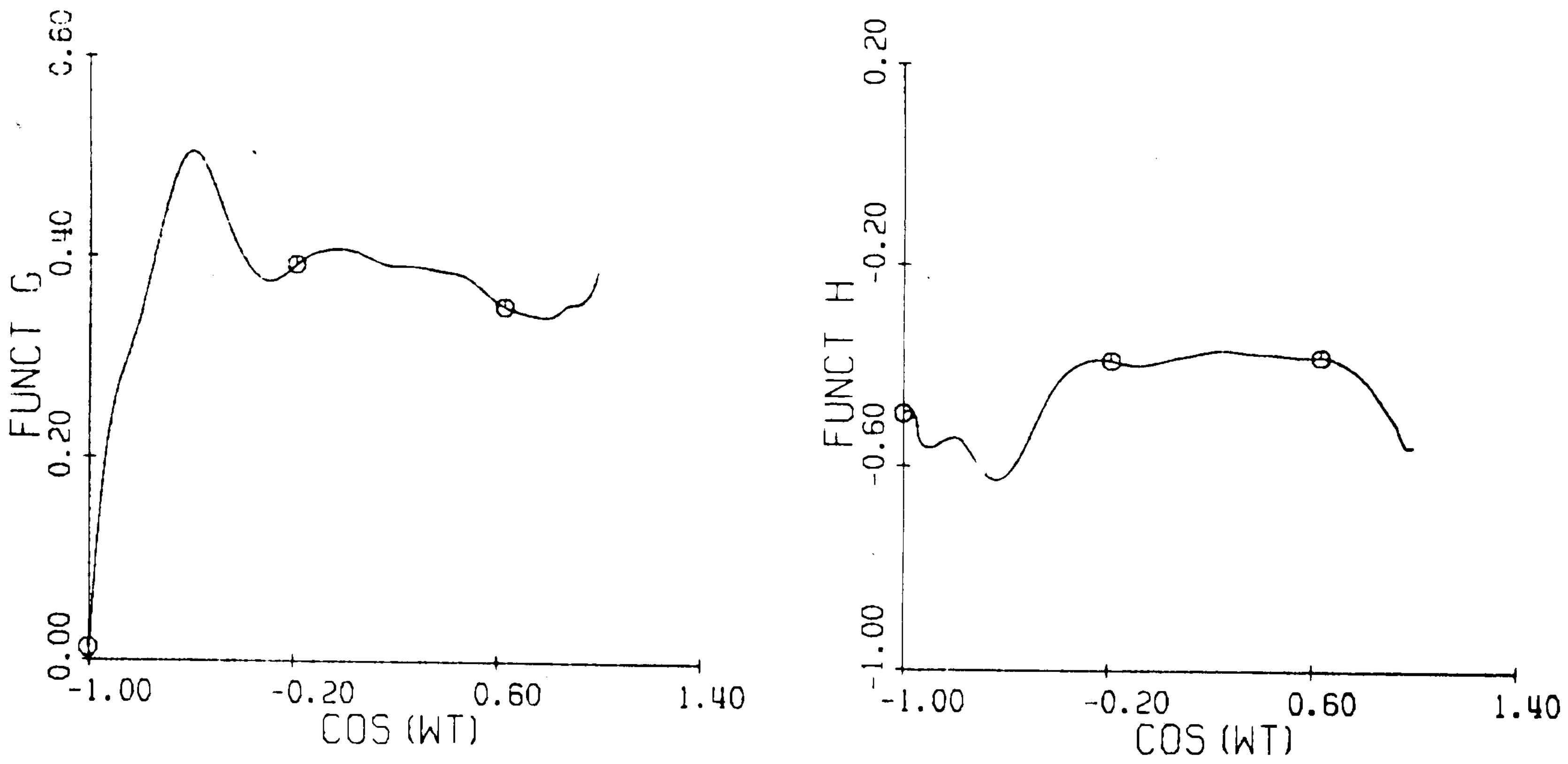

Figure 28. Plots of 'g' and 'h' functions for the ankle extensor muscle for cat #1 for walking at 1.12 c/s.

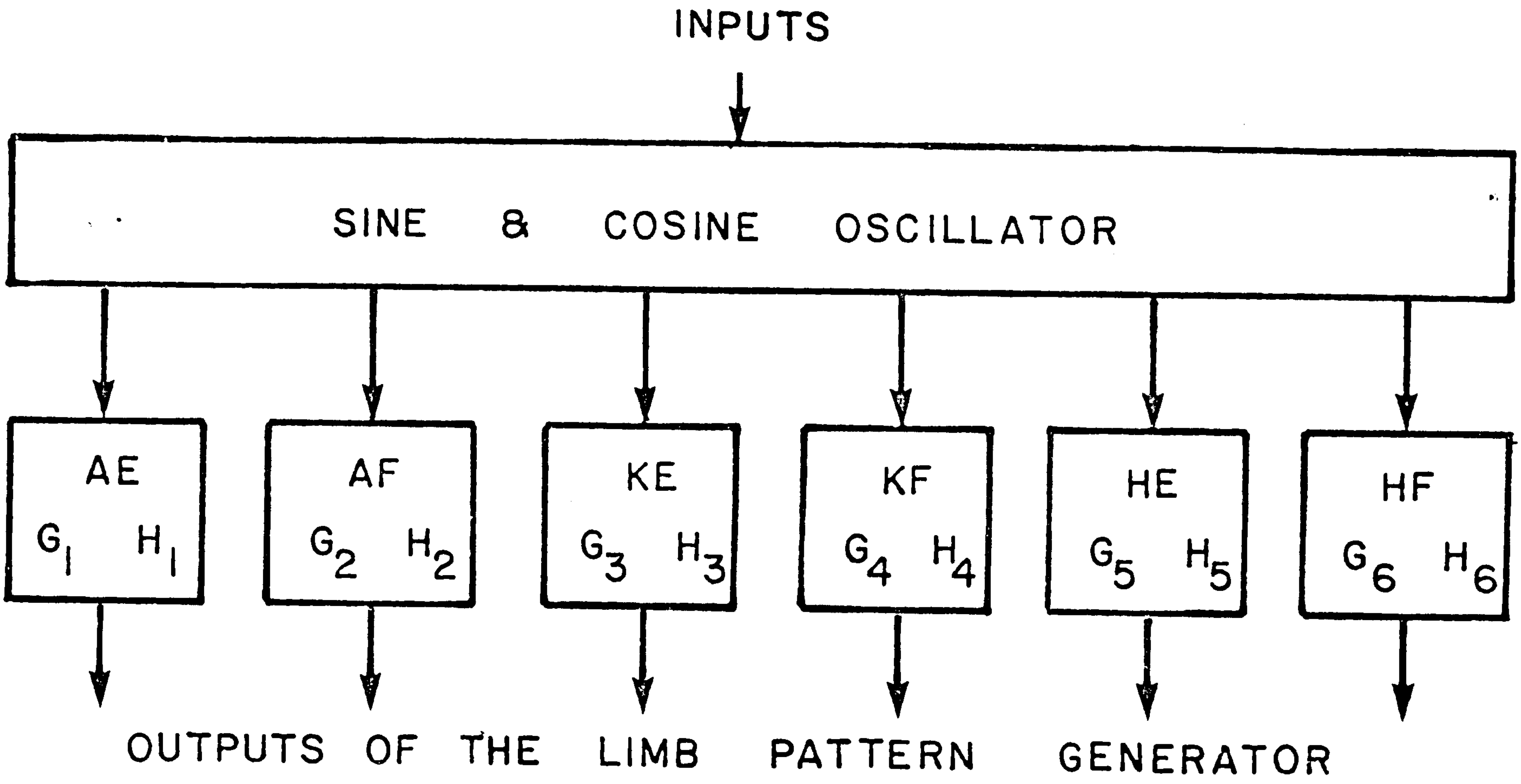

Figure 29. A schematic diagram of the revised limb pattern generator model.

generator. In fact, it is very likely that to improve the realibility, the mammalian nervous system has evolved more than one fundamental frequency oscillator per limb. Redundancy, to improve realibility, seems to be the rule rather than the exception as evidenced by the ability of the nervous system to function normally even when some parts of it are damaged (82).

5.3 Performance of the Model over a range of Input Signals - Cat Data

An analytical model of the limb pattern generator has been derived. The most important test of the usefulness of the model would be to determine its performance over a range of input signal. The input to the model is the tonic excitation to the MLR. When this input is altered, the speed of locomotion is modified. This alteration in the speed of locomotion is due to the change in the generator output which will be reflected in the changes in the model parameters 'ω', 'g' and 'h' for each of the six channels.

The model parameters were determined from a data set for three speeds of locomotion from cat #1. Three 'g' and three 'h' functions corresponding to the three speeds of locomotion were plotted for each of the six muscles used in the study (see Figures 30a-30f). As the graphs show, the 'g' and 'h' curves change with speed of locomotion. The fundamental frequency 'ω' also changes with speed of locomotion. The changes in the fundamental frequency of oscillation with changes in the tonic input can be seen in the simulation result of Figure 31.

Each of the 'g' and 'h' curves can generate up to thirtieth harmonic in the output waveform. Visual inspection of the 'g' and 'h' curves from Figures 30a-30f reveals that the changes are smooth. To corroborate this deduction, each curve was fitted with a polynomial series (fifth order) and the coefficients of the terms in the expansion (ranging from -1 to 1 for the particular subroutine used) were plotted against the normalised period. The normalised period is proportional to the tonic input. These plots (Figures 32a-32f) show a smooth change of coefficients with changes in tonic input to the generator.

Similar results were obtained from another cat preparation. These results are shown in Appendix III. Thus the model can handle different input conditions reasonably well.

Figures 30a-30f. These figures contain the plots of 'g' and 'h' curves for the three speeds of locomotion for each of the six channels of the Cat EMG data set. Each curve in the figures is generated from 100 points joined by a smooth line. The symbols used in the figures represent the following :

□ --- 1.12 c/s

△ --- 1.49 c/s

✱ ---- 1.85 c/s

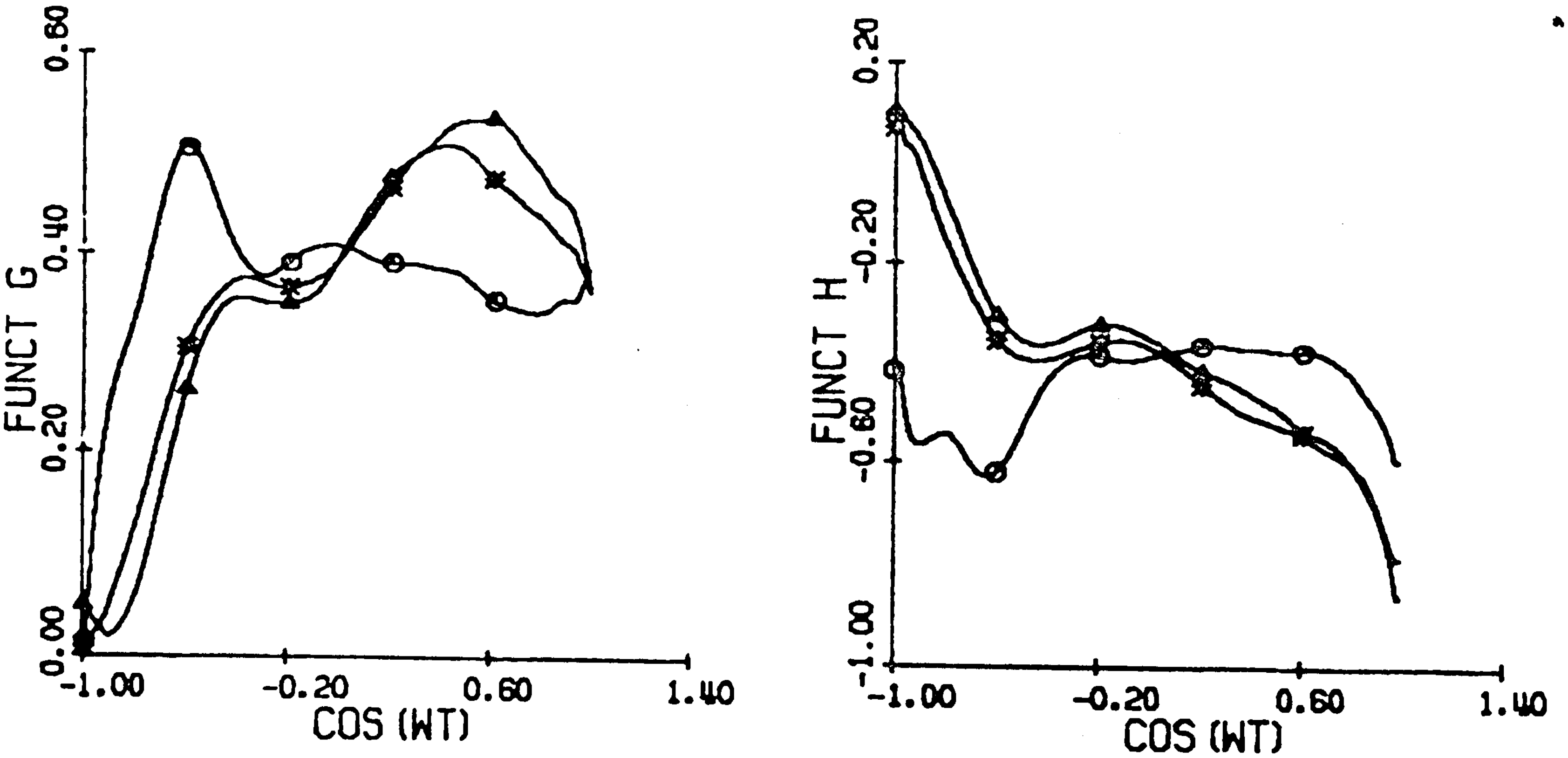

Figure 30a. Plots of 'g' and 'h' curves for the ankle extensor muscle, soleus.

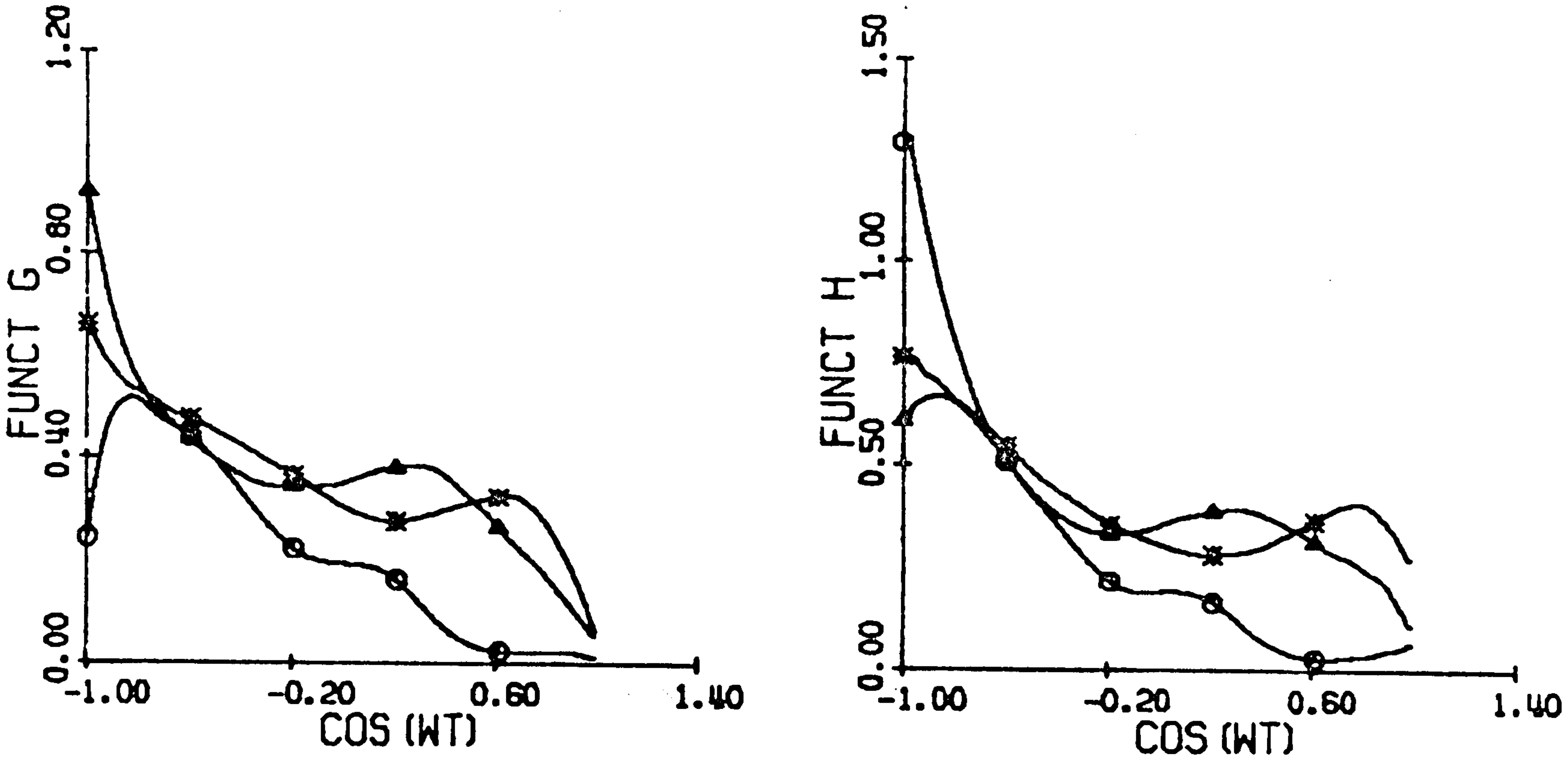

Figure 30b. Plots of 'g' and 'h' curves for the ankle flexor muscle, tibialis anterior-

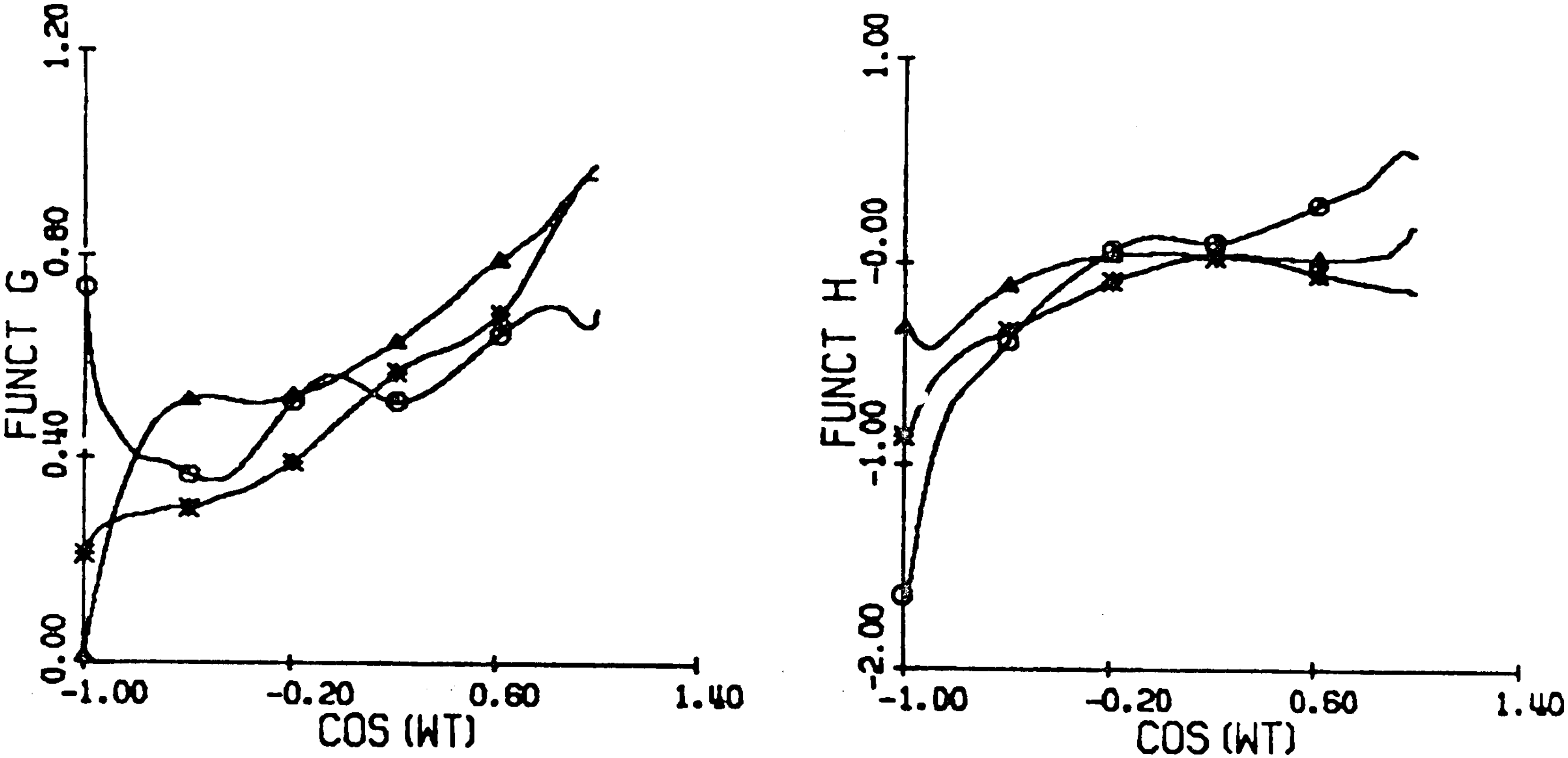

Figure 30c. Plots of 'g' and 'h' curves for the knee extensor muscle, vastus lateralis.

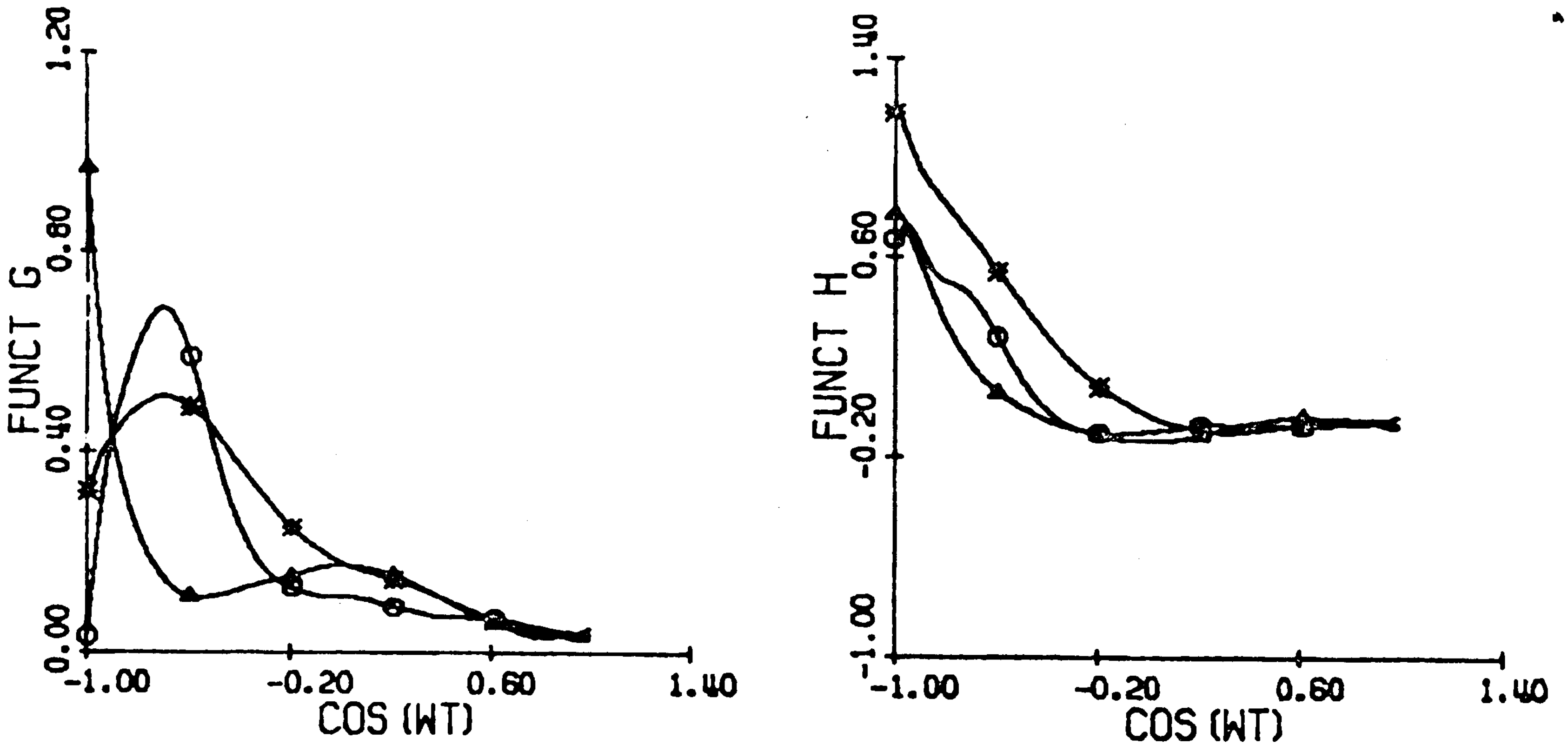

Figure 30d. Plots of 'g' and 'h' curves for the knee flexor muscle, semitendinosus.

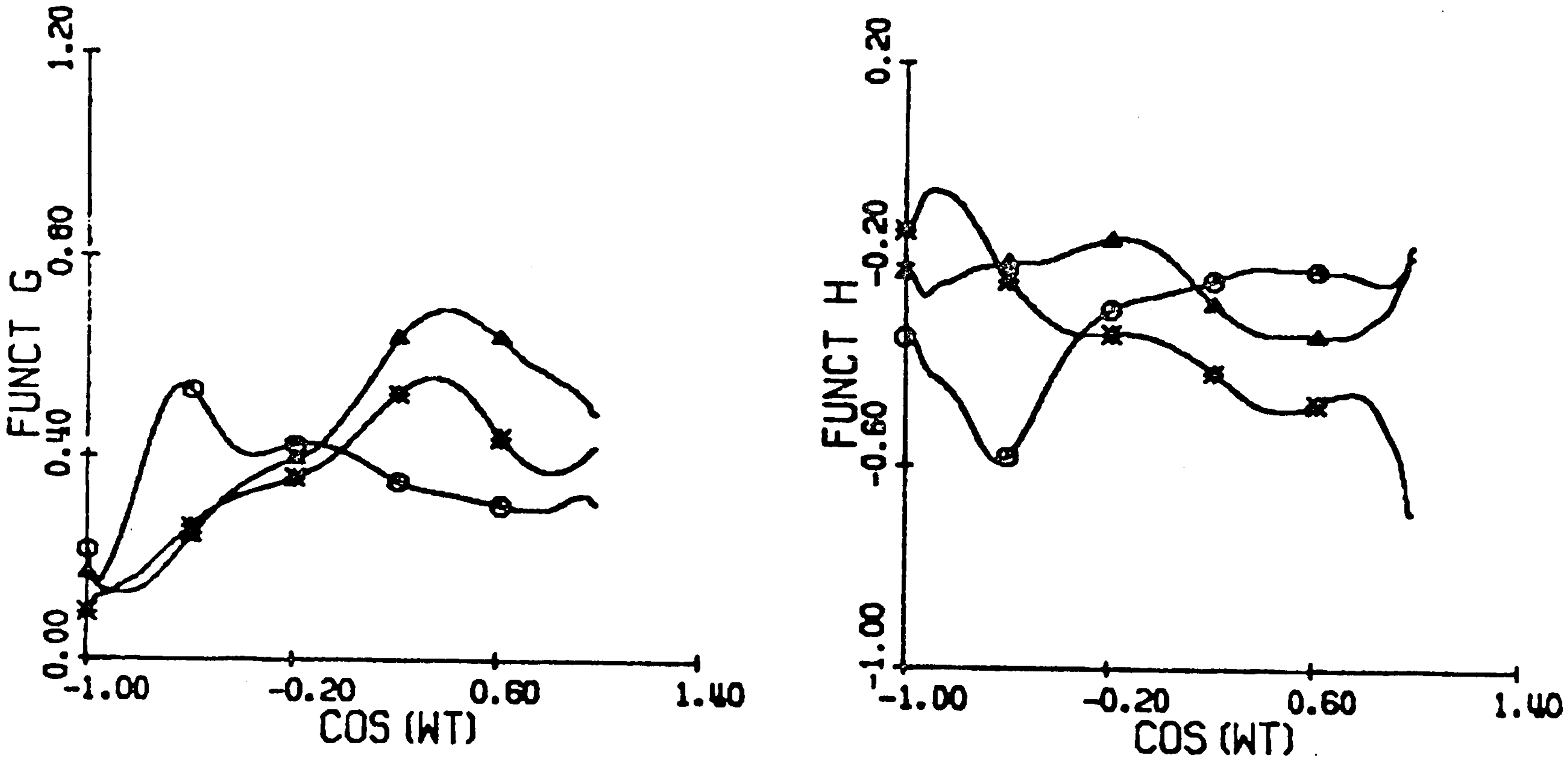

Figure 30e. Plots of 'g' and 'h' curves for the hip extensor muscle, biceps femoris.

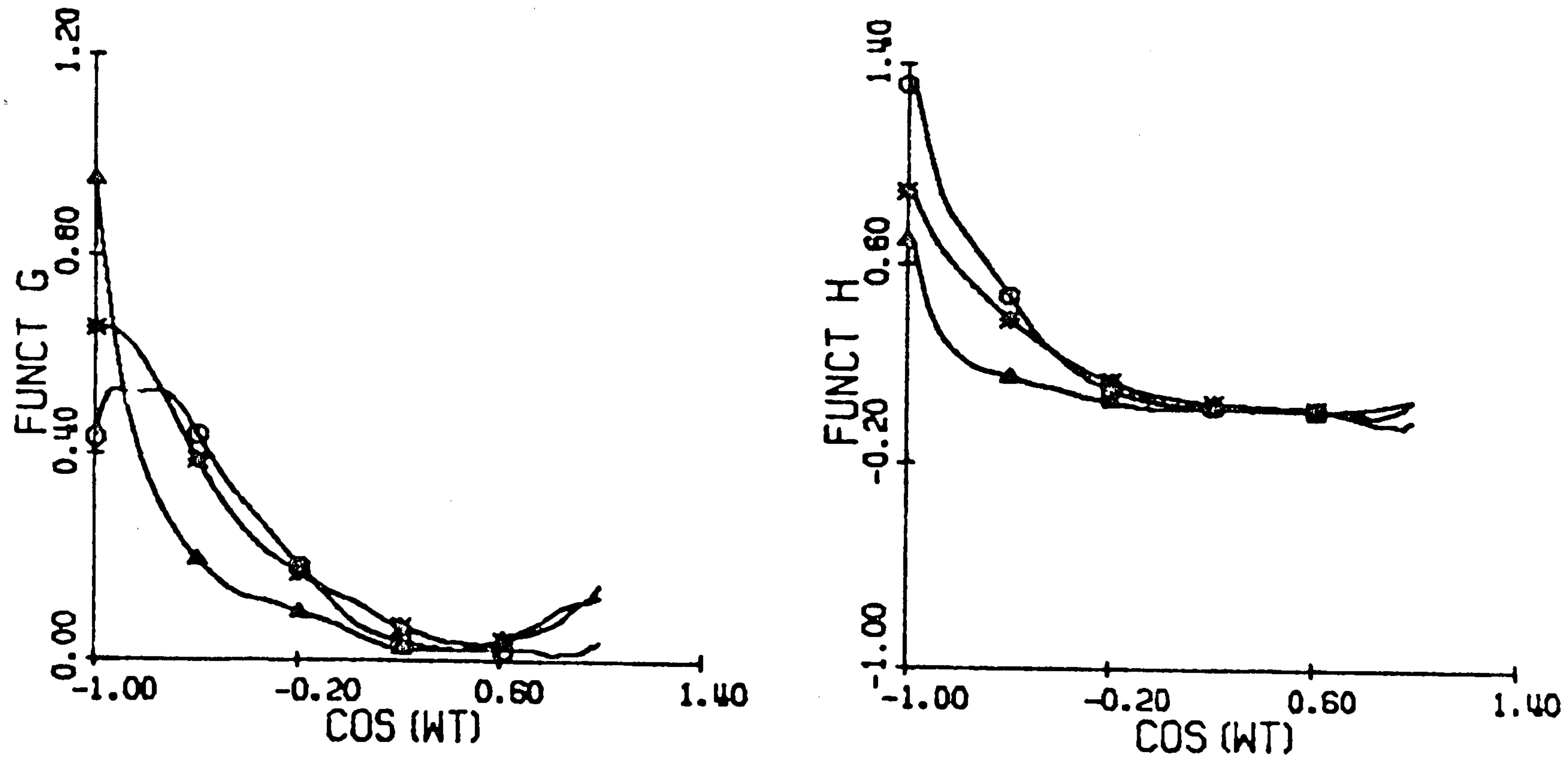

Figure 30f. Plots of 'g' and 'h' curves for the hip flexor muscle, iliopsoas.

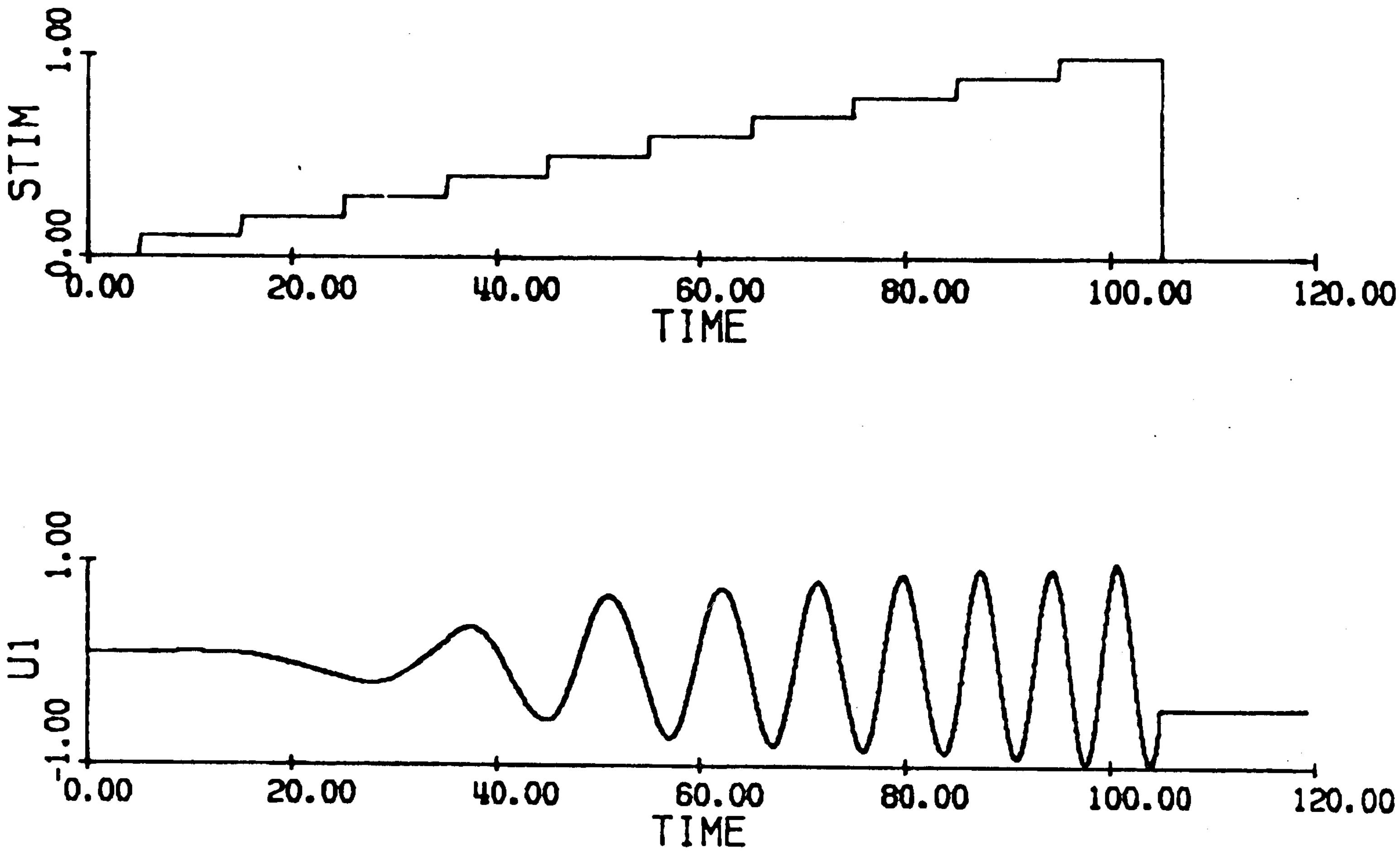

Figure 31. Simulation result showing changes in frequency with change in stimulus for the labile sine/cosine relaxation oscillator.

Figures 32a-32f. These figures contain the plots of the five coefficients of the series expansion of the 'g' (ag1 - ag5) and the 'h' (ah1 - ah5) curves versus the normalised period (np) for each of the six channels of the Cat EMG data set.

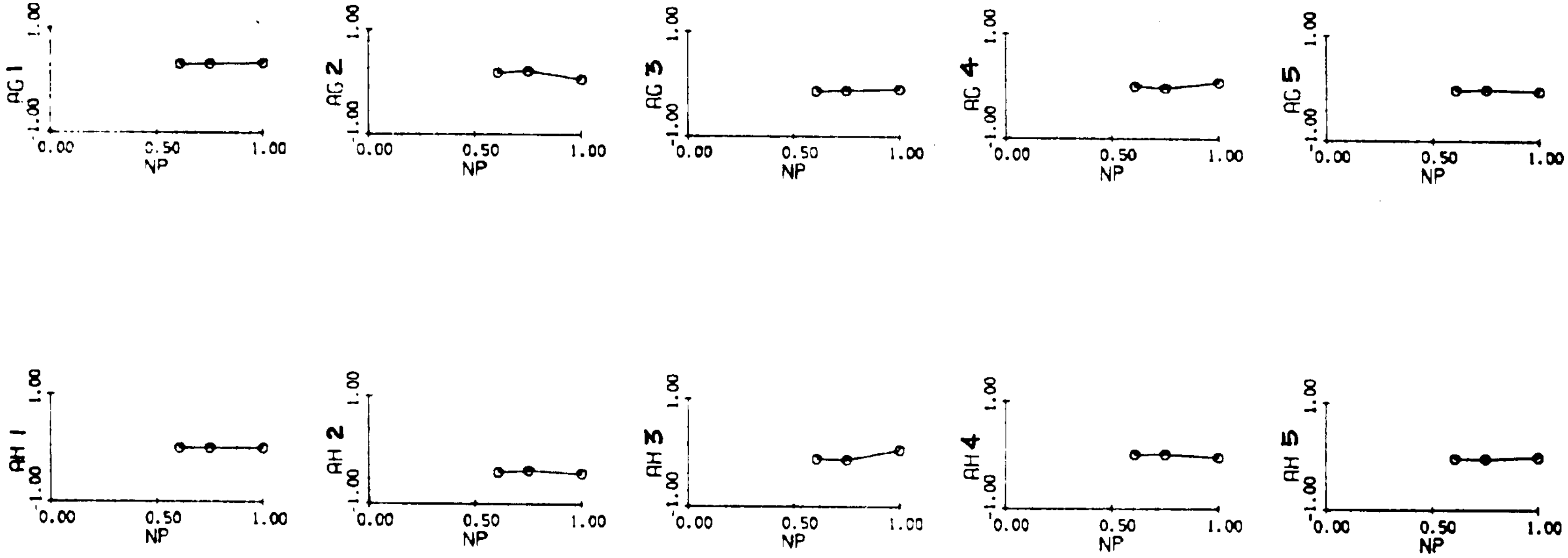

Figure 32a. Plots of the five coefficients versus normalised period for the ankle extensor muscle channel.

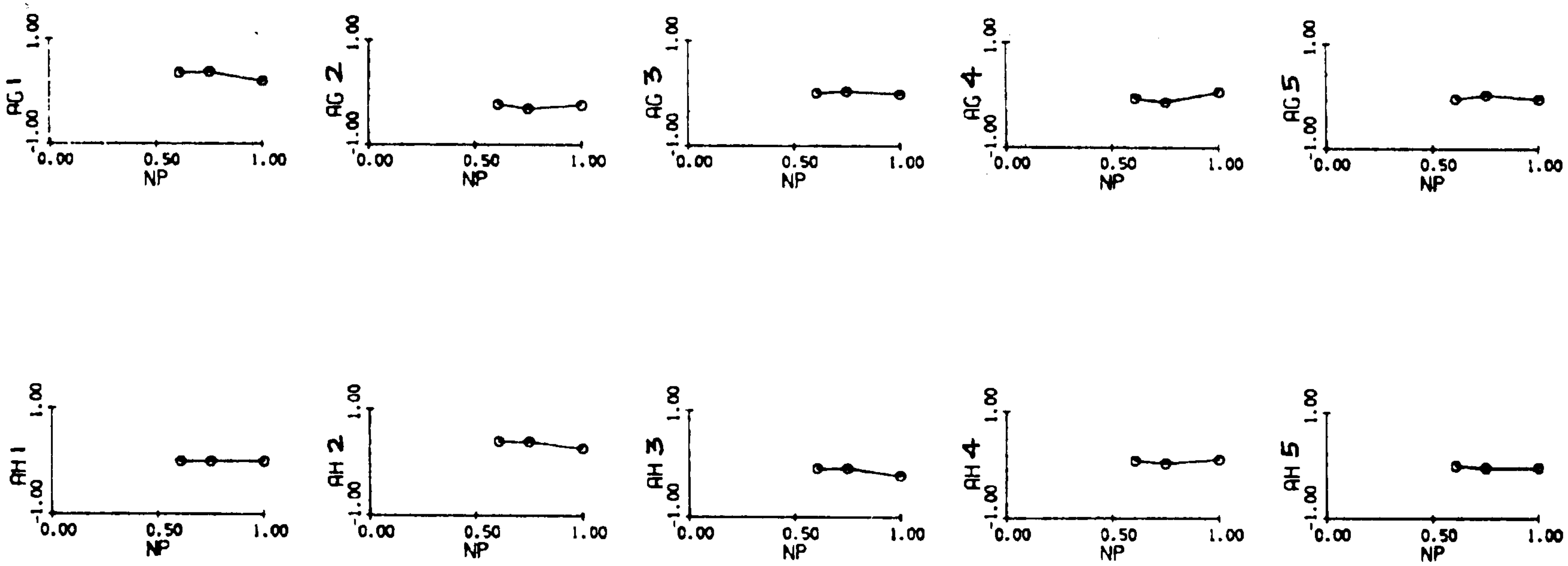

Figure 32b. Plots of the five coefficients versus normalised period for the ankle flexor muscle channel.

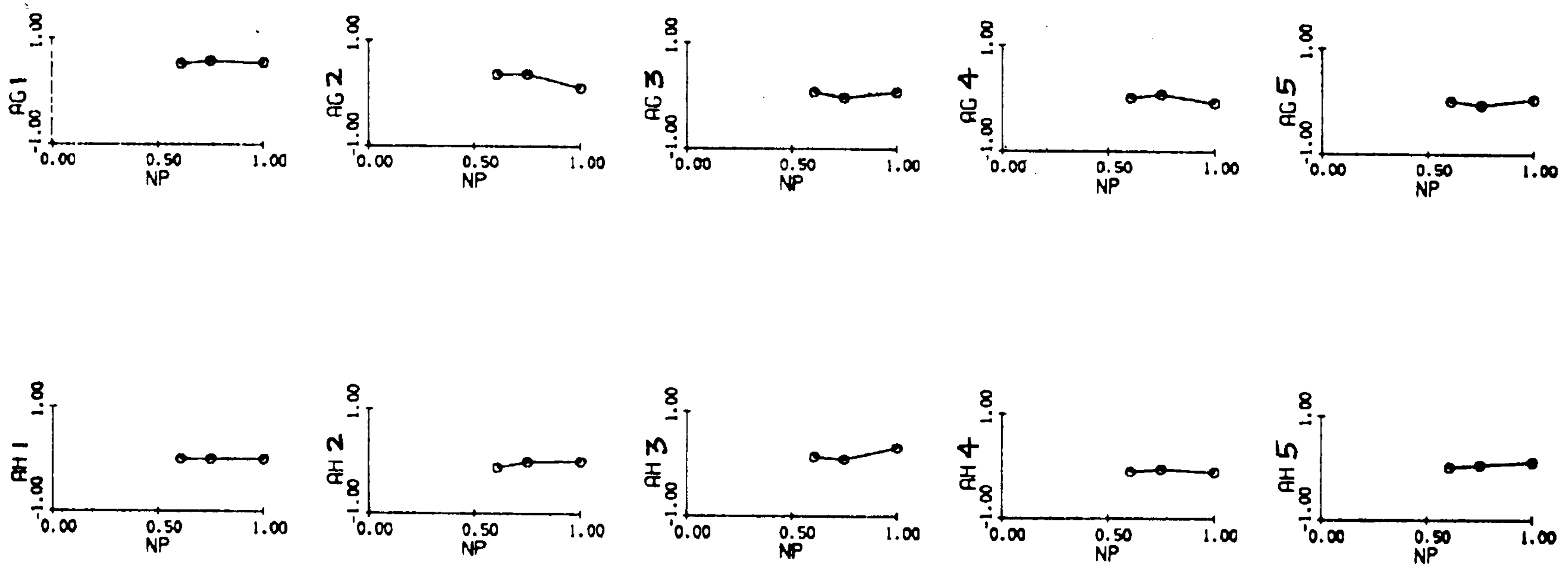

Figure 32c. Plots of the five coefficients versus normalised period for the knee extensor muscle channel.

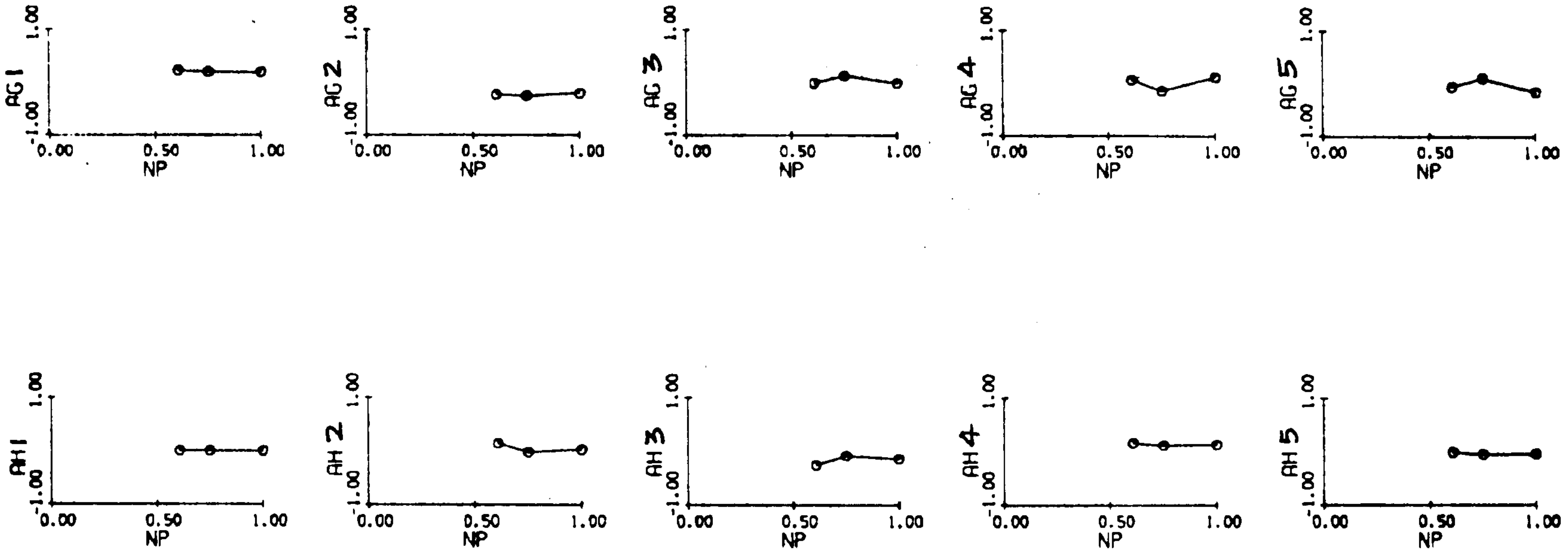

Figure 32d. Plots of the five coefficients versus normalised period for the knee flexor muscle channel.

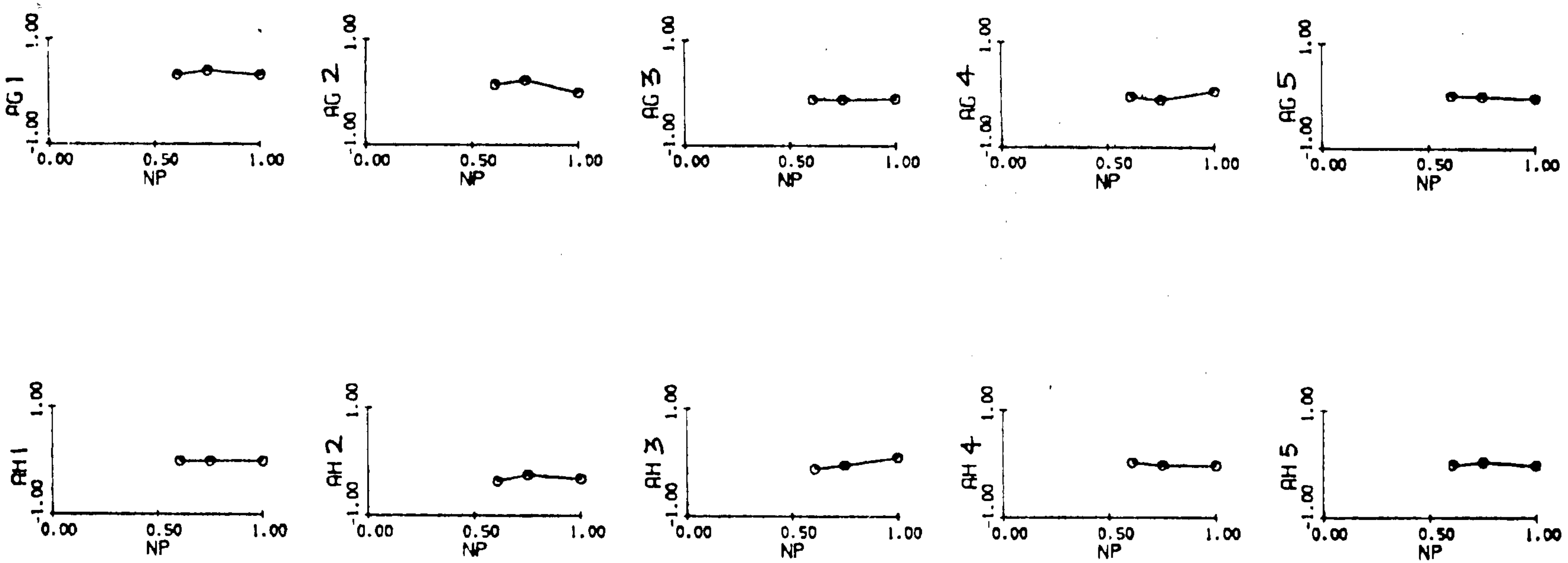

Figure 32e. Plots of the five coefficients versus normalised period for the hip extensor muscle channel.

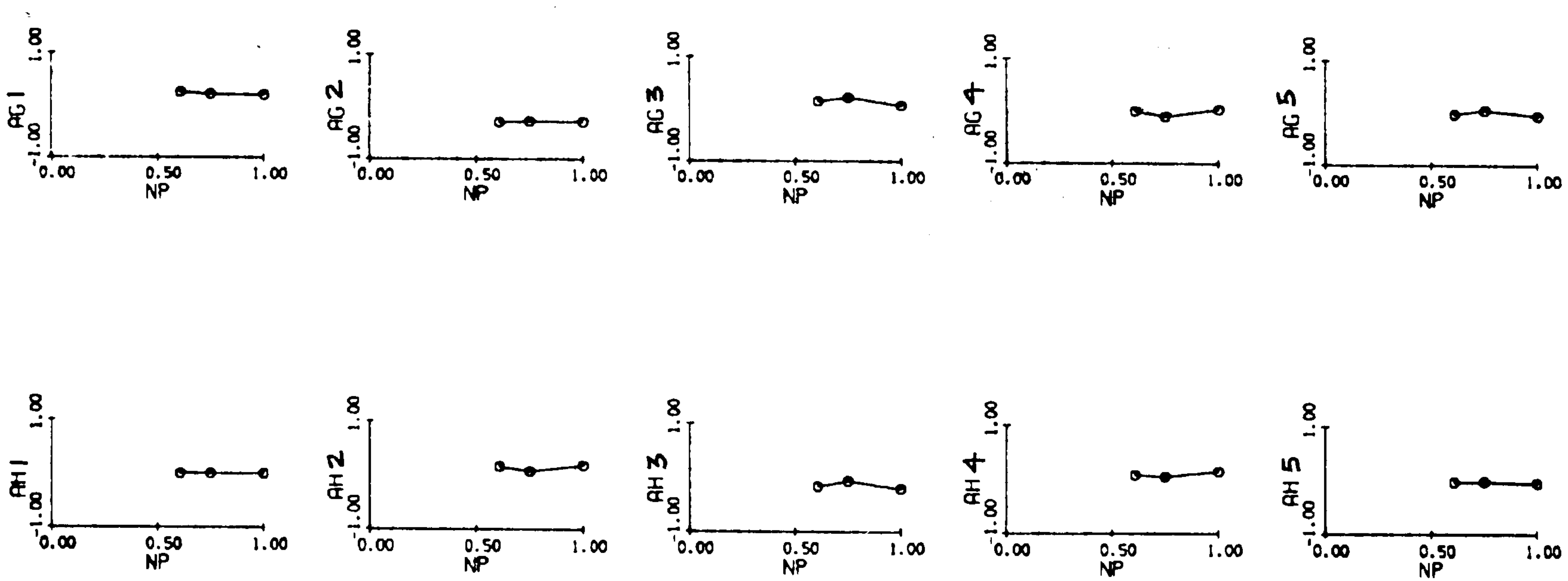

Figure 32f. Plots of the five coefficients versus normalised period for the hip flexor muscle channel.

5.4 On Validity of using Cat Pattern Generator Model for Humans

One of the principal motives for this research has been the desire to gain insights into the processes involved in human locomotion. The neurophysiological studies mentioned in the previous chapters have been done on mammals other than man. Are the conclusions derived from these experiments valid for human locomotion ? It is not possible to give an absolute and unqualified answer to this question, but by comparing cat and human locomotion one can make an educated guess. The similarities between cat and human locomotion are:

a) Cats use digitigrade locomotion. Though man uses plantigrade locomotion for walking, he does convert to the digitigrade form of locomotion during running (26).

b) The stance/swing phase duration as a function of speed in cats (26) is similar to that in man (83).

c) The intra-joint and inter-joint displacements in cats and man are similar (26).

d) Although there is no one-to-one correlation between the muscles involved in locomotion in cats and in humans the overall pattern of muscle activation is similar, (7,26,83).

e) The shoulder to hip phase relation in man has been shown to have some similarity to that described in the cat (84,85).

f) A preliminary study by the author suggests that in man there is the same phasic control of the reflex arc as has been described for cats (34-37).

In summary it can be argued that the differences between quadripedal and bipedal ambulation is more due to differences in postural structure than to differences in the neural control system.

It is apparent that we do not consciously control each appropriate muscle at a given instant in our stepping cycle and thus there seems to be a motor program for human locomotion. Studies on infants have shown reciprocal activation even before the child learns to walk (86). From an evolutionary point of view there would seem to be no reason to discard the neural scheme for producing the rhythmic patterns during locomotion. A case can be made for having more control over these generators so that they can be adapted for new rhythmic movements of the lower limb observed in activities such as cycling and climbing stairs.

5.5 Performance of the Model for Human Data

The performance of the limb pattern generator model was studied for various types of rhythmic activities such as walking, cycling and climbing stairs.

5.5.1 Changes in Model Parameters with Speed of Locomotion

The analysis carried out on the cat data was repeated here on the human data. The EMG data was available for only two speeds of level walking. The 'g' and 'h' functions for these two speeds were plotted (see Figures 33a-33f). Visual inspection revealed a smooth change in the 'g' and 'h' functions with speed of locomotion. The kinematic data (Appendix C) for walking gave similar results.

5.5.2 Changes in Model Parameters with Different Modes of Rhythmic Activity

Besides walking, humans use their lower limbs for various other stereotypical rhythmic activities such as cycling and climbing stairs. Is it possible to adapt the locomotor system for use in other rhythmic activities ? To answer this question the 'g' and 'h' curves for walking and climbing stairs were studied (see Figures 34a-34f).

Figures 33a-33f. These figures contain the plots of 'g' and 'h' curves for two speeds of level walking (□ - normal, △ - fast) for each of the six channels of the Human EMG data set. Each curve in the figures is generated from 100 points joined by a smooth line.

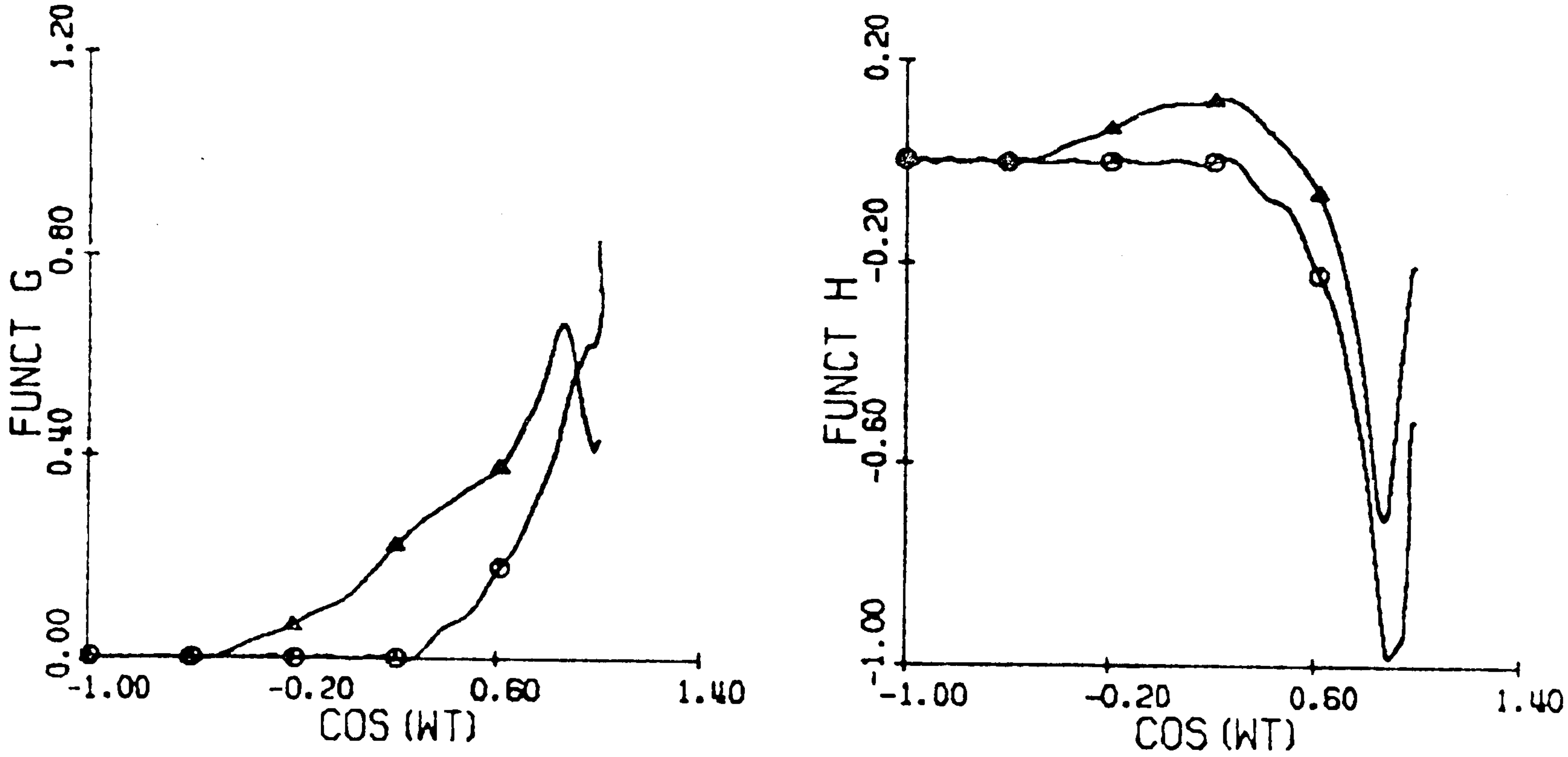

Figure 33a. Plots of 'g' and 'h' curves for the hip extensor muscle, biceps femoris.

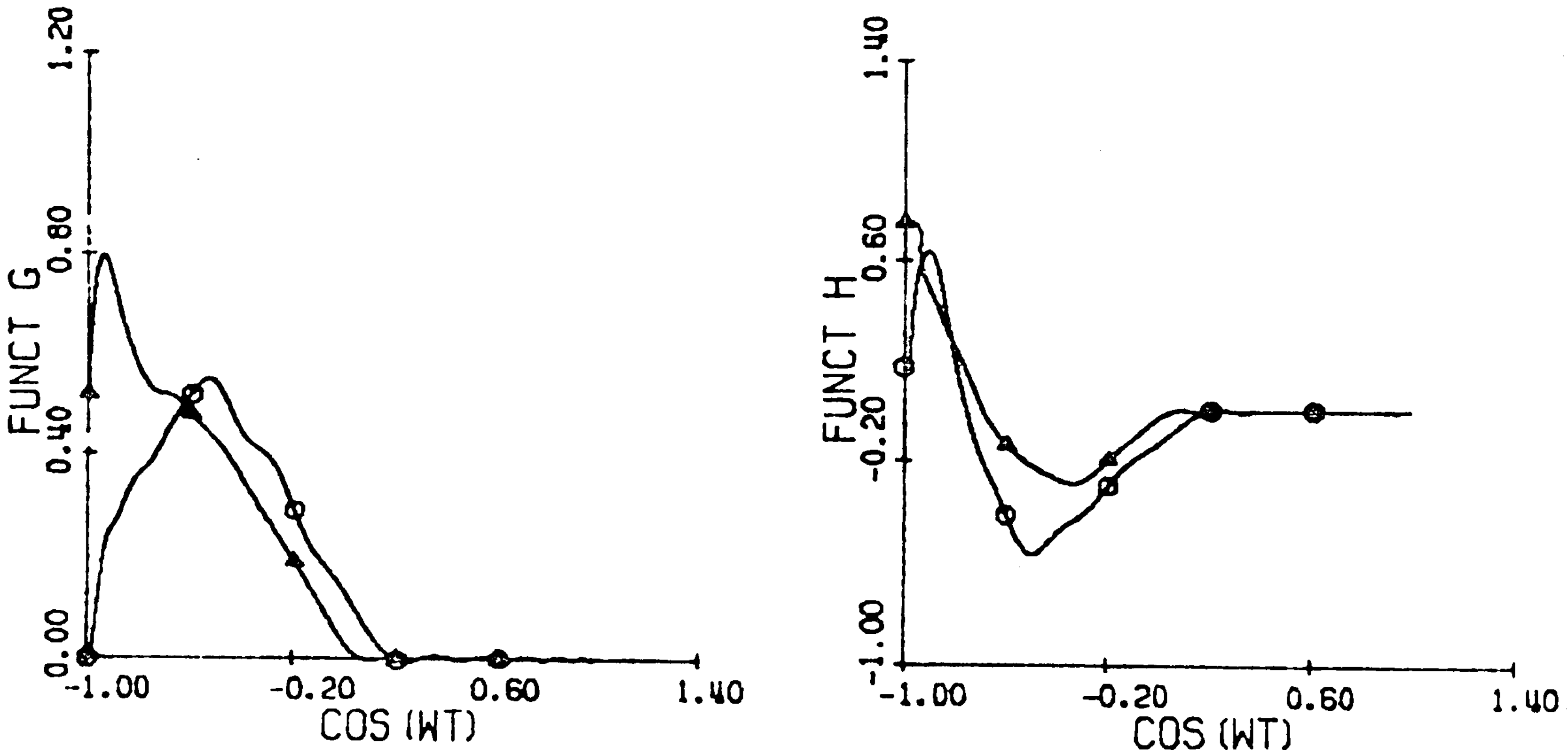

Figure 33b. Plots of 'g' and 'h' curves for the hip flexor muscle, iliacus.

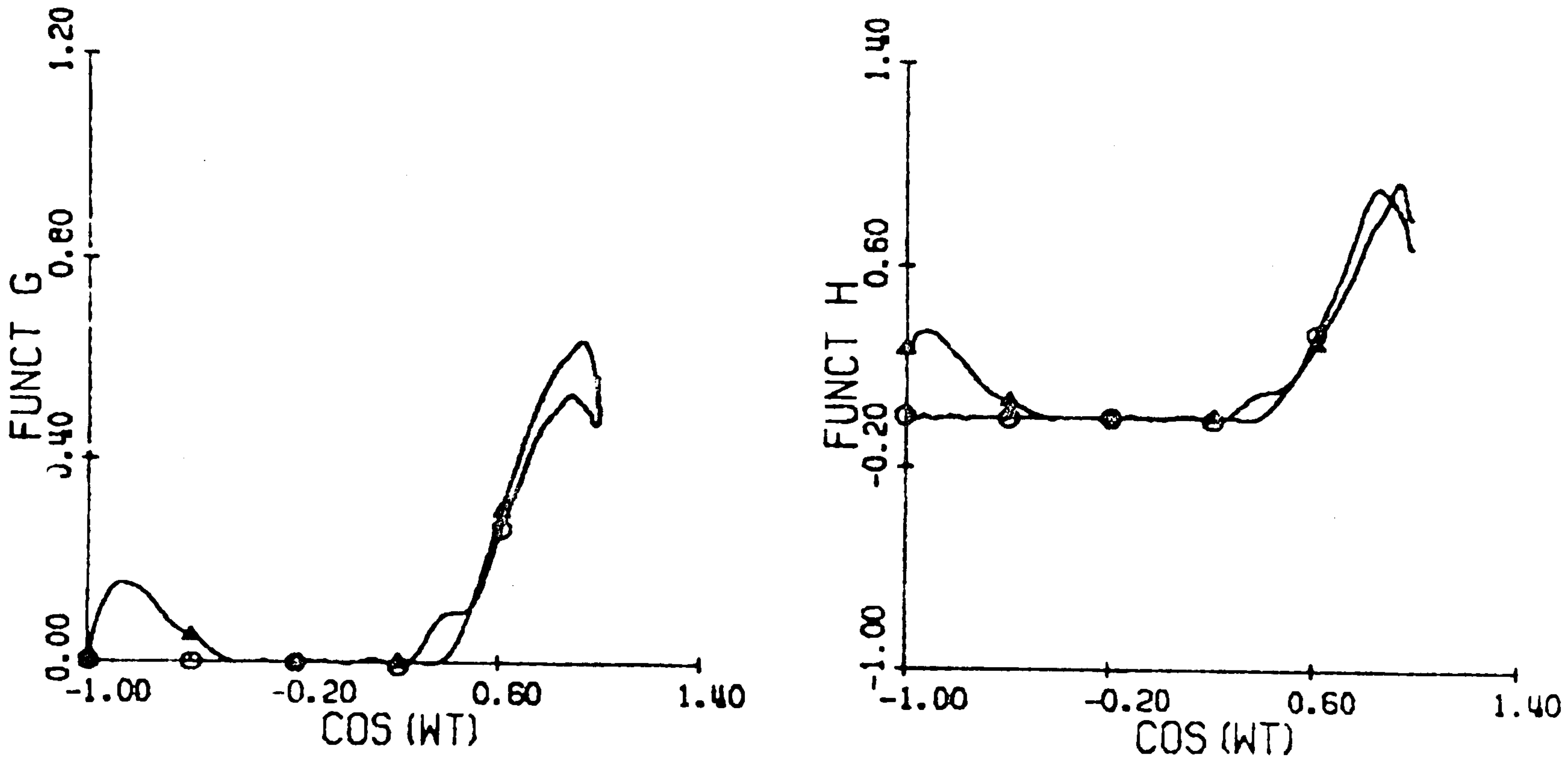

Figure 33c. Plots of 'g' and 'h' curves for the knee extensor muscle, vastus lateralis.

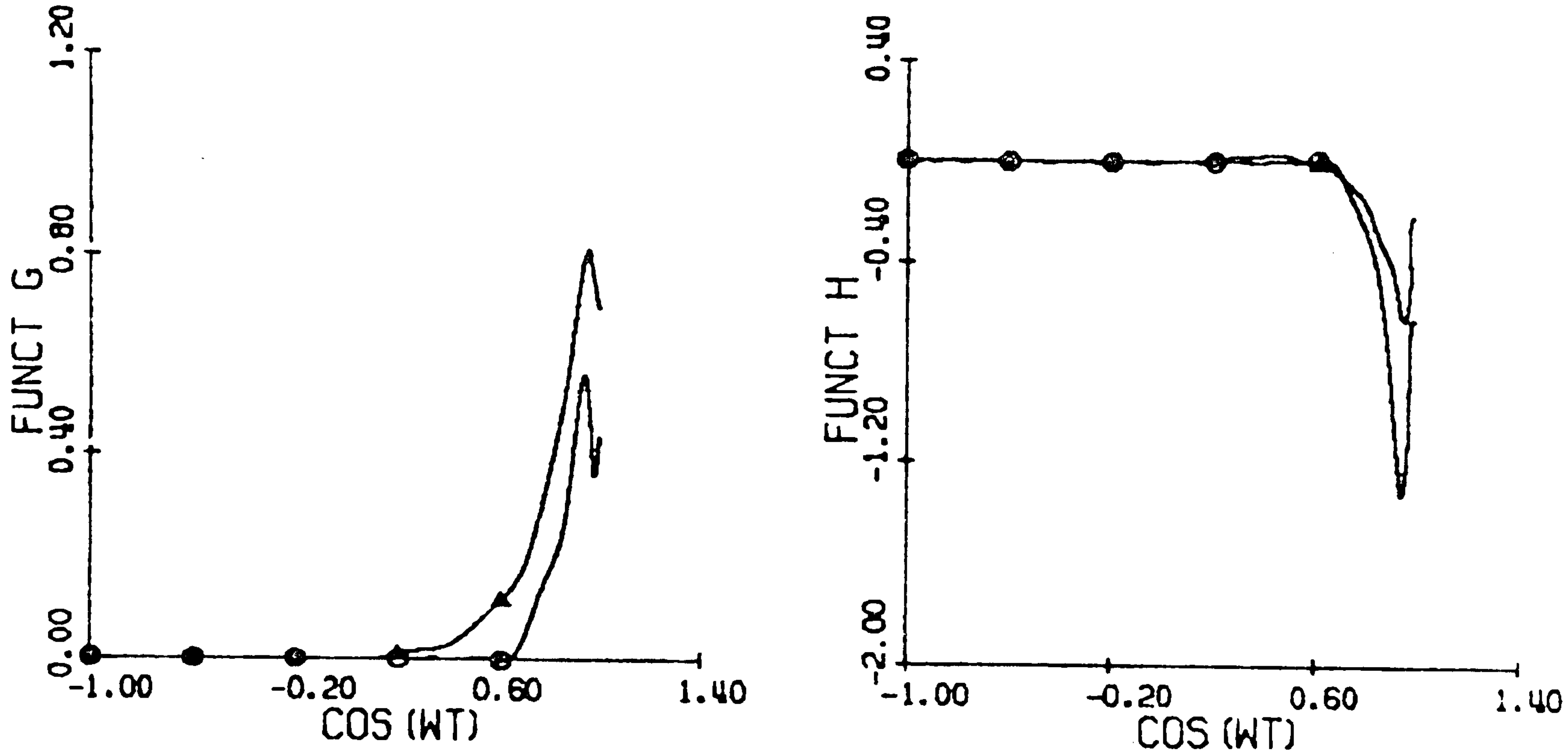

Figure 33d. Plots of 'g' and 'h' curves for the knee flexor muscles, semitendinosus.

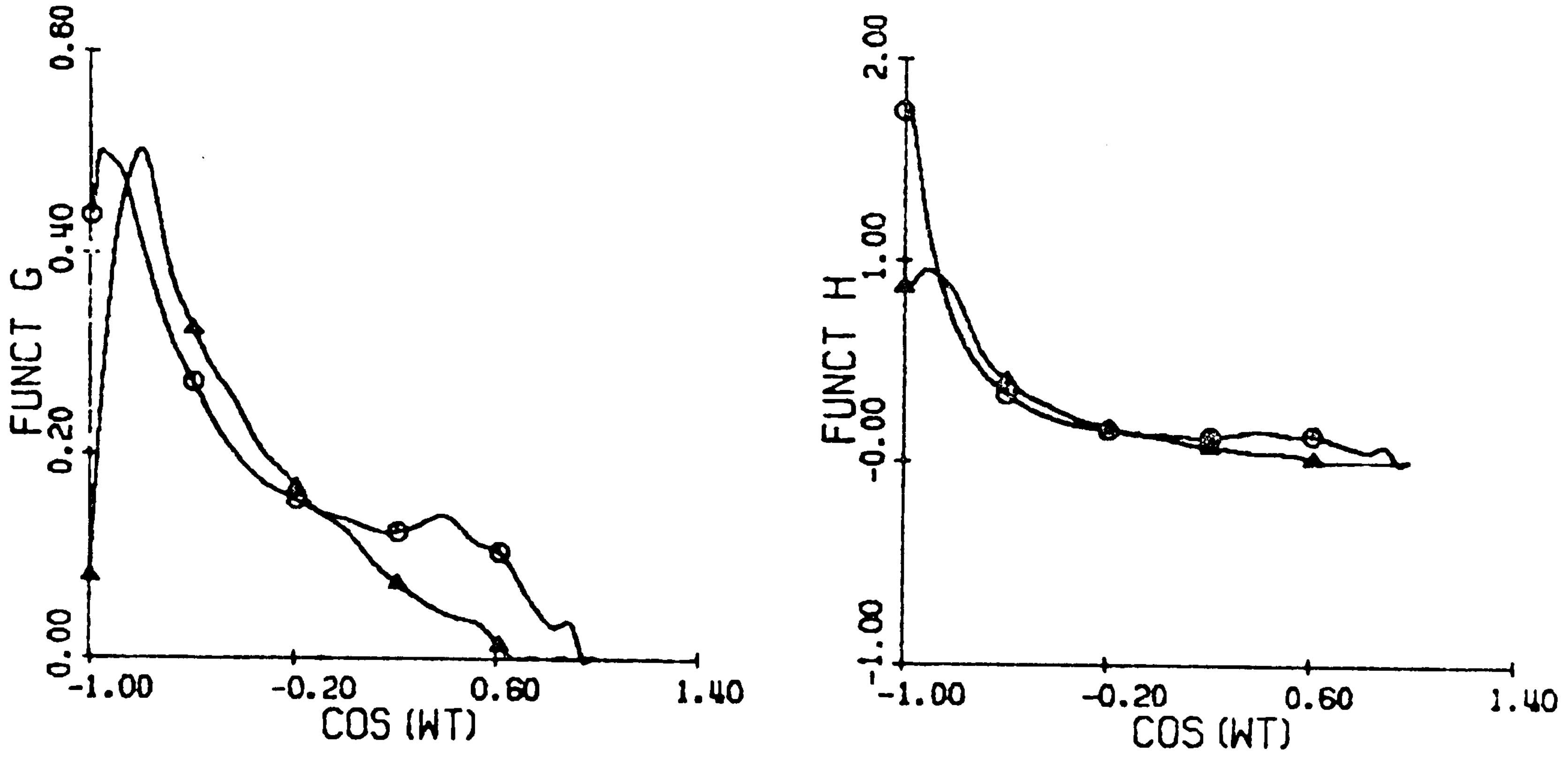

Figure 33e. Plots of 'g' and 'h' curves for the ankle extensor muscle, soleus.

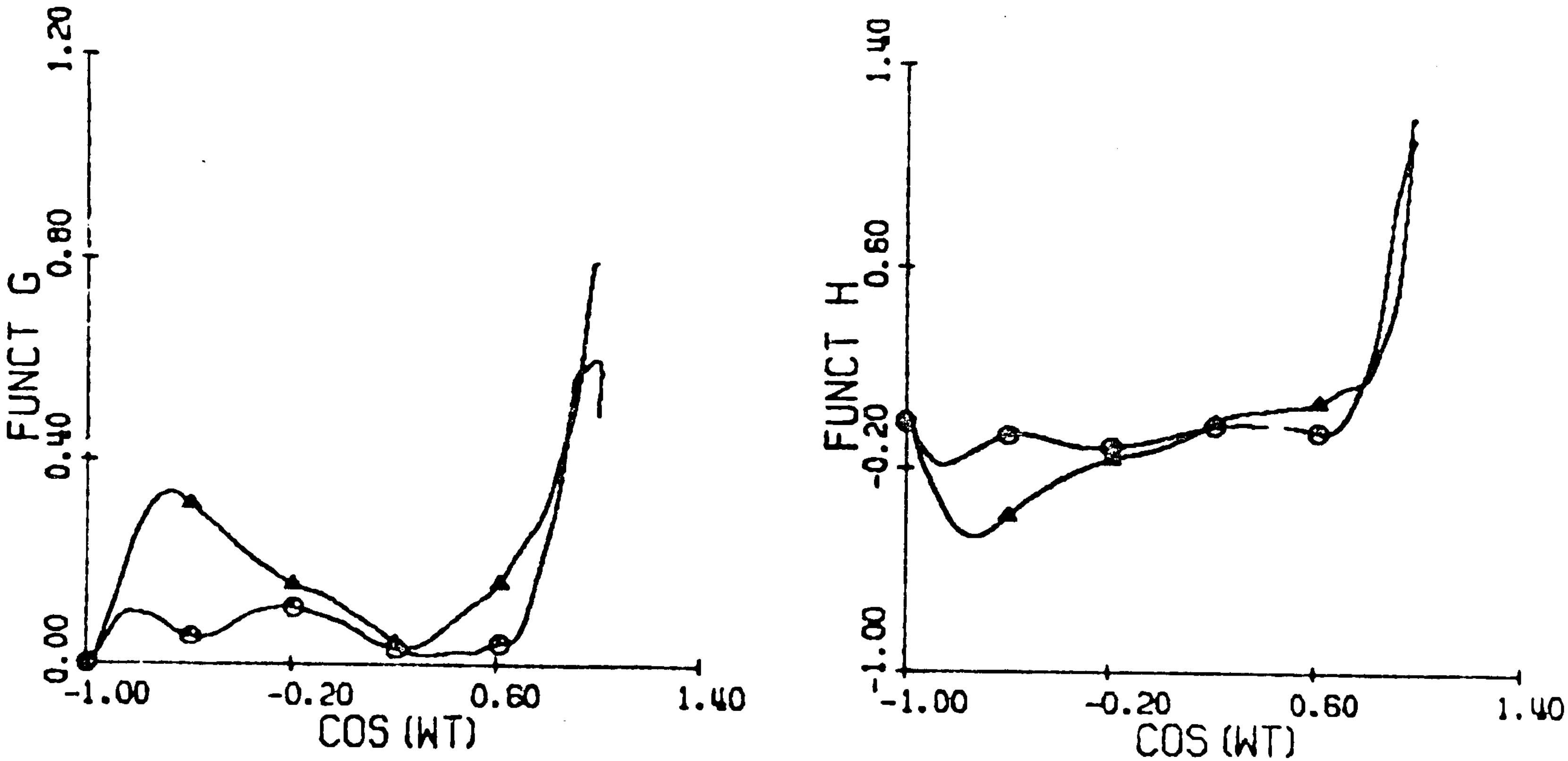

Figure 33f. Plots of 'g' and 'h' curves for the ankle flexor muscle, tibialis anterior.

Figures 34a-34f. These figures contain the plots of 'g' and 'h' curves for walking (□) and climbing stairs (△) for each of the six channels of the Human EMG data set. Each curve in the figures is generated from 100 points joined by a smooth line.

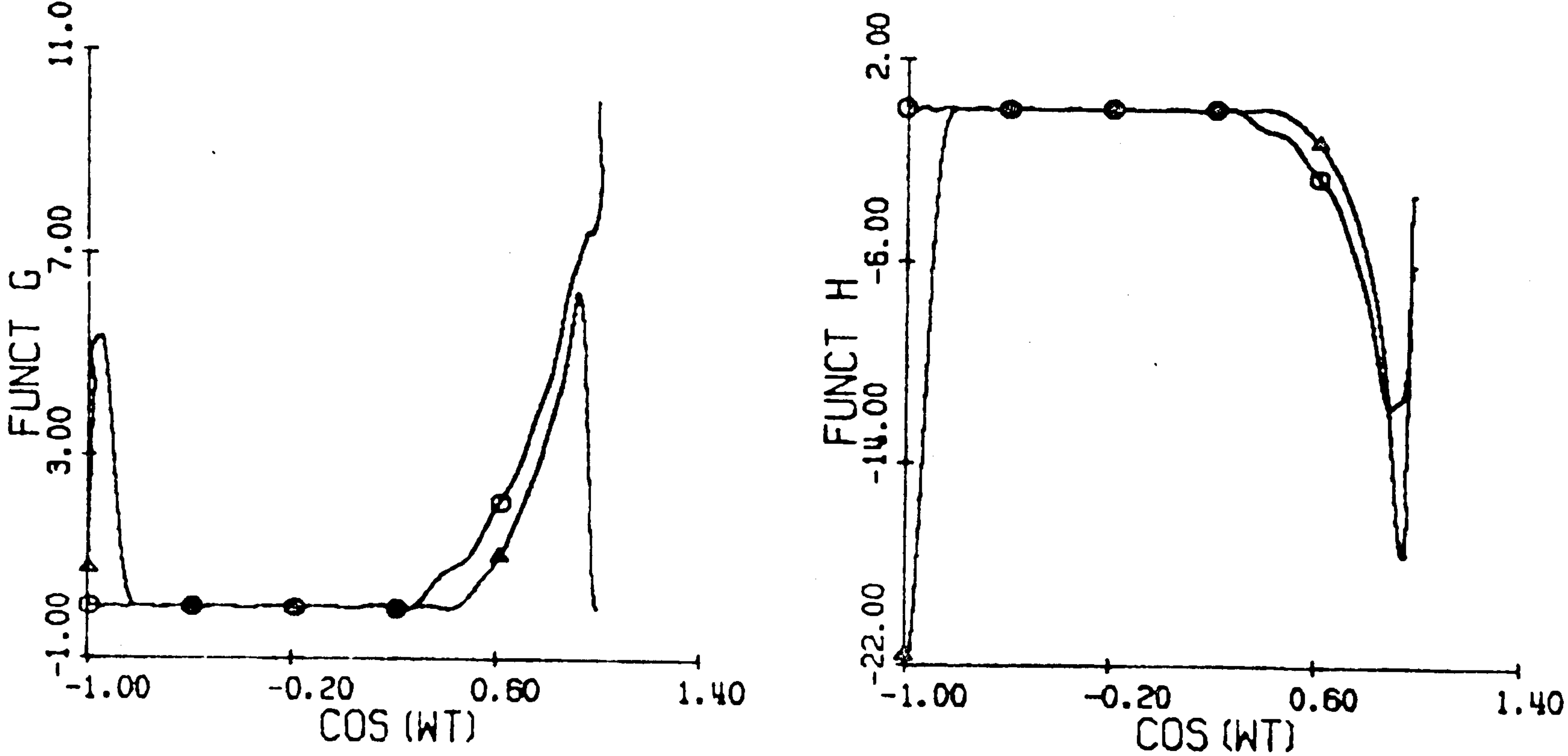

Figure 34a. Plots of 'g' and 'h' curves for the hip extensor muscle, biceps femoris.

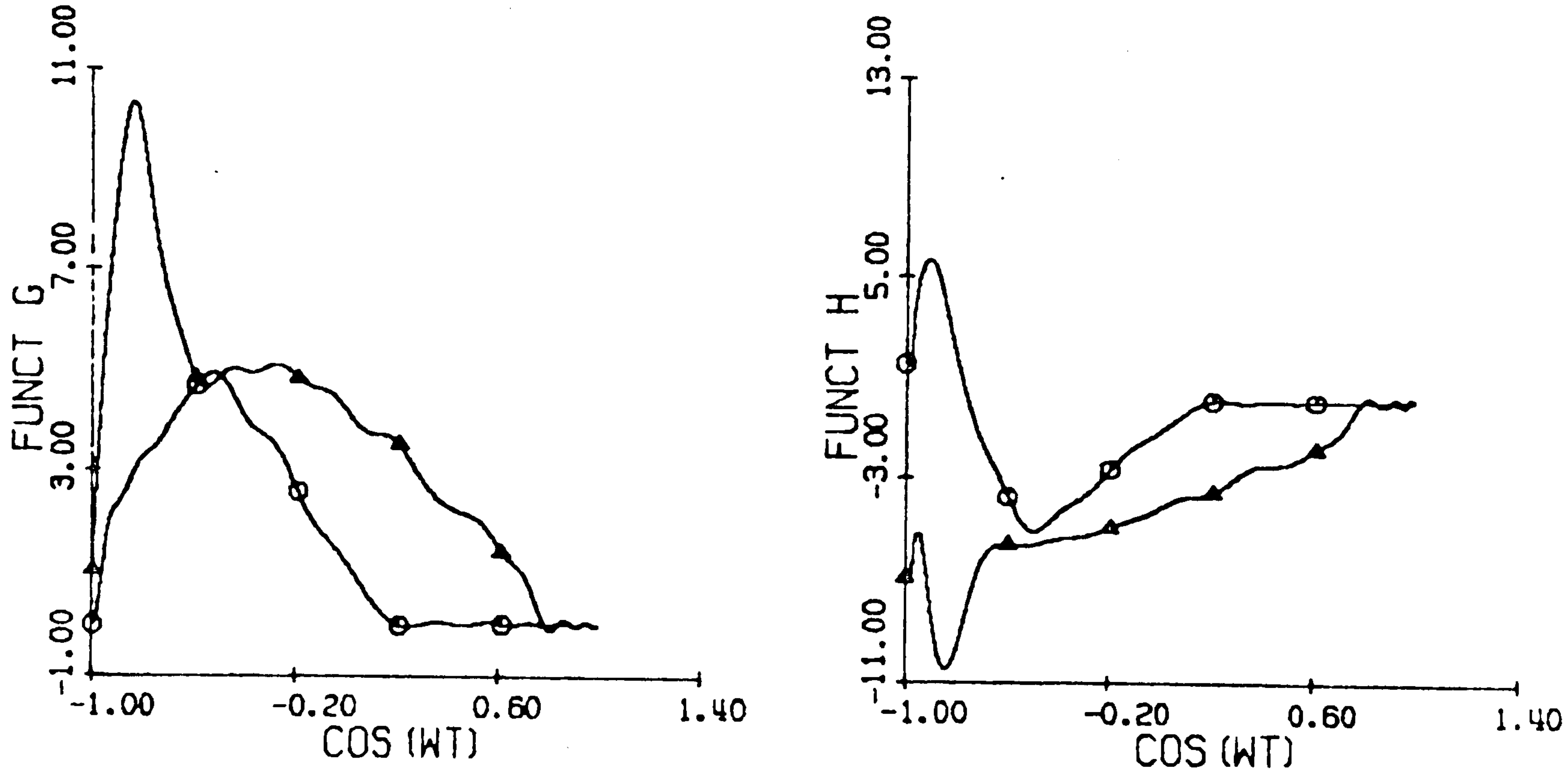

Figure 34b. Plots of 'g' and 'h' curves for the hip flexor muscle, iliacus.

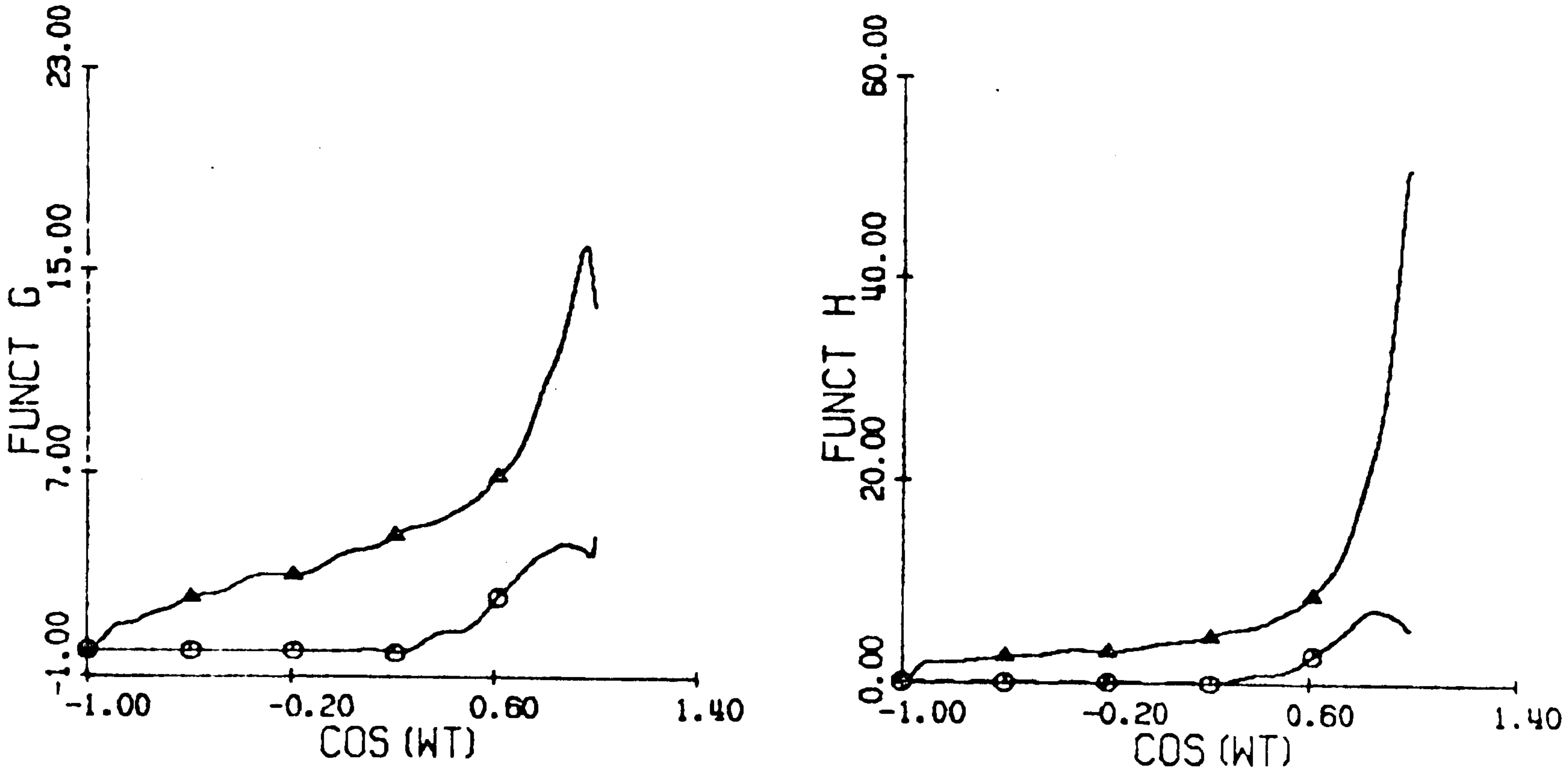

Figure 34c. Plots of 'g' and 'h' curves for the knee extensor muscle, vastus lateralis.

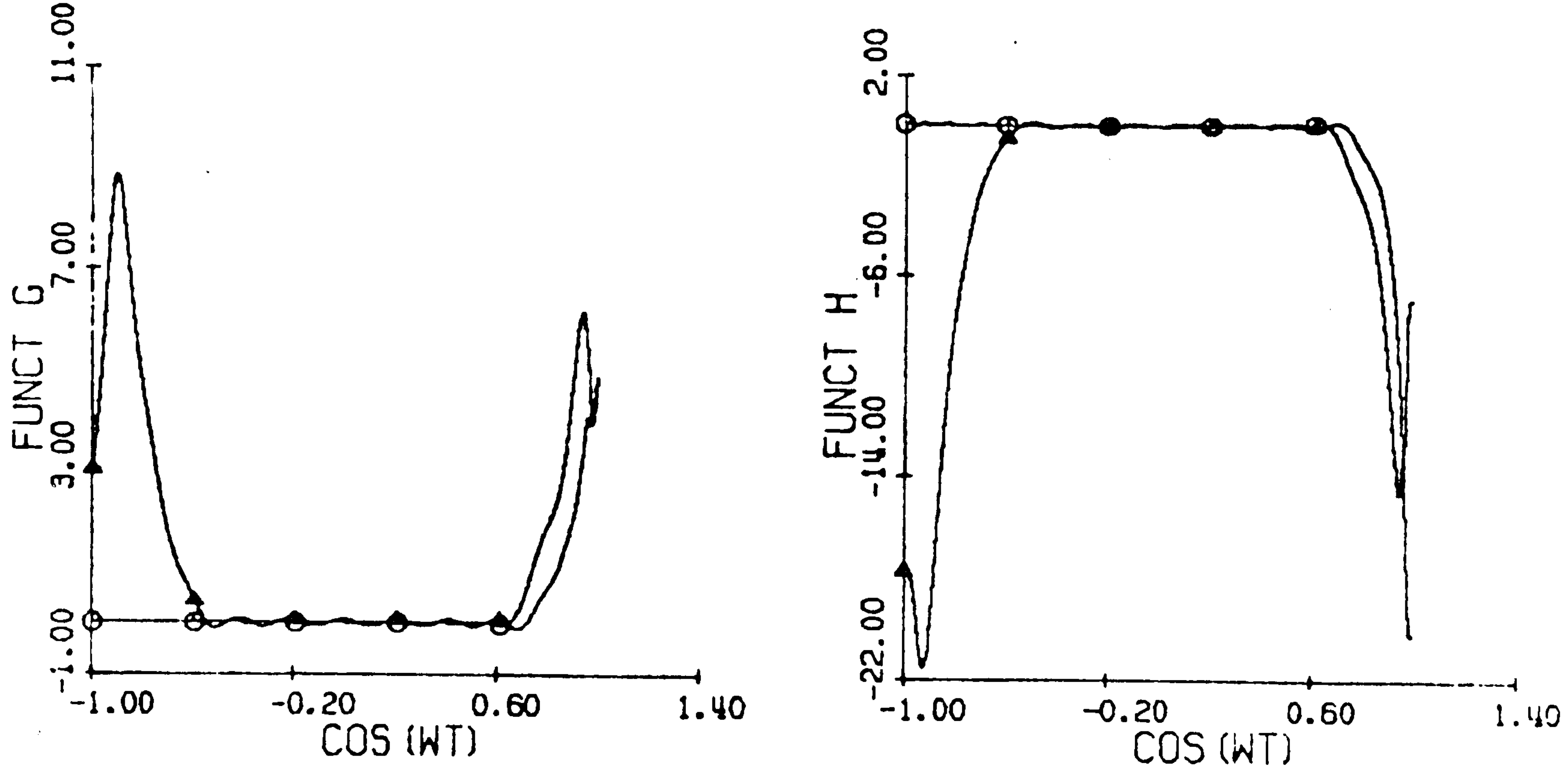

Figure 34d. Plots of 'g' and 'h' curves for the knee flexor muscle, semitendinosus.

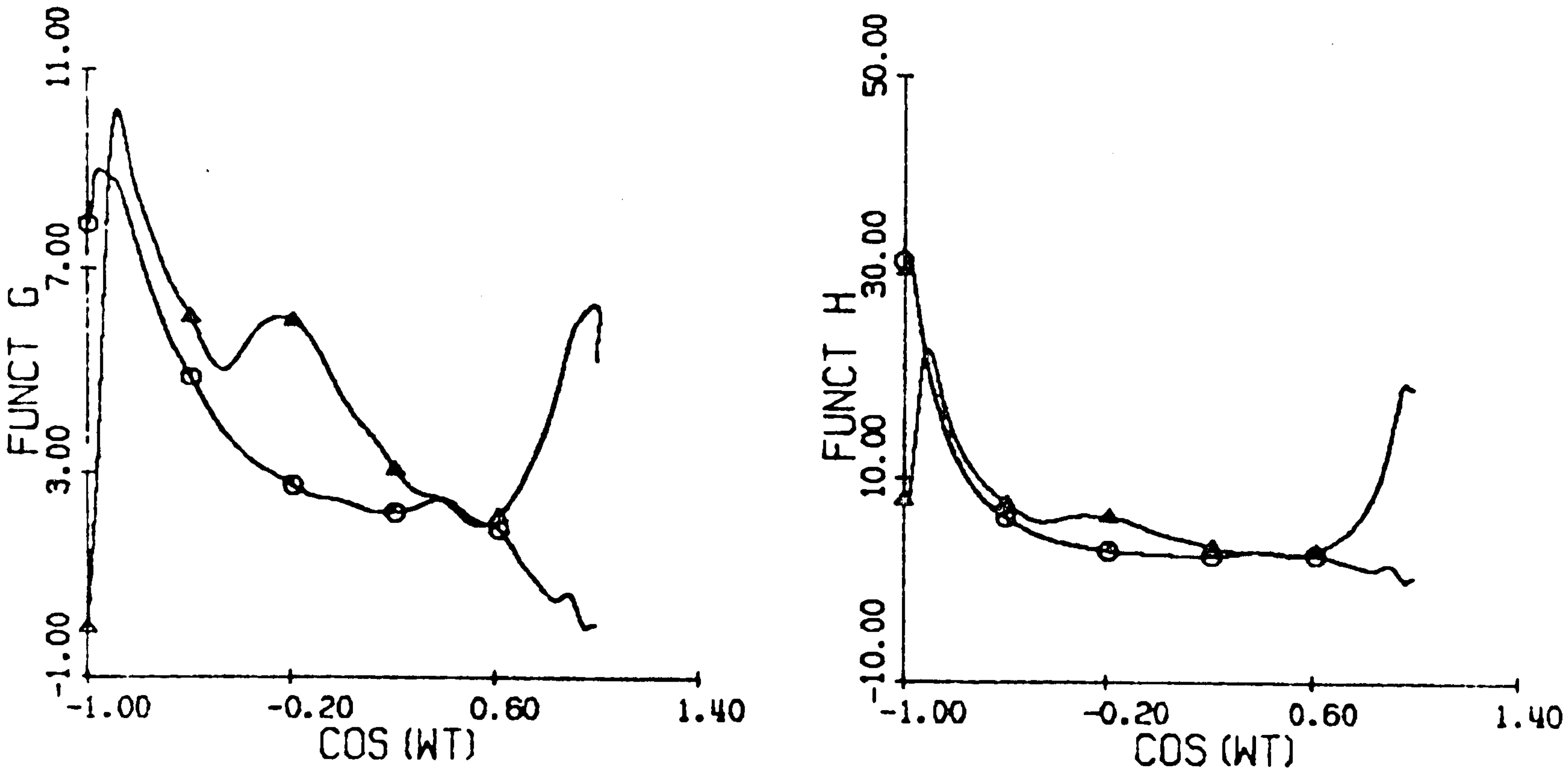

Figure 34e. Plots of 'g' and 'h' curves for the ankle extensor muscle, soleus.

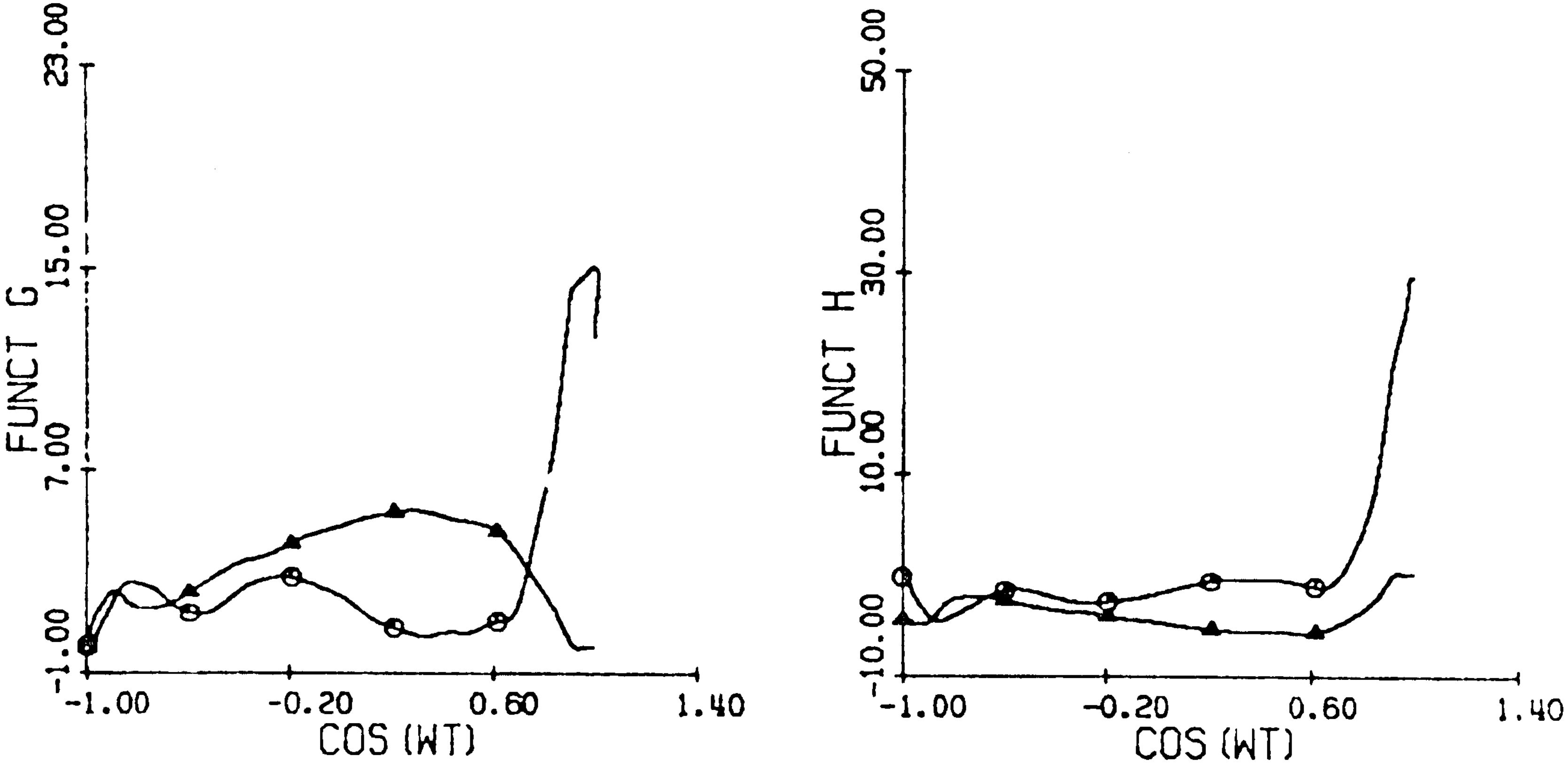

Figure 34f. Plots of 'g' and 'h' curves for the ankle flexor muscle, tibialis anterior.

From visual inspection of these plots, it seems possible that one can modify the 'g' and 'h' functions used for walking to functions that can be used for climbing stairs. Comparison between other forms of rhythmic activities, using EMG and Kinematic data is shown in Appendix C.

5.6 Neural Network Realisation of the Limb Pattern Generator Model

A case has been made for the analytical model's ability to explain experimental results for cats and human subjects. Since one of the goals of this study is to understand the structure of the pattern generator, a valid question that can be asked of the model is ' Can the model be implemented by a neural network ? '. To answer this question, one possible implementation is described below. The first section describes a network for the sine/cosine oscillator and the next one describes a network for the 'g' and 'h' functions.

5.6.1 Network for sine/cosine oscillator

The properties of recurrent cyclic inhibitory networks have been studied extensively (38,39,40). A four neuron network can produce four activity phases each leading the other by 90 degrees (39). These types of network seem to be the most likely candidates for realising the sine/cosine oscillator.

Willis (45) has described a model where each of the four neuron-like elements represents a pool of actual neurons and is described by a first order differential equation. The network model is defined by four coupled first order differential equations (Appendix D). A nonlinearity is introduced into the model since the output cannot be negative. This model was simulated using a CSMP program and Figure 35 shows a simulation result for particular values of the model parameters.

Thus a simple four cell network (Figure 36), based on known neuronal properties, is a suitable analog for the sine/cosine oscillator.

5.6.2 Networks for 'g' and 'h' Functions

The 'g' and 'h' are static nonlinear functions of the amplitude of cosine(ω t). The problem of producing these functions is equivalent to generating an arbitrary function of a single variable. In analog computer simulation of

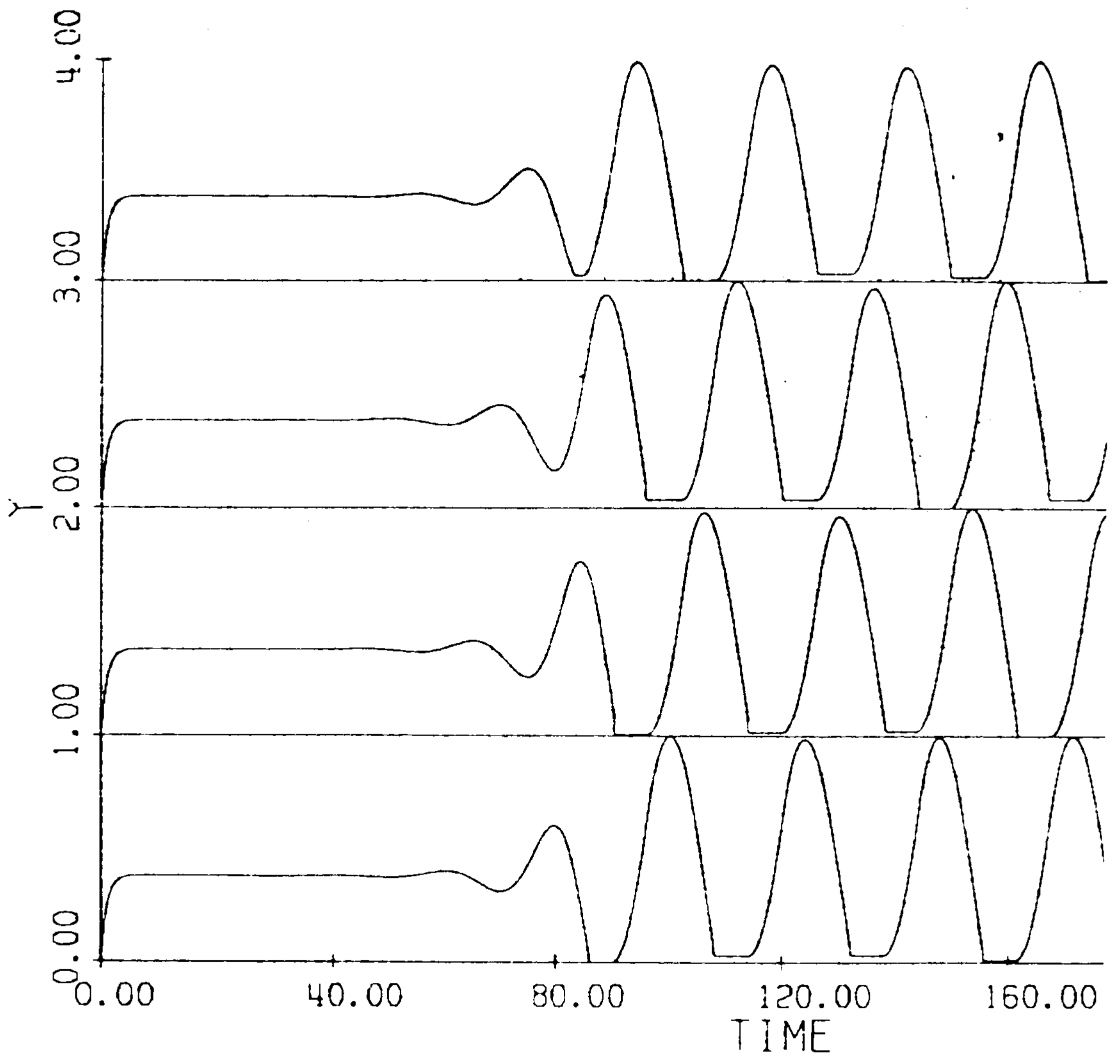

Figure 35. Simulation result of the neural network for the sine/cosine oscillator (k=1,a=0.28, b=0.32,c=0.4,d=0.0)

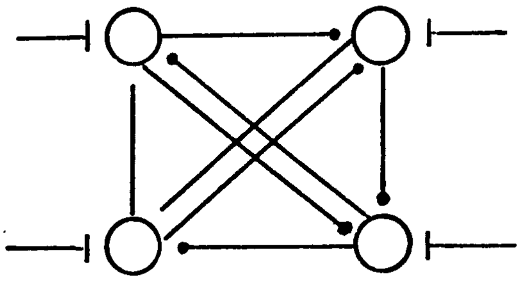

Figure 36. Neural network for the labile sine/cosine oscillator.

models, one is often faced with a similar problem. One solution which is relevant to our problem, is a piece-wise linear approximation of the function by a diode function generator (87). This solution can be directly applied to the problem at hand and is illustrated by the following example.

Let us assume that we wish to implement the function given by the dashed line in Figure 37a with a two segment straight line approximation as shown. It is apparent that this two segment approximation of the function is a sum of separate functions shown in Figure 37b and 37c. The function of Figure 36b can be produced by a neuron with a threshold x_1, gain k_1, and saturation at x_2. The second function (Figure 37c) can be generated by another neuron with a threshold x_2, gain k_2, and saturation above x_3. Thus a parallel network of neurons (Figure 37d) with different threshold, gain and saturation values can, in principle, generate an arbitrary function of a single variable.

Since neurons exhibit a threshold phenomenon and saturation due to the refractory period, this method of producing the 'g' and 'h' functions is feasible.

It is reassuring that a simple neural network implementation of the model can be proposed. This enhances

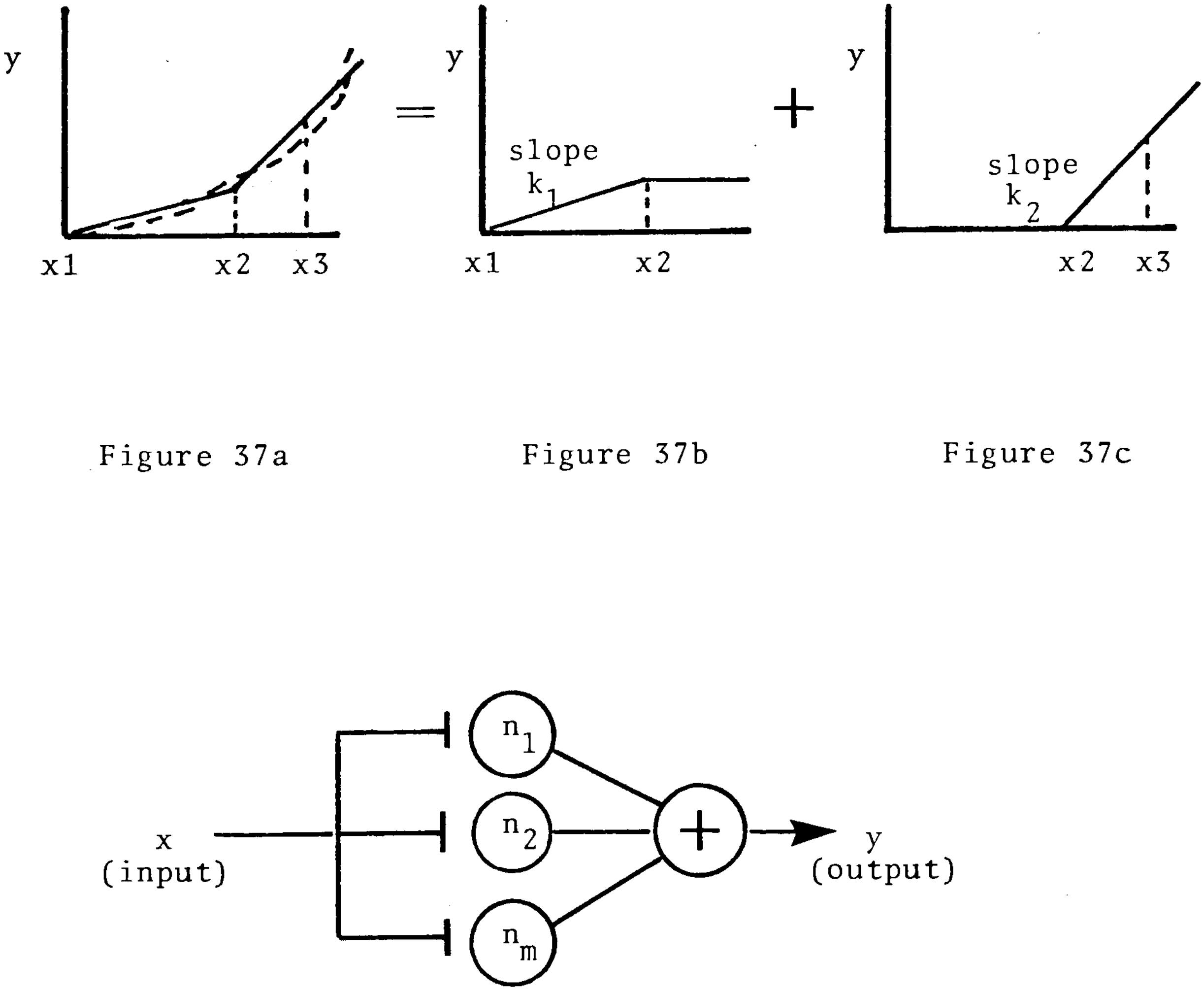

Figure 37a

Figure 37b

Figure 37c

Figure 37d

Figure 37. Neural network realisation of the 'g' and 'h' functions with an illustrative example.

the usefulness of the analytical model. These suggestions are not unique and it would be easy to describe other suitable analogs. Evolution of neural networks in the nervous system has been guided by numerous constraints, including those imposed by phylogeny, ontogeny, and the basic structural and operational limitation of neurons (46). Thus it has been difficult to deduce a network based on the operation of a system, that is known to be anatomically correct. However, the results are very useful in elucidating the operational principles of the system under study.

5.7 Interlimb Corodination in Cats

Upto now we have concentrated on a single hind limb pattern generator. To study the interlimb coordination we concentrate on the sine/cosine oscillators for the two hind limbs.

In normal locomotion along a straight line, despite large variations, two main forms of hindlimb coordination can be observed : alternate mode as in walking and in-phase mode as in gallop (26,27,48). The change from alternate to in-phase gait seems to be abrupt.

The alternate gait would require the sinusoidal output from the two oscillators to be 180 degrees out of phase whereas in-phase gait would require them to be in phase. A simulation of the the oscillators for the two hind limbs was carried out. They were bi-directionally coupled with the coupling coefficients varying from 0 to 1.. The simulation results show that this form of coupling can phase lock the two waveforms but cannot alter the phases to provide alternate and in-phase coupling. Thus this type of interaction cannot coordinate the limbs appropriately.

A solution to this problem can be found in the simulation of the network for the sine/cosine function. The use of four neurons provided us with four sinusoidal outputs each leading the other by 90 degrees. Thus we have two sets of sine/cosine functions that are 180 degrees out of phase. To provide the two forms of coupling, the oscillators of the two limbs are connected as shown in Figure 38. Either the velocity, duration of the extension or the duration of the support phase can probably be a critical factor in determining the switch from alternate to in-phase gait (48).

Another complex form of interlimb coordination occurs when an animal walks along a circular path. This can be studied by having the cat walk on a split treadmill. This

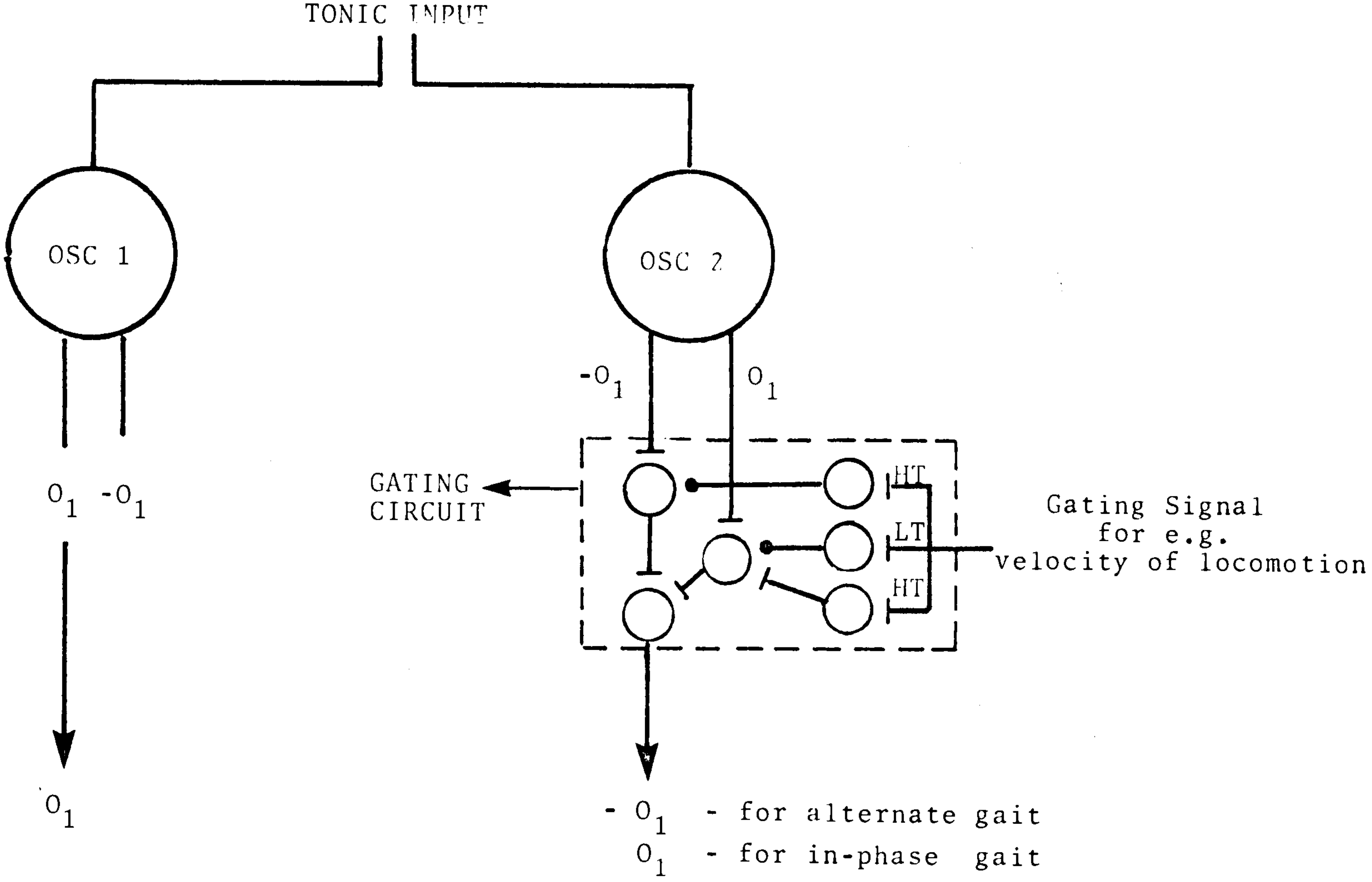

Figure 38. Interlimb coordination between the hindlimbs (osc1 & osc2) for locomotion in a straight line. A possible neural gating circuit is also presented. (LT- low threshold, HT- high threshold)

situation was simulated for two limb oscillators using bidirectional coupling. The two oscilators were 180 degrees out of phase. When the difference in frequency of oscillation was 10%, the simulation result (Figure 39) shows as unstable behaviour. There is no phase locking of the waveforms. But when the difference in frequency of oscillations is two fold, the simulation result (Figure 40) shows a stable phase locked outputs. It also shows that there is an asymmetry in the step cycles of the fast limb. These results have been observed by Kulagin & Shik (88) and Forssberg et al (48).

Researchers have proposed that long ascending and descending propiospinal pathways are the primary substrate for the neural control of forelimb-hindlimb coordination during locomotion (89,90). The trotting form of forelimb-hindlimb coupling is most prevalent in intact cats (89). Diagonal couplet coordination may be considered to be a subset of the trotting mode of coupling (89). It may be that the initial condition accounts for the phase difference between the forelimb and the hindlimb , and the propiospinal pathways provide the bidirectional coupling to phase lock the oscillations of the two limbs.

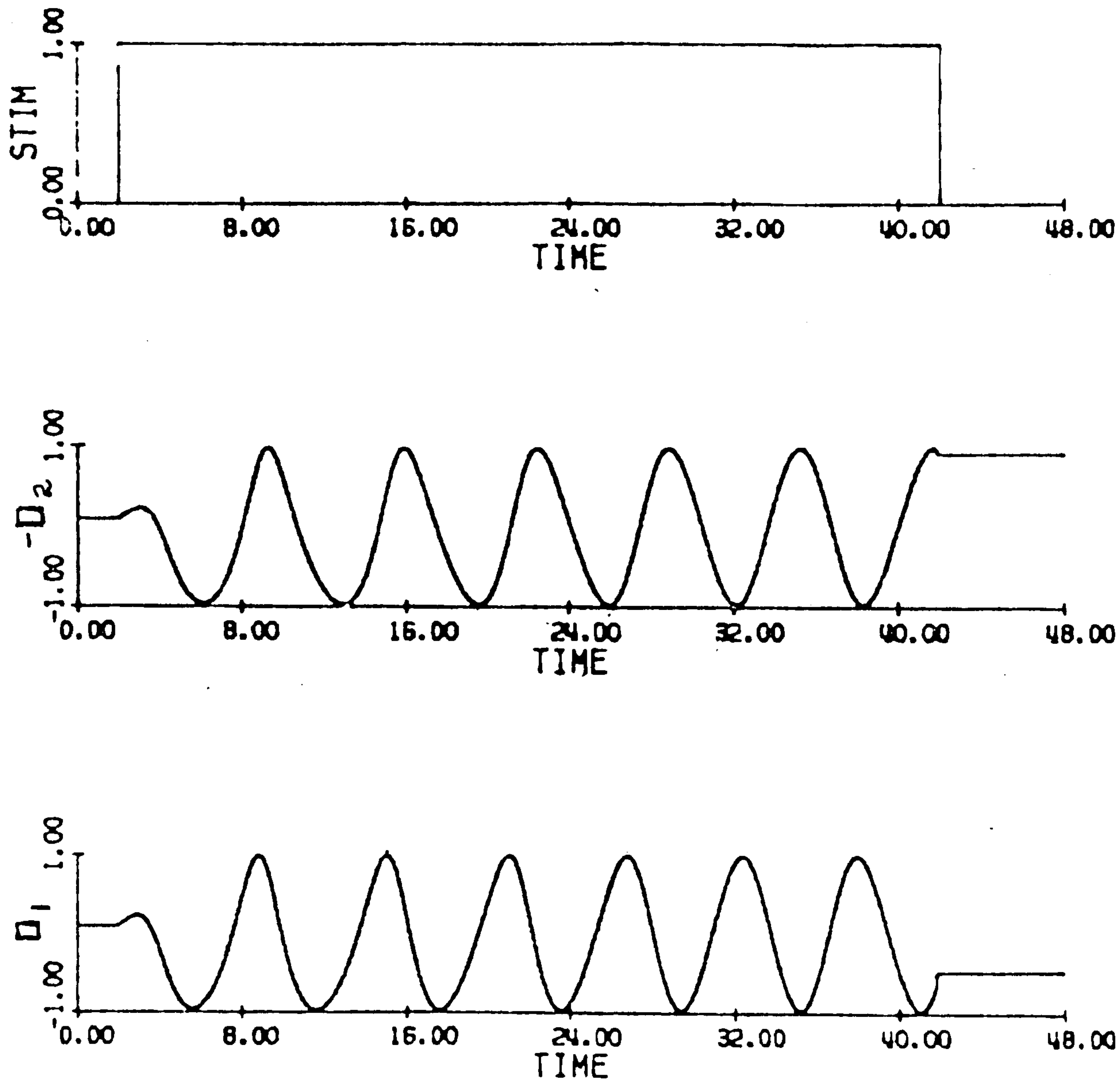

Figure 39. Simulation result of interlimb coordination between the hindlimbs during locomotion on a split treadmill (10 % speed difference between the two belts).

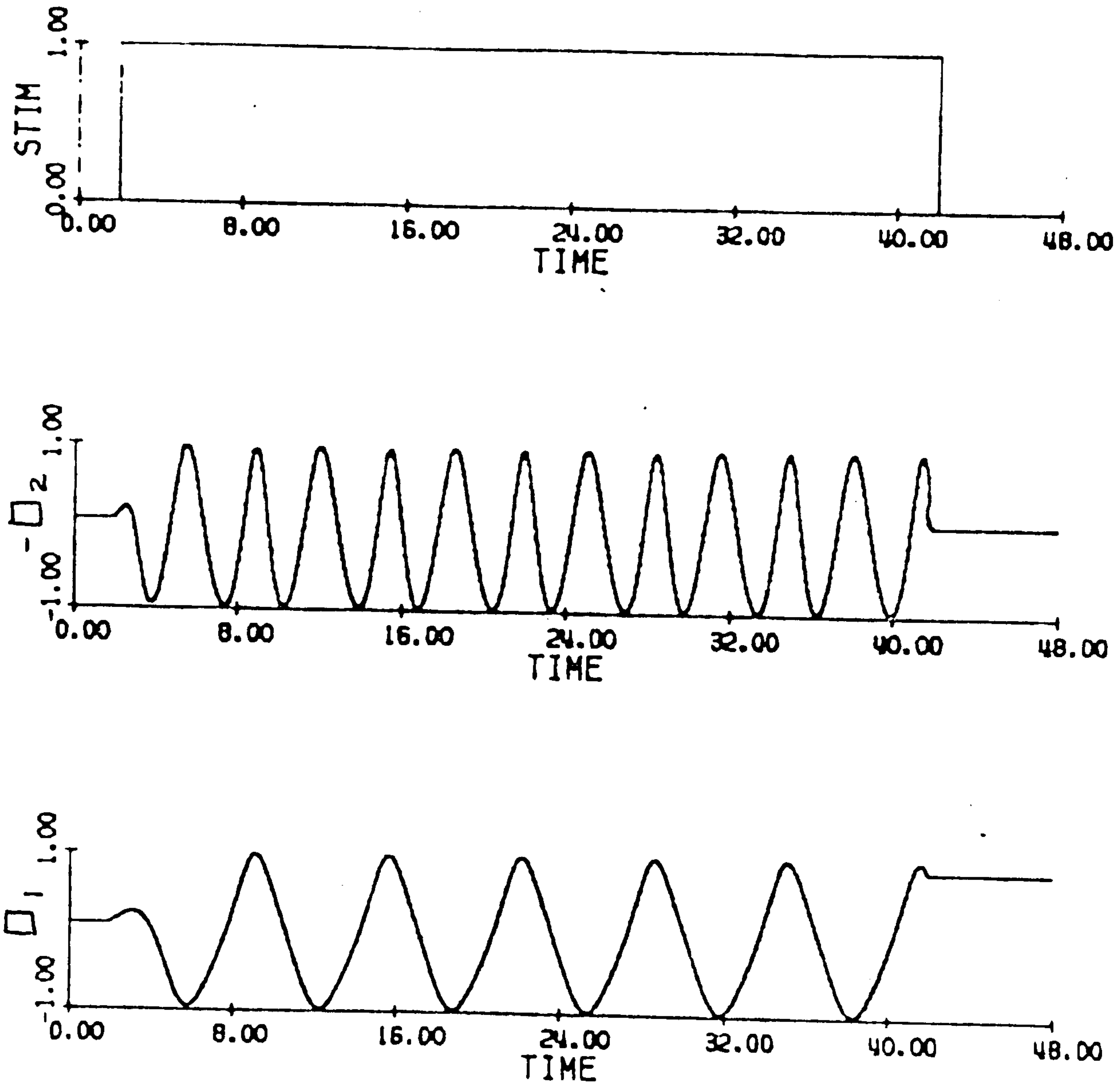

Figure 40. Simulation result of interlimb coordination between the hindlimbs during locomotion on a split treadmill (one belt moving at twice the speed of the other).

5.8 Limitations of the Model

The data recorded from the cat preparations were affected by other descending tract inputs besides the tonic input and by peripheral feedback. Since research has demonstrated that these inputs to the pattern generator are not necessary (26,27), the problem is not serious. Despite this knowledge, one would prefer to collect the generator ouptut under ideal conditions of only tonic input and no peripheral feedback. There are practical problems in getting a successful preparation that will meet these conditions (30,74).

Though difficult, locomotor activity in a deafferented preparation has been studied by other researchers (26,30). Their quantitative results can be accomodated by the model easily. For instance, it is known that in the absence of peripheral feedback, the frequency of rhythmic activity of the limb is slowed down (26). It has been suggested (70) that nonspecific afferent input may provide some extra drive to the pattern generator. The simulation result of Figure 31 show the reduction of frequency with decrease in the tonic drive to the pattern generator. This observation indicates that the peripheral feedback acts on the sine/cosine oscillator. Does it also affect the 'g' and 'h' functions ?

Grillner (30) has observed no qualitative difference in the muscle activity with and without feedback. This would suggest that the 'g' and 'h' functions are not affected by peripheral feedback. This needs to be confirmed by quantitative analysis of the data.

The phase dependent, compensatory reaction to a mechanical or electrical stimulus is an important aspect of the locomotor behaviour. These reactions have been reviewed in the first chapter. It has been suggested (91) that the compensatory response is controlled by the spinal locomotor generator. This behaviour was not studied experimentally, but model simulation studies were carried out.

The behaviour of the sine/cosine oscillator that is disturbed by a rectangular pulse was studied. This oscillator representing one hind limb was bidirectionally coupled to the other hind limb oscillator. The simulation results are shown in Figure 41. The response of the stimulated oscillator is always a transient increase in the amplitude of the sine wave. Depending on which part of the step cycle the stimulus is applied, one either gets an increase in flexor muscle activity or an increase in the extensor muscle activity. This follows from the model. Thus

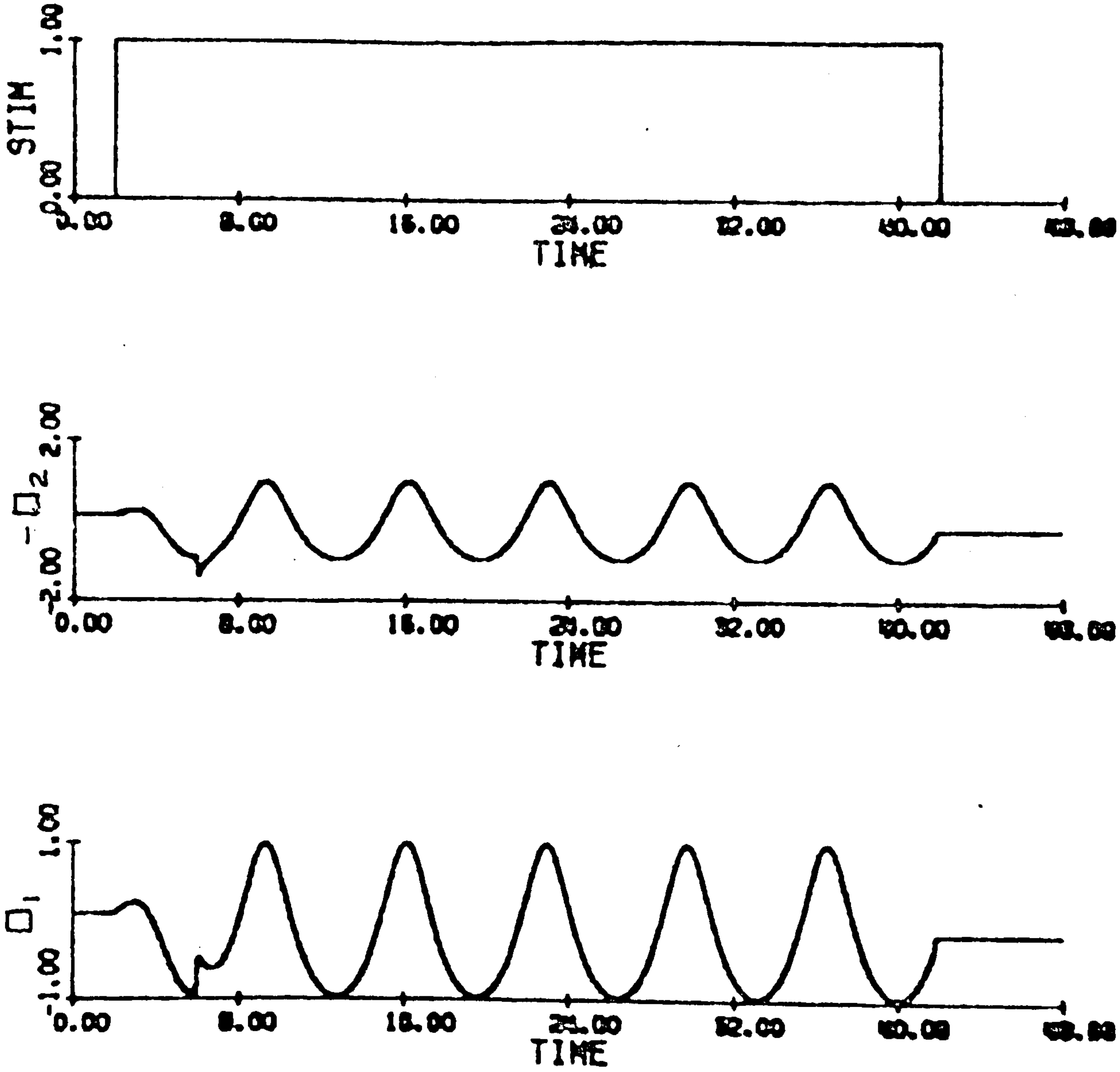

Figure 41. Simulation result of the bidirectionally coupled limb oscillators disturbed by a rectangular pulse.

the phase dependant compensatory response seems to be a property of the oscillator. But there is one problem. As seen from the simulation result, the disturbance introduces a phase change in the output of the oscillator. Duysen & Stein (37) have observed that after the corrective response, the disturbed limb regains its phase relationship with the other limb. Bidirectional coupling could not correct this phase change. But it is known that whenever a stimulus evokes an ipsilateral flexor reaction during swing, a crossed extensor activation also occurs (91). This effect on the other limb could aid in aligning the phase of the stimulated limb with the other limb (Figure 41).

The model assumes only six outputs from the pattern generator. There are more than six muscles involved in locomotion. As seen from the model, adding more muscles would increase the number of nonlinear function modules. The basic structure of the model will not alter. It may be that the theory of basis functions could be useful in finding a common denominator in the synergies observed during locomotion.

It is evident from the above discussion that though there are limitations to this study, they do not diminish the analytical model's usefulness.

5.9 Discussion

The thesis started with the concept that analytical modelling of the pattern generators in mammals would provide a useful basis for studying and understanding the system. Though tacit modelling is always associated with experimental design, measurements, description, and interpretation of results, this was a specific attempt at analytical modelling designed to complement experimental neurophysiology.

The analytical model derived for the limb pattern generator is able to explain a large body of experimental results obtained not only by the author but by other researchers as well. This ability to focus experimental evidence and interpretations into a coherent, parsimonious view, indicates the usefulness of the model. The model is amenable to simulation studies and hence may be useful. Another attractive feature of the model is that it can be realised by a neural network. Thus it is not only analytical but also physiologically feasible.

Though the model cannot be claimed to be unique, it is an adequate representation of the system based on the present knowledge. Thus, it can be said that the goals of this thesis have been met. It is hoped that the model has provided some new insights and will be an useful tool for future studies.

CHAPTER VI

CONCLUSIONS AND SUGGESTIONS FOR FURTHER RESEARCH

6.1 Conclusions

In this thesis an analytical model of a limb pattern generator has been described. The model generator is considered to have one input and six outputs. The only input is tonic and is treated as a signal level. For each of the three joints, a flexor and extensor output in the form of a general periodic waveform is used. The model suggests that the limb pattern generator consists of a labile sine/cosine oscillator that produces the fundamental frequency of the output in response to a tonic signal. The output of this oscillator is then fed into modules for each muscle used in the study, to produce the output pattern that we observe during locomotion.

The model is able to explain experimental data collected in this study. Computer simulation of the model for interlimb coordination produced results in concurrence with the observations made by other researchers. A possible neural implementation of the model has also been suggested.

6.2 Suggestions for Further Research

Some possible areas of the further research which arise from this thesis are :

a) A rigorous quantitative analysis of myoelectric signal recorded from a deafferented cat preparation needs to be done. The effect of feedback on the nonlinear functional modules can thus be determined.

b) A similar analysis should be done on the data obtained from a spinal cat preparation. Along with the results obtained from step (a) , this would help establish the pattern generator output with only tonic input.

c) It may be helpful to study a single joint in detail. The EMG from all the muscles acting at this joint should be recorded during locomotion and analysed. This would be helpful in understanding a functional unit of the generator better.

d) Transition between two forms of rhythmic activity such as walking and climbing stairs for humans should be studied in detail. This could shed light on how the locomotor system adapts to new activities.

APPENDIX A

DETERMINATION OF BASIS FUNCTIONS

In this appendix the theoretical determination of the basis functions is examined. This is based on the book by Young & Calvert (55) and the paper by Fukunaga & Koontz (56).

Let $o_i(t)$ $(i=1,2,\ldots,N)$ be the set of time functions represented by n discreet sampling points. Then the functions may be represented as column vectors

$$o_i = \begin{bmatrix} o_i(t_1) \\ o_i(t_2) \\ \cdot \\ \cdot \\ \cdot \\ o_i(t_n) \end{bmatrix} \qquad (i=1,2,\ldots\ldots,N) \;\ldots\; (1)$$

These functions can be expanded as a linear combination of basis functions, u_j (t) $(j=1,2,\ldots,N)$, as follows :

$$o_i = \sum_j c_{ij} \cdot u_j \qquad \ldots\ldots\ldots\ldots \quad (2)$$

where U_j is a vector representation of the jth. basis function as

$$U_j = \begin{bmatrix} u_j(t_1) \\ u_j(t_2) \\ \cdot \\ \cdot \\ \cdot \\ u_j(t_n) \end{bmatrix} \quad (j=1,2,\ldots\ldots,N) \quad .. \quad (3)$$

The coefficients c_{ij} in equation 2 are given by the following equation

$$c_{ij} = U_j^T \cdot O_i \quad \ldots\ldots\ldots\ldots \quad (4)$$

where the U_j^T represents the transpose of U_j.

The basis functions $u_j(t)$ $(j=1,2,\ldots,N)$ are the eigenvectors of the autocorrelation matrix, S, given by

$$S = E_i \left[O_i \cdot O_i^T \right] \quad \ldots\ldots\ldots \quad (5)$$

where O_i^T is the transposed vector of O_i, and

E represents the operation in which the expected value (average) of the sum in the square bracket is taken.

Since the basis functions are eigenvectors they are mutually orthonormal. Thus

$$U_j^T \cdot U_j = \begin{cases} 1 & \text{for} \quad i = j \\ 0 & \text{for} \quad i \neq j \end{cases} \qquad \ldots. \quad (6)$$

The basis functions U_j were calculated using a standard subroutine for evaluating the eigenvectors. From equations 4 & 6 , the expansion of the time functions O_i given by equation 2 follows.

APPENDIX B

SOLUTION OF THE SINE/COSINE RELAXATION OSCILLATOR

In this part of the thesis, the solution for the second order system, S (x_1, x_2), defined by the equations :

$$\dot{x}_1 = \omega \cdot [\ x_2 + x_1 \ (1 - x_1^2 - x_2^2)\ ] \quad \ldots\ldots \quad (1)$$

$$\dot{x}_2 = \omega \cdot [-x_1 + x_2 \ (1 - x_1^2 - x_2^2)\ ] \quad \ldots\ldots \quad (2)$$

is developed. This is based on the work by many authors (61,62,63).

Using polar coordinate transformation given by the equations

$$r = \sqrt{x_1^2 + x_2^2} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (3)$$

$$\phi = \tan^{-1} (x_1 / x_2) \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (4)$$

the second order system S (x_1, x_2) is transformed into

$$\dot{r} = \omega \cdot r \cdot (1 - r^2) \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (5)$$

$$\dot{\phi} = \omega \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (6)$$

where $\dot{r}$ is the first derivative of r with respect to time.

Excluding $r = 0$, equation 5 shows that $r = 1$ is the only positive value of r for which $\dot{r} = 0$. Also from equation 5 it follows that $\dot{r} < 0$ for all $r > 1$ and $\dot{r} > 0$ for all $0 < r < 1$. Hence all solutions approach $r = 1$ as a limit.

At $r = 1$, equations 1 & 2 reduce to

$$\dot{x}_1 = \omega . x_2 \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (7)$$

$$\dot{x}_2 = -\omega x_1 \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (8)$$

Hence in the limit, we have

$$x_1(t) = \text{sine}\ (\omega t + \theta) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (9)$$

and

$$x_2(t) = \cos(\omega t + \theta) \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (10)$$

where θ is the constant phase angle. By choosing appropriate initial time, this phase angle can be set to zero.

APPENDIX C

ADDITIONAL RESULTS FROM THE THESIS

In the following pages, additional results from the data collected for the thesis are presented. The data were analysed according to the procedures listed in the main text. The description of the figures is given below.

Figures C1a-C1f. These figures contain the plots of 'g' and 'h' curves for the three speeds of locomotion (□ - 0.91 c/s, △ - 1.1 c/s, ✱ - 1.43 c/s) for each of the six channels of the cat EMG data set. Each curve is generated from 100 points joined by a smooth line.

Figures C2a-C2c. These figures contain the plots of 'g' and 'h' curves for the three speeds of locomotion (□ - 0.68 c/s, △ - 0.94 c/s, ✱ - 1.00 c/s) for each of the three channels of the human kinematic data set. Each curve is generated from 100 points joined by a smooth line.

Figures C3a-C3c. These figures contain the plots of 'g' and 'h' curves for the three different rhythmic activities of the lower limbs (□ - walking, △ - cycling, ✱ - hopping) for each of the three channels of the human kinematic data set.

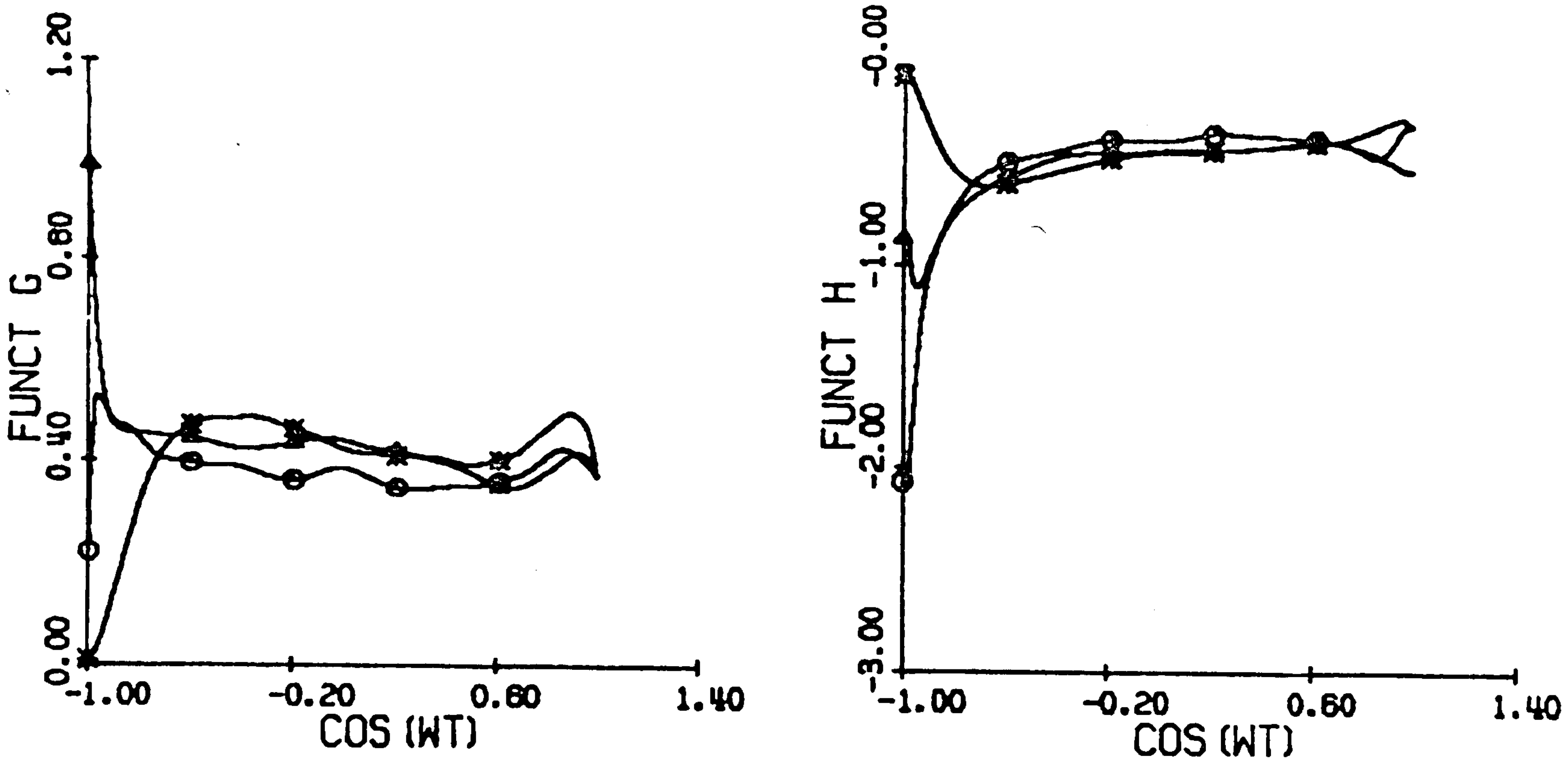

Figure C1a. Plots of 'g' and 'h' curves for three speeds of walking for the ankle extensor muscle channel.

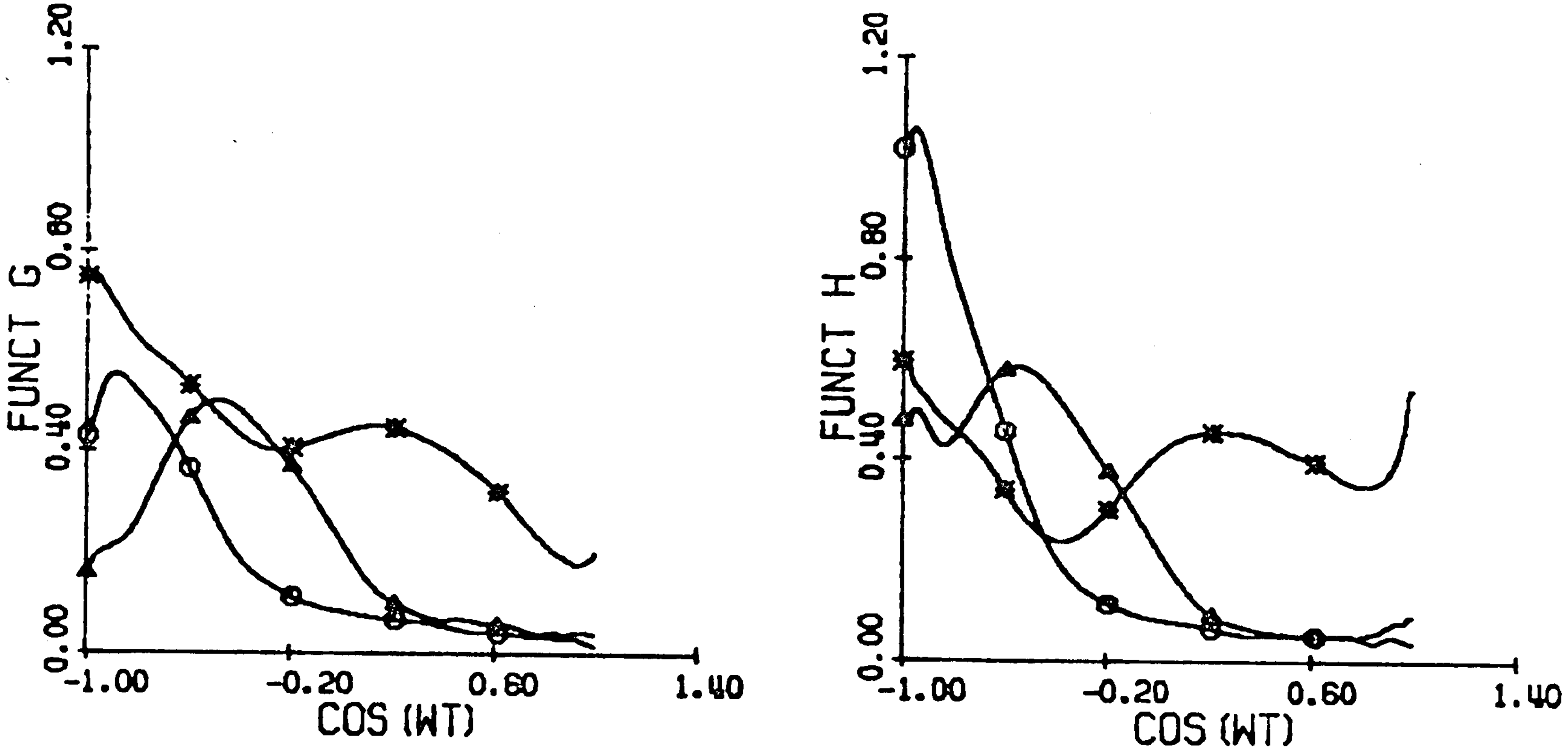

Figure C1b. Plots of 'g' and 'h' curves for three speeds of walking for the ankle flexor muscle channel.

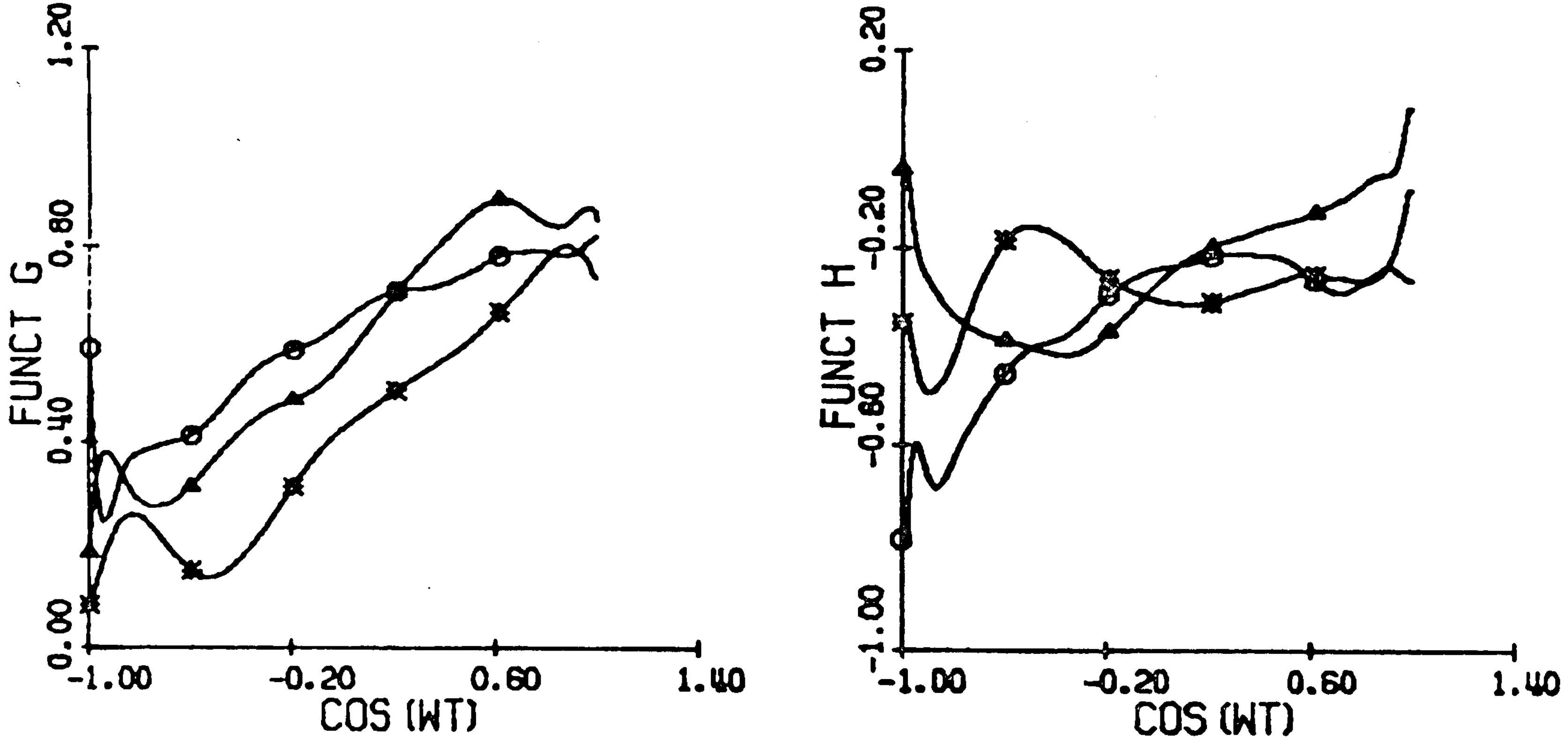

Figure C1c. Plots of 'g' and 'h' curves for three speeds of walking for the knee extensor muscle channel.

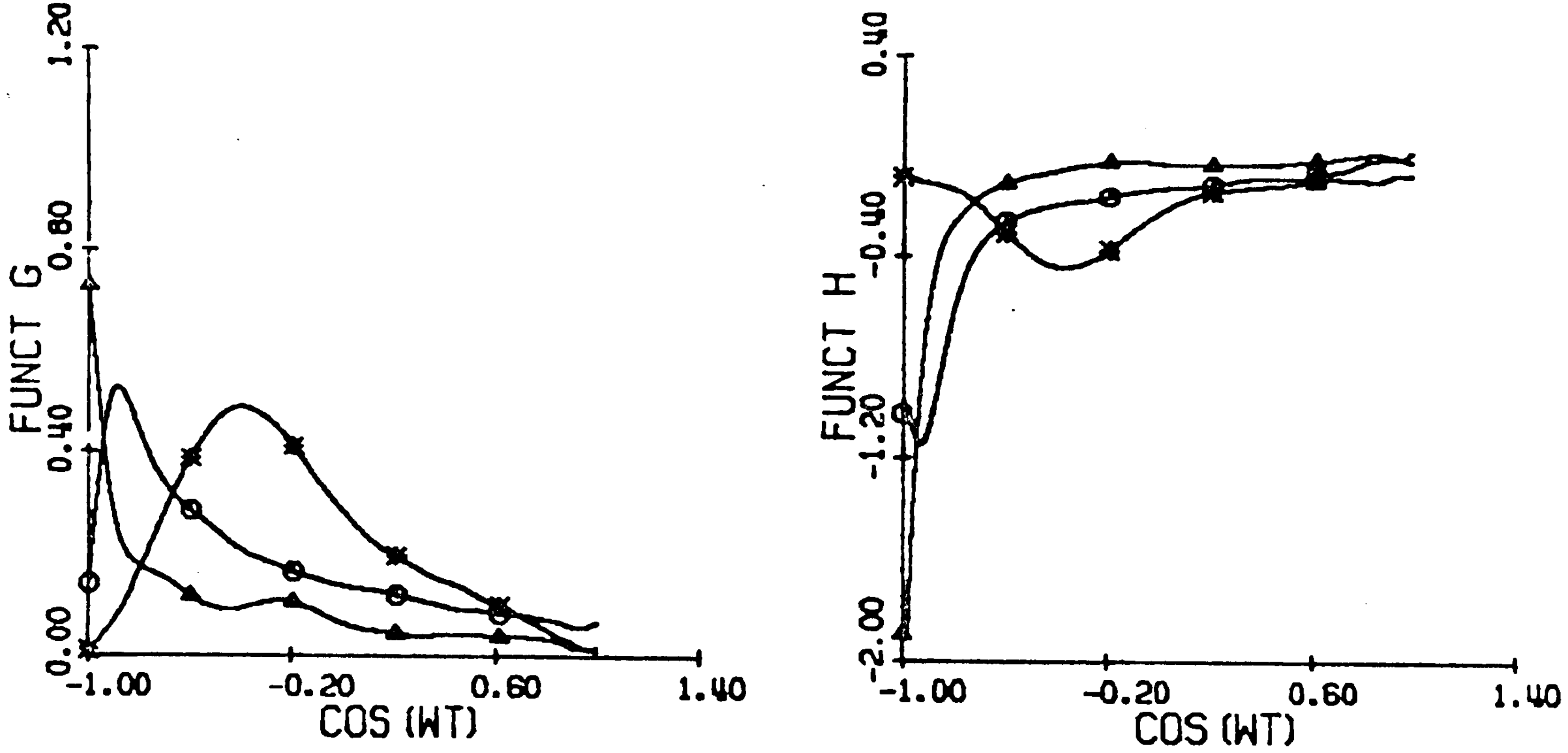

Figure C1d. Plots of 'g' and 'h' curves for three speeds of walking for the knee flexor muscle channel.

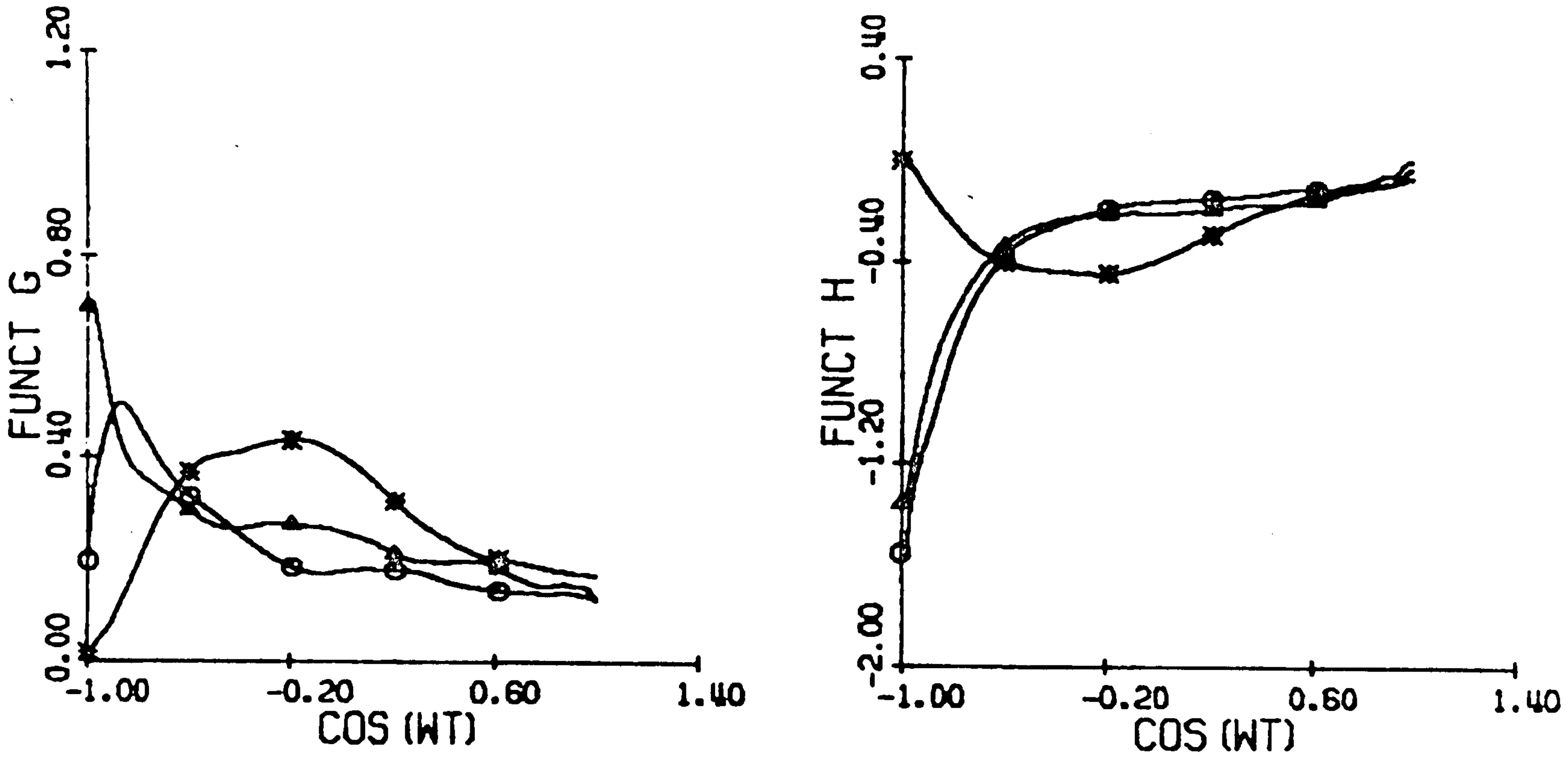

Figure C1e. Plots of 'g' and 'h' curves for three speeds of walking for the hip extensor muscle channel.

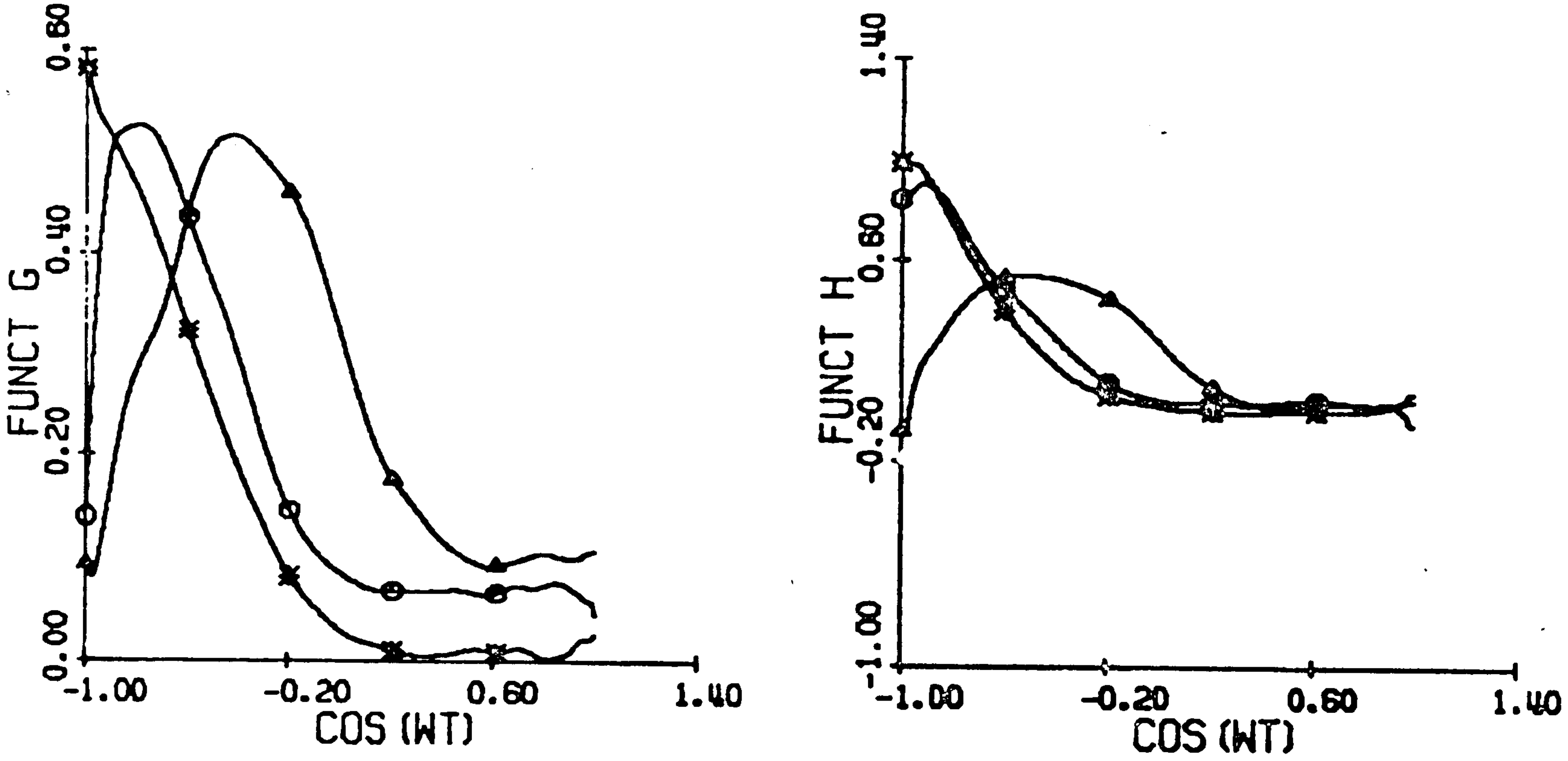

Figure C1f. Plots of 'g' and 'h' curves for three speeds of walking for the hip flexor muscle channel.

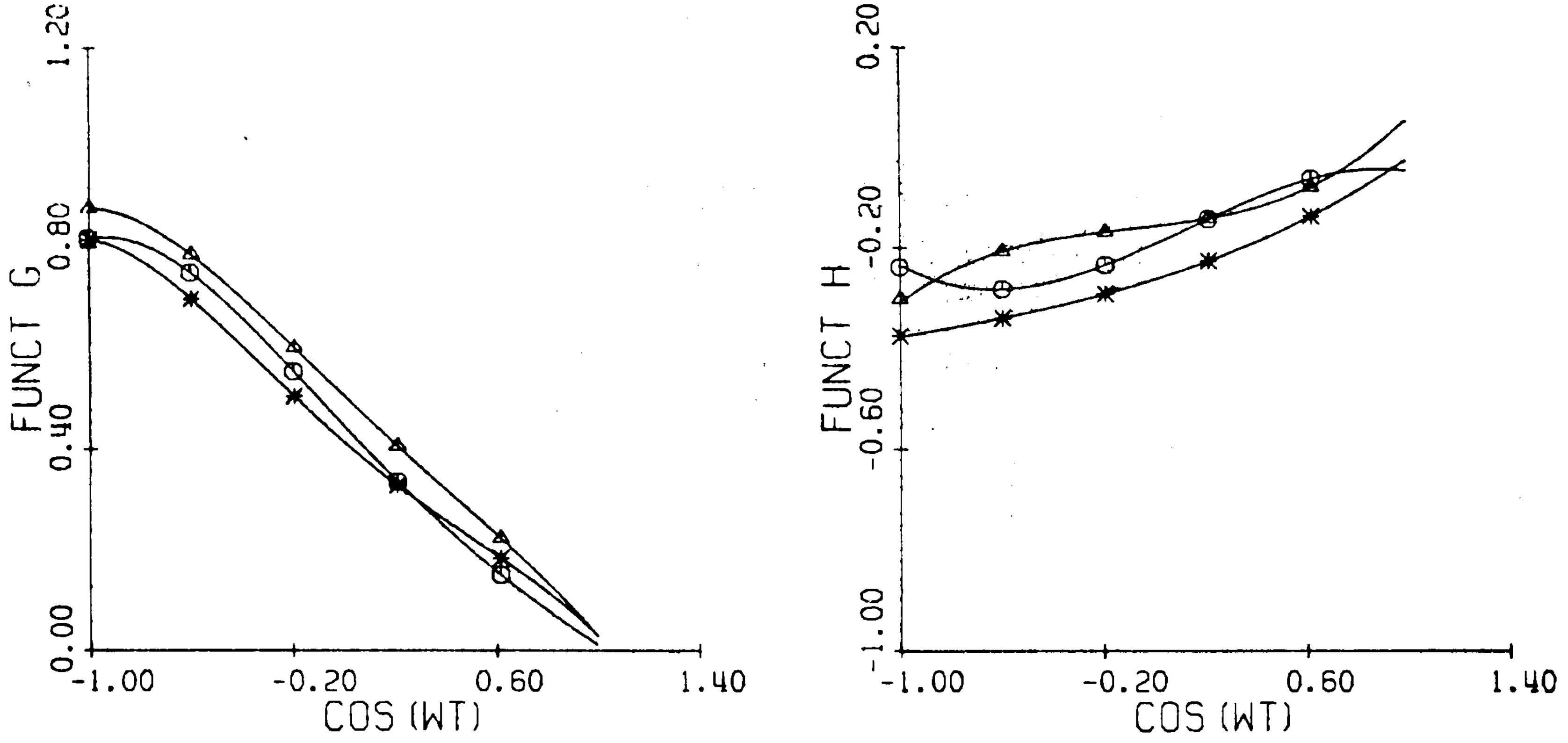

Figure C2a. Plots of 'g' and 'h' curves for three speeds of level walking for the hip kinematic data.

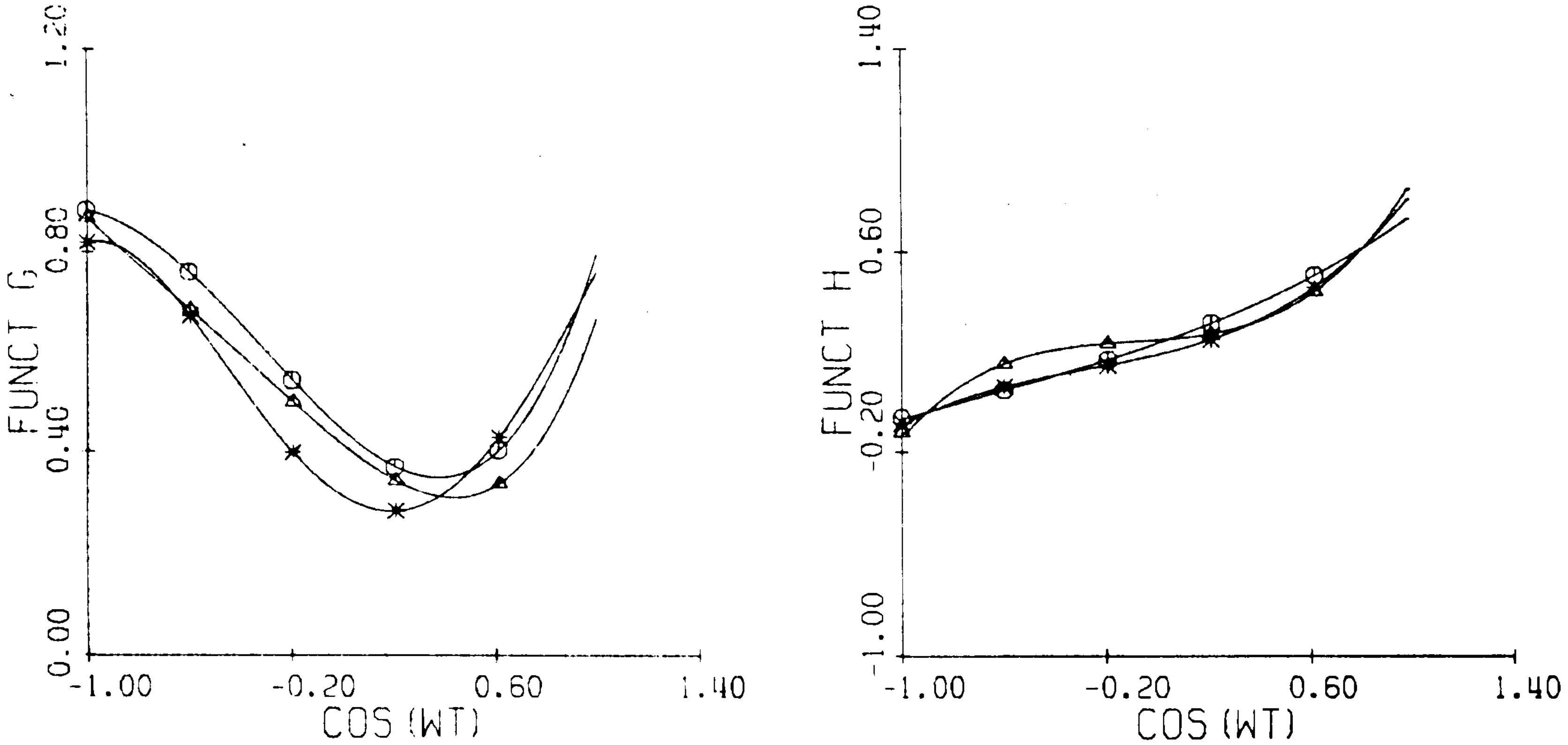

Figure C2b. Plots of 'g' and 'h' curves for three speeds of level walking for the knee kinematic data.

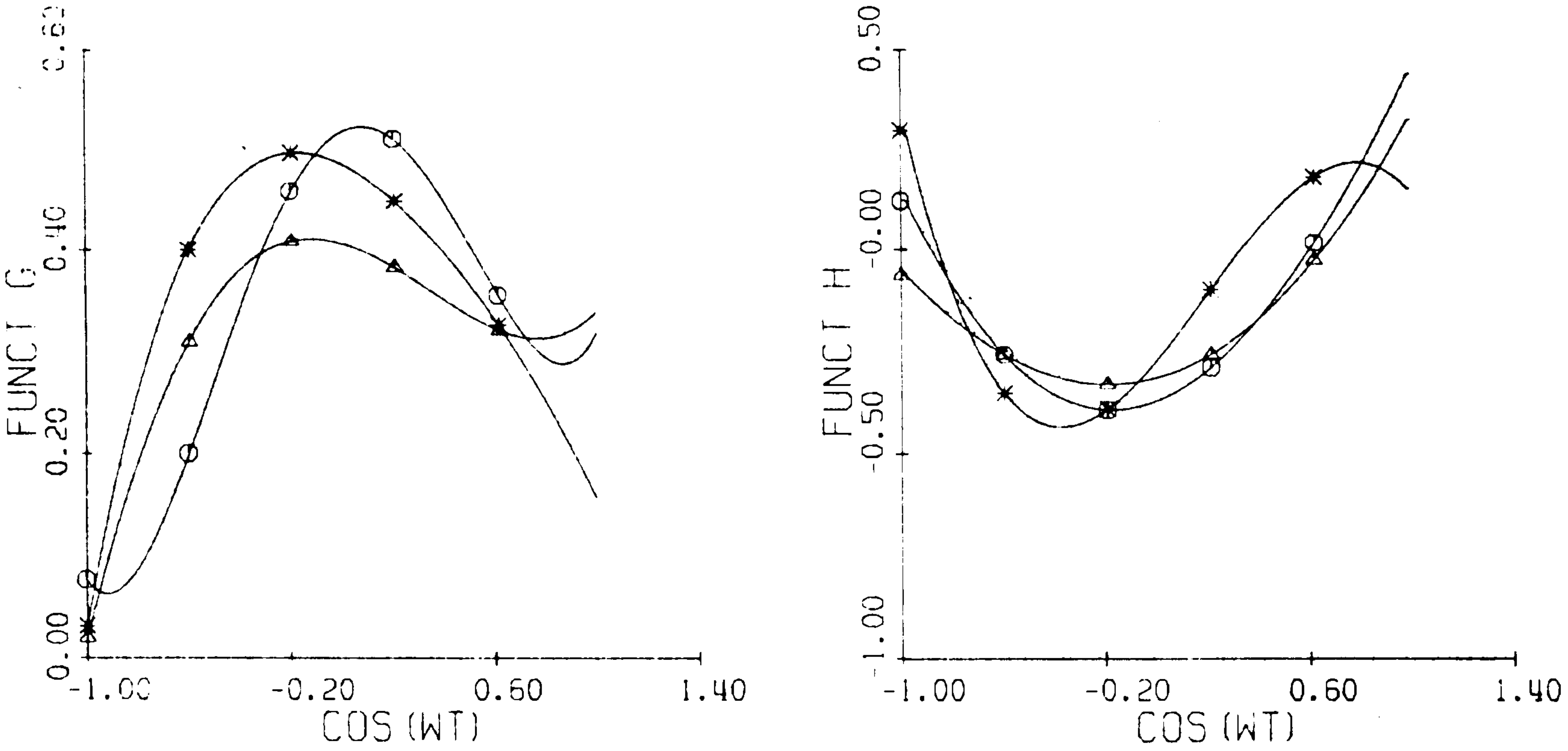

Figure C2c. Plots of 'g' and 'h' curves for three speeds of level walking for the ankle kinematic data.

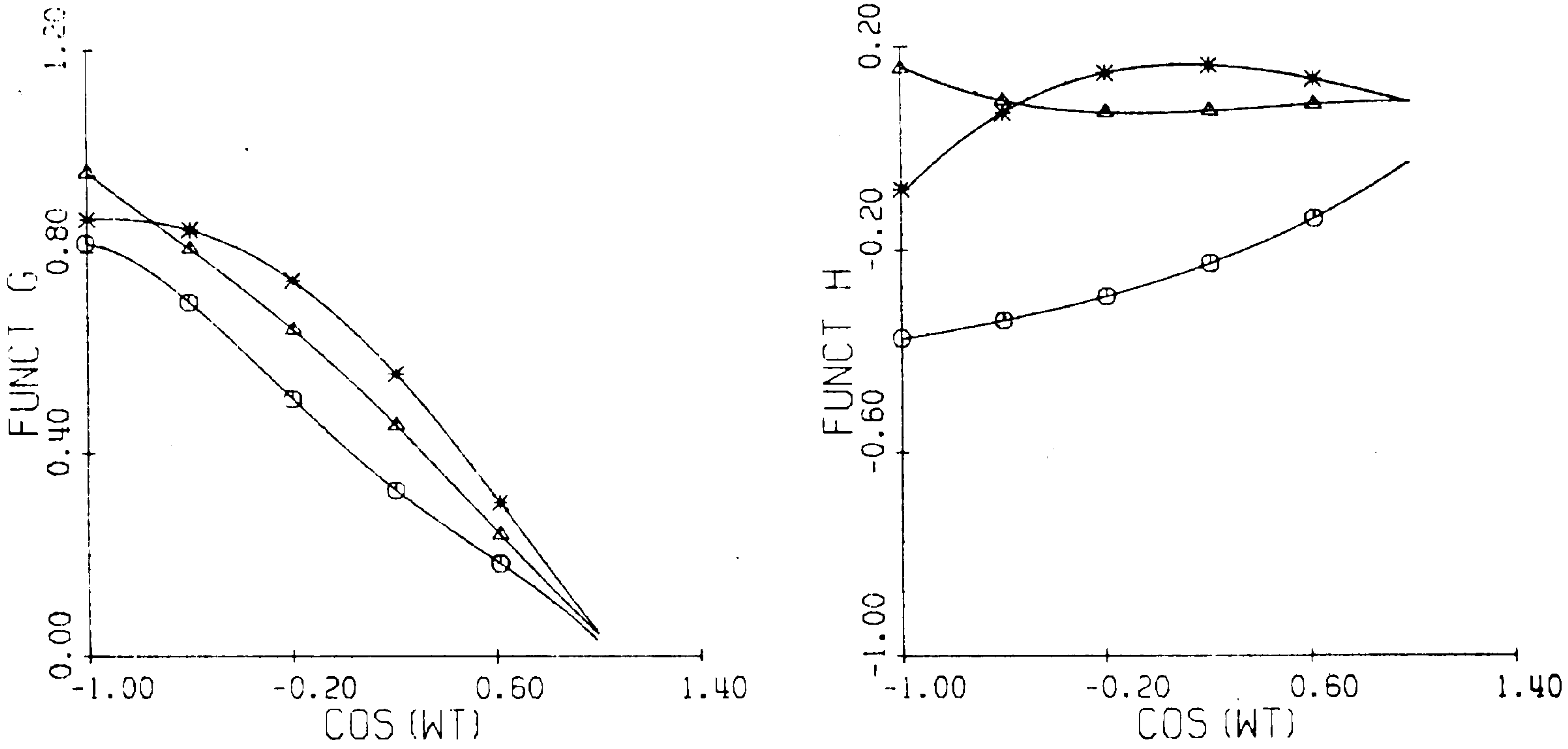

Figure C3a. Plots of 'g' and 'h' curves for three different rhythmic activities of the lower limb for the hip kinematic data.

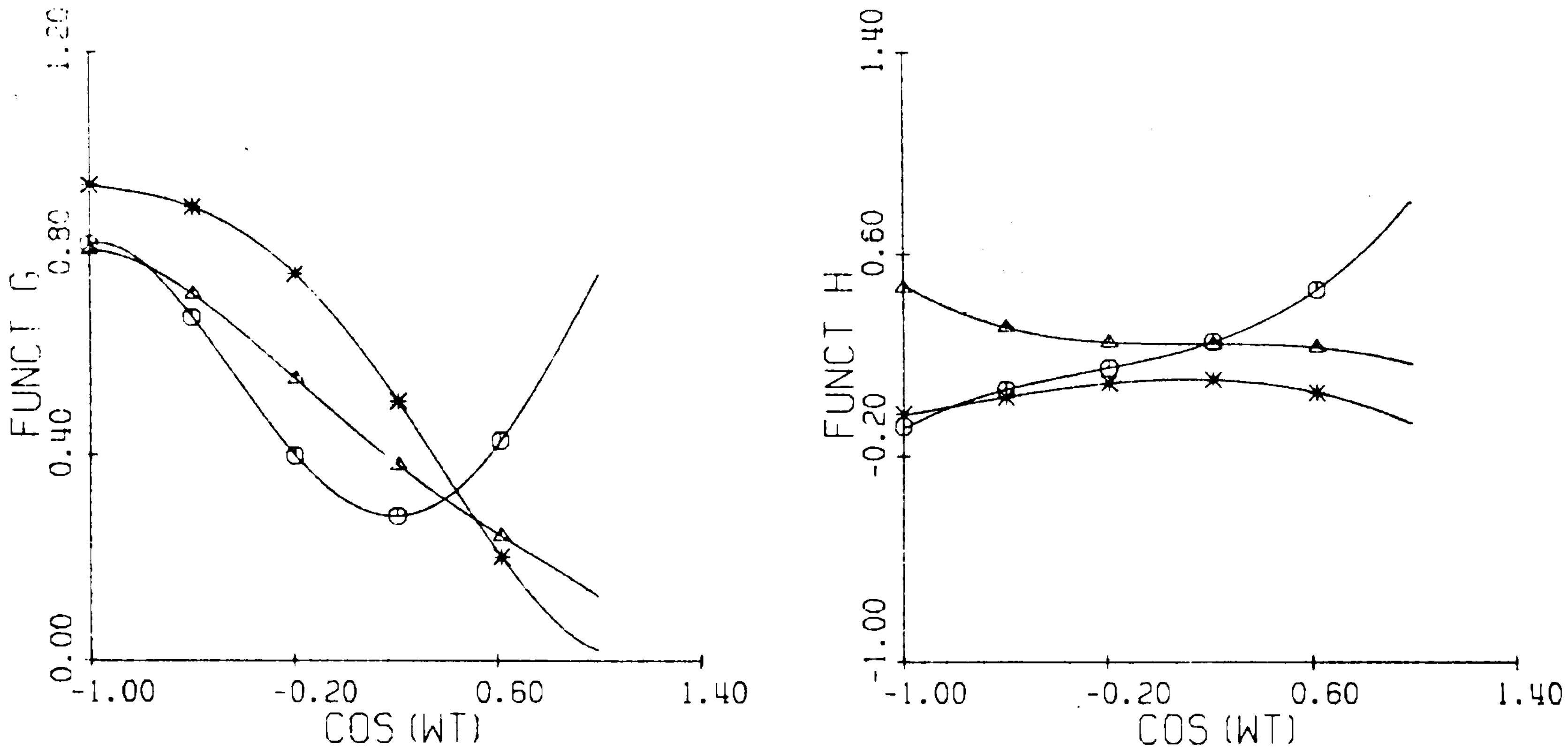

Figure C3b. Plots of 'g' and 'h' curves for three different rhythmic activities of the lower limb for the knee kinematic data.

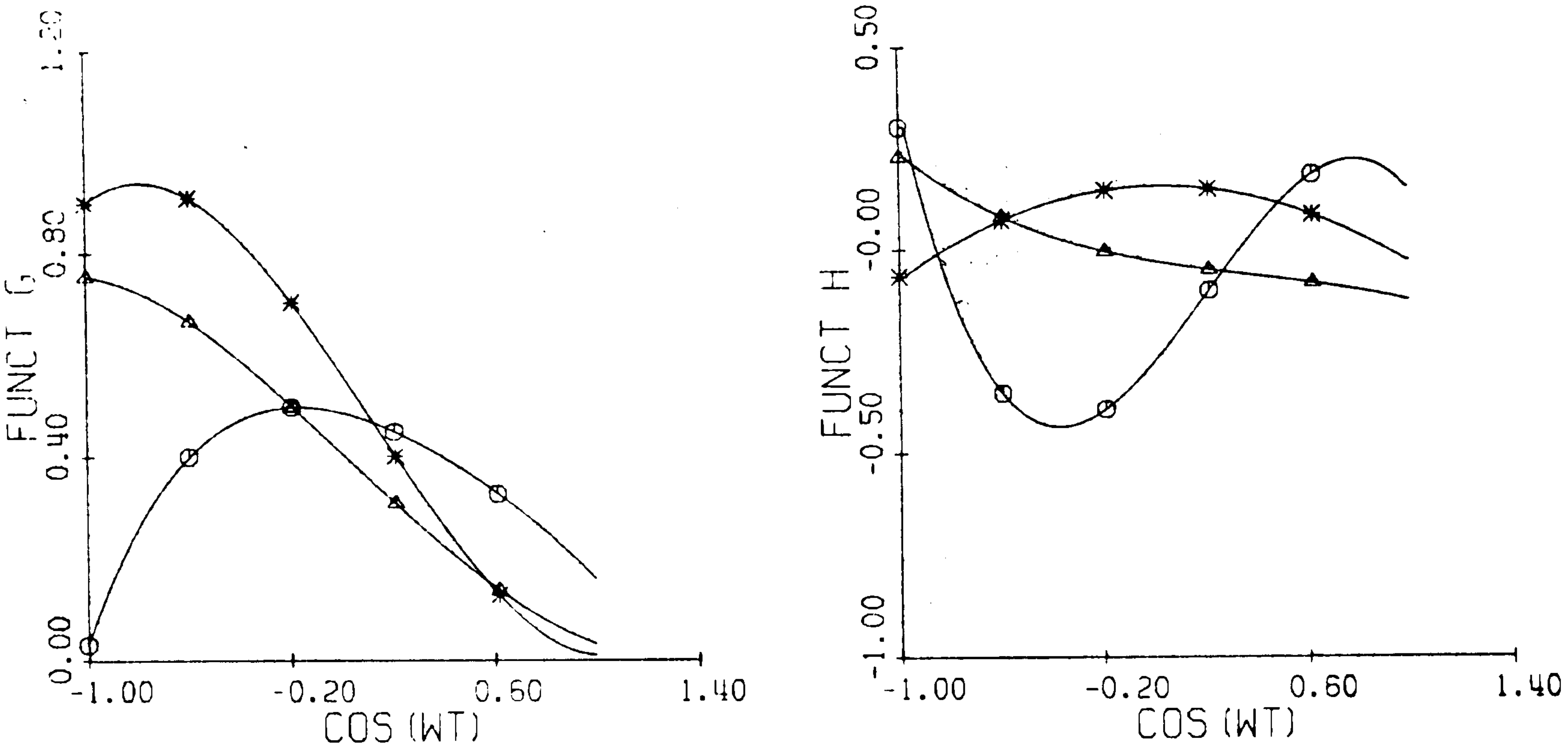

Figure C3c. Plots of 'g' and 'h' curves for three different rhythmic activities of the lower limb for the ankle kinematic data.

APPENDIX D

NETWORK FOR SINE/COSINE OSCILLATOR - MATHEMATICAL MODEL

A mathematical model of a four neuron recurrent inhibitory network, based on Willis's work (45), is described in this appendix.

To synthesise a network to produce a sinusoidal output, one needs to select a model for a single neuron. A number of neuronal models of varying complexity are available in the literature (46,92). One has to choose a model that includes the most important characteristics of real neurons, yet is simple enough to permit detailed analysis of network properties.

The model selected for this study is described by a first order differential equation

$$\dot{y} = k - a \cdot y \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

where y is the rate of generation of nerve impulses

k is the tonic input to the neuron

a is (1 / (time constant)) that describes the change in 'y' for a step change in 'k'

$\dot{y}$ is the first derivative of y with respect to time.

The model neglects the refractory period and adaptation in neurons and assumes a linear relationship between the input and the steady state rate of nerve impulse generation.

Using this neuronal model, a recurrent inhibitory network consisting of four neurons can be described by four coupled first order differential equations

$$\begin{bmatrix} f_1 \\ f_2 \\ f_3 \\ f_4 \end{bmatrix} = \begin{bmatrix} k \\ k \\ k \\ k \end{bmatrix} - \begin{bmatrix} a & b & c & d \\ d & a & b & c \\ c & d & a & b \\ b & c & d & a \end{bmatrix} \begin{bmatrix} y_1 \\ y_2 \\ y_3 \\ y_4 \end{bmatrix} \quad \ldots\ldots\ldots\ldots \quad (2)$$

where the variables $f_{\dot{i}}$ (i = 1,2,3,4) are defined by the following equations

$$\dot{y}_{\dot{i}} = f_{\dot{i}} \quad \text{if} \quad f_{\dot{i}} \geqslant 0 \quad \text{or} \quad y > 0 \quad \ldots\ldots\ldots \quad (3)$$

$$\dot{y}_{\dot{i}} = o \quad \text{if} \quad f_{\dot{i}} < 0 \;\&\; y = 0 \quad \ldots\ldots\ldots \quad (4)$$

The constraints of equations 3 & 4 ensure the that ouputs y_i are always positive. These discontinuities in the first derivative of y_i introduce nonlinearity in the model equations. These equations were solved numerically using the CSMP program.

The discrete time lags involved in the interactions between neurons are neglected in the simulation of the network shown in Figure 36 of the text of the thesis. Because of the noise in the nervous system, imbalance in the initial conditions can occur and the system will oscillate with appropriate choice of the parameters. Figure 35 shows a simulation result for particular values of the system parameters.

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