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Muscular Synergies in the Human Hand

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1 Kurzfassung

Aus der Perspektive eines Ingenieurs stellt die menschliche Hand mit ihrer Vielseitigkeit ein kleines Wunderwerk der Natur dar. Alle bisherigen Versuche, die Morphologie und Physiologie der Hand zu imitieren, führten zu aufwändigen technischen Konstrukten, die auch nicht annäherungsweise die Geschmeidigkeit und Beweglichkeit einer menschlichen Hand nachzuahmen vermochten. Das Ziel dieser Studie war es, Prinzipien zu finden, mit denen diese Geschmeidigkeit und Beweglichkeit erreicht werden. Das "Substrat" war die menschliche Hand selbst. Mittels elektronischer Signalverarbeitung versuchten wir Hinweise auf synergistische Muskelaktivität aus Elektromyogrammen herauszufiltern. Die Hypothese war, dass durch das Koppeln von mehreren Effektoren - Muskeln, Muskel-Kompartimenten oder motorische Einheiten - die biomechanische Überbestimmtheit der Hand gelöst und somit diese Redundanzen aufgabenspezifisch angewandt würden.

Im Detail suchten wir zu erst nach synergistischer Muskelaktivität, welche aktiv bei der Ausübung von isometrischen Kräften zwischen Daumen und Zeigefinger (Präzisionsgriff) eingesetzt wird. Die Versuchspersonen mussten unterschiedlich stark auf einen Kraftsensor drücken, während die elektrische Aktivität von insgesamt vierzehn Muskeln der Hand gemessen wurde. Diese Elektromyogramme wurden dann in die Potentiale der einzelnen motorischen Einheiten zerlegt. Deren Auftretenszeiten wurden sodann mit der jeweiligen ausgeübten Kraft und der Auftretenszeiten anderer simultan gemessener motorischen Einheiten korreliert. Dadurch konnten wir die Kraft einer Einzelzuckung einer motorischen Einheit, sowie deren Synchronisation mit anderen Einheiten beschreiben. Basierend auf diesen Korrelationen, versuchten wir die Vorhersagen unserer Hypothese zu stützen. Des weiteren untersuchten wir den Einfluss des motorischen Cortex auf die Synchronisation mittels trans-cranialer magnetischen Stimulation. Wir haben unter verschiedenen experimentellen Bedingungen - verschiedene Kraftstufen, Kraft- und Aktivität-Feedback, Kraftzunahme und -abnahme, Präzisions- und 'Power'-griff, mit und ohne Cortexstimulation - unterschiedlich stark synchronisierte motorische Einheiten gefunden und versucht, diese Unterschiede plausibel zu begründen. So dann diskutieren wir mögliche Ursprungsorte für Muskelsynchronisation und die Relevanz der Muskelsynergien in der menschlichen

Hand. Mögliche neue Ansätze für Roboterhände und Handprothesen werden zum Schluss aufgezeigt.

2 Abstract

From an engineer's point of view the human hand and its versatility is a miracle of nature. Any attempts to technically mimic the morphology and physiology of the human hand have resulted in rather bulky constructs that cannot nearly match the suppleness and versatility with which any human being can apply his or her hands to a certain task. The goal of this study was to find rules that govern this suppleness and versatility. The "substrate" of the study was the human hand itself and by electronic signal processing we tried to find indications in the electromyograms for synergistic motor activity. The hypothesis was that the problem of excess degrees of freedom in the hand is resolved by the coupling of agents - muscles, muscle compartments or motor units - and that these coupled agents are controlled as one entity. Furthermore, we attempted to find varying levels of synergistic activation under varying experimental conditions and tasks.

More specific, we determined whether synergistic muscle activation is present and active during grip force application between the tips of thumb and index finger (precision grip). Subjects were asked to perform a visuo-motor step tracking paradigm exerting isometric grip force at predefined levels, while the electrical activity of totally fourteen different hand and forearm muscles was recorded. The electromyographic activity of these muscles was then decomposed into the constituting potentials of single motor units. The occurrence of these motor units was related to the applied grip force and the simultaneous occurrence of other units to describe twitch force and synchronisation of motor units. From these correlations, we attempted to bolster the predictions made in the hypothesis that motor units are activated synergistically. Furthermore, we directly determined the influence of the cortex on the synchronisation of motor units by applying trans-cranial magnetic stimuli to the contralateral motor cortex of our subjects during the performance of the motor task. We found synchronisation under the various experimental conditions - different force levels, increase and decrease of force, force and motor unit activity feedback, precision and power grip, with and without stimulation - to various degrees. Possible origins of motor unit synchronisation and the relevance of motor synergies are discussed with a more global view on the motor control of the human hand. Finally, new approaches to the design of robot hands and their controls are proposed.

3 Introduction

3.1 Goal of this Work

Muscles are co-activated in synergy so that a specific limb or body part adjusts its compliance, applies isometric force on an object or performs a movement with the right amplitude, direction, at an appropriate and economic velocity and acceleration. The goal of this work is to characterise muscular synergy that occurs in the human hand during the precision grip and the power grip. Thereby, we want to uncover putative rules that govern the synergistic activation of the involved muscles and contribute to the understanding of a possible biological control strategy for such a redundant system. This might lead eventually to computer simulations and finally physical models that mimic the human hand both in its versatility and dexterity. Furthermore, understanding the synergistic activation of muscles in the hand may, in the long run, lead to more complex functional electric stimulators for patients with hands that are paralysed due to neuronal disorders or damages.

In our understanding, "muscles acting together" or muscular synergy can be quantified by synchronous and coherent activity of groups of muscles or muscle parts. In this work we mainly focus on synchronous motor unit activation as illustrated by the cross-correlation analysis.

3.2 Goal of this Chapter

The goal of this chapter is to acquaint the reader with the neuro-motor system of biology, its terminology and the human motor system in specific. This is especially done with the reader of technical background in mind. We will then show that the muscular system is highly redundant and we will investigate how the neuro-muscular system might resolve these redundancies for the human hand. Furthermore, we will list the studies we perform to answer some of the issues of the muscular redundancies.

In the first section of this chapter a general anatomical and physiological overview of the neuro-muscular system shall be gained. Highlights will be put a) on the effectors: the muscles and their sub-ordinate structures; b) on sensors, from where the central nervous system gains information on force, position and the state of the subject. In part c) the

flow and processing of information through the structures of the central nervous system (CNS) are addressed.

In section two of this chapter we investigate muscular redundancies and how the neuro-muscular system deals with these redundancies. The *acting together* of muscles, or sub-structures of muscles, is addressed. This *acting together* of muscles will hereafter be referred to as *muscular synergy*. Several motor sub-systems will be mentioned where muscular synergies are a prerequisite for the vital contribution to the subject organism.

In the third section the neuro-muscular system of the hand is analysed in more detail. Sensory input, synergistic activation of muscles in function of anatomy, physical practice and manual task will be mentioned.

The fourth section shall give a short overview on machine grippers and anthropomorphic robot hands, to show the difference between biologic and technical systems.

In the final, fifth section we state the specific questions that have triggered this piece of work, and we specify the issues that we investigate experimentally.

3.3 Concepts of Motor Activity in Humans

The motor system is one of the fundamental systems of living organisms and voluntary movement is an essential function of the nervous system. The motor system reacts on the sensory input and volitional drive of the nervous system with purposeful behaviour, thus representing the final output of an animal or human being. As Bernstein (1967) pointed out: "... movements are almost the only expression of the life activity of the organism...". Charles Sherrington, an English physiologist at the beginning of the twentieth century termed this behaviour as the *integrative action* of the nervous system (1906). Given the motor system, animals and human beings alike, have the ability to react to stimuli of the senses, to decide on actions, based on past experience or inherited behavioural patterns, and to undertake and execute movements. In order to successfully act on the needs of the organism the motor system requires at least three sub-systems to perform these behavioural patterns: first - the sensors or receptors that feed information from the outside world and the periphery on the state of the system and its members to - second - a controller or rather a network of controllers that generate, based on the

sensory input and the volitional drive, the appropriate action signal to - third - the effectors or the motor part which transforms electro-chemical command signals into purposeful action. In the whole loop, from sensory input to motor action the signals are modulated, adjusted to the momentary needs, the transmission of the signal is facilitated or inhibited, so that only in the most basic reflex loop one-to-one connections can be identified.

3.3.1 The Effectors

The executing organ in man and animal is the muscular system, in particular the striated muscles, that can be activated at will. Of physiological interest are the motor unit (MU), the muscles per se and their spatial and temporal activation in the whole system.

3.3.1.1 The Motor Unit

The MU constitutes the functional "quantal" entity that can be addressed by the CNS at any one time. A MU is defined as the combination of a single α-motoraxon, its terminal branches and all the muscle fibres which the branches innervate (Liddell and Sherrington, 1925). Today, in addition to the original definition, the entire motoneurone is included in the MU (Burke, 1981). The muscle fibres of one single MU - that are disseminated over a certain area (territory) of the muscle, up to 10-30% of the total muscular cross sectional area according to Buchthal, Guld and Rosenfalck (1957) and Rothwell (1994) - contract, when the action potentials of the supplying motoneurone trigger the muscular contraction. Upon arrival of the action potential at the presynaptic site of the neuromuscular junction the neurotransmitter acetylcholine is released into the synaptic cleft. This transmitter diffuses from the pre-synaptic axonal ending of the motoneurone through the synaptic cleft to the post-synaptic muscular membrane and binds to the acetylcholine receptors, which in turn leads to the depolarisation of the muscle membrane along the muscle fibres and consecutively to muscle contraction. The MU action potential recorded in the electromyogram (EMG) is the spatial and temporal summation of the individual muscle action potentials for all the fibres of a single MU. The more force a muscle exerts and the cruder the movement, the more muscle fibres are innervated by one motor axon (1000 fibres in the gastrocnemius of the leg, less than 100 in the extraocular muscles: Buchthal and Schmalbruch, 1980).

Two basic kinds of muscles fibres exist in the striated muscles, i.e. the muscles that can be activated by volition: the twitch and the tonic fibres. The twitch or fast fibres are triggered in an all-or-none, digital mode. These fibres belong to fast MUs. They reach the peak tension and relax more rapidly than the slow units. The tonic or slow fibres of these latter units can be activated in a graded, analog manner. The fast units are further subdivided into *fast fatiguing* and *fast fatigue-resistant* units. The classification into fast and slow twitch units has first been made in the cat (Andersen and Sears, 1964). Later on Sica and McComas (1971) showed that these two unit classes also exist in the human extensor hallucis brevis muscle in the foot. Motor units can further be classified by their twitch tension, i.e. the contraction amplitude and velocity of the fibres of one MU to one nerve action potential. Fast MUs have a larger twitch tension and contract faster than slow units. However, Thomas et al. (1991) showed that there is no distinct boundary between the two groups of MUs.

The question as to how graded force is generated by the nervous system revealed two fundamental mechanisms: a first mechanism was introduced by Liddell and Sherrington (1925): the concept of recruitment of MUs. This concept was refined by Henneman and co-workers in the mid-sixties (1965) who formulated the *size principle* showing a specific recruitment order of motoneurones, in that small motoneurones would start to discharge at lower force thresholds before larger ones and consequently small MUs were first recruited. Thus varying force levels could be achieved by one muscle. Adrian and Bronk (1929) proposed frequency modulation, or *rate coding*, as a second mechanism to grade force. They suggested that a higher discharge rate of the MU would generate a higher contraction force. Motor units typically discharge at rates of about 8 to 25 Hz, the higher the discharge rate, the higher the contractile force. However, the relationship of discharge rate and the motor output is linear only on a very narrow frequency range. Above this range the single twitches start to fuse in a tetanus and the contractile force output of the MU saturates. Nevertheless, these two fundamental mechanisms for grading force can be found in varying proportions depending on the muscles (DeLuca et al., 1982) that have been investigated.

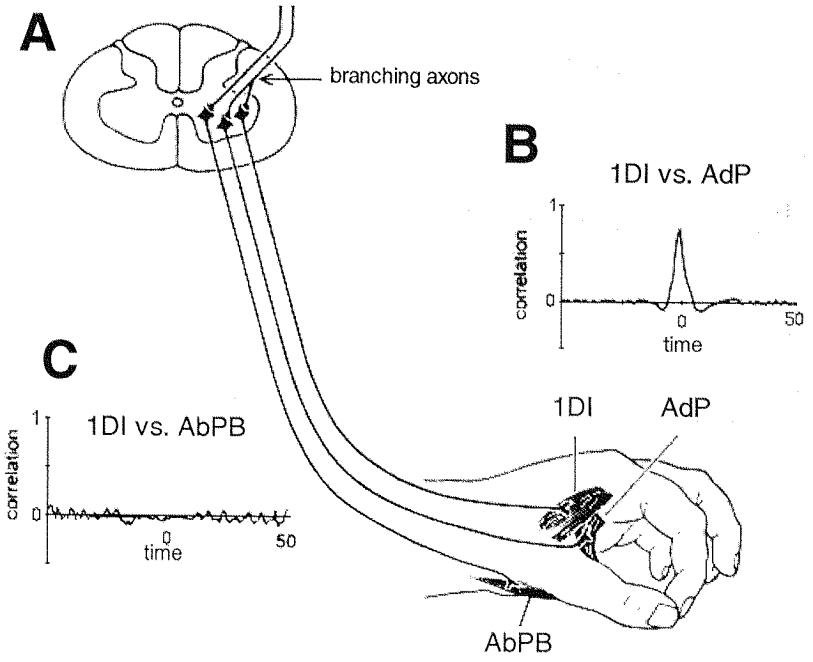


Figure 3-1. Synopsis of theoretical issues and analytical approaches. *A:* Example of three hand muscles active in precision grip and their respective innervation (AbPB, abductor pollicis brevis; AdP, adductor pollicis; 1DI, first dorsal interosseus). In this example, AdP and 1DI receive a common input (branching axon) in the spinal cord, while AbPB is individually innervated. *B:* Synchronous activation of AdP and 1DI in the time domain is reflected as a peak in the cross-correlation function. *C:* In this hypothetical example, AbPB and 1DI are not correlated as shown by the 'flat' cross-correlogram.

3.3.1.2 The Muscle

Anatomically, the striated skeletal muscle is built from muscle fascicles which represent a group of muscle fibres surrounded by a connective tissue sheath. A fibre contains myofibrils which, in turn, are built from thin and thick filaments composed of actin and myosin molecules. Physiologically, the striated muscles can be grouped in two types: the *phasic* and the *tonic* muscles. The phasic muscles are used in dynamic contractions, while the tonic muscles maintain the posture of the body and act over longer periods of time. The muscles impinge, in general, on the skeletal framework and by contracting the myofibrils produce the movement seen macroscopically. Unlike many technical effectors, muscles can only exert tensile forces, in addition, the input-output relationship of muscles is highly non-linear as already seen in the MU. In biomechanical research, muscles are mechanically modelled as visco-elastic elements with contractile, dampening and spring elements. Together with other muscles at one joint this mechanical behaviour generates the movement and stiffness of the limb at a given joint. The stiffness or compliance can be controlled by the co-contraction of several muscles that act at a joint.

The exerted force depends on the impulse rate of activation through the motor nerves, on the direction of the contraction and on the relative length of the muscles at the moment of contraction. The higher the impulse rate is, the higher is the generated force, again depending on the momentary muscle length, length change rate and fatigue condition (Bigland-Ritchie et al., 1983). Together with the muscle length and the joint flexion angle also the moment arm, i.e. the tendon excursion at the joint, can vary (Chao et al., 1989). In addition, the highest contractile force is obtained at a specific contraction speed. Depending on the activation state in forced muscle-shortening, higher or lower forces can be obtained than in the isometric force generation. The contractile force reaches a maximum at its optimum working length based on the biochemical nature of the contractile apparatus and falls off if the muscle is over-stretched or too lax.

3.3.1.3 The Muscular System

Only rarely is one degree of freedom in a joint related to just one muscle. On the contrary, in the majority of the cases several muscles act at one joint, and, in addition, many muscles extend over several joints generating movements and torque around

several axes at different joints. The resultant force measured or movement seen depends on the correct temporal and spatial activation of all the muscles - agonists, antagonists and synergists - involved in the kinematic chain for the involved motor program.

3.3.2 The Mechanical Receptors

The sensory information needed to close the feedback loop to the CNS is provided by proprioceptive receptors, i.e. sensors that measure the internal state of the body, such as length of the muscles and contractile force, the relative position of one body part to the next. The sensors that provide the information on the muscle state are the muscle spindles and Golgi tendon organs. Additional information on the position of the limbs, i.e. kinaesthetic information, is provided by sensors in the joints and in the skin (Edin and Johansson, 1995; Collins and Prochazka, 1996). The signal of all these receptors is used at various levels in central nervous processing: at the lowest level in spinal reflexes (e.g. stretch reflex, see below), at highest levels through the cerebral and cerebellar cortex in motor planning.

3.3.2.1 The Muscle Spindle

The muscle spindle generates a signal related to the length of the muscle. Interestingly, the muscle spindles are adaptive sensors with efferent innervation from the spinal cord (γ-motoneurones), enabling the CNS to adjust the sensitivity of the sensors by contracting muscle fibres that pass through the spindle. The muscle spindle is a spindle-like structure, hence its name, also "fusiform", within the fleshy part of the muscle with a length of a few millimetres. The structure is surrounded by a connective tissue capsule and comprises incoming and outgoing neural endings and the so-called "intrafusal" muscles fibres, controllable by the CNS. This structure is in *parallel* to the ordinary, "extrafusal" muscle fibres.

The sensory signal depends on the momentary length of the muscle (static fibres) and the rate of length changes (dynamic fibres). In general, the firing rate of the sensory ending is proportional to the length, the more the muscle is stretched, the higher the discharge rate of the response signal.

3.3.2.2 The Golgi Tendon Organ

Another independent and complementary feedback measure is the muscle tension, which is conveyed by the Golgi tendon organ. The sensor is located at the junction of muscle and tendon, *in series* to the extrafusal fibres. In a simplistic description, Golgi tendon organs respond to muscle contraction rather than to stretch of the muscles. Spindles, in contrast, reduce their firing rate when the muscle contracts because, as the extrafusal fibres shorten with contraction, the parallel intrafusal fibres also shorten.

The discharge of Golgi tendon organs may, in fact, be more related to the variations in contractile force than to the static contraction level (for review see Jami, 1992).

3.3.2.3 Deep and Joint Receptors

In addition to the two above mentioned main sensory receptors further information of the muscle state is gained from free nerve endings and Paciniform corpuscules. Due to the difficulty to characterize these sensors *in vivo* little is known about their action. It is hypothesised that the free nerve endings code for nociceptive and high-threshold stimuli.

Joint receptors code for the relative position of the joint. They comprise free nerve endings located in the connective tissue of the joint apparatus, Golgi endings in the joint ligaments comparable to the Golgi tendon organs, and Ruffini endings in joint capsules. The physiological action of these sensors is still a matter of debate. While Skoglund (1956) showed that joint afferents discharge in relation to a certain joint angle, more recent findings suggest that - at least - some of the receptors work as "end switches", in that they discharge when the joint angle reaches the extremes.

3.3.2.4 Cutaneous Receptors

The mechanoreceptors of the skin are of interest for the motor control in that they convey mechanical signals such as vibration, pressure and shear force. Four physiological responses have been described (Vallbo and Hagbarth, 1968): fast and slow adapting receptors type I with small circumscribed receptive fields, i.e. sensory uptake areas. These receptors are specifically sensitive to objects that cause indentations in the skin. The palmar tips of the fingers are especially densely innervated by these receptors. The density of innervation gradually decreases to the glabrous, dorsal side of the hand;

fast and slow adapting receptors type II have much larger receptive fields. These receptors signal stretch of the skin and have a directional sensitivity. The activity of all these sensors has nicely been shown by Westling and Johansson (1987). This part will further be extended in the chapter "The gripping hand". Furthermore, Edin and Johansson (1995) as well as Collins and Prochazka (1996) showed in two parallel investigations that skin receptors can convey kinaesthetic information of the hand and movement illusions when the skin was stretched over the finger joints.

3.3.3 Motor Control

Hitherto, engineering and computer science have shown considerable difficulties in mimicking with robots the large movement repertoire a human being can produce, such as bi-pedal walking or handling a large variety of tools and items with dimensions at different orders of magnitude. The difficulty to model the musculo-skeletal apparatus is certainly caused by the complexity of the system. A human skeleton consists of around 200 bones, about 100 degrees of freedom in the joints between adjacent bones and more than 600 muscles (Cordo, Harnad 1994). Moreover, Bernstein in his "small collection of papers" on the coordination and regulation of movements (1967) described the indeterminancy of motor coordination stating a whole series of sources that compounded the problem: first the anatomical sources "the presence of a large number of degrees of freedom of movement at the joints, and more so in the complex kinematic chains found in the make-up of the organism", hinting to e.g. the variation in the function of muscles at multi-axial joints, the multiplicity of muscular action, and the convergence of incoming neuronal pathways; second the mechanical indeterminancy, e.g. the high degree of mechanical complexity in the multi-segmental kinematic chains (of the body as a whole, of the hand, in particular). The third source of indeterminancy was of physiological origin. The activating signal that originates in the pyramidal cells of the motor cortex is modulated, facilitated or inhibited on its way to the muscles by many peripheral agents. Furthermore, the muscles have varying properties depending on their length, fatigue and the rate of movement. Bernstein's conclusion, therefore, was that the "motor effect of a central impulse cannot be decided at the centre but is decided entirely at the periphery..."

The complete motor apparatus encompasses not only the skeletal and muscular system but also large parts of the neural system. Important parts of the cerebral cortex, the basal ganglia, cerebellum, brain stem and spinal cord are involved in motor control. Thereby the control aspects cannot be reduced to one single controller of movement. In the following chapters the main contributions of some of the important motor control structures are high-lighted. In the past, with the observation of pathological effects of brain damages in human patients by clinicians and then in the recent decades by direct electrical brain stimulation and chronic recordings of the brain activity with single cell measurements in the monkeys' brain, areas could be identified and correlated to specific functions that the brain has to perform in order to generate commands to the muscles (for review cf. Hepp-Reymond, 1988).

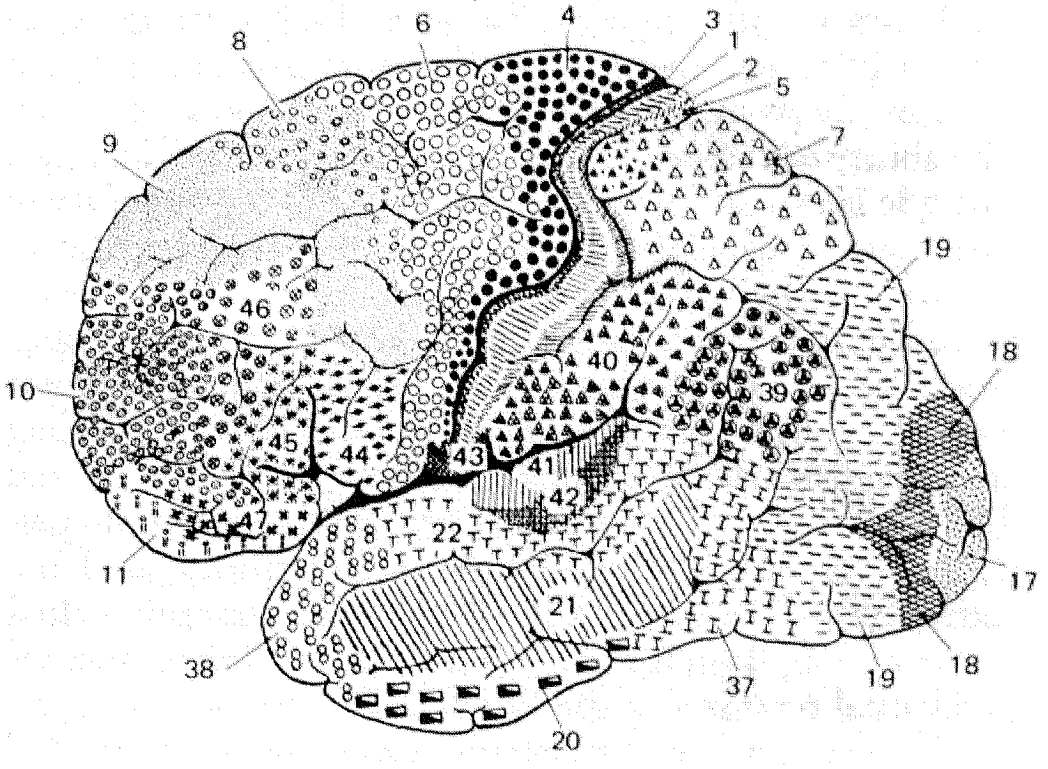


Figure 3-2. Brodmann's map of the human cerebral cortex. Based on cell structure and arrangement, Brodmann divided the human cerebral cortex into 52 discrete areas, a number of which are illustrated in this lateral view. Each symbol represents a distinct area, numbered as shown. Area 4, the motor cortex, occupies most of the precentral gyrus. The postcentral gyrus, where the primary somatic sensory cortex is found, is divided into three distinct areas (1,2,3).

In very recent time, a new non-invasive technique to investigate the cortical regions has been introduced into clinical and scientific laboratories: transcranial magnetic brain

stimulation (TMS) in humans. It has provided more insights into cerebral motor functions of man (Merton and Morton, 1980; Day et al., 1989; for review see Rothwell et al., 1991; Meyer, 1992). Last but not least functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have eased the way in non-invasively exploring the human brain functions.

3.3.3.1 Motor Areas of the Cerebral Cortex

On the cerebral cortex following main motor areas have been identified that play a role in the volitional control of movement and force: the primary motor cortex (M1) in the frontal lobe in the anterior bank and in front of the sulcus centralis; the supplementary motor area (SMA), in the medial wall of the brain hemispheres; and the premotor cortex located more anteriorly and dorsally to M1.

The complete cerebral cortex was mapped cyto-architectonically by Brodmann (1909). Later it was found that the cyto-architecture of his area 4 (Figure 3-2) correlates well with the physiologically defined M1. Cyto-architectonically, the motor cortex can be identified by the laminar appearance of the superficial layers (Campbell, 1905) and by the large pyramidal cells in the fifth layer (Ramon y Cajal, 1909, 1911) which represents the final output stage in the cerebral motor control to the spinal cord.

A complete somatotopic representation of the muscles is present in the M1 as Penfield and Rasmussen (1952) described after electrically stimulating the brain of patients during operations. This somatotopic representation was termed homunculus for the human beings. In homology to the motor representation in humans a large body of work has been performed on monkeys (He, Dum and Strick, 1993; for review see: Porter and Lemon, 1993). Both in man and in monkey it has been noted that the output areas of the fingers and the face are relatively over-represented in comparison to other body parts hinting to their importance in motor control (Figure 3-3). In recent years, this homuncular representation has a bit altered with the advent of the higher topographical resolution of intracortical microstimulation. When looking at the motor representations in more detail, a mosaic-like structure opens up with the intermingling of motor representations of many output zones (Sanes et al., 1995).

It was found already very early that M1 can be characterised as the region of the cerebral cortex with the highest excitability to evoke motor responses in the muscles of the

fingers (Fritsch und Hitzig, 1870). In addition, the response times of the MUs to an electrical intracortical stimulus in this region are shortest, advocating a direct innervation via the pyramidal tract (6.6 - 14.5 ms in the *Macaca nemestrina* with spike-triggered averaging; Lemon, Mantel and Muir, 1986).

The pyramidal cells have direct monosynaptic connections via the pyramidal tract to the motoneurones in the contralateral motor nuclei of the spinal cord and from there onwards to specific muscles (Lemon et al., 1986; Buys et al., 1986). This cortico-motoneuronal (CM) system can be found in most mammals, but it is in humans and in some other sub-human primates that it reaches its greatest size and importance. Lawrence and Kuypers (1968) showed by transsecting the pyramidal tract at the height of the brainstem that the CM neurones are a prerequisite for fractionated finger movement in primates, including human beings. Much of the CM functions deal with voluntary control of the upper limbs, especially the hand (Clough et al., 1968; Muir and Lemon, 1983) and lower limbs (Jankowska et al., 1975).

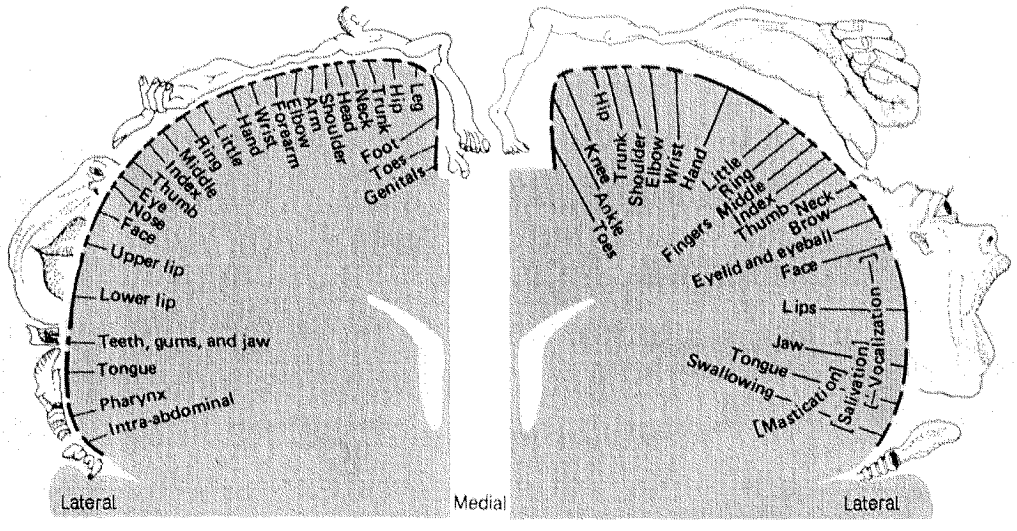


Figure 3-3. Penfield Map. Somatic sensory (*left*) and motor projections (*right*) from and to the body surface and muscle are arranged in the cortex in somatotopic order. *Left:* Sensory information from the body surface is received by the postcentral gyrus of the parietal cortex (areas 1, 2 and 3). Here the map for area 1 is illustrated. Areas of the body that are important for tactile discrimination, such as the tip of the tongue, the fingers, and the hand, have a disproportionately larger representation, reflecting their more extensive innervation (adapted from Penfield and Rasmussen, 1950). *Right:* The analogous motor map exists for the motor cortex. Note the large representation of the hand, fingers and, in close vicinity, the face.

From another region on the medial wall of the brain hemispheres, the SMA, electrical stimulation was also found to show motor responses (Penfield and Rasmussen, 1952). In addition, as shown with retrograde tracer studies from the spinal cord in monkeys, the SMA has also a somatopically organised output-pathway to the spinal cord for the generation and control of movement (He et al., 1995). Today, it is thought that the SMA is mainly involved in the co-ordination of synergistic bilateral tasks but it may also subserve other functions such as the programming of complex movements (in man: Roland et al., 1980; in monkeys with bimanual tasks and co-ordinated movements: Brinkman, 1984).

In the past years, the premotor cortex (comparable with Brodmann's area 6) of macaque monkeys was extensively investigated. The cyto- and myeloarchitecture of the sub-areas were described and tracer studies showed the connections to other motor areas and the spinal cord (Barbas and Pandya, 1987; He et al., 1993). It was found that the premotor cortex, too, has a certain degree of somatotopical organization (Matelli et al., 1986; Gentilucci et al., 1988; for review Godschalk and Wise, 1987). Functional studies revealed that this region represents higher order motor functions, such as preparation and motor planning for amplitude and direction of movements (Weinrich and Wise, 1982; Kurata, 1993; Godschalk et al., 1985). Several groups have shown that neurones of this region also had movement-related activity with respect to the hand (Gentilucci et al., 1988). Rizzolatti et al. (1988) demonstrated that neurones in the ventral premotor area 6 were activated during combined finger and hand movements, e.g. holding, tearing and grasping. In most cases sensory inputs were also coded. Hepp-Reymond et al. (1994) and Qi (1996) characterised premotor neurones located in various finger representations and their relationship to the performance of a precision grip task and grip force control.

Furthermore, it has to be stated that all these regions, i.e. M1, SMA, and the premotor regions, also receive direct sensory input from the visual system and the periphery, e.g. Rizzolatti et al. (1988); Wannier et al. (1991); Qi (1996). More recently Hepp-Reymond et al. (1999) have shown that in M1 and three premotor regions context-dependent force coding occurred hinting towards a normalisation of the firing rate for cortical neurones, enabling the neurones to discharge at an optimal work range for output modulations.

3.3.3.2 Basal Ganglia and Thalamus

The basal ganglia in the brain include the globus pallidus internus and externus, the putamen, the caudate (putamen and caudate = striatum), the subthalamic nucleus and the substantia nigra (pars compacta and reticularis). The functions of these nuclei are still a matter of debate. As shown by pathologies in these regions, e.g. Parkinson's disease, it is evident that they form a part of motor control pathways. The basal ganglia do not directly act on the motoneurones of the spinal cord and do not receive direct sensory input. However, the basal ganglia are involved in control loops that originate in the cerebral cortex travelling through the striatum, the globus pallidus, the subthalamic nucleus and via the thalamus return to the cerebral cortex and influence various cortical motor areas (see Figure 3-4; Alexander and Crutcher, 1990).

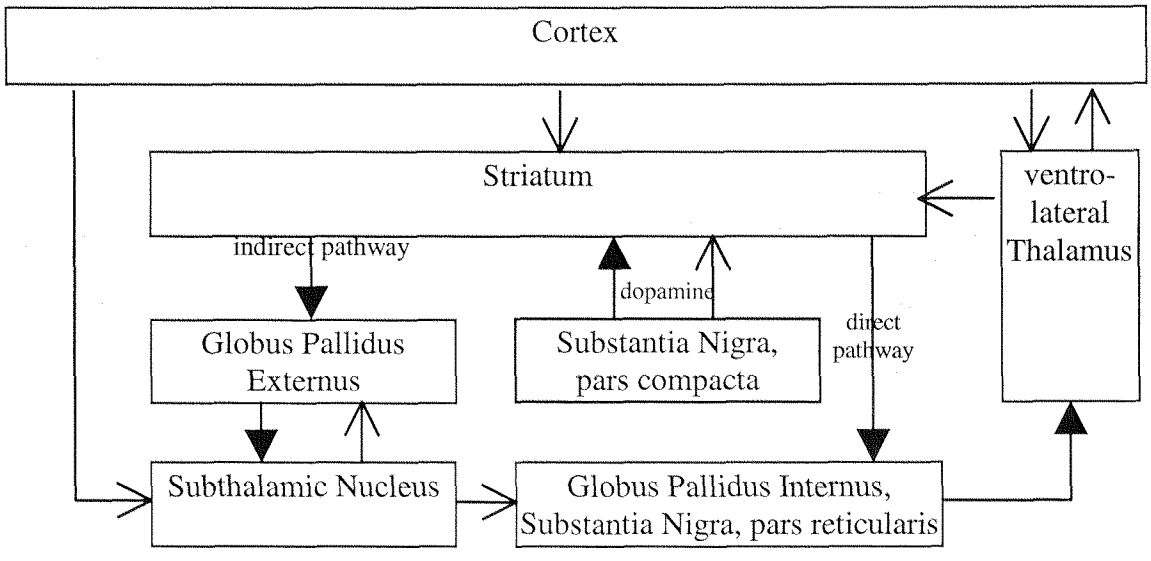


Figure 3-4. Cortico-basal ganglia-cortex circuit. For every muscular region, e.g. oculomotor, face, arm, leg, there exists a separate parallel loop. Little functional convergence has been found. Excitatory connections are shown as open arrows, inhibitory connections as filled arrows (adapted from Alexander and Crutcher, 1990a).

The two main outputs from the globus pallidus and the subthalamic nucleus are neurones secreting either inhibitory (γ-aminobutyric acid: GABA) or excitatory

(Glutamate) neurotransmitters. The interplay of these neurones can nicely be shown in the direct pathway through striatum, globus pallidus internus and thalamus. The striatum receives excitatory input from the cortex. The striatum then inhibits the inhibitory neurones in globus pallidus internus via GABAergic synapses. This results in a disinhibition of the thalamus, which, in turn, activates the cortex. The indirect pathway through the subthalamic nucleus seems to have an inhibitory effect on the motor cortex. The function of the basal ganglia in movement control is not quite clear. It has been shown that movement-related cells fire phasically in relation to direction of movement and not force (Crutcher and DeLong, 1984). Alexander and Crutcher (1990b) further demonstrated that preparatory neurones of the putamen coded for movement direction. The discharge on- and offset were, in the mean, later than that seen in either SMA or M1, though still overlapping. This preparatory activity was found in the rostral part of the putamen. In an accompanying paper, they stated to have also found muscle-related activity in the putamen neurones, but that their proportion was about half that of directionally sensitive neurones (Alexander and Crutcher, 1990c).

Important is the innervation of dopaminergic cells from the substantia nigra, pars compacta and other midbrain regions to the striatum. The clear functional pathway is unclear, since in the indirect pathway, the dopaminergic cells act inhibitory, while in the direct pathway they are excitatory. In Parkinson's disease, these cells degenerate with no clear reason. Symptoms seen are akinesia: lack of spontaneous and associated movements, slow movements, slow or lacking reaction movements; resting (3-5 Hz) and action (6-8 Hz) tremor (Dietz et al., 1974) and rigidity due to co-contraction of antagonists. The patients have difficulties in releasing their muscle tone. Abnormal stretch reflex activation of the muscles is seen.

3.3.3.3 Cerebellum

The cerebellum is a convoluted structure residing posteriorly under the cerebral hemispheres over the brain stem at the height of the fourth ventricle. The cerebellum is connected to the brain stem via three input/output fibre tracts. As the cerebral brain, the cerebellum is divided into two hemispheres connected by a structure called vermis. These hemispheres are transversally divided into three lobes, separated by deep fissures.

Four nuclei with somatotopic body maps are located in the depth in each side of the cerebellum (Thach et al., 1993).

The cerebellum receives input from the vestibulum, the pons, the olive and the spinal cord. The bulk of input comes from the pons, followed by afferent input from the olive, the spinal cord, visual, vestibular and other sources. The pons acts as a relay station for the cerebral input. Starting from the pons, mossy fibres project through the pontocerebellar projections into the cerebellum. Here these fibres contact the granule cells, the axons of which ascend to the most superficial layer, where they bifurcate in a "T"-junction and contact, as parallel fibres, as many Purkinje cells as possible. The Purkinje cell is the largest cell in the cerebellum. The cell has a dendritic tree that extends superficially in sagittal direction. It constitutes the only output cell of the cerebellar cortex and inhibits neurones of the cerebellar nuclei.

In the inferior olive several tracts from the spinal cord, the motor cortex and other nuclei converge and are relayed to the contralateral part of the cerebellum via the climbing fibres. The climbing fibre of one olivary neuron contacts exactly one Purkinje cell. All the connections to the Purkinje cells are excitatory. Other inputs from cerebellar stellate and basket cells are inhibitory. Finally, Golgi cells inhibit granule cells. Via the cerebellar nuclei the output goes to the brain stem and the thalamus, from where the cortical areas 4 (M1) and 6 are somatotopically innervated.

As to the function of the cerebellum three hypotheses exist: the cerebellum as timing device, as learning device and as muscle coordinator. The first hypothesis postulates that the cerebellum gives the exact timing of agonist and antagonist muscle activity. It proposes that the cerebellum is used to time the duration of agonist muscle activity and the latency of antagonist activity, so that any movement is halted at the correct point. Brooks and Thach (1981) showed evidence for this hypothesis with single joint movements in the monkey: by cooling (thermal inactivation) of the cerebellar nuclei reaction times increased, and rapid, self-terminated movements tended to overshoot the target. Furthermore, antagonist activation was delayed in rapid, repetitive movements. The second hypothesis is based on experiments that show that specific kinds of motor learning are no longer possible after acute or chronic inactivation of the cerebellar cortex and nuclei. The third hypothesis puts forward the idea of an open-loop controller

that sets the temporal and amplitude values for muscle activation. These functions are all a matter of debate (for review see Bloedel, 1994; and accompanying comments).

With the introduction of new visualisation techniques such as PET and fMRI it has become possible to scan the cerebellum for neuronal activity related to force exertion (besides all other cerebral areas). And indeed, the group around Frackowiak (Dettmers et al., 1995) showed with PET that parts of the cerebellum - the vermis and possibly other areas - are also involved in the control of fine motor commands.

3.3.3.4 Spinal Cord, Reflexes

The spinal cord is that structure of the CNS which extends from the brainstem through the vertebral channel down into the lumbar region of the spine. In cross-section with appropriate staining methods the spinal cord has a very characteristic aspect. The cord is oval shaped and in the centre lies a butterfly-like structure - the grey matter - with the cell bodies of the spinal neurones. The sensory input from the periphery enters through the dorsal root into the dorsal horn of the grey matter. The cell bodies of a large number of interneurones, and - in the ventral horn - the motoneurones are located in the grey matter. In the white matter, surrounding the grey matter, the input and output pathways lead to or come from supraspinal centres or other spinal segments.

In 1981, Shinoda, Yokata and Futami showed with the help of tracer studies the existence of divergent projection of corticospinal neurones in the spinal cord to motoneurones of different muscles in the monkey. These findings speak in favour of hard-wired synergistic muscle control, at least for the hand system in these monkeys. Apart from these tracer studies, investigations on reflexes have helped enormously to elucidate the set-up and function of the spinal network. Reflexes are involuntary and relatively stereotyped responses to specific sensory stimuli. They are graded depending on the locus and strength of stimulation. In spinal reflexes the sensory stimuli arise from receptors in muscles, joints and skin. In these reflexes the neural circuitry responsible for the motor response is entirely contained within the spinal cord. Best understood today are the reflex pathways from the Ia muscle spindle afferents (cf. Figure 3-5). Activation of the muscle spindles lead to monosynaptic excitation of the homonymous α-motoneurones (the main motoneurones, as opposed to the γ-motoneurones innervating the muscle fibres of the spindle) in the parent muscle and heteronymous excitation to

those motoneurones supplying other muscles, which act mainly as mechanical synergists at the same joint as the parent muscle, and via the Ia-interneurone to inhibition of the antagonist α-motoneurone (reciprocal Ia inhibition).

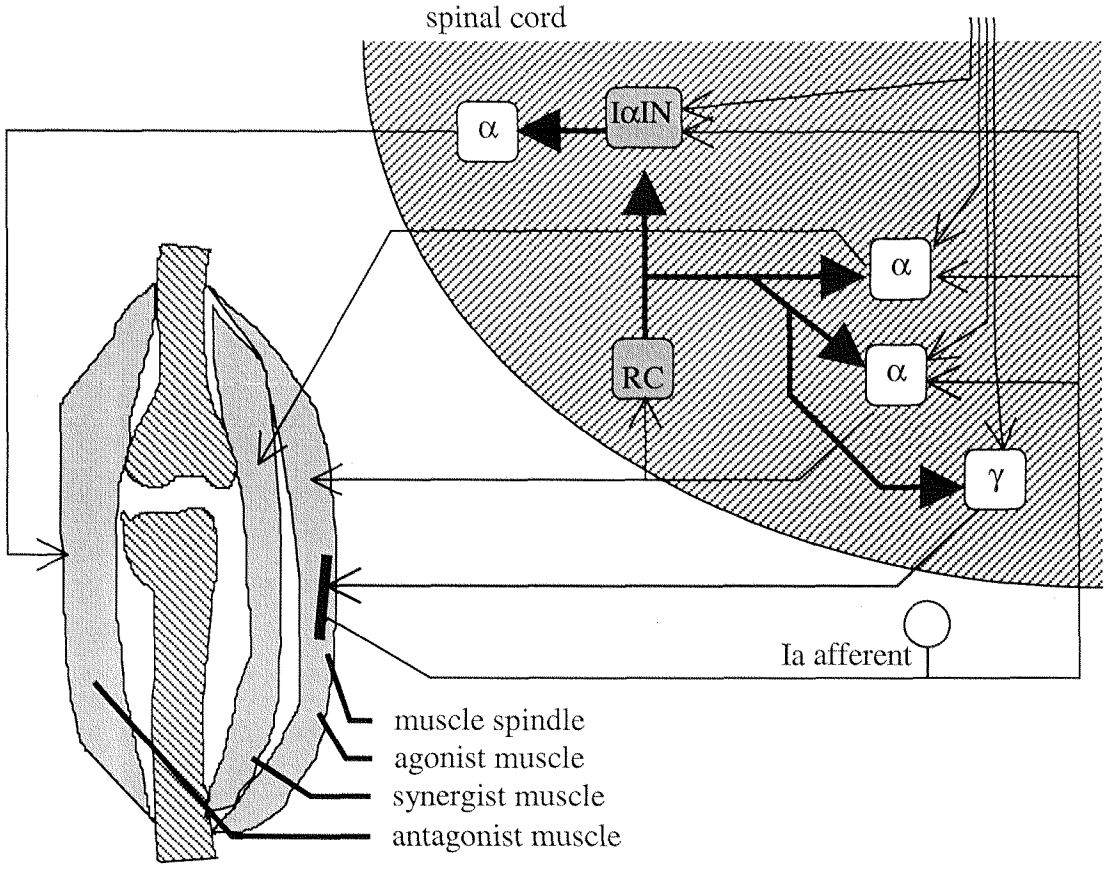


Figure 3-5. Schematic circuitry of the Ia afferents and inhibitory Renshaw cells (RC). Ia afferents project monosynaptically to the homonymous α-motoneurones and disynaptically, via the Ia inhibitory interneurone (IaIN) to the α-motoneurones of the antagonistic muscle. Renshaw cells are excited by axon collaterals of α-motoneurones and project back to the same motoneurones, the γ-motoneurones and the associated Ia inhibitory interneurones. Dotted arrows represent input from higher centres. Adapted from Hultborn, Lindström and Wigström, 1979.

The scheme drawn in Figure 3-5 is a vast over-simplification of the real circuitry found in the spinal cord, however, it suffices to show the basic wiring. The neurones and interneurones receive, in addition, an enormous input from other sources such as the corticospinal tract, group Ib afferents, cutaneous afferents, flexor reflex afferents.

The Renshaw cell, another inhibitory interneurone in the spinal cord, recurrently inhibits the α-motoneurones that project to it, as well as the homonymous and synergistic γ– and

α-motoneurones and the Ia interneurones of antagonist muscles. It is thought that the function of the Renshaw cell is contrast enhancement of motor commands, gain control of the output stage and prevention of maximum excitation of the motoneurones.

Further spinal reflexes have been detected such as the inverse myotactic reflex of the Ib Golgi tendon organ afferents and the flexor reflex afferents. Given all these reflexes the spinal cord resembles rather a hard-wired network that can react to specific stimuli. But in the day-to-day life the organism has to be able to flexibly answer the needs that might not fit into the stereotypic framework given by these reflex loops. The question, therefore, arose, whether other means to modulate the responses of the muscles might exists. One possible mechanism to influence muscle responses might be conveyed by the presynaptic axo-axonal synapses (Hultborn and Illert, 1991).

3.3.4 Summary

In this first part of the introduction, the physical components or the hardware that constitute the motor system have been described: first, the effectors, ranging from the MU via the whole muscles to the muscular system. The way how MUs function - recruitment, rate coding and size principle - has been listed, as well as their classification in *slow*, *fast-fatigue resistant* and *fast-fatiguing* MUs. The working principle of muscles has been stated. It was shown that the contractile force of a muscle depends on various parameters, among others length and contractile speed. The muscular system is the combination of all muscles with their respective origins and target locations on the skeleton. In this arrangement, the muscles exert their activity in concert to produce co-ordinated movements. Second, the receptors that return meaningful information to the CNS have been described. The muscle spindle, measuring the length in a muscle and the Golgi tendon organ measuring the tension in a muscle have been mentioned as well as deep, joint and cutaneous receptors. Third, the control instance, the CNS, was discussed. Starting at the motor cortical areas of the brain, motor pathways through the basal ganglia and thalamus have been described. The function of the cerebellum was discussed in brief with its unique cellular architecture and the three hypotheses concerning its function in timing, learning and muscle co-ordination. Finally, the spinal cord and spinal reflexes have been highlighted showing

the spinal circuitry of Ia-afferents, α- and γ-motoneurones as well as inhibitory Renshaw cells and Ia interneurones.

3.4 Problems of Motor Control: The Nature of Muscular Synergies

As shown above, the whole hard-wired neuronal circuitry is set up in the CNS to receive information from the outside world, process this information and generate the motor commands. The question now is: how are smooth and sensible movements generated by the CNS? Taking a simplistic approach and relying on stacking together of reflex loops to perform voluntary movement will not suffice in real life situations. On the contrary, this might lead to rather jerky movements depending on the timely or untimely triggering of the reflexes. Another issue is the biomechanical set-up of the musculo-skeletal system. Only in very few cases is one muscle responsible for one specific movement. On the contrary, smooth movement at any one joint relies on the concerted action of a large number of agonistic, synergistic and antagonistic muscles that show - to aggravate the problem even further - non-linear input/output properties. In addition, the movement around one joint results in reaction forces at the neighbouring joints that have to be counterbalanced. Furthermore, muscles are in general poly-articular, i.e. they act on more than one joint, e.g. the biceps brachii muscle acts both at the shoulder and the elbow joint. This results in the coupling between joints (Hogan, 1985). Furthermore, Schieber (1993) has shown that even compartments of muscles can be selectively activated to achieve specific movements, thus increasing the number of controllable units. And finally, what is known as the "degrees-of-freedom problem" in neurophysiology and -psychology further compounds the computation of the inverse kinematics, i.e. the determination of joint co-ordinates from the global position of e.g. the hand. A specific location and orientation of the hand is described by six spatial co-ordinates. When taking into account all joints of the kinematic chain from the feet to the hand, even when disregarding locomotion, as a consequence of the inherent redundancy an indefinite number of possible joint positions to reach the specified hand position and orientation in space can be chosen.

Chao et al. (1989) tried to model biomechanically the precision grip of the hand, i.e. the thumb in opposition pressing against the index finger, and predict the resultant force that would occur between the two fingers. The complete biomechanical modelling resulted in an overdeterminate system with two degrees of redundancy. They proposed to solve the indeterminacy in two ways: first, by taking the system apart and systematically assigning known forces to redundant variables; second, they suggested to use the

principles of optimisation and thus gain a determinate solutions. Indeterminate problems have also been described for other parts of the body, e.g. the head-neck system (Keshner et al., 1992), or the hand in space with at least seven joint angles when counting from the shoulder (Hogan, 1985).

The main question now arises as to how this indeterminacy is resolved by the CNS and how the multitude of control-parameters are brought together to produce sensible actions. Which muscles are activated when and how much? Several concepts have been proposed. Bernstein (1967) suggested that when an organism acquires new skills the CNS locks several kinematic degrees of freedom and only with the progress in learning releases these joints and incorporates them in the increasingly smooth flow of movement. Saltzman (1979) proposed that functional synergies such as the coupling of joint velocity or locking of joints might solve the degrees-of-freedom problem to calculate the inverse kinematics. In addition, similar strategies might be applied to resolve the situation at the single joint where an excess number of muscles act on one joint. Lee (1984) discussed in his essay the idea that neuromotor synergies might be involved in the co-ordination of intentional movements. In his words these synergies manifest themselves as "... a) coherent patterns of electromyographic activity in sets of muscles which can be elicited by electrical stimulation of localised supraspinal neural structures; b) action patterns generated by spinal circuitry; c) multi-muscle postural reaction; d) classically defined responses such as stretch, vestibular, cervical, and flexor-withdrawal reflexes..." He hypothesised that the low-level, neurally based patterns constrain intentional actions, i.e. that a wide range of movement is executed by the combination of various neuromotor synergy modules. Based on his hypothesis these synergies can only be uncovered by statistical investigation of neuromotor activation patterns. These patterns should be observable either spatially (same set of muscles always activated), temporally (coherence, synchronisation, or fixed phase relationship) and in scaling, i.e. all patterns behave the same way throughout the working range. According to Lee, however, results of performed experiments were not clear enough to speak in favour or against this hypothesis.

In 1988, Macpherson recorded the ground reaction forces and the muscular activity in the legs of the cat placed on a moving platform. By translating the platform in several horizontal directions she hoped to find clear correlation of synergistic muscle activation

with forces exerted at the platform in response to its translation. Against her working hypothesis, the muscles behaved not in a simple synergistic organisation. Although the corrective force exerted at the platform was invariant to a given stimulus, the muscle activation changed. She came to the conclusion that the synergies might be tuned to the momentary requirements. Such tuning would consequently allow for more flexible synergies (for review see Macpherson, 1991). Looking at muscle coordination from the two extremes: fixed synergies at the muscle level vs. independent muscle control she found no conclusive indication for fixed muscular synergies. On the other hand, she also rejected the idea of independent muscle control. Her conclusion was, that movement control is conveyed by a set of mechanical strategies with appropriate muscle patterns that are used in specific situations. Maier and Hepp-Reymond (1995a) showed that even though the motor output in the human precision grip was always invariant (mechanical strategy), the activation pattern of finger muscles might change considerably with no obvious reason (see also Hepp-Reymond et al., 1996). Their conclusion was that the CNS was using short-term synergies to produce a certain motor output. Gielen et al. (1995) reviewed several strategies how the kinematic redundancies could be dealt with. He pointed out that most strategies that had been developed in the past years had all short-comings, in that the predictions could not be matched with what was found experimentally. He proposed that a neural network approach which closely matches the biological situation might be an appropriate way to proceed. Nevertheless, it is very likely, that the predictions did not match the experimental outcome purely by the overwhelming number of uncontrolled or difficult to quantify parameters, e.g. anatomy, fatigue, physical and psychic fitness, practice, a.s.o., that might have interferred with the muscle activation. Furthermore, given the relatively confined biomechanical system of the eye with its three rotational degrees of freedom and exactly six muscles - two for each degree of freedom - it might be hypothesised that accuracy (two muscles per degree of freedom, visual system with very high accuracy) was traded off against an unknown evolutionary-sensible criterion which favoured a redundant musculature.

In conclusion, there are two main issues that compound the control of movement: the kinematic and the muscular degrees-of-freedom problems. After elaborating on manifestation and origin of muscle synergies, the latter aspect will be addressed more in

detail, and mainly with a view to the muscular system in man in the following sub-chapters. A large chapter is dedicated to the human hand.

3.4.1 Manifestation of Muscle Synergies

As mentioned above the term "synergy" has various usages: muscles linked within a reflex or higher level organising principles for movements (cf. Macpherson, 1991). "Synergy" in this work shall be used as it is defined by Macpherson (1991) namely "a group of muscles acting together" and, more detailed in the present context, "synchronised muscles and MUs". To determine synergistic activation in specific muscle groups such as in the hand the means of investigation is the EMG. Smith and Bourbonnais (1981) showed that most of the 24 forearm and hand muscles in a monkey were active with the force exerted between thumb and index finger in a precision grip task. Rufener and Hepp-Reymond (1988) elaborated on this experiment to show that the muscle activation covaried with variable precision grip force in a more refined task. Schieber (1995) showed that individuated finger movements in rhesus monkeys were due to the combined action of more than one extrinsic multi-tendoned muscle.

On a much finer time scale, by calculating the cross-correlation and coherence functions of paired EMG records both the temporal and frequency locking of pairs of muscles or MUs can be uncovered. The statistical description as well as several derivations of these functions have been introduced into electrophysiological research and especially motor-control research in the past decades with temporal resolutions down to the order of 10 kHz (Perkel et al., 1967; Moore et al., 1970); synchronised MU activity (Milner-Brown et al., 1973a); synchronisation of MUs in tremor (Dietz et al., 1976); spike-triggered averaging in cortico-motoneuronal cells and fore-limb muscles (Fetz and Cheney, 1980); cross-correlation in intracortical neurons in the motor cortex (Allum et al., 1982); time series analysis (Brillinger, 1988).

3.4.2 Short-Term and Broad Peak Synchrony

Short-term synchronisation between muscles or their MUs is considered an indicator for common input to the motoneurones activating the muscles. Kirkwood and Sears (1991) described in their review on synchronisation the synergies in the respiratory system and discussed several possible neuronal connections that might cause this phenomenon.

From the various forms of cross-correlation peaks of two simultaneously discharging MUs they proposed that only the cross-correlograms with the narrowest peak (half-width of peak less than 2.1 ms) would be caused by the branching axon of one motoneurone. Other cross-correlograms with a broader but nevertheless significant peak would result from oligo- or poly-synaptic inputs, where synchronisation may originate from neurones further upstream. Furthermore, broad-peak synchronisation has been associated with central nervous lesions in the cortex or brain-stem (Datta et al., 1991; Farmer et al., 1993) and with physiological tremor (Logigian et al., 1988).

There is a large variability of muscle or MU synchronisation within the same individual over time, let alone the inter-individual variability. Both intra-individual and even more so inter-individual analyses (e.g. Maier et al., 1995b) resulted in varying degrees of muscle synchronisation. Nordstrom et al. (1990) uncovered synchronisation of chewing muscle, masseter, MUs in four out of their five subjects during the long period of 15 minutes recording time. Also Bremner et al. (1991b) indicated the inter-individual fluctuations in their recording of finger muscle activity.

3.4.3 Localising the Neural Origin of Synchronisation

Many hypotheses have been put forward and experiments performed as to uncover the substrates involved in generating MU synchronisation. Supra-spinal and cortical (Baker et al., 1988; Datta et al., 1991; Farmer et al., 1993), intra- and inter-segmental connections as well as reflex loops have been investigated for their involvement in generation of synchronisation seen at the MU level. This was usually done with stroke patients who had relatively circumscribed areas of the CNS affected by the infarct. For example, Farmer et al. (1993) studied MU synchronisation in intrinsic hand muscles of stroke patients with an infarct in the cerebral cortex, the internal capsule, the cerebral peduncle, the lateral medulla, or the upper cervical spinal cord. They found a loss or reduction of synchronisation associated with a corresponding slowing in the performance of rapidly alternating finger movements. In a very elaborate, complementary experiment with the auditory feedback of the degree of synchronisation, Schmied et al. (1994) demonstrated that the synchronisation of MUs in the extensor carpi radialis muscle could voluntarily be influenced and altered by the test person. This fact speaks clearly in favour of the central origin of muscle and MU synchronisation.

Furthermore, Adams, Datta and Guz (1989) studied the MU activity in the sternocleidomastoid muscle during voluntary and reflexively induced breathing. They found that synchronisation was stronger during voluntary breathing. Bremner and Baker (1990) tested the influence of peripheral input. They applied mechanical vibration at 50 Hz on the 1DI but did not see any changes in the levels of synchronisation in the adjacent second dorsal interosseus muscle. It would be expected that by the very potent stimulus homonymous MUs would be brought into synchrony through the reflex loop, which was not the case.

3.4.4 Physiological Evidence

Indeed, various neuromuscular systems have been identified that display synergistic muscle activation. Physiologically this was usually shown by synchronisation of pairs of MUs, of fixed sequences of muscle activation in specific movements.

3.4.4.1 The Respiratory System

Probably one of the most extensively researched area for muscle synchronisation is the respiratory system. In the respiratory system the muscles of the ribcage and the diaphragm have to be activated in a relatively stereotyped spatio-temporal manner in order to allow respiration. Sears and Stagg (1976) showed a high degree of MU synchronisation in intercostal muscles of the cat. They proposed that this phenomenon was due to branching of presynaptic fibres. Kirkwood and Sears (1991) reviewed the findings they had obtained in their research and came to following conclusions: there exist three types of pre-synaptic synchronisation: a) the high-frequency oscillation which probably originates in the medullary respiratory neurones. This type of synchrony can be potentiated by chemical stimuli for respiration such as too much carbon dioxide in the blood (hypercapnia) or the lack of oxygen (hypoxia); b) the "broad-peak" synchronisation with peaks that have a base width of up to 20 ms. This type of synchronisation seems to represent some sort of pathological function as seen after central nervous lesions and in tremor. In addition, the authors implied that this sort of synchronisation may be conveyed by interneurones that are synchronised to each other or fire in bursts, c) and finally a synchronisation with a periodicity of 30 Hz which they ascribed to the purring function in the cat.

In their conclusion, however, "... only the narrowest of these peaks, ..., can confidently be ascribed to the branched axon hypothesis alone and the others should be regarded as containing a greater or lesser component resulting from presynaptic synchronisation."

3.4.4.2 The Trigeminal System, Speech

During mastication a multitude of muscles is involved. In the trigeminal system too, synchronisation between MUs in the masseter muscle have been described (Nordstrom et al., 1990). In contrast to other muscular systems the reflex loops of the masseter muscle is much more restricted to a small portion of motoneurones and there exists no evidence for recurrent inhibitory pathways analogous to the Renshaw system in the spinal cord. Only after a relatively long time of data recording were Nordstrom and colleagues able to demonstrate that MU synchronisation was also present in the masseter muscles. During the recording period of 15 minutes they followed the time course of synchronisation and found a fluctuation in the strength of synchronisation. In contrast to the generally accepted notion that synchronisation would increase with fatigue, they could not find any trend towards stronger time locking in the discharge of the MUs.

In speech the precise temporal activation of various muscles is a prerequisite for this system to function properly. Here the muscles are innervated by a large number of different cranial nerves: from the fifth, the trigeminal nerve down to the twelfth cranial nerve, the hypoglossal nerve. Gracco and Abbs (1986) asked several subjects to pronounce the word "sapapple" while they recorded upper and lower lip and jaw position but no EMG. In spite of the restrictive temporal regimen the position and velocities of the three measured landmarks showed a considerable scatter. Thus temporal patterns are kept invariant, while other aspects of the control process may vary.

3.4.4.3 Lower Limb and Trunk Musculature, Head and Neck Musculature

In the leg muscles, synchronisation between MUs of the soleus and gastrocnemius muscles (two synergistic calf muscles) were described by Dietz et al. (1976). In addition, Gibbs et al. (1995) compared the synchronisation in the muscles of the small toe with that found between finger muscles and concluded that more widespread

synchronisation was present in the foot than in the hand, speaking in favour of a higher degree of functional coupling of muscle groups in the foot.

In the axial muscles two main direction of spatio-temporal activation can be defined: the homologous muscles on either side of the middle axis and the muscles along the body axis. During stance the posture has to be constantly adjusted against sway mainly in the sagittal and frontal planes. While more synchronous activation can be expected in the homologous muscles (Carr et al., 1994) a fixed cascade of muscle activation along the body starting at the muscles acting on the ankle joint has been shown in response to perturbation of the support platform (Nashner, 1977). This cascade was the same, regardless of the stimulus being either vestibular (translatory movement of the supporting platform) or kinaesthetic (rotation of the platform around the ankle). In a later study Horak and Nashner (1986) showed that in forward or backward support platform perturbations standing subjects responded to the stimuli depending on the platform length - long platform with the weight distributed over the whole foot and short platform with a length of 9 cm - with two distinctly different strategies: the ankle strategy on long platforms with the largest counteracting torque at the ankle joint and the hip strategy on small platforms with compensatory movement mainly around the hip. For intermediate lengths of platform the compensatory movements were executed with combinations of the two strategies. Finally, recent experiments have shown that the switch from one experimental situation to the next had also an influence on the selection of the strategy. Hirschfeld and Forssberg (1994) proposed that for a first fixed muscle activation a central pattern generator for postural responses is used which reacts to acceleration. In a second step this pattern would be finely tuned by all additionally activated sensory systems, such as tactile sensors in the sole of the foot that return information of the supporting platform length. Based on experiments with infants they suggested that the first pattern was produced by a neural network, while the modulation is due to a learning process in the network. In a similar experiment where head displacement was compared to support displacement, Horak et al. (1994) found that both types of completely different inputs (vestibular vs. somatosensory) could trigger the same central pattern when other sensory information was unreliable. In their conclusion, a discrete, innate set of muscle activation patterns seems to control stance and posture. This set of patterns is modulated by post-natally acquired experience.

3.4.4.4 The Upper Limb

Several studies have been performed to address the question of muscle synergy at the upper limb. Buchanan et al. (1986) had subjects perform isometric force of the forearm in flexion, extension, varus, valgus and intermediate directions. The elbow system too is redundant in terms of degrees of freedom. Buchanan and co-workers found that for certain directions only the coactivation of at least two muscles was needed to fulfil the specified task. Given the results of muscles being active over a wide angular range the authors proposed four possibilities for the origin of the patterns: muscle afferent fibre divergence; interneuronal connections to different motoneurone pools; divergence of descending motor axons such as corticospinal or rubrospinal neurones; and finally coherent descending commands. Arguing that the activation patterns look very much similar as the stretch reflex responses, they favoured the possibility of the interneuronal divergence as a very important source of muscle synergy and rejected the notion of fixed synergies. In a second paper, Buchanan et al. (1989) go even further in arguing that fixed muscle synergies at the human elbow joint are rather uncommon and that the relationships between muscle activities are situation-dependent: first, based on the torques of single polyarticular muscles that have to be counterbalanced at the adjacent joints either by muscular, bony or ligamentous constraints. And second, they argue that in almost no muscle pair a consistent coactivation pattern could be detected when going over a broad range of load levels. Soechting and Lacquaniti (1989) could not find any consistent fixed muscular synergies in a three-dimensional arm pointing task, either.

Muscular synergies of the hand will be discussed in the next chapter.

3.4.5 Summary

In this chapter we addressed the coactivation of the muscles in several parts of the human body. Given the analytical indeterminacy of the muscular system, i.e. more degrees-of-freedom than necessary, we pointed out several of the hypotheses that are related to this problem. Further, we showed what experiments were performed to identify biological strategies to tackle the problem of indeterminacy. The means of choice was the cross-correlation analysis of the discharge of MUs with which synchronised events down to fractions of milliseconds could be disclosed, keeping in mind, however, that intra- and interindividual fluctuations of MU synchrony occurs.

Evidence has been put forward that relates the origin of synchronisation to central nervous structures. Several muscular systems have been described where muscular synergy is present: the respiratory system, where the intercostal muscles have to be activated in such a timely manner, that the complete rib cage is moved according to the requirements of the ventilation; further, the trigeminal system is mentioned with strict temporal sequences of muscular activation functions during mastication. Invariant speech but kinematically varying muscle activation have been addressed, speaking in favour of flexible muscle synergy. Next, synchronisation could be found in different leg muscles. Activation patterns were shown on the trunk where a specific cascade of muscle activation was started depending on the experimental constraints and perturbations the test volunteer experienced. Finally, for the upper limb experimental evidence was shown that muscular synergy at the elbow was flexible, adjusted to the momentary need of the action.

3.5 The Hand: Function and Muscular Synergies

3.5.1 The Gripping Hand

The structure of the hand and wrist consists of 27 small bones. Thirty-nine muscles originating in the forearm (extrinsic) or in the hand itself (intrinsic) move the hand and the individual fingers to the required tasks. As already shown in the systems enumerated above, the hand is also biomechanically redundant, with an excess number of muscles compared to the joint degrees-of-freedom. In addition, the muscles span over more than just one joint and contribute to a variety of movements. Given this complex structure we were interested in how the CNS would control such a system, keeping in mind the large variety of tasks at hand.

Indeed, a large number of studies has been performed to determine the rules that govern the control of the hand and the force application in various grips starting with Napier (1956, 1960). These studies have been performed in human beings or monkeys, that have a similar morphology of the hand. Napier first classified the various types of grips in the human hand suggesting two main classes: the power grip and the precision grip. While in the former, all fingers are used to hold an object and press it against the palm, in the latter only smaller forces are used to hold an object between the tips of the thumb in opposition and the index finger. Later on, Landsmeer (1962) defined in more detail these two grips and came to the conclusion, that for the power grip there was a dynamic starting phase and then a static phase after the fingers were brought into contact with the object to be held. In contrast, the precision grip would have no static phase, since the 15 muscles involved would have to keep this delicate system under tight control. In 1967, Close and Kidd described - with the help of EMG recordings - the activity of hand muscles during several handling tasks and defined the muscular functions in these tasks.

In the monkey, Smith and Bourbonnais (1981) showed that almost all the forearm and hand muscles were involved in a precision grip task where a monkey had to press a button during a prescribed period of time. When aligned to grip onset "...virtually all the various antagonist pairs, flexor and extensor, adductor and abductor, pronator and supinator groups all contract in approximate synchronicity...". Lemon et al. (1986), in fact, demonstrated this synchronisation in hand muscles of the monkey. Rufener and Hepp-Reymond (1988) elaborated on the findings of Smith and Bourbonnais and

showed that the EMG activity in many finger muscles covaried with precision grip force. Finally, Chao and colleagues tried with a very elaborate biomechanical model - summarised in their book (Chao et al., 1989) - to quantify the influence of each separate muscle to grip force. They concluded that three classes of muscles exist that contribute to the maintenance and stabilisation of the precision grip: the first group of muscles would covary their activity with the load (FDP, AdP, 1DI, OPP), the second group would get recruited only at higher force levels (EPL, AbPL) and finally a third group of muscles, consisting of the AbPB and EPB, would provide stabilisation of the joints.

One team of investigators that contributed vastly to the understanding of grip control in human beings is that of Roland Johansson in Umeå. This group characterised in great detail the various parameters that are involved in grip control: first they determined the factors that influence the force exerted during the precision grip: friction, cutaneous afferent input and sensory motor memory (Johansson and Westling, 1984). They also showed that an invariance existed between grip force and perpendicular load force with a safety margin that was dependent on the surface texture of the manipulandum. The grip force could be much smaller with object-finger pairings that had large coefficients of friction. In the next step they went on to characterise with microneurography the sensory receptors that conveyed the tactile stimuli, namely the FA I, fast adapting with small receptive fields; FA II, fast adapting with large receptive fields; SA I, slowly adapting with small fields; and finally the SA II, slowly adapting with large fields. In this study, Westling and Johansson (1987) correlated the neurograms of sensory nerves with mechanical measures and EMG recordings, and proposed that the SA II units were involved in the motor control processes in registering the current balance between grip forces and other manipulative forces. They showed that the SA II units were strongly influenced by both indentation forces and lateral forces with directional preferences. According to the authors, the FA I units with a pronounced dynamic sensitivity reliably signalled the occurrence of slip between the fingers and the object held (Johansson and Westling, 1987). In the following series of experiments they demonstrated that grip force is programmed and automatically effectuated on the basis of sensorimotor memory. They gave subjects different boxes with invariant outer dimensions but various weight to lift, and could show that the motor program for grip force active in one trial was very much related to the program used in the previous trial (Johansson and

Westling, 1988a). The investigation was then extended to preparatory actions to unknown impact loads. This preparation consisted of a general stiffening of the hand/arm system prior to an expected impact. This action took all the foreseeable parameters into account, such that at impact of a ball onto the manipulandum which was held by the subject the grip was firm enough to counter the imposed loads. Only when unexpected load changes with partial slip in the grip did occur automatic muscles responses restored the stability of the grip (Johansson and Westling, 1988b). In later studies, pediatricians at the Karolinska Institute in Stockholm and the Johansson group (Forssberg et al., 1991, 1992) demonstrated that the performance of grip has to be acquired from infancy on and that it takes several years before the precision grip performance becomes fully automated under feed-forward control. Then the Johansson group focused on the grip reaction to actively moving manipulanda. These experiments showed that a first muscular reaction, as seen in the EMG, was due to subcortical commands, while a later activity increase in the involved hand muscles could be related to cortical activity as demonstrated with TMS (Johansson et al., 1992a,b; Johansson et al., 1994).

Other groups tried to uncover neuronal connectivity in both man and monkey with acute and chronical recording of muscles and neurones. The test subjects, either man or monkey, were required to perform a precision grip task, exerting force with the thumb and index finger. Lemon and his collaborators identified cortical neurones in the monkey motor cortex that had direct monosynaptic connections to motoneurones and from there onwards to muscles in hand (Lemon et al., 1986). This group further described that intrinsic hand muscles showed more often post-spike facilitation than muscles of the forearm, speaking in favour of more cortico-motoneuronal cells terminating on hand motoneurones than on those innervating the more proximal muscles. In addition, they claimed that the former connections were also stronger (Lemon, Bennett and Werner, 1991). They further pointed out, that any given cortico-motoneuronal cell would also diverge and impinge on other muscles, claiming that one such cell would facilitate, on average, 1.9 muscles, noting however, that this divergence was smallest in the intrinsic finger muscles. This group proposed, given the restricted number of facilitated muscles in the hand, that this focused pattern of facilitation contributes to the fractionation and individuation of hand muscle activity. And finally,

they stressed the point that there was, by no means, a fixed relationship between the cortico-motoneuronal cell in the cortex and the muscles. As was already shown by Fetz and Cheney (1980), neurones and muscles need not be recruited together, even if they show post-spike facilitation. Coming back to the homunculus of Penfield, these results indicated that the organisation in the motor cortex would be much more complex, rather, an output map with multiple representation, convergence and overlap arises with dynamically changing muscular synergies (for review see Lemon, 1993). The anatomical hardware for the physiologically described synchronicity of muscles and MUs (forearm muscles in the monkey: Fetz and Cheney, 1980; hand muscles in the monkey: Lemon et al., 1986) was shown in 1981. Shinoda, Yokata and Futami (1981) proved the existence of divergent projection of corticospinal neurones to motoneurones of different muscles in the monkey by staining of corticospinal axons with horseradish peroxidase. Of course, these findings speak in favour of hard-wired synergistic muscle control, at least for the system they described.

3.5.2 Functional Synergies/Antagonies

Muscular synergy in the hand was thoroughly tested by Bremner et al. (1991b). In their study they compared the level of synchronous firing in adjacent muscles to that of more distant muscles. These authors showed that the firing of MUs that act on widely separated fingers was less synchronised than the firing of MUs acting on adjacent fingers. In addition, MU firing in the finger flexor muscles was less synchronised than the firing of MUs in either the finger abductor or the finger extensor muscles. They concluded that the presynaptic organisation associated with the different tasks is not constant but varies characteristically and consistently with different voluntary motor commands.

3.5.3 Lateralisation

It has often been hypothesised that handedness may be due to better connection of the dominant hand to its controlling structures. Schmied et al. (1994) determined the influence of handedness in extensor carpi radialis on MU synchronisation. Their two main findings were that short-term synchronisation of MU discharges was stronger when the subjects were using their preferred arm, especially for the low-threshold, slow-contracting MUs, and that the presynaptic input synchronisation was also stronger on

the preferred side, especially for the high-threshold, fast-contracting MUs. They proposed that these findings were a sign of the enhancement of efficiency of the motoneurones' common inputs in slow MUs and the enhancement of presynaptic synchronisation of the motoneurone inputs for fast MUs.

Semmler and Nordstrom (1995) came to a different conclusion. They had 51% of MU synchronisation in the dominant hand and 81% in the non-dominant hand. The synchronisation peaks of the MU pairs in the dominant hand were smaller and broader. In addition, MU synchronisation was significantly different between the two hands of right handers, while in left handers no difference, neither in strength, nor in incidence of synchronisation could be determined. Their conclusion was that "... the reduced MU synchronisation in the dominant hand of right-handers may reflect a more restricted distribution of direct projections from motor cortical neurons within the hand motoneurone pool, or reduced excitability of the cortical neurons during the task". In other words, they argued that the dominant hand requires a finer distribution of innervation for more fractionated finger movement. Bremner et al. (1991b) argued in the same line. They described better synchronisation between finger extensor MU pairs than between flexor pairs. Their explanation was that finger flexion usually has to accomplish interaction with the environment, bring the fingers into contact with external objects and, therefore, the flexor muscles have to be controlled separately to reach the optimum position of the individual fingers. In contrast, finger extension is usually non-interactive with the outside world, and thus need not be separately controlled.

3.5.4 Physical Practice

It has been found that physical practice could enhance synchronisation (Milner-Brown et al., 1975). The authors demonstrated a weak trend towards increased synchronisation of 1DI MUs in weight lifters, which in their eyes, is associated with the way in which muscles are used. They concluded that the synchronisation observed in the weight lifters was a direct result of training and not due to other physiological differences which may distinguish them from the general population. De Luca et al. (1982) investigated, among other issues, MU synchronisation in the 1DI muscles of long-distance swimmers, powerlifters, pianists and normal subjects. From their Fig. 2 it can be assumed that pianists have relatively small levels of MU synchronisation, while powerlifters showed

higher degrees of synchronisation. This can be seen as an indication for the specific muscle activation modes these two professional groups require, the pianists intricate, fast movement with the fingers activated separately, and the powerlifters with relatively crude and general muscle activation in a short time.

3.5.5 Summary

First, the biomechanical complexity of the hand was high-lighted. Then, the two main grip forms, the power and the precision grip were mentioned. The unstable bone configuration in the precision grip started several investigation on the muscular activation in this specific grip. These investigations have shown that the grip force is due to the concerted action of a majority of finger muscles. Moreover, the muscular activation is in close correlation to the exerted force. Using the EMG recordings the muscles could be classified with regard to their action. The Johansson group described the sensory "instrumentation" in the hand and showed several programs that are active to maintain stable gripping. This group could show the influence of sensory information, such as haptic and visual cues, on muscle activation. Finally, the development of stable gripping in infants was also investigated.

Another approach to the neuronal connectivity of the muscles was by synchronisation analysis between different muscles and various central nervous structures such as the cortico-motoneuronal tract. This approach gave insight into the origin and organisation of muscle activation in the cerebral cortex.

Finally, three aspects are shown that have been related to specialised connections: synergistic and antagonistic muscles, lateralisation into dominant and non-dominant hand and the influence of physical exercise on enhanced connectivity.

3.6 Robot Hands

In the technical world and industrial applications grippers are used for picking up, holding, manipulating, transferring, placing and releasing workpieces. In general, grippers are mounted on the distal end of a robot arm, enabling the robot to interact with its environment and providing the universality of the machine. Although anthropometric designs of grippers resembling the human hand exist, the general grippers are much simpler, tailored to the specific item they manipulate and to the specific task. In some cases vacuum cup operated grippers are more than sufficient. Other common designs incorporate two- or three-finger grippers, resembling pliers with one degree of freedom (Schunk: Greif Systeme, Product Catalogue, 1998/1999 and 1999). However, these sort of grippers lack the versatility of a multi-purpose gripper, in other words, they have no possibility of dextrous manipulation of grasped items.

Dextrous robot hands, in particular anthropometric grippers, are especially prevalent in academia, where they have been developed from the late seventies and early eighties onwards. However, the theory of stable gripping of dextrous robot grippers had first to be established (Mason and Salisbury, 1985; Cutkosky, 1985). Many challenges such as the kinematical layout in regard to maximum work space, the control of a stable grip in the presence of disturbances such as slipping or compliance control had to be tackled. And last but not least, a large amount of sensory information, e.g. ultra-sonic, optical and tactile information, was to be acquired, fused and analysed in order to develop strategies for stable grasping. Only with this theoretical background of grasping and gripping could the development of anthropomorphic - e.g. the Utah/MIT (Jacobson et al., 1986) or the Belgrade/USC hand (Bekey et al., 1990) - or non-anthropomorphic hands such as the Stanford/JPL hand (Salisbury, 1984; Figure 3-6) or the COR-gripper (Scherrer, 1993), to mention just a few, be made possible.

The most modern example, probably, with a sophisticated integrated design is the DLR articulated hand (Hirzinger, 1999) with four modular fingers, each featuring four joints and three degrees of freedom. The fingers are arranged in a configuration with one thumb and three opposing fingers, enabling the precision grip. Furthermore, 25 sensors - joint angle and torque sensors, tactile foils to detect centre and size of external forces, optical, temperature, limit and motor position sensors - are integrated into the fingers.

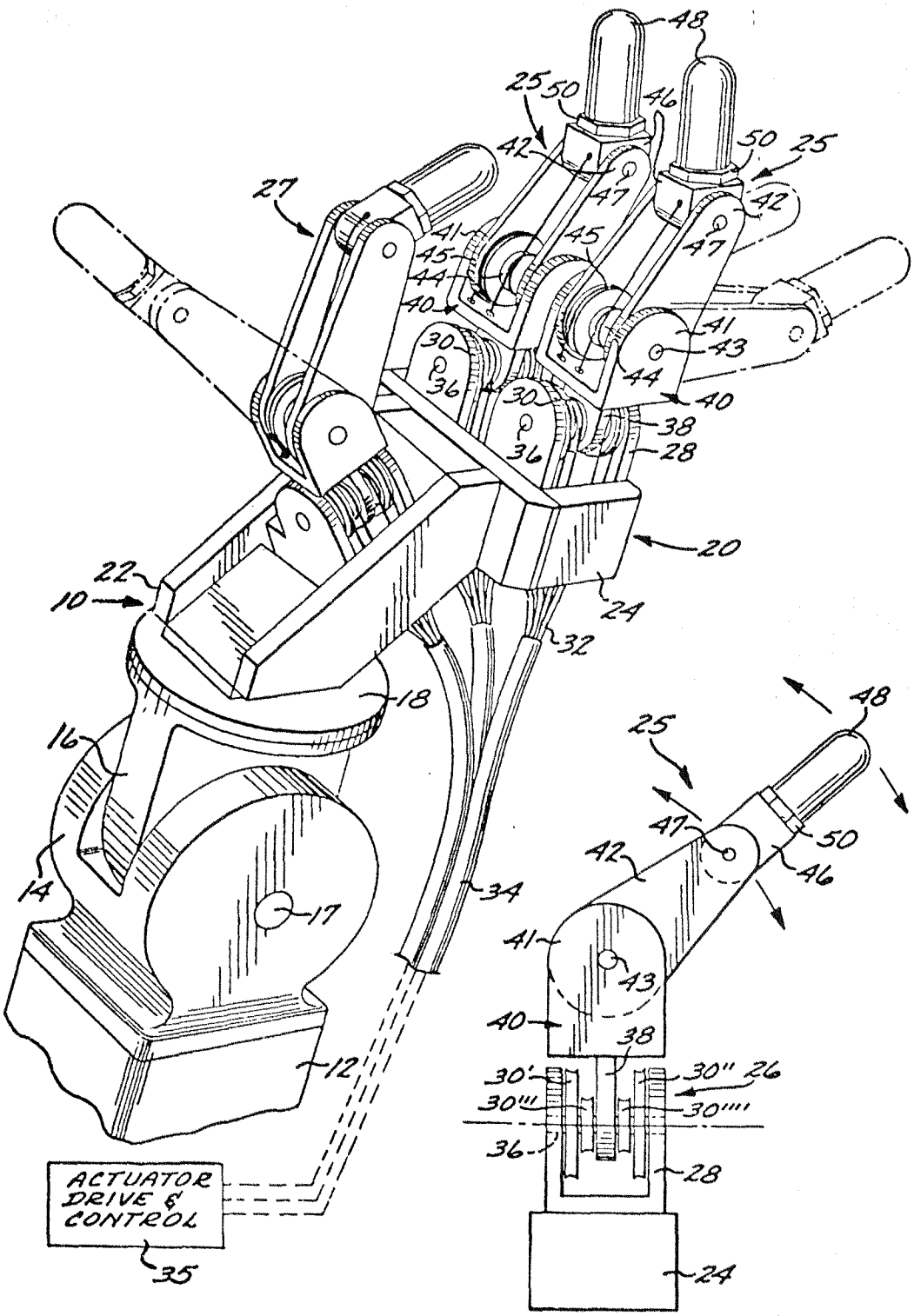


Figure 3-6. Stanford/JPL hand with three fingers. The hand is shown mounted on a Unimate 600 manipulator. *Detail:* A side view of one modular finger with three joints. The joints are moved through pulleys by actuator drives located outside the hand.

The maximum force at the fingertip is 11 N. The control architecture is split into two levels, the global hand control level and the local finger control level.

Cutkosky (1985) described design rationales that have to be considered in robotic hands: he proposed a system that included both the hand and the wrist. In his opinion, the hand had to be sufficiently versatile for grasping and sufficiently precise for manipulation. He preferred a realisation with separate subsystems for the two tasks, or better leave manipulation to the wrist. The fingers needed sensors to measure normal and shear forces at the fingertips. In addition, the location of the centre of the contact area on the finger of the grasped device should somehow be determined. Furthermore, he considered size, uniformity and general shape of the pressure distribution of the contact area to be useful. And finally, the joint angles and torques would be needed. With regard to the controller, Cutkosky proposed basic reflexes for hand and wrist controllers, thereby compressing sensory information before sending it to the task controller. Above the reflexes in a hierarchy are algorithms for choosing a grip, determining internal forces to impose on the object and making fine motion in fulfilment of a task. Salisbury (1985) developed the concept of the grip matrix, then he went on to develop the basic relationships necessary for performing force (wrench), velocity (twist) and stiffness control with an articulated hand.

In more recent years, sensory fusion was one focus of research. With the prevalence of more powerful computers, the number-crunching workload of visual data analysis was made possible. This involved problems as object and pattern recognition, hand-eye calibration and 3D vision, all in real-time. Another area of interest was the planning of object grasping (Woelfl, 1995), where the complete process of target acquisition up to stable grasping and handling is simulated and performed.

The robot hands that evolved over the years are significantly different from their biological counterparts both in design and control. First, the robot joints have, in general, only one degree of freedom and the designers take care that the hands are kinematically determinate or show only a limited number of redundancy. Furthermore, the actuators are mostly rotatory stepper motors applying torque over pulley drives in contrast to the translational muscles in humans and animals. Furthermore, there is no such thing as the size principle or rate coding in technology. Probably closest to these

control parameters is the asynchronous electrical engine where frequency and electric current are controlled.

On the other hand, there is a striking correspondence of all these robot hands with the human hand: they feature a thumb slightly positioned proximally and in opposition to the remaining fingers enabling and emphasising the importance of the precision grip!

3.7 Questions and Hypothesis

Our goal for this whole work is to determine muscular synergies in the human hand. It has been shown before, that MU synchronisation between finger muscles exists. We are interested, whether this previously described phenomenon is influenced or even enhanced by the experimental set-up; whether the CNS has access to synchronisation as a tool to reduce computational complexity, and if so under what circumstances would synchronisation be used, or whether this phenomenon occurs purely at random.

The above compiled results on MU synchronisation have mostly been based on experiments with clear-cut feedback conditions, both visual and auditory feedback of the firing rate of at least one discharging MU under investigation. In a first attempt, study 1, we will extend the analysis of MU synchronisation to a more natural, behavioural task, where the subject has no knowledge of the MU activity underlying the force exertion but, where he only gets feedback of the grip force exerted between thumb and index finger. Furthermore, we want to improve our understanding on some of the results obtained by Maier and Hepp-Reymond (1995b) from whole muscle EMGs, namely the fluctuating and unstable muscle synergies in an invariant motor task and the relatively rare occurrence of synchronisation when compared to other studies. Parts of the data generated by Maier and Hepp-Reymond (1995a,b) are used for the post-hoc analysis of study 1, where we want to show that synchronisation occurs both in pairs of intra- and intermuscular MUs of hand muscles during the precision grip and at different force and activation levels. In addition, we want to show, that synchronisation is occurring preferentially just above recruitment threshold of the MUs and thus may be directly involved in recruitment.

In study 2, we will address several questions that arise from the results of study 1: first, we want to validate the results gained in the first study; second, we want to find out whether the phenomenon, that force release in a controlled manner is considerably more difficult to achieve (e.g. Johansson and Westling, 1987) is related to a different level of MU synchronisation; third, for us the most intriguing question, is there any influence of the MU activity feedback onto MU synchronisation, as advocated by the study of Schmied et al. (1993) and the high percentage of MU synchronisation described by other groups in comparison to number Maier and Hepp-Reymond (1995b) proposed; fourth,

we are interested in the biomechanical properties, i.e. the twitch tension and contraction time, of our MU data pool.

For study 3, we test the muscular activation in two complementary tasks, the precision grip and the power grip (Napier, 1956). Flament and colleagues (1993) showed a task dependence of the responses in the first dorsal interosseous muscle (1DI) to TMS. These responses are stronger with increasingly more complex grip tasks. Based on these findings, we put forward the hypothesis that different degrees of synchronisation should be obtained in selected hand muscles during different tasks. In particular, we expect to find less MU synchronisation in the precision grip, were all the fingers have to be activated separately, and the power grip, with its coarse finger muscle activation. The experiments will be performed to investigate the degree of synchronisation between the whole muscle EMG signals of muscle pairs during the two grip tasks. Furthermore, we determine the influence of TMS on this synchronisation. Comparison of synchronisation between MUs with or without TMS in the precision grip task alone will also be performed.

All these results will be analysed with a view to the importance of muscular synergy in the hand. On the one hand, this shall help to understand how the CNS is involved in the control of the precision grip, on the other hand, the results shall also highlight the amount of muscular synergies in different tasks. This might lead to predictions on control strategies to cope with or, rather, sensibly utilise the given muscular redundancies.

4 Study 1: Muscular Synchronisation

Parts of this chapter have been published in Experimental Brain Research (Huesler et al., 2000, EMG Activation Patterns during Force Production in Precision Grip. III. Synchronisation of Single Motor Units)

4.1 Goal and Motivation

In study 1, we investigate to what extent MU synchronisation is present and robust in a natural, behavioural task in which the subjects are not aware of the MU activity underlying force production, but only get a feedback of the grip force exerted between the tips of thumb and index finger. This is in clear contrast to the majority of studies that have been performed so far, where test subjects had to control and maintain the MU discharge at a specific level.

Furthermore, we wanted to find out which MU characteristics may account for the relatively small degree of temporal coupling and the fluctuating and unstable muscle synergies disclosed by Maier and Hepp-Reymond (1995b) in whole muscle EMG during grip force. The isometric task in those experiments was invariant, i.e. the subject had to repeat twenty times an isometric step-tracking task by increasing grip force from zero to three Newton force with increments of one Newton. Given this task, it was expected to find an ample amount of synchrony between the various muscles involved. This was not only not the case, moreover, synergies turned out to be only present in a restricted set of test sweeps, but not in all sweeps originating in one experimental session. This analysis now goes more into the details of the data and tries to characterise MU synchronisation in muscles active during the precision grip. We expect to find more synchrony at the MU than at the muscle level. Furthermore, we expect that MU synchronisation increases with increasing force, based on higher discharge rates and a stronger volitional drive from the CNS to the muscles to generate in synergy higher forces.

4.2 Study 1: Means and Methods

4.2.1 Experimental Set-Up

The data analysed in this part is a subset of data (EMG and force signals) gathered in the experiments of Maier and Hepp-Reymond (1995a, b). The experimental set-up, task,

EMG and force recording procedures are described in these two papers. In brief, five healthy subjects - all right-handed - were seated comfortably in front of a computer screen. The right hand was immobilised with the wrist in the resting position, i.e. in slight extension (~20°) with an individually fitted thermoplastic cast. The subjects had to perform a visuomotor step-tracking task by exerting isometric force on a transducer which was held between the tips of thumb and index finger, and to match three consecutive target force levels (1, 2 and 3 N, i.e. less than 10% maximum voluntary contraction, MVC) during approximately 3 s each. The whole sequence of required target forces was constantly displayed on the screen in front of the subject while the exerted force was represented as a running cursor. The intramuscular electromyographic activity of up to eight varying hand and forearm muscles (see Table 4-1) was recorded with bipolar, intramuscular needle electrodes and stored simultaneously with the three force signals (thumb, index and resultant total force) on an analog 13-track FM tape for later off-line analysis.

The subset sample used in this study was selected under two criteria: first, we wanted to achieve a maximum variety of muscle combinations for later correlation analysis and, second, the EMG signals should be such that discrimination into single MU potentials was possible, i.e. the signal should not display tetanic fusion of the potentials.

4.2.2 Data Acquisition and EMG Decomposition

The data of one experimental session consisted of up to four simultaneous multi-unit EMG records (10 kHz sampling frequency/channel, 50 Hz notch and anti-aliasing filtering at 3 kHz), and the resultant force (40 Hz sampling frequency, gain: 1 V/N, 0.13 N resolution, range: ±5 N) acquired from 20 trials of 15 s duration each. The limited time and amplitude resolution of the force channel were determined by the software and hardware configuration of the data acquisition system and could not be altered. This system (ARTMUP; Haas and Meyer, 1989) was tailor-made for an integrated acquisition of EMG signals and their decomposition into constituent MU potentials (MUPs; see Figure 4-1) and therefore, did not suit all the requirements for this study, i.e. relatively poor resolution for the force signals both in time (40 Hz) and amplitude (0.13 N resolution).

Muscle	Innervation	Function	# of MUs
Thumb Muscles			
Abductor pollicis brevis (AbPB)	median	abduction & flexion at metacarpophalangeal joint	1
Abductor pollicis longus (AbPL)	radial	abduction & dorsal flexion at metacarpophalangeal joint	4
Adductor pollicis (AdP)	ulnar	adduction & opposition at metacarpophalangeal joint	18
Extensor pollicis brevis (EPB)	radial	abduction & extension at metacarpophalangeal joint	6
Extensor pollicis longus (EPL)	radial	adduction & extension of the thumb	1
Flexor pollicis brevis (FPB)	median/ ulnar	adduction & flexion at carpometacarpal joint	5
Flexor pollicis longus (FPL)	median	flexion at metacarpophalangeal & interphalangeal joint	7
Opponens pollicis (OPP)	median	opposition & adduction at carpometacarpal joint	7
Index Finger Muscles			
First dorsal interosseus (1DI)	ulnar	abduction & flexion at metacarpophalangeal joint, flexion at metacarpophalangeal joint, extension at proximal & distal interphalangeal joint	16
First lumbricalis (1LUM)	median	flexion at metacarpophalangeal joint, extension at proximal & distal interphalangeal joint	8
First palmar interosseus (1PI)	ulnar	adduction & flexion at metacarpophalangeal joint, extension at proximal & distal interphalangeal joint	7
Extensor digitorum communis (EDC)	radial	extension at proximal & distal inter- & metacarpophalangeal joint	3
Flexor digitorum profundus (FDP)	median	flexion at metacarpophalangeal, proximal & distal interphalangeal joint	4
Flexor digitorum superficialis (FDS)	median	flexion at metacarpophalangeal & proximal interphalangeal joint	5

Table 4-1. Overview of all the muscles, whose MUs were analysed in this study. The functions are described only as far as they are relevant for the precision grip task. FPB: deep part innervated by ulnar nerve, superficial part by median nerve (Feneis, 1988).

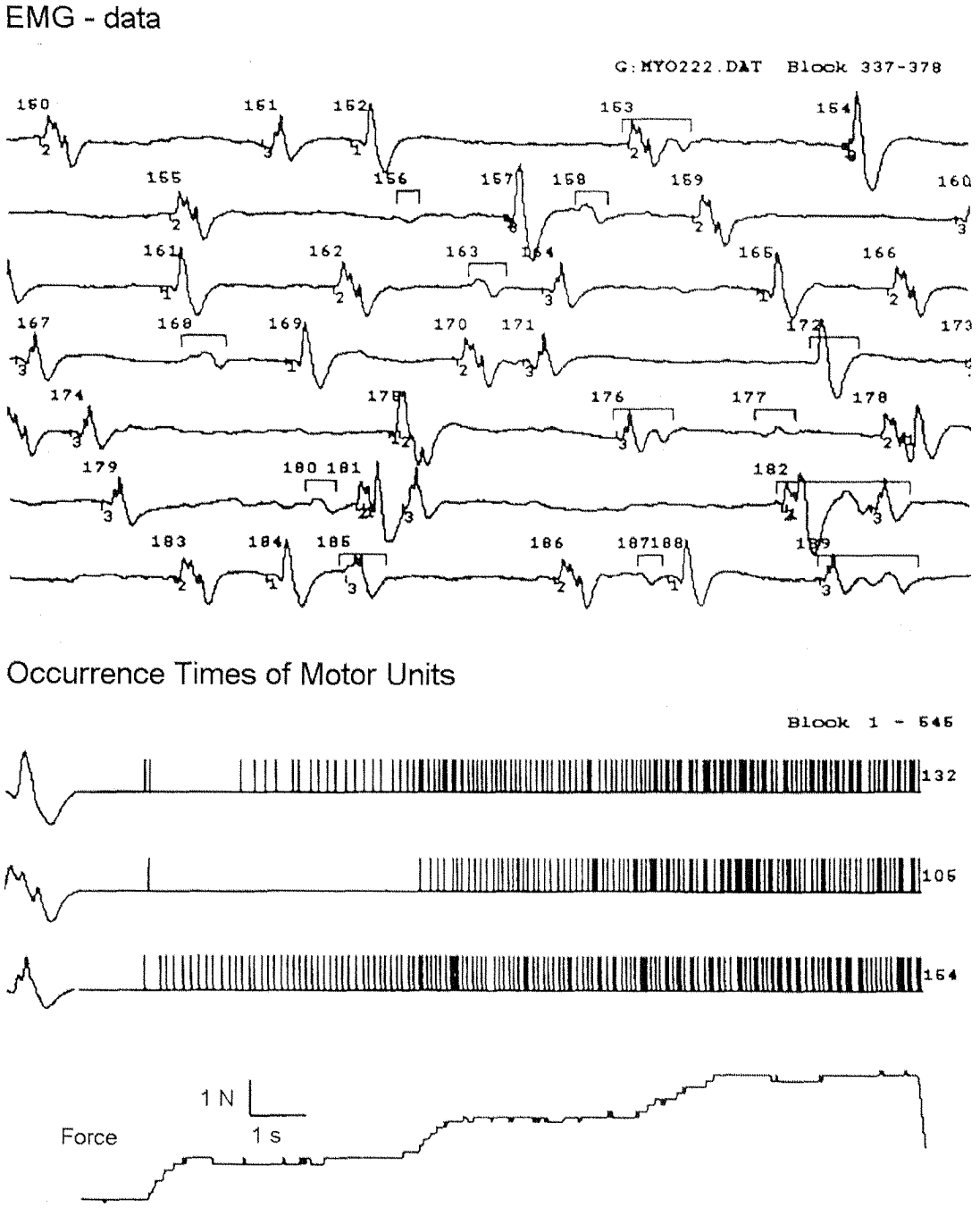


Figure 4-1. Example of an EMG decomposition by ARTMUP for an AdP electromyogram. *Top:* Original EMG signal of 1.05 s duration - seven lines with 0.15 s each. Numbers above the signal trace indicate the identified segments (150 - 189), the numbers below the trace denominate the successfully discriminated MUPs (1, 2 & 3). Not completely decomposed data segments are indicated by a square bracket. *Bottom:* Occurrence times of the three discriminated MUs in a 15-s trial with the averaged force trace.

The ARTMUP's strategy to discriminate MUPs within multi-unit EMG signals is based on several phases. First, the algorithm detects segments of activity (Figure 4-1 *top*) in the multi-unit EMG where the signal exceeds a background level of activity. These segments putatively contain one or more MUPs. These segments are marked until final decomposition and identification of all enclosed MUPs. In the next phase the algorithm extracts templates for single MUPs from these segments by a nearest-neighbour cluster analysis considering the following MUP features: maximal positive amplitude, peak-to-peak amplitude, area, duration of an active segment, maximal positive slope, maximal negative slope, number of extremes. Finally, using the estimated mean repetition rate, superimposed potentials are automatically decomposed. This is confirmed by subtracting the templates from the summed signal in the segment. The user can control and interactively optimise the results of the program by checking the inter-potential interval histogram (IPIH) for plausibility, and by subtracting single potentials from overlapping potentials. A list with all occurrence times of each potential is exported. These processes have to be repeated for every 15 s recording, in other words, the MU templates have to be regenerated each time, since they are not conserved from one trial to the next. Finally, the templates of each trial are compared with those in the preceding and subsequent trials by visual inspection. Templates that could be identified and followed over several sweeps were retained for further analysis, while others were discarded, that did not show any characteristic feature and could not be classified. This may be an arbitrary decision making process, but it assures that the retained template is always originating from the same MU.

In the low force range used in this investigation (<10% MVC) ARTMUP reliably detected up to four different potentials in one EMG channel (single electrode recording). With higher forces the potentials of a multitude of MUs start to fuse and thereby prevent satisfactory discrimination by ARTMUP.

All in all, 232'372 segments were identified. Of these, 53'659 segments were rejected a-posteriori due to poor discrimination of the MU potentials. This was indicated by implausible firing rate distribution as shown in the IPIHs, or by insufficient quantity of data points, i.e. less than 200. Thus 178'713 segments were retained for further analysis. Of this number, 139'193 or 77.9% segments were fully decomposed, while 39'520 or 22.1% were only partially decomposable, nevertheless yielding at least one occurrence

time of one MU potential to the total number of occurrences. In the 178'713 segments a total of 92 MU potentials with a total of 199'264 occurrence times could be identified.

From a more global perspective 18 records with one MU/channel, 12 records with two MUs/channel, 14 records with three MUs/channel and two records with four MUs/channel were obtained.

Finally, the occurrence times of each MU potential were printed out together with the respective force traces in raster form, the peri-response time histogram and the IPIH (Figure 4-2) using a custom-made program (std/mtd) based on X-Plot (open-source C-language program). As example, Figure 4-2 shows the activity of one OPP MU during 20 trials. This MU was one amongst four discriminated within the multi-unit EMG signal. As soon as the MU was recruited, it fired regularly and the firing frequency was correlated with force (r: 0.80). The variability of recruitment is attributed to the different contraction rates of the muscles, since this parameter was not controlled in this experimental situation. The IPIH shows a unimodal distribution of the firing frequency, even though the intervals were derived from the three force levels.

4.2.3 Data Selection

Three-second epochs, one for each of the three steady-state force levels of a trial were automatically selected by a sliding window with two weighted criteria: smallest standard deviation of the actual force signal in the window and least difference between the averaged applied force in the window and the target force. The times of occurrence of MUPs and the averaged applied grip force during these epochs were then extracted for further processing. Neither the transition phases from one force step to the next step, nor the force release at the end of the trials were used since the intended analysis with the cross-correlation method relies on stationary data.

4.2.4 Motor Unit Behaviour

The participation of the MUs to grip force was estimated by correlating the mean firing rate with the mean applied force of each epoch. The relationship between force and firing rate - rate coding - were determined by a correlation and linear regression analysis. Recruitment was determined statistically over the twenty trials. Given the stepwise force increase following definitions were used.

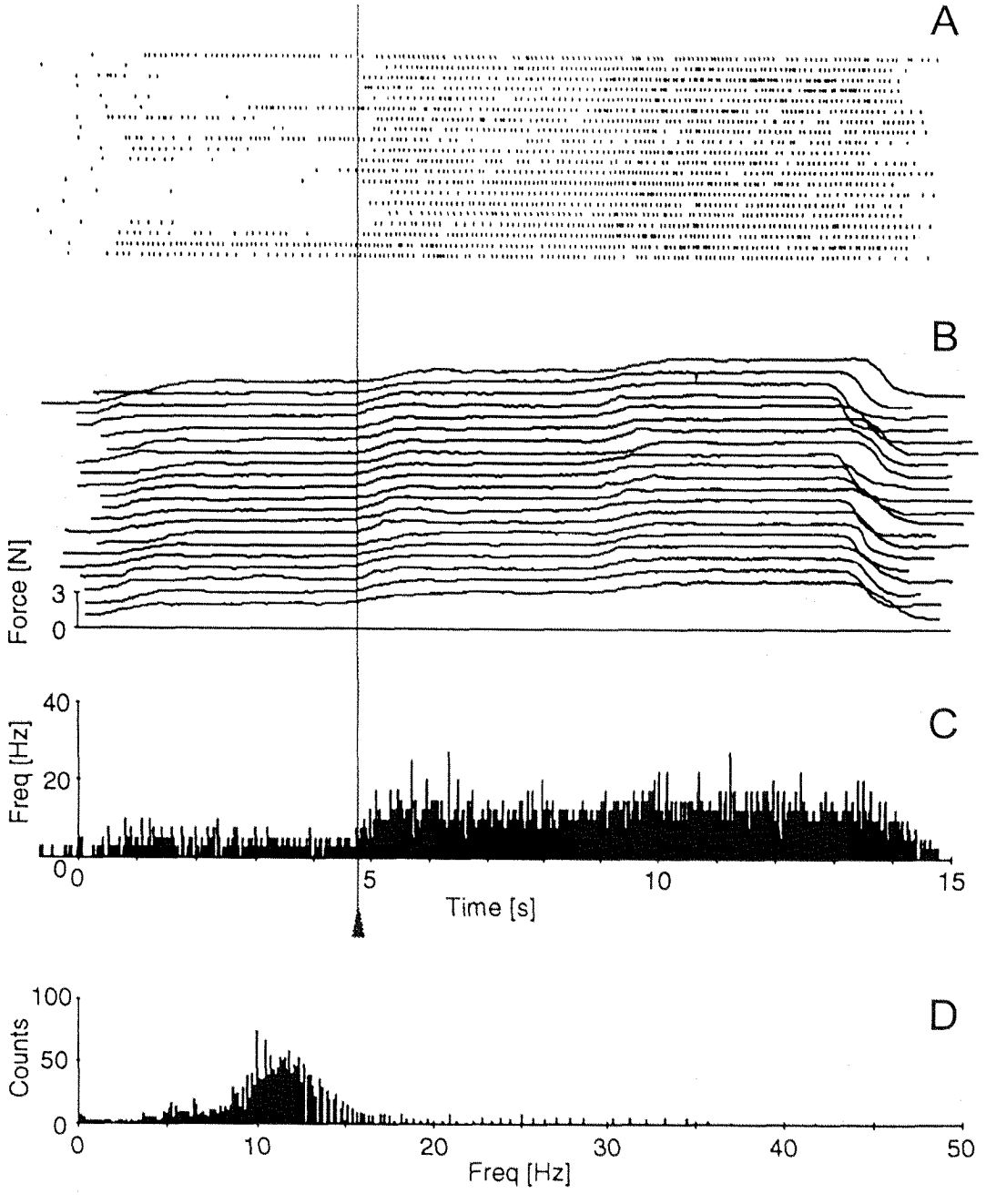


Figure 4-2. Opponens motor unit activity during 20 trials. This MU was amongst four others that were discriminated within the whole muscle EMG signal. *A:* Raster histogram of the MUP train, 20 trials, lowest trial being the first one. *B:* Corresponding force traces. *C:* Peri-response time histogram: summation of the occurrence times of the MU potential in the 20 trials. The vertical line indicates the point of alignment, i.e. the onset of force increase from 1 to 2 N. The MU firing rate clearly increases with force (correlation coefficient $r = 0.80$). The columns in the histogram have a binwidth of 20 ms, thus the height of the columns is quantified by the number of counts in each bin divided by 20 ms. *D:* Inter-Potential Interval Histogram showing a unimodal distribution of the firing frequency even though the data is derived from all three force levels.

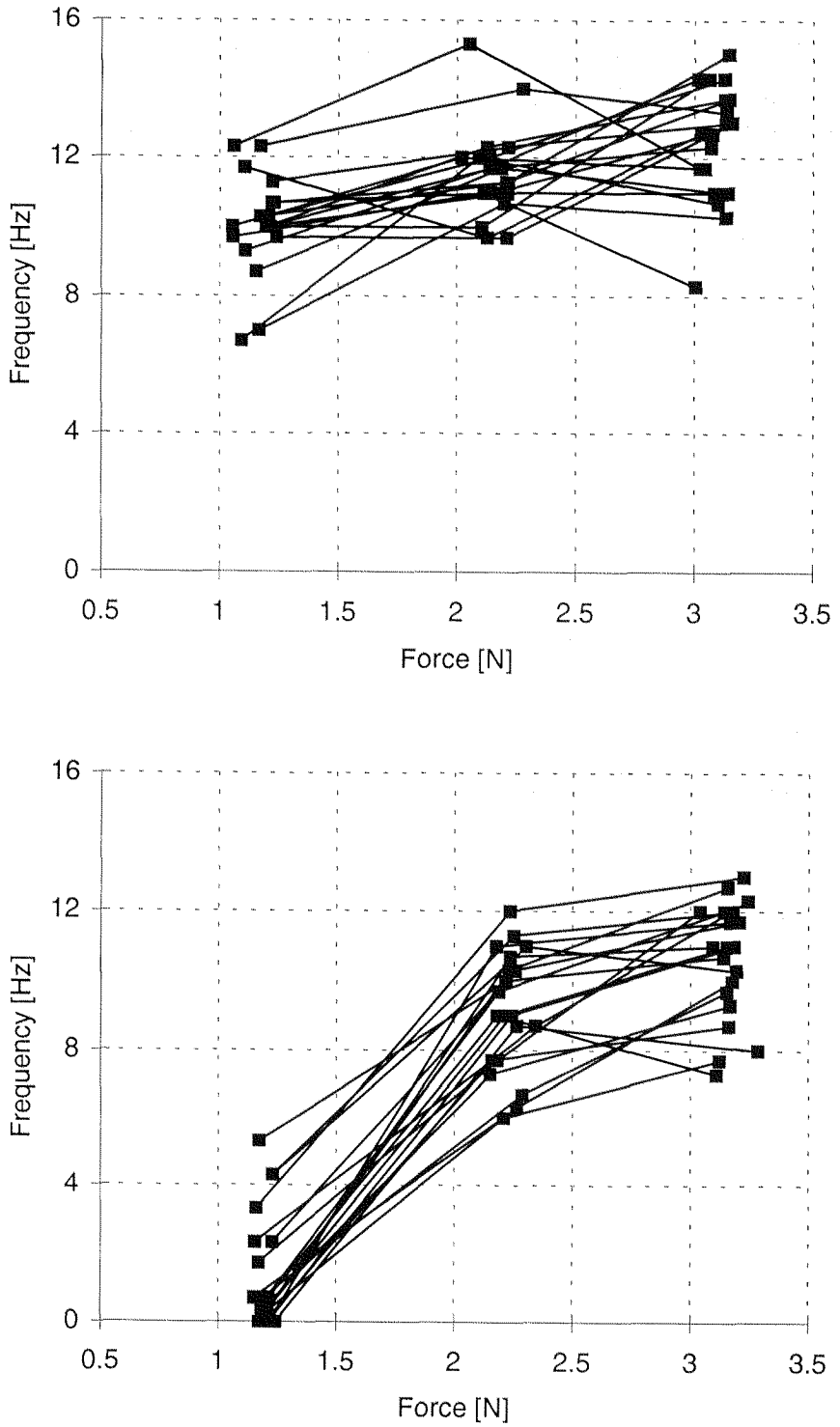


Figure 4-3. Relationship between firing frequency and force for on FPL MU (*top)* and one AdP MU (*bottom)*. The firing rate as a function of force for the FPL MU is already relatively high at the 1 N level and only increasing slightly over the subsequent levels, typical for extrinsic MUs. In contrast, the AdP MU is just becoming active at the 1 N level, jumping to a stable discharge at the 2 N level and from there increasing slightly to the discharge rates at the 3 N level. This behaviour is typical for intrinsic MUs.

The *single trial recruitment level* of the MUs with positive correlation of firing rate and force was determined trial-by-trial interactively. The *single recruitment threshold* was defined as the lowest level, i.e. 1, 2, or 3 N, on which the MU discharge was becoming stable, i.e. without missing discharges, and regular, i.e. with a constant frequency. This value was obtained by averaging the single trial recruitment levels over the 20 performed trials. To classify the MU, this value, rounded-up, was taken as its overall *recruitment level*, i.e. 1, 2 or 3 N.

Scatter diagrams were created for all MUs, with the three data points of one trial (three epochs) connected to visualise the stability of the firing rate/force relationship (see Figure 4-3 and Maier and Hepp-Reymond, 1995a).

4.2.5 Motor Unit Synchronisation

To detect the existence of synchronised discharge of MU pairs a time-discrete cross-correlation analysis was performed for both intramuscular (IAM) and intermuscular (IRM) pairs on each force level separately for a maximum of 20 trials. The cross-correlation was calculated only when a minimal number of 200 spikes/MU channel was given. Thus a maximum of three cross-correlations per MU pair could be obtained for further analysis. The cross-correlation (E 4-1) was calculated using the Spike2 software (CED, Cambridge UK) on a time interval of ±100 ms, with a binwidth of 2 ms.

$$Corr(g,h)_j \equiv \sum_{k=0}^{N-1} g_{j+k} h_k$$

E 4-1

Based on the results of Maier and Hepp-Reymond (1995b) and of other groups we confined the search for significant short-term synchronisation peaks to a time window of ±20 ms around time-lag zero. Cross-correlogram peaks were identified as a sustained rise in the CUmulative SUM derivative (CUSUM, cf. Davey et al., 1986, E 4-2). The on- and offset of the peak were defined as the first and last bins that were part of the CUSUM rise, respectively, and their difference determined the peak width. The statistical significance of the synchronisation peaks obtained was determined using the CUSUM:

$$S_i = \sum_{j=1}^{j=i} \left(x_j - \bar{x} \right)$$

E 4-2

The CUSUM had to exceed the significance limits based on the variance of either Poisson (E 4-3) or stochastic point processes (E 4-4) whichever was more stringent.

Variance of a Poisson process:

$$V_{Poisson} = \frac{nt}{m}$$

E 4-3

Variance of a stochastic point process:

$$V_{po\,int} = n\left[\frac{c^2 t}{m} + \frac{1}{6} - \frac{c^4}{6} + \frac{(ct)^2}{um} \right]$$

E 4-4

where t is the time after a control reference period of duration u, m is the mean interval of the discharge train used to construct the cross-correlogram of n trials and c is the coefficient of variation.

At least one point in the CUSUM had to exceed the 0.1% significance limit during the critical period of ±20 ms (3 times standard deviation of the Poisson or stochastical point process, respectively). Cross-correlogram and CUSUM with significance limits were printed out together (Figure 4-4). To determine the strength of synchronisation the peaks were quantified with four indices: *k:* relative peak amplitude (Sears and Stagg, 1976); *k'*: relative peak area (Ellaway and Murthy, 1985); *b:* peak area normalised with total number of trigger plus response spikes (Bremner et al. 1991a); *CIS,* common input strength*:* peak area normalised to total recording time (Nordstrom et al. 1992). The *mpi* index (mean percent increase above baseline, Cope et al., 1987) can directly be derived from the *k'* index and was, therefore, not used. Even more, the values *b* and *CIS* were rejected later on, because the values *k* and *k'* best represented the cross-correlogram in relation to the visual impression.

The robustness of the CUSUM calculation for evaluating significance of cross-correlogram peaks was demonstrated by Bremner et al. (1991a) with segments of independent records of 100 trigger pulses each, i.e. half of the 200 spikes we specified as minimum criterion: they showed a faulty estimation in less than 1% of the 360 cases.

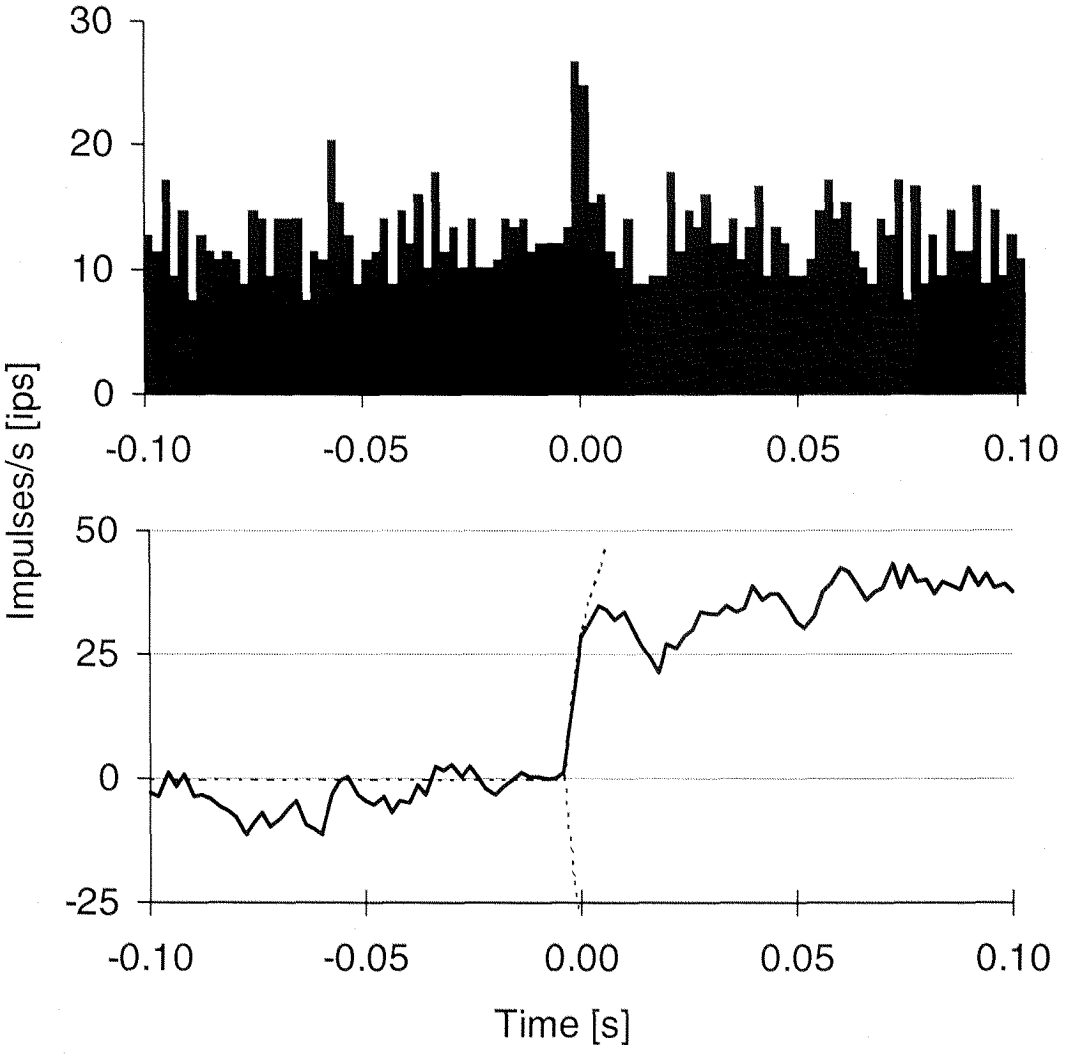


Figure 4-4. *Top:* Cross-correlogram of two AdP MUs on the 2 N level with a peak centred at time 0. *Bottom:* corresponding cumulative sum derivative (CUSUM, heavy line) with confidence limits (dashed lines) showing significant short-term synchronisation. Same MUs as MU1 and MU2 of Figure 1. The mean firing rates were 10.1 and 11.0 Hz, respectively. The number of triggers contributing to the cross-correlogram is 559 for MU1 and 547 for MU2. The strength of synchronisation is given by the relative peak amplitude *k*: 3.00, the relative peak area *k'*: 1.53. *Abbreviations*: ips: impulses/sec as given by counts per bin/(binwidth x number of sweeps).

Further, the IRM MU cross-correlograms were compared with the cross-correlograms of the corresponding multi-unit EMGs obtained from Maier and Hepp-Reymond (1995b). In brief, cross-correlations between EMG activity of the two muscles were computed by multiplying the Fourier transform of the EMG from one muscle by the complex conjugate of the other muscle's Fourier transform of the EMG. This product was then inversely transformed and summed over all trials of a single force level. Muscle pairs were considered synchronous if the size of the peak exceeded four standard deviations of the total signal.

4.3 Study 1: Results

4.3.1 Motor Unit Sample and Behaviour

The data were gained in 15 experimental sessions from five healthy subjects. The discrimination of the selected multi-unit EMG signals yielded 92 MUs, 30 located in extrinsic, 62 in intrinsic muscles.

Of the 92 MUs 29 MUs were tonically active already at the 1 N level, 42 MUs were recruited between 1 and 2 N, and 21 MUs above 2 N. The mean firing rates varied between 5 to 14 Hz for the 1 to 3 N force range. The mean firing rate at recruitment threshold was 8.6±1.9 Hz.

Four statistical values were compared to show the differential contribution of extrinsic and intrinsic MUs to grip force: the recruitment threshold, the correlation coefficient of the force/firing rate relationship, the slope and the intercept of the corresponding regression analysis. For the former two values all 92 MUs were taken into account, for the latter two only the 77 significantly and positively correlated MUs.

First, the mean recruitment threshold was 1.4±0.7 N (range: 0.2 - 2.9 N). The recruitment thresholds were significantly lower for the extrinsic MUs as compared to the intrinsic ones (1.0±0.6 N, n_{extr} = 30 vs. 1.6±0.7 N, n_{intr} = 62, respectively; *t*-test, $P<0.001$).

Second, seventy-seven MUs showed significant positive correlation coefficients (18 extrinsic and 59 intrinsic MUs, Figure 4-5). Significant negative correlations were found in three extrinsic and one intrinsic MUs. The activity of eleven MUs, nine extrinsic and two intrinsic MUs, was unrelated with the resultant grip force in the task. Further

differences between intrinsic and extrinsic MUs were: a) relatively more MUs of intrinsic muscles displayed a significant force/firing rate relation than extrinsic MUs (intrinsics: 60 out of 62, 97% vs. extrinsics: 21 out of 30, 70%; χ^2-test, $P<0.001$); b) the MUs of intrinsic muscles showed significantly better positive correlation than the extrinsic MUs (r_{intr}: 0.68±0.17, n = 59, vs. r_{extr}: 0.57±0.22, n = 18; t-test, $P<0.05$) ; c) with regard to positive significant correlations, the MUs of intrinsic muscles had a smaller scatter in the force/firing rate relationship (variance σ^2 of correlation coefficient r: 0.028, n = 59) in comparison to the MUs of extrinsic muscles (variance σ^2: 0.049, n = 18). However, this difference was not significant (F-test, $P>0.05$).

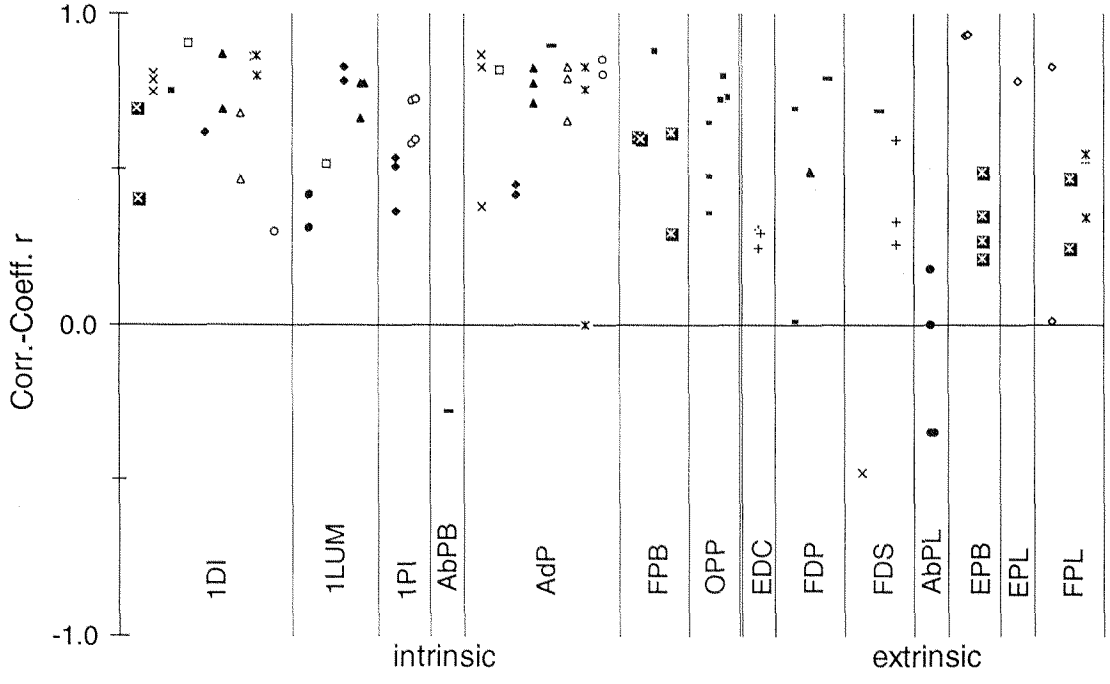


Figure 4-5. Correlation coefficient r for the force/firing rate relationship of intrinsic and extrinsic MUs. Each marker denotes a correlation of one MU. Same symbols originate from the same experiment, markers in the same column originate from the same needle electrode recording. The intrinsic MUs show a significantly smaller scatter of the coefficients. Except for two intrinsic MUs, all coefficients are positive. The extrinsic MUs display much stronger scatter.

Third, the slopes of the regression lines for 77 positively correlated MUs varied between 0.5 and 6.0 Hz/N, with an average of 3.3±1.5 Hz/N. The slopes of the intrinsic MUs were steeper (3.56 Hz/N vs. 2.45 Hz/N) when compared to the extrinsic ones (t-test,

$P<0.01$, $n = 77$). The slope of the four negatively correlated MUs had a range of -1.0 and -1.3 Hz/N.

Finally, the y-axis intercepts of the intrinsic MU regression lines were more negative (-0.92 Hz vs. 2.91 Hz) when compared to the extrinsic ones (*t*-test, $P<0.001$, $n = 77$). Negative intercepts are indicative of recruitment at higher force levels within the investigated force range.

In Figure 4-3, the two exemplary scatter diagrams and in Figure 4-6 the two cumulative plots of the slopes and intercepts, the latter originating from the significant positive force/firing rate regression lines, highlight the differences between the MUs in intrinsic and extrinsic muscles. Figure 4-6 *top* (cumulative plot of slope values) shows that intrinsic MUs have steeper slopes, i.e. the cumulative graph of the intrinsic MUs is shifted more to the right compared to the extrinsic one.

Figure 4-6 *bottom* demonstrates that the y-intercept values for the intrinsic MUs are more negative. The cumulative graph of the intrinsic MUs is, therefore, shifted to the left in comparison to the extrinsic graph.

4.3.2 Motor Unit Synchronisation

To detect synchronisation between two MUs the respective times of MUP occurrence were cross-correlated. Narrow peaks in the cross-correlograms around time zero, indicating synchronised activity, were found in the majority of the cases.

4.3.2.1 *Intermuscular Motor Unit Synchronisation*

Out of 328 possible MU pairs resulting from the 92 analysed MUs, 166 IRM pairs could be gained with simultaneously active MUs. In 59 pairs the MUs were coactive on one force level only, in 68 pairs on two levels and in 39 on all three levels, yielding 312 cross-correlograms. Synchronisation was found on at least one force level in 45% (75) of the MU pairs: 65 pairs on one, nine pairs on two, and a single pair on three levels, yielding 86 cross-correlograms with significant synchronisation peaks. The mean and standard deviation of the synchronisation strength was given by the indices *k*: 2.19±0.50, and *k'*: 1.70±0.30 ($n = 86$).

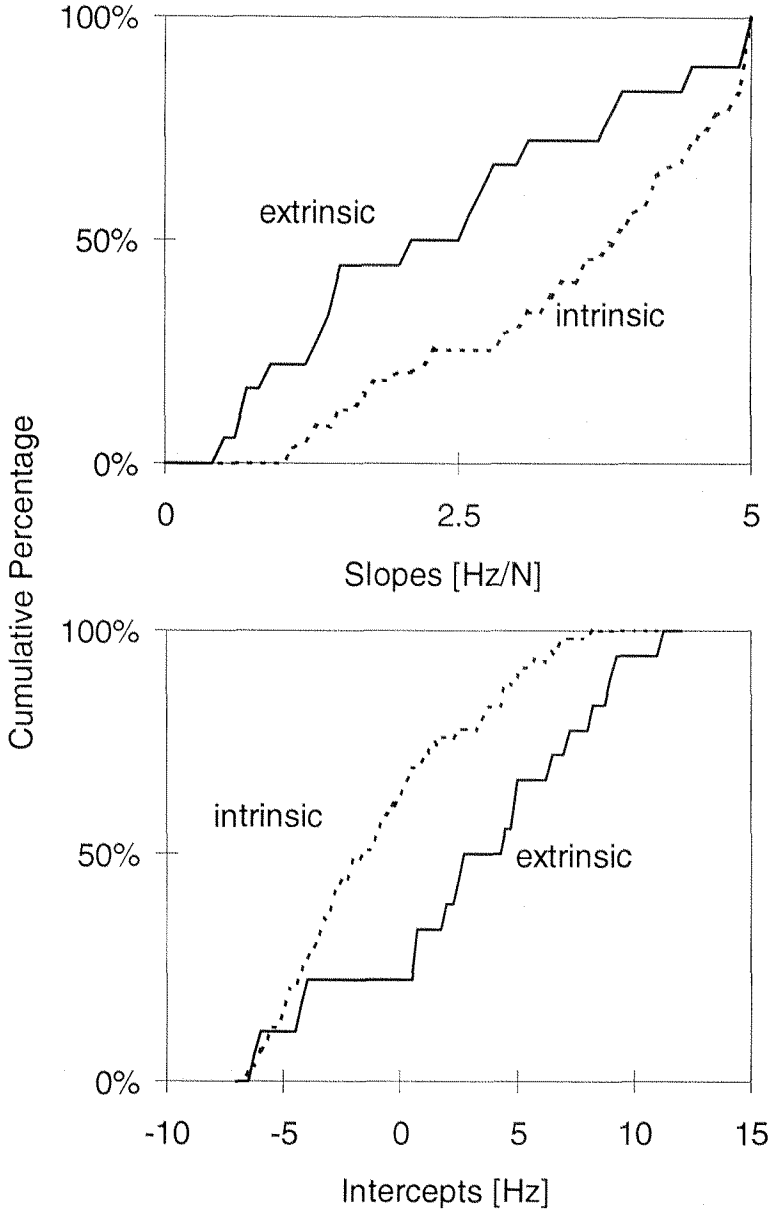


Figure 4-6. Relationship between firing rate and force for populations of intrinsic and extrinsic MUs. *Top*: Cumulative percentage calculated from the values of the slope of the force/firing rate regression lines for 59 intrinsic (stippled lines) and 18 extrinsic (continuous lines) MUs. About 50% of the extrinsic MU population has a slope below 2 Hz/N in contrast to less than 20% of the intrinsic MUs, indicating a generally steeper slope for intrinsic MUs. *Bottom:* Cumulative percentage of the intercepts of the force/firing rate regression lines for intrinsic and extrinsic MUs. About 63% of intrinsic MUs show negative intercepts indicating recruitment during the increase of force, whereas most extrinsic MUs have positive intercepts due to activity prior to 1 N.

4.3.2.2 *Intramuscular Motor Unit Synchronisation*

From a total of 83 IAM MU pairs, 69 pairs were accepted for further processing. In 22 pairs the MUs were coactive on only one level, in 27 pairs on two levels and in 20 on all three levels, yielding 136 cross-correlograms. Fifty-four MU pairs (78%) showed significant synchronisation on at least one force level. Among those, only four pairs were synchronised on all three force levels (2 AbPL, 1 AdP and 1 FPL pairs), fifteen at two and 35 at one level only, yielding 77 cross-correlograms with significant synchronisation peaks. The mean and standard deviation of the synchronisation strength was given by the indices k: 2.49±0.88, and k': 1.81±0.46 (n = 77).

4.3.2.3 *Comparison of Inter- and Intramuscular Synchronisation*

The percentage of synchronised MU pairs was significantly larger for the IAM pairs than for the IRM ones (IAM: 54 out of 69 vs. IRM: 75 out of 166; χ^2-test, $P<0.001$). The synchronisation strength was also significantly stronger for the IAM pairs (t-test, $P_k<0.01$, $P_{k'}<0.05$, n = 163). There was no significant difference in mean peak width between IAM and IRM MU pairs (7±4 ms vs. 6±4 ms; t-test for means, Kolmogoroff-Smirnoff-test for the distribution, Figure 5). The median peak width was 6 ms for both populations (see Methods). There was no correlation between the number of spikes (geometrical mean of the two MUs in a pair) and the peak width in the cross-correlograms (r = 0.081; $P>0.05$, n = 163).

4.3.3 Factors Influencing Synchronisation

We attempted to elucidate some of the factors, such as innervation, anatomical location, and mean recruitment level, that could possibly influence MU synchronisation in the present experimental situation.

4.3.3.1 *Innervation and Anatomical Location*

We first tested the hypothesis according to which the innervation by the same nerve would increase the probability of synchronisation in IRM MU pairs. The pairs innervated by the same peripheral nerve had significant peaks in 45% of the 76 cross-correlograms. The probability of synchronisation in pairs with different innervation reached a similar percentage (46%, n = 90).

Secondly, the *IAM* pairs, with both MUs belonging to either an intrinsic or extrinsic muscle, were more often synchronised than MUs in *mixed* IRM pairs (intrinsic: 37/45, extrinsic: 17/24, mixed: 20/58; χ^2-test, $P_{intr}<0.001$, $P_{extr}<0.01$). The *IRM* pairs, with both MUs belonging to either an intrinsic or extrinsic muscle, were more often synchronised than the mixed MU pairs (intrinsic: 45/87, extrinsic: 10/21, mixed 20/58; χ^2-test, $P_{intr}<0.05$, $P_{extr}<0.05$). When all MU pairs (IAM and IRM) were analysed together, the synchronisation was significantly stronger in extrinsic than in intrinsic or mixed MU pairs (ANOVA, $P<0.05$, Table 4-2).

Thirdly, IAM MU pairs in *thumb* muscles had a higher probability to synchronise than IAM MU pairs of *index finger* muscles (thumb: 36/41; index: 18/28; χ^2-test, $P<0.05$). This was not the case for IRM MU pairs (thumb: 16/32; index: 12/31; χ^2-test, $P>0.05$). With respect to the synchronisation strength no further significant differences were found between thumb and index MU pairs, neither for IAM, nor for IRM pairs. The data are summarised in Table 4-2 without the distinction of IAM and IRM MU pairs.

	Intrinsic Pairs			**Mixed Intrinsic/Extrinsic Pairs**			**Extrinsic Pairs**		
Occurrence	*n*	sync	%	*n*	sync	%	*n*	sync	%
total	*132*	82	62	*58*	20	34	*45*	27	60
Strength									
Index *k*	2.13 ± 0.39			1.94 ± 0.30			2.72 ± 0.66 *		
Index *k'*	1.70 ± 0.28			1.54 ± 0.18			1.94 ± 0.35 *		
	Thumb Pairs			**Mixed Thumb/Index Finger Pairs**			**Index Finger Pairs**		
Occurrence	*n*	sync	%	*n*	sync	%	*n*	sync	%
total	*73*	52	71	*103*	47	46	*59*	30	51
Strength									
Index *k*	2.36 ± 0.71			2.11 ± 0.35			2.20 ± 0.56		
Index *k'*	1.76 ± 0.36			1.69 ± 0.29			1.66 ± 0.24		

Table 4-2. Occurrence and strength of synchronisation in all IAM and IRM MU pairs grouped according to their location in intrinsic or extrinsic muscles (*top*) and in thumb or index finger muscles (*bottom*). *Abbreviations:* sync, synchronised MU pair; *, $P<0.05$ ANOVA, see text

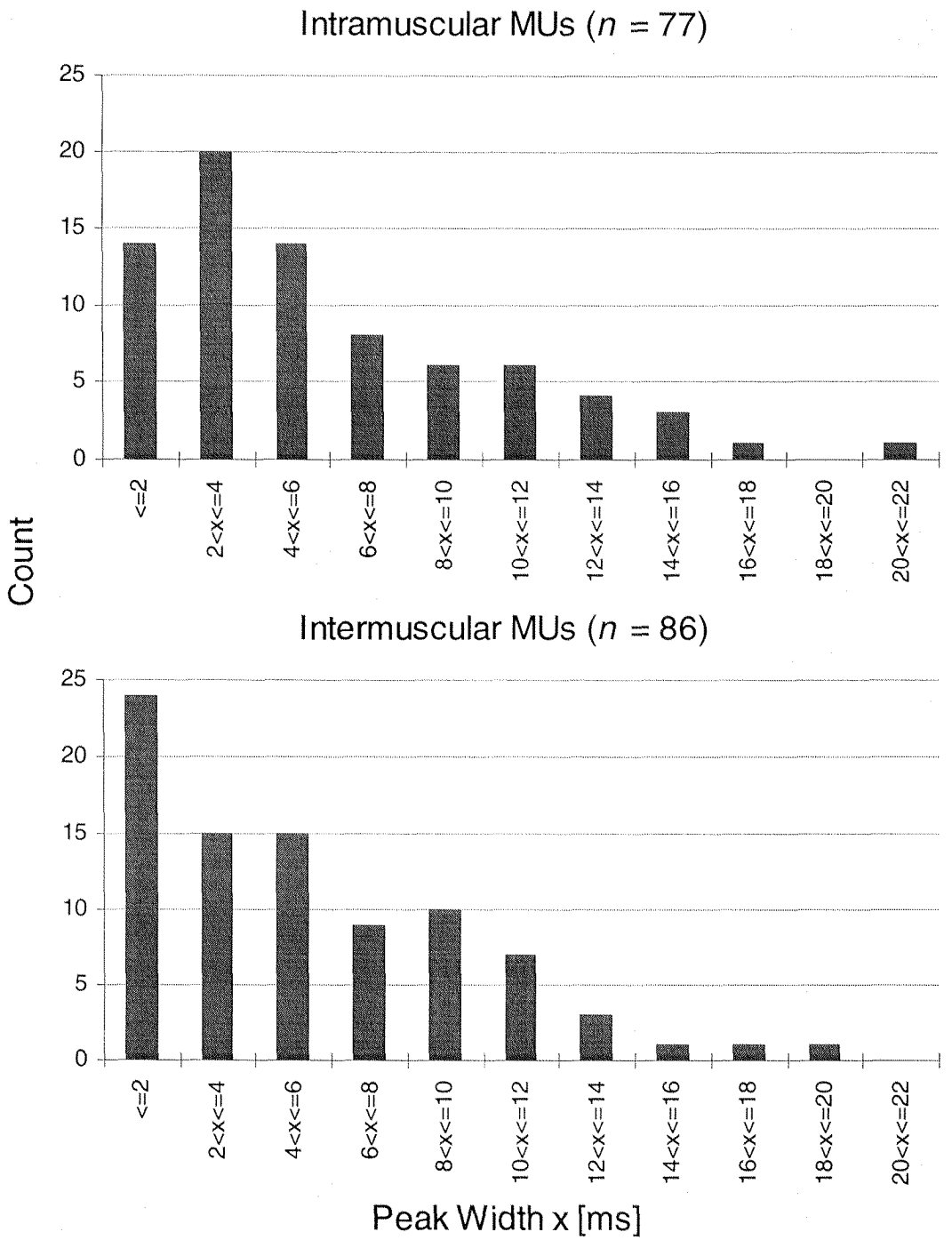


Figure 4-7. Distribution of the cross-correlation peak widths determined at the base of the peak for IAM (*top*) and IRM (*bottom*) pairs. About 50% of the IAM and 40% of the IRM pairs have peak widths smaller than 6 ms, indicative of monosynaptic effects mediated by branched last-order fibres.

4.3.3.2 *Influence of Recruitment Level*

The MU pairs were classified according to the recruitment level of the MU with the higher level in the pair (i.e. lowest level of stable firing: 1, 2 or 3 N), and the occurrence of synchronisation was analysed with respect to the force levels above this recruitment. A higher probability of synchronisation could be shown at the level where recruitment occurred regardless of the absolute force. Among the IAM pairs, synchrony was mainly found at recruitment in 47 out of 69 pairs (68%) or at one force level above recruitment (24 out of 47 pairs, 51%). Only 30% (6 of 20 pairs) were synchronised at two levels above recruitment. The same trend was also observed for the IRM pairs: 36% (59/166) at recruitment, 21% (23/107) and 10% (4/39) for two and three force levels above recruitment, respectively (Figure 4-8). This finding was highly significant (χ^2-test, $P<0.01$ for IAM and $P<0.001$ for IRM pairs).

Furthermore, we checked whether the difference between the recruitment level of the two MUs in a pair affected synchronisation. The MU pairs were grouped into three classes: pairs without difference in recruitment level between their two MUs, pairs with difference of one and of two force levels. MUs with similar recruitment level were firing synchronously in 71% IAM and 48% IRM pairs (25/35 and 33/69 pairs, respectively). Among the MU pairs with one force level difference, 71% IAM and 31% IRM pairs showed synchrony (20/28 and 21/68 pairs, respectively). Finally, synchronisation occurred only in a minority of pairs with a difference of two levels (33% IAM and 17% IRM pairs, i.e. 2/6 and 5/29 pairs). This higher synchronisation probability with small differences in recruitment level was, however, only significant for the IRM pairs (χ^2-test, $P<0.01$, Figure 4-8 bottom).

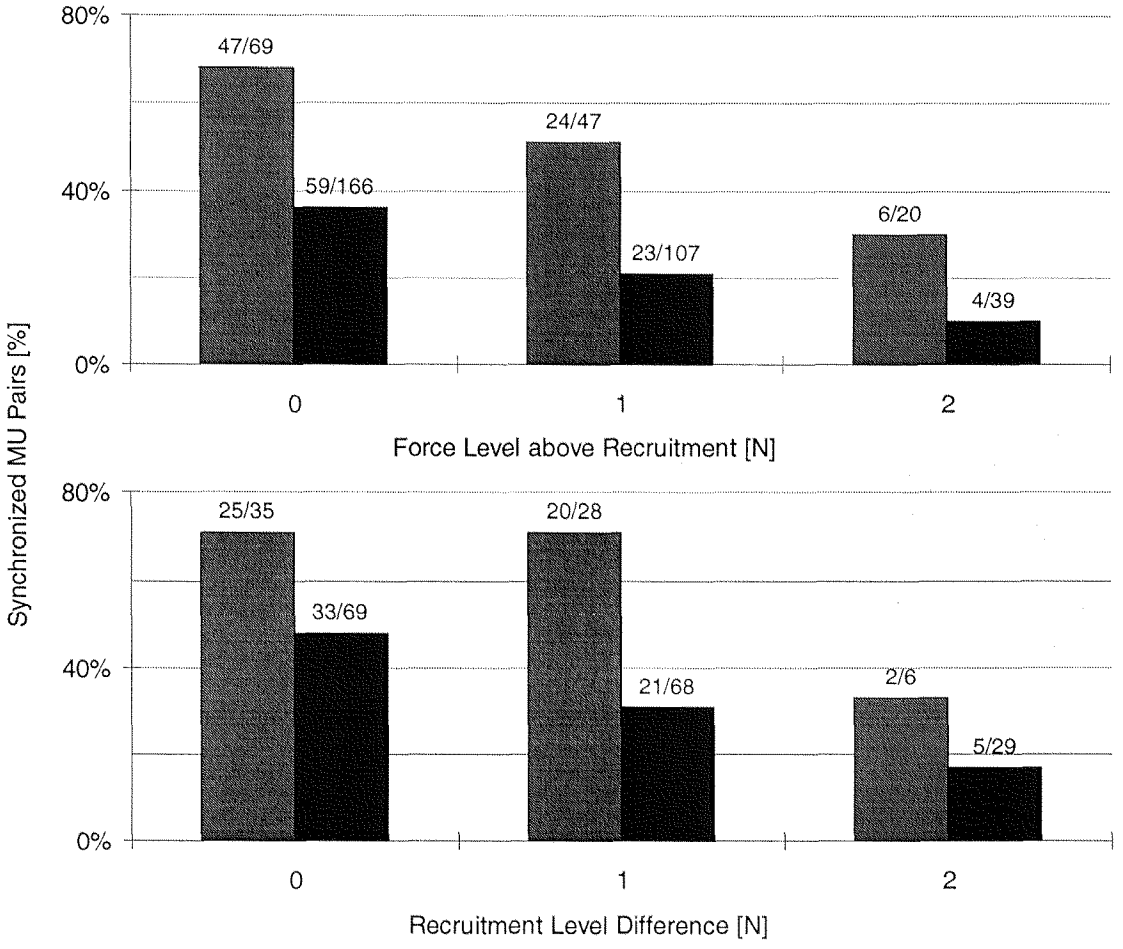


Figure 4-8. Synchronisation at levels above recruitment (*top*) and in function of the difference between the recruitment levels of the two MUs in a pair (*bottom*). The synchronisation probability decreases as force increases above recruitment (*top*). The larger the difference between the two recruitment levels, the smaller is the synchronisation probability (*bottom*). IAM pairs in grey, IRM pairs in dark columns.

4.3.4 Stability of Synchronisation

Synchronisation on all three force levels was observed only in five out of 235 IAM and IRM MU pairs, and only 24 pairs showed synchronous firing on two force levels.

The two variables that determine the overall MU behaviour in force production are recruitment and rate coding. If, as suggested by our data, the recruitment level is a determining factor in synchronisation, we can make two predictions that should account for instability in synchronisation over the force range tested. First, because most MUs were recruited at low forces, synchronisation should occur preferentially at low force levels with, as a consequence, a loss of synchrony at higher forces and higher firing

rates. Secondly, synchronised MU pairs should generally display lower firing rates than non-synchronised ones.

These two predictions could indeed be confirmed. To analyse the relationship between exerted force and synchronisation stability only those MU pairs with both MUs activated on at least two force levels were taken into account (93 IAM and IRM MU pairs). The MU pairs were grouped into four mutually exclusive classes: *low, high, stable, alternating* (Table 4-3). The class "low" contained the MU pairs that were synchronised only on the lower force level but not on the higher ones. For the class of "high" pairs, synchronisation was observable on the higher force levels only. A pair was assigned to the class "stable", when synchronisation was seen on all force levels (two or three, depending on the MUs recruitment level), while "alternating" denoted those pairs that showed occurrence, disappearance and again resurgence of significant synchronisation, or vice versa, on the three force levels respectively. Figure 4-9 displays two pairs of MUs that are synchronised on all three force levels ("stable").

	n	**Low**	**High**	**Stable**	**Alternating**
Intramuscular	*39*	17*	6	15	1**
Intermuscular	*54*	29***	11	7	7
total	*93*	46***	17	22	8***

Table 4-3. Occurrence of synchronisation in 93 MU pairs (IAM and IRM) with activity on at least two levels grouped according to their distribution in the four classes *low, high, stable* and *alternating*, as explained in the text. Statistical significance: *, $P<0.05$; **, $P<0.01$; ***, $P<0.001$; F-test.

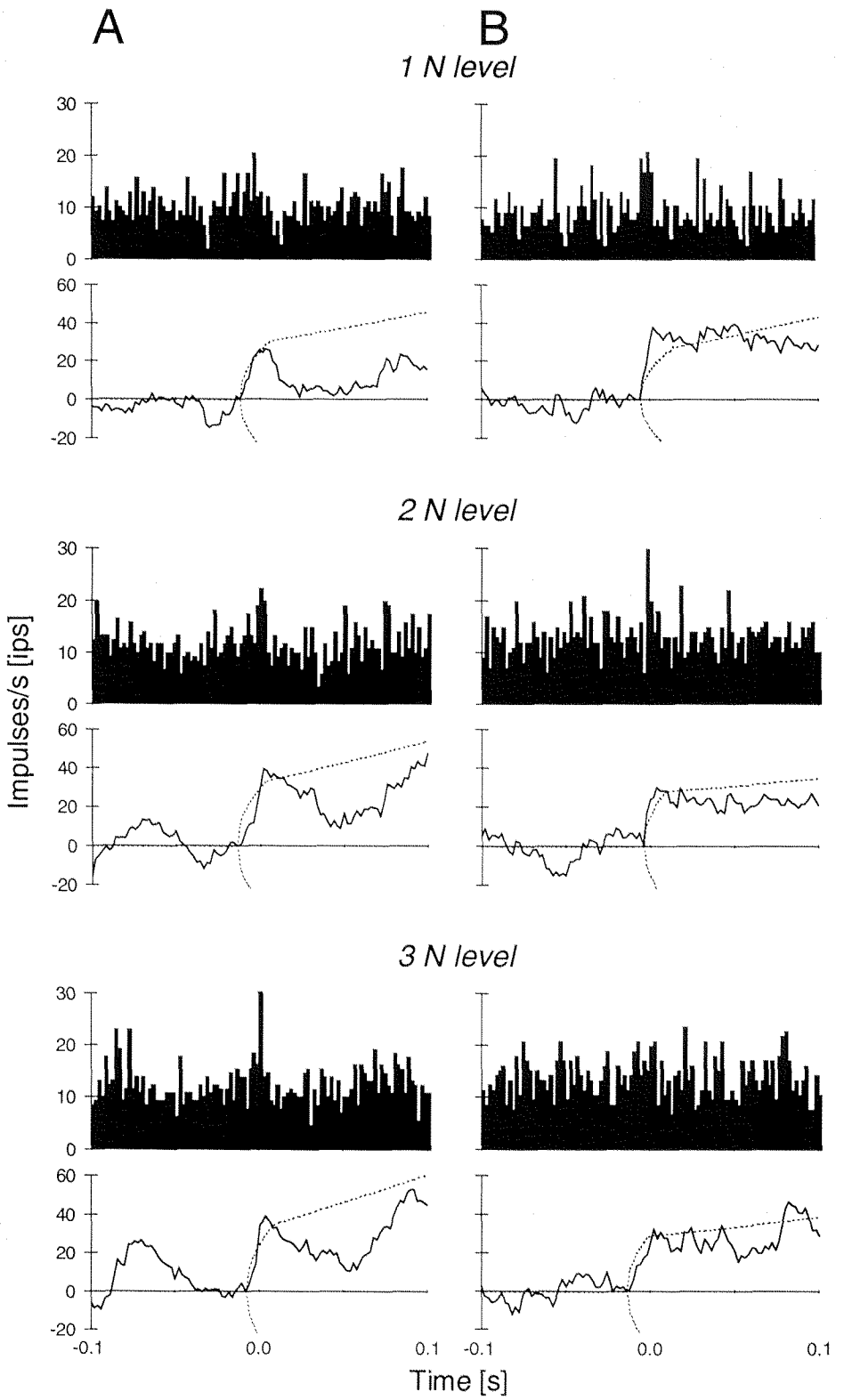


Figure 4-9. Synchronisation of two MU pairs at all three force levels. In *A* the temporal coupling of an *IAM* FPL pair increases with force. Synchronisation indices for the three levels: k_{1N}: 2.08, k_{2N}: 2.02, k_{3N}: 2.71. In *B* for an *IRM* 1DI/1PI pair the synchronisation is stronger at the lower two force levels. Indices for the three levels: k_{1N}: 2.27, k_{2N}: 2.34, k_{3N}: 1.55.

In example A synchronisation is getting stronger with force increase, while the opposite is the case for the example B, nevertheless both show "stable" occurrence of synchronisation. According to prediction one, the majority of the MU pairs (71/93, 76%) was not synchronised on all force levels tested (Table 4-3). Of these 71 MU pairs, a significant majority fell into the category "low", indicating a preference for synchronisation at low force levels (46/71, 65%; χ^2-test, $P<0.05$). The strength of synchronisation did not increase systematically with force.

	Force Level	**Synchronised MU Pairs**		**Non-Synchronised MU Pairs**	
	[N]	*n*	Firing Frequency [Hz]	*n*	Firing Frequency [Hz]
Inter-muscular	1	*26*	6.87±1.97	*58*	7.90±2.48
	2	*64*	8.14±2.37	*150*	9.27±2.00
	3	*82*	9.43±1.77	*244*	10.10±1.97
Intra-muscular	1	*26*	8.51±0.96	*14*	9.34±1.18
	2	*56*	9.45±1.54	*38*	10.41±1.41
	3	*72*	10.03±1.96	*66*	10.92±1.84

Table 4-4. Firing frequencies of synchronised and non-synchronised MU pairs (average ± standard deviation). The firing frequencies of the synchronised MU pairs are lower than those of the non-synchronised ones (ANOVA, $P<0.001$).

Guided by prediction two, we also investigated whether the firing rates of the synchronised and non-synchronised MU pairs differed. The MUs in the synchronised IAM and IRM pairs fired at the respective force levels on average at a lower rate than non-synchronised ones (ANOVA, linear contrasts according to Scheffé, $P<0.001$, Table 4-4).

4.3.5 Relationship to Multi-Unit Muscle Synergies

As the multi-unit EMG represents the spatial integral of the underlying MU activity a considerable overlap between the synchronisation at both the multi-unit and single MU level was expected. This assumption was tested at each force level separately.

We first compared the temporal coupling of the constituent IRM MU pairs with that found for the multi-unit EMG by Maier and Hepp-Reymond (1995b). The first important observation was that temporal coupling at the multi-unit EMG level did not require the synchronisation of the ensemble of underlying MUs. In the 45 muscle pairs displaying significant temporal coupling, only 5 muscle pairs showed synchronisation for all the discriminated MUs. Nineteen muscle pairs had only partial MU synchronisation. Figure 4-10 shows an example of a MU pair with synchronisation at the 1 N level only, while the multi-unit EMG from which the MUs were extracted displayed synchrony on all three force levels. Thus, either one MU pair with strong synchronisation or the weaker synchrony of several MU pairs can lead to the short-term temporal coupling detected at the multi-unit EMG level.

We then investigated to which extent MU synchronisation could be generally seen at the multi-unit EMG level. Only 55% of the 86 muscle pairs containing synchronised MUs showed significant synchronisation peaks in the multi-unit EMG. This seems to indicate that the specific contribution of the synchronised MUs was quite low in comparison to other non-synchronised MUs dominating the integrative EMG signal. A further clear finding was that the synchronisation strength of MU pairs was significantly higher when the multi-unit EMG of both muscles was also synchronised (one-sided *t*-test, $P<0.05$ for index k, $P<0.01$ for index k').

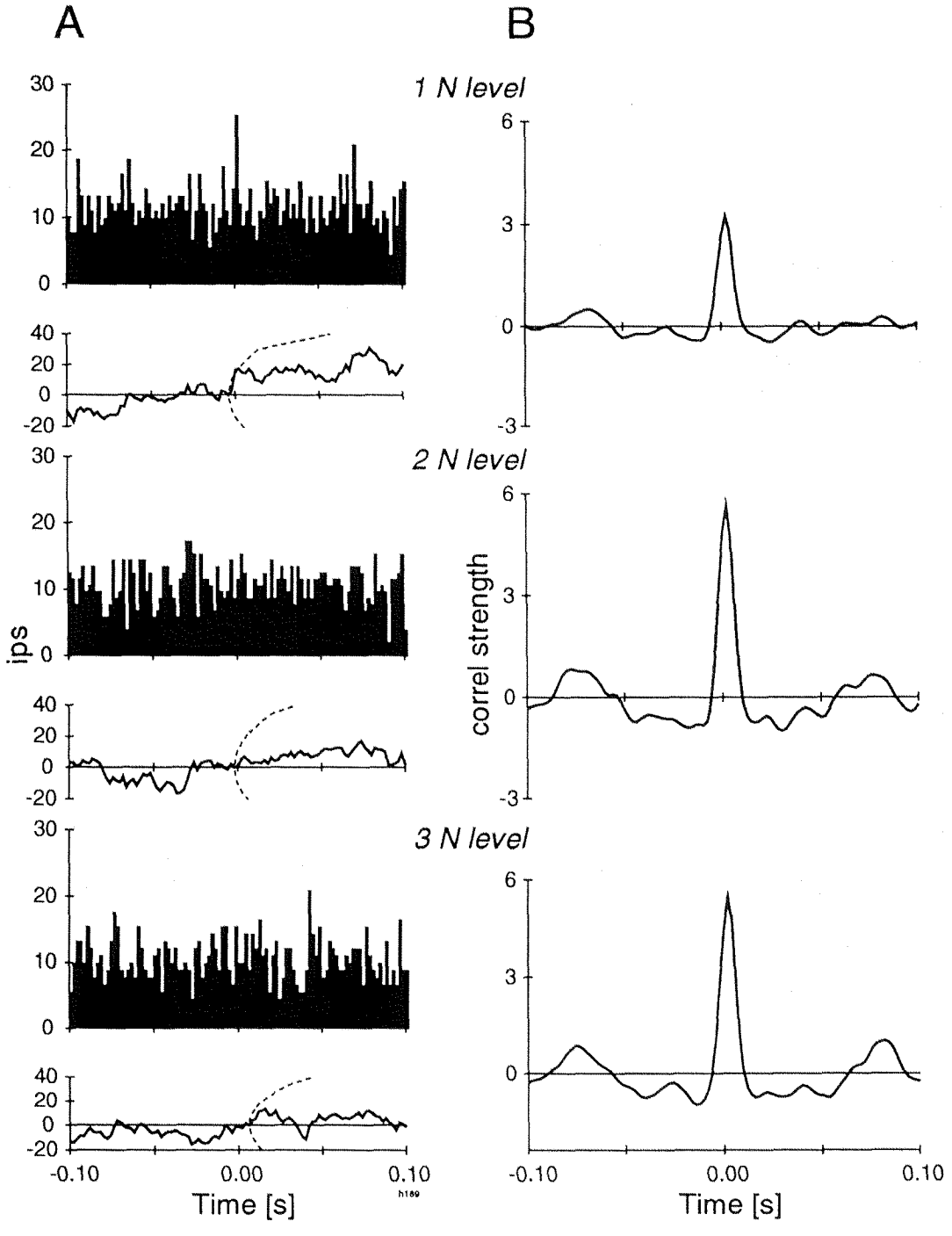


Figure 4-10. Comparison of synchronisation at the single unit (*A*) and multi-unit EMG (*B*) level for an FDS-OPP pair. The two MUs used in *A* were extracted from the multi-unit EMG signals of the FDS and OPP muscles, respectively. The synchronisation of the MU pair is only significant at the 1 N level, while multi-unit synchronisation is present at all three levels reaching its maximum at 2 N force level.

4.4 Study 1: Discussion

4.4.1 Methodological Considerations

The EMG decomposition algorithm ARTMUP that was used in the first phase of this work to discriminate MUs in multi-unit EMG records showed a good grade of maturity. The authors of ARTMUP claimed a mean discrimination rate of 95% for their algorithm with several benchmark tests (Haas, 1989). Although only 78% of our EMG data could fully be discriminated - the remaining 22% were partially discriminated - we are confident that the system produced valid data. MU potentials could be traced over longer periods of time (twenty 15 s trials with rest periods of about 10 s between the trials). This is in spite of the fact that the templates had to be regenerated anew for each trial. Furthermore, the potential trains and the inter-potential interval histograms that were generated are feasible with the MU characteristics that is published, i.e. discharge rates within physiological ranges (e.g. Milner-Brown et al., 1973b). In contrast to the software, the hardware at the time was the limiting factor. Due to the limited computer storage capacity, only sequences of up to 15 s duration could be digitised in one sweep. Furthermore, the number of channels as well as the amplitude and time resolution of the force channels were not sufficient to perform an in-depth analysis of the MU behaviour with regard to twitch tension. Finally, sampling the EMG at 10 kHz and low-pass filtering at 3 kHz is in the range of other studies (e.g. Bremner et al., 1991a: 4 kHz sampling; van Bolhuis et al., 1997: 16 kHz sampling, 0.3 - 5 kHz band-pass filtering).

Synchronisation analysis is the method of choice to describe temporal muscle coupling. With the parameters (time resolution 2 ms, cross-correlogram width ±100 ms) we had chosen, we were able to describe MU synchrony. MUs typically discharge at frequencies in the order of 10 Hz. However, this analysis is not capable of detecting muscle coupling, where various muscles increase activity in parallel but asynchronously. This would require another analysis, e.g. correlation of the mean discharge rates of two MUs at the three force levels (Lee, 1984; amplitude domain analysis, Maier and Hepp-Reymond, 1995b). Furthermore, cross-correlograms require stationary data. To fulfil this requirement, we had to cut the whole recording in relatively short periods, which were then analysed separately. This again resulted in a reduced number of events that could be correlated.

The task with stationary periods of 3 s duration and twenty repetitions yielded a relatively low spike count/MU. With a MU continuously discharging at 10 Hz this results in 600 spikes/force level. This number is relevant since most of the comparable studies with synchronisation analysis used minimal spike counts one order of magnitude higher than our number, arguing that the signal to noise ratio in the case of small spike counts is weakening the results. However, the method applied here has been validated with spike counts as little as 100 and shown a remarkable robustness (Bremner et al., 1991a).

A further methodological aggravation of the present task for the analysis was that only a minority of the MUs (29 of 92) was active through-out the investigated force levels. Each force level had thus to be investigated separately, MUs with disparate recruitment thresholds could not be compared over all three force levels. On the other hand, with recruitment threshold included in this study we could show that this level showed some enhanced synchronisation of MUs.

4.4.2 Motor Unit Behaviour

The vast majority of MUs (77/92) showed significant positive correlation between their firing rate and the grip force. This speaks in favour of a broad pattern of muscle coactivation in the precision grip, with only a few muscles involved in stiffness or postural control of wrist and/or finger joints. Within individual finger muscles the MU behaviour was not always homogeneous. While a large majority of intrinsic muscles usually contained MUs with highly significant positive correlations between firing rate and force, other MU populations, mainly in extrinsic muscles, displayed weaker correlations with a large variance. In the force range investigated, the MUs of intrinsic muscles also had a considerably higher force sensitivity than those of extrinsic muscles. On the other hand, it has to be mentioned that with the extrinsic muscles more "mechanical compliance of tissue (e.g. skin and tendons)" is interposed between the active unit and the force transducer which can introduce a higher degree of distortion than in the intrinsic muscles with small muscles and short tendons that do not have to pass anatomical bottle necks like the wrist (Monster and Chan, 1977). On the whole, the results obtained on the MU level, namely the more important contribution of the intrinsic finger MUs to the fine regulation of isometric grip force, support the findings

of the previous multi-unit analysis (Maier and Hepp-Reymond, 1995a). The possible influence of fatigue (Bigland-Ritchie et al., 1986) was controlled and found to be of minor importance. The discharge rate in the 20 consecutive trials of one experimental session significantly increased in 9 of 92 MUs, while insignificant rate change was seen in the majority (67 MUs). In 16 MUs the firing frequency significantly decreased, however, whether this can be attributed to fatigue or a change in strategy remains open.

4.4.3 Motor Unit Synergy

If muscle synergy is a means for the CNS to co-ordinate muscle activation, then this should be manifested in short-term synchronisation within and between the large MU pools during our task which required a high level of muscle co-ordination. We based our analysis mainly on the occurrence rather than the strength of synchronisation as the commonly used synchronisation indices seem to be frequency-dependent (Nordstrom et al., 1992; Matthews, 1996). According to Vaughan and Kirkwood (1997), the peak width in cross-correlograms of synchronised MUs can give some indication on the underlying synaptic connectivity. In our findings, the presence of narrow peaks in 50% of the cases - less than 5 - 6 ms measured at the base of the peak (which compares to approximately 2.5 ms half-width of Vaughan and Kirkwood, 1997) - speaks indeed in favour of monosynaptic short-term motoneurone synchrony mediated by last-order branched axons. However, broader IAM and IRM peaks also indicate the existence of di- or oligosynaptic divergence at a non-premotoneuronal, probably spinal or even cortical level. It has to be noted, however, that the peak widths we report here are narrower than most of those reported in the literature (e.g. Bremner et al., 1991a, mode 13 ms; Schmied et al., 1994, mean 8.5 ms). Notably, Nordstrom et al. (1990) reported 3 ms peak widths for masseter MU pairs. Moreover, our distribution of peak widths is skewed, in contrast to most others.

It may be possible that the narrower peaks are due to the low signal-to-noise ratio in our data. We think that the present data set, though based on relatively few triggers, does have a sufficient robustness in terms of occurrence (see Methods), but may be at the limits for detecting finer details such as peak width. In particular, two methodological aspects may lead to narrower peaks: the shorter period for calculating the CUSUM baseline, and the criterion of monotonic growth of the CUSUM for establishing the

width. These aspects could account for the skewed distribution. However, there was no significant correlation between numbers of spikes and peak width, i.e. within our sample the peak width was independent of the spike count. Nevertheless, consistent with Bremner et al. (1991a) we did not find any difference in peak width for the differently innervated IRM MU pairs.

MU synchronisation was found in 78% IAM and in 45% IRM pairs. These results are, compared to other studies, well within the range for the IAM pairs but are at the lower boundary for the IRM ones (Table 4-5). Several factors may account for differences with those studies: first, the motor task and the experimental paradigm, second, the feedback condition, third the firing rates and forces, and finally, the recruitment level.

First, in most studies the subjects were asked to continuously exert weak torque around one joint over several minutes without modulation of joint torque or MU firing rate. In our paradigm, in contrast, the subjects had to follow a ramp-and-hold force trajectory repeatedly between 0 and 3 N by applying force on a transducer held between thumb and index finger, thereby recruiting the discriminated MUs in each trial. Another non-negligible factor is the type of muscle activation pattern investigated. While in our experimental set-up the subjects were asked to exert isometric force in the precision grip, i.e. with a large number of coactive muscles, other investigators generally restricted their task to isometric contraction of a limited number of synergist muscles at one joint (Bremner et al., 1991a,b,c; Datta and Stephens, 1990; Milner-Brown et al., 1973; Nordstrom et al., 1992). Moreover, coactivation of different muscles has been rarely investigated (Bremner et al., 1991a; DeLuca and Mambrito, 1987).

Second, the type of feedback signal presented to the subjects during performance of the tasks varied considerably among studies. In the majority of the cases, visual and/or auditory feedback of the MU activity was the rule whereas in our experiments only the total exerted grip force was presented to the subjects. Thus, the results in most other studies may have been biased by the feedback of the MU discharge, as demonstrated by Schmied et al. (1993), who showed that the level of synchronisation could voluntarily be changed by giving an appropriate feedback. This point will be an issue in study 2, where we want to determine the influence of auditory feedback of the MUs to the subject.

Authors	Muscles	Degree of Synchronisation	Feedback	Firing Rate, *Force*	Comment
Bremner et al., 1991a	1DI, 2DI, 4DI, EPB, EDC, FDS	67-100% IAM 68-77% IRM	vis. & aud.	~10 Hz	Table 1: class A-C, class D
Datta and Stephens, 1990	1DI	88% IAM	vis. & aud.	~10 Hz	-
DeLuca and Mambrito, 1987	FPL, EPL	not quantified, IAM/IRM	force	< 60% MVC	-
DeLuca et al., 1993	TA Delt 1DI ECU ECR	54% IAM 45% IAM 71% IAM 74% IAM 69% IAM	force	30% MVC	-
Logigian et al., 1988	ECR	68% IAM	not specified	not specified	tremor
Milner-Brown et al., 1973a	1DI	100% IAM 0% IAM	vis. & aud.	5-10 Hz	1 subject 100%, the other 0%
Nordstrom et al., 1992	1DI	not quantified, IAM	vis. & aud.	7.5-17.5 Hz	-
Schmied et al., 1993	EDC	70% IAM	vis. & aud.	'regular'	-
Schmied et al., 1994	ECR	88% IAM 69% IAM	vis. & aud.	not specified	dom n-dom
Semmler and Nordstrom, 1995	1DI	51% IAM 81% IAM	vis. & aud.	constant rate	dom n-dom
Study 1	15 intr. & extr. finger muscles	78% IAM 45% IRM	force	1, 2, 3 N	
Study 2 force feedback	AdP, 1DI	74% IAM 47% IRM	force	1, 2, 3 N	
Study 2 activity feedback	AdP, 1DI	91% IAM 48% IRM	vis. & aud.	8, 13, 18 Hz	one MU feedback

Table 4-5. Prevalence of single motor unit synchronisation as described by several authors. This overview shows the wide range of synchronisation in the various studies. *Abbreviations:* TA, tibialis anterior; DELT, deltoid muscle; ECR, extensor carpi radialis; ECU, extensor carpi ulnaris; vis.&aud., visual and auditory feedback of motor unit; IAM and IRM, IAM and IRM motor unit pair, respectively; dom./n-dom, dominant/non-dominant hand, intr. & extr.: intrinsic and extrinsic finger muscles.

Third, the occurrence of short-term synchronisation should statistically increase with increasing discharge rate of the MUs as the cortical drive - a putative main source for

synchronisation (Datta et al., 1991; Farmer et al., 1993) – also increases with higher forces (Fetz et al., 1989). Therefore, we expected to find more short-term synchronisation at higher force levels. However, the main present result is that MU synchronisation occurs predominantly at lower force, just at or after recruitment.

This suggests that the large number of central and peripheral afferent inputs to the motoneuronal pools at higher force decreases the influence of any particular synchronising presynaptic source, in other words the ratio of synchronising vs. non-synchronising input is getting smaller. In particular, the synchronising input delivered by the cortico-motoneuronal system may reach the limit of its working range and saturate earlier than other non-synchronising inputs. Indeed, several investigators have already mentioned the higher degree of MU synchronisation at low activation levels (Dietz et al., 1976; Nordstrom et al., 1992; Matthews, 1996). Moreover, in the present investigation synchronisation is rarely stable over the whole investigated force range. In fact, synchronous firing on all active force levels occurs in only seven of 166 inter- and in 15 of 69 IAM pairs (Table 3). If synchronisation arises preferentially in the lowest range of the MU firing frequency, then the increase in firing rate with higher forces, due to rate coding, may well be the cause of the less frequent and unstable synchronisation observed at higher forces. Similarly, Schmied et al. (1994) showed that the smaller the difference between the MU firing rates the greater was the degree of synchronisation. In several of the experiments performed by other groups, the low firing rates required (usually about 10 Hz, i.e. close to recruitment level) may, as our results suggest, be a central factor giving rise to synchronisation.

Finally, the main observation of the present investigation, i.e. the fact that the highest probability of synchronisation occurs just at the force level above recruitment, is in contradiction with DeLuca et al. (1993) who concluded that the MU recruitment threshold had no influence on synchronisation. However, they had tested MU pairs for synchronisation at 30% MVC and not at the level of recruitment as we did. We, in addition, could demonstrate that the difference between the recruitment levels of the two MUs in a pair definitely plays a role in synchronisation. The closer the two levels are, the higher is the probability to synchronise. This may be a reflection of the fact that the contribution of any excitatory post-synaptic potential, whether synchronous or not, to the precise timing of motoneurone firing is strongest close to recruitment threshold. This

finding which suggests that MUs with similar force ranges share a common input is in line with Datta and Stephens (1990) who, for 1DI MUs, had come to the conclusion that the synchronisation strength was inversely related to differences in recruitment threshold.

4.4.4 Relationship between Temporal Coupling of Motor Units and of Multi-Unit EMG

The differences between synergistic activation of single MUs in this study and the corresponding multi-unit activity (Maier and Hepp-Reymond, 1995b) are to a certain extent due to the selection of MUs. Since our analysis was based on discrete digital data due to the MU discrimination process, we could extract only part of the spectral richness of the multi-unit EMG. Therefore, it is not surprising that the results of the two analyses do not overlap to 100%. The essence of this comparison is that usually only part of the constituent MU population is temporally coupled in an otherwise fully synchronised muscle. At least for IAM pairs, this may be surprising in view of the fact that cortico-motoneuronal cell axons branch to most if not all motoneurones in a pool (Porter and Lemon, 1993). However, since the same pool receives input from many, not necessarily synchronised, cortico-motoneuronal cells, as well as asynchronous input from other sources, it seems likely that only parts of the constituent MUs are synchronised. In consequence, depending on the ratio between asynchronous and synchronous contribution of underlying MUs, not each MU synchronisation could be detected at the multi-unit EMG level.

4.5 Study 1: Summary

The MUs were first characterised with regard to their behaviour in the respective muscles. Compared to MUs in extrinsic muscles, intrinsic MUs had steeper regression lines with negative intercepts, indicating higher force sensitivity and higher recruitment thresholds.

The cross-correlation analysis was performed for 69 IAM and 166 IRM MU pairs while steady grip force was exerted at three different levels. Synchronisation, for at least one force level, was found in 78% of the IAM and in 45% of the IRM MU pairs. This occurrence of synchronisation was, however, not stable over the investigated force range. Force increase did not induce increased synchronisation between MUs, in contrast, most MU pairs showed synchrony just at the level of recruitment. In addition, the more similar the thresholds of the two MUs in a pair, the greater the likelihood for them to be synchronised. Finally, when synchronisation was found, lower discharge rates of the two MUs could, in general, be shown.

The short-term synchronisation we describe, speaks in favour of monosynaptic short-term motoneurone synchrony mediated by last-order branched axons. In contrast, to many other studies, which disclosed a high amount of MU synchrony, we found only a limited percentage of synchronised MUs. We attribute this differences mainly to the different natures of experimental tasks. First, in contrast to the precedent studies where the subjects were actually asked to control MU discharge, our volunteers were not aware of the discharge activity in their hand muscles, whatsoever. Second, our task required a large number of muscles to be active simultaneously, while other experimental tasks required only a limited number of synergist muscles around one joint to be active. Third, our task necessitated the subject to follow a force profile where he or she had to match the resultant force to three different force levels, thus recruiting and inactivating MUs over time. Other experiments required constant discharge over longer periods.

Finally, we expected that the synchronous drive to the MUs would increase as force increased. But contrary to our expectations, we not only found unstable synchrony but rather synchrony mainly confined to the recruitment levels of the MUs under scrutiny. These findings are in contrast to the notion of synergy being a means for the CNS to reduce excess degrees of freedom in the hand.

5 Study 2: The Validation of Study 1 and Influences on Synchronisation

5.1 Goal

This study was performed to validate the results gained in study 1 and to find and understand mechanisms that may lead to MU synchronisation. Following investigations were performed:

Test A: confirm the findings of study 1, i.e. general level of synchronisation, IAM and IRM synchronisation, relationship of synchronisation with regard to recruitment of the MUs.

Test B: extend those findings and investigate, whether there is a different muscle activation "mode" operational with respect to synchronisation during the *increase* of grip force compared to the *decrease*. Identical experiment as Test A, but different analysis.

Test C: find out, whether the level of MU synchronisation can be altered by having the subject control its MU activity by providing *auditory feedback* of the MU activity in contrast to force feedback. In the text "auditory feedback" and "MU activity feedback" are used interchangeably. No distinction is made between these two terms.

Test D: characterise the twitch tension of 33 MUs and classify these MUs.

Furthermore, a new force transducer was purposefully made for this study to avoid the short-comings of the previous set-up, i.e. the old sensor was fixed to the hand support and was only movable around the vertical axis of the fixation, thus forces in the axial and radial direction could be exerted but were not observable.

5.2 Study 2: Means and Methods

5.2.1 Experimental Set-Up

In order to answer the questions mentioned above, a complete new experimental set-up was established with a modified and extended paradigm, a new data acquisition system and a purpose-made new force sensor. A schematic drawing of the experimental set-up is given in Appendix A.

The subjects were seated in front of an oscilloscope, on which a target signal and two feedback signals, thumb and index finger force, or - for Test C - a target signal and the discharge frequency of one MU were displayed in *SCROLL* mode on the feedback oscilloscope. The right hand in resting position of the subject was individually fitted to a thermoplastic cast (Polyform) which was attached to the force transducer platform to ensure isometricity during the whole experimental session and reproducibility between multiple sessions with the same subject. A force sensor for each finger was designed and built with a force range from 0.5 mN to 5 N (Appendix B, two transducers in series). The milli-Newton force range resolution was measured with a Kistler piezo-transducer (Typ 9205/9207; charge amplifier 5011). This measurement was used to characterise the twitch tension of single MUs and classify them (force twitch due to the contraction of one MU, Test D). The Newton force range signal was measured with a strain gauge-transducer (HBM, Typ 6/120LY11, full Wheatstone bridge; Analog Devices 2B30/2B31 force amplifiers). This signal was also used for force feedback. All force sensors were reset before each experiment. The EMG activity was recorded from the surface and intramuscularly from the two investigated muscles, in general, the AdP and the 1DI (surface electrodes: silver/silver oxide disk electrodes, Ø1 cm or custom-made Ø6/4 mm outer/inner diameter ring electrodes; intramuscular needle electrodes: Dantec Medical, 26Gx1½", Ref 13L49, 13R01). The two EMG signals gained with the needle electrodes (amplification: 500 - 5000x; notch filter: 50 Hz; bandpass filter: 3 Hz - 1 kHz) were fed on-line into a BAK-1 discriminator (time and amplitude window) and manually searched for clear MU potentials on an oscilloscope. Only the TTL acceptance pulses of the BAK-1 discriminator (TTL: transistor-to-transistor logic, 5 V pulses of 600 ms duration) were stored. For the experimentor to verify that only one MU was discriminated at a time the acceptance pulses were also sent to a loudspeaker before the experiment onset. The data acquisition system was based on a National Instruments system (ADC: AT-MIO-64F-5.VI, 12 bit resolution, LabVIEW) running on a Pentium PC with the IMAGO software developed at the Swiss Paraplegic Centre of the Orthopaedic University Clinic Balgrist (Prof. V. Dietz). We recorded and digitised simultaneously two surface EMG signals (amplification: 1'000 - 100'000x; notch filter: 50 Hz; bandpass: 3 Hz - 600 Hz), two on-line pulse trains of the discriminated intramuscular EMG signals, two strain-gauge force signals, two piezo force signals and

one channel, which served to synchronise on-line recorded data with off-line discriminated MU pulse trains. The sampling frequency was 2 kHz per channel. The surface EMG and the strain-gauge force signals were desampled off-line to 500 Hz (LabVIEW Desample.VI) for data reduction. In addition to the data acquisition on the computer, all signals, and in particular the raw needle EMG signal, were backed up on a Bio-Logic DTR 2601 digital DAT recorder. The EMG signals gained with the needles were later played back. The two MUs that had already been gained on-line and additional MU potentials that could not be captured on-line during the experiment due to hardware limitations, were discriminated to gain - in the former case - cleaner and - in the latter case - additional MU discharge trains. Templates of the MU potentials were sketched during this process in order to prevent double discrimination of the same MU.

This experimental set-up was used for all tests A to D. For Test C, force feedback was replaced by MU activity feedback. Here, the pulse train of one discriminated MU was fed to a loudspeaker - for each pulse a click was audible - and a moment-rate meter, which generated an output signal that was linearly correlated to the momentary discharge frequency of the MU. This signal was digitally filtered (E 5-1) and displayed for the subject on the oscilloscope (Philips PM 3384, Math option filter) together with the target signal.

$$S_r[n] = \sum_{k=-\frac{K-1}{2}}^{k=+\frac{K-1}{2}} S_1[n+k] \times \frac{1-\cos\left(\frac{\pi+2\pi k}{k+1}\right)}{k+1}$$

E 5-1

Where $S_r[n]$ denotes the signal displayed at sampling time n, K = window width (19 samples), k = convolution index, sampling duration is 62.5 ms, n = sampling index.

5.2.2 Experimental Task

After training, Tests A to D were performed one after another provided the discharge of a MU could be followed over the three experiments, Test A and B being the identical experiment. With MUs becoming silent over time, more data could be gained with Tests A and B as opposed to Tests C or D. On the other hand, new MUs were recruited during

the course of the tests, thus only a partially overlapping MU data pool was obtained. For all tests, the subjects were naive to the purpose of the study. The sole instruction given to them was to match the feedback signal with the target signal as accurately as possible.

5.2.2.1 Tests A, B: Validation, Activation Modes

In this first experiment, the subjects had to exert grip force on the force transducer and thereby match the force with the running target signal. After a first training session of approximately 20 minutes, with the identical target signal and feedback as in the upcoming experiment, when relatively high precision tracking was achieved, the muscles to be investigated and recorded from were identified according to Delagi & Perotto (1980). The surface EMG electrodes were applied on the bellies of these muscles, and fixed with scotch tape when a good signal was obtained. The needle electrodes were inserted between the surface electrodes and moved until a MU could cleanly be discriminated. After that, the force transducers were reset and the subjects began the 25 force trials (force levels: 0, 1, 2, 3, 2, 1, 0 N; holding time of 5 s on each force level; transition periods of 1 s between each level; total duration: 25x41 s, cf. Figure 5-1). These force amplitude and holding periods were chosen as to avoid the occurrence of subjective feeling of fatigue in the muscles and gain as much data as possible.

5.2.2.2 Test C: Motor Unit Activity Feedback

If the MU recording was still stable after the first 25 trials in Tests A and B, i.e. the MUs were still well discriminable, Test C was performed. In this task the subject had to match on the oscilloscope the target signal with the frequency signal of one discharging MU (MU activity level: 0, 8, 13, 18, 13, 8, 0 Hz, same time frame as above). The frequency levels were chosen such that the activity levels were in the normal working range of MU discharge (Monster and Chan, 1977) and coincided approximately with the force levels. The subjects were allowed enough training time to match the MU activity signal to the target signal. This recording was performed as long as the discriminated MUs were well isolated, or up to a maximum of 25 trials.

The word "stage" is used here and subsequently to denote either force level (1, 2 or 3 N) or MU activity level (8, 13 or 18 Hz) or both together.

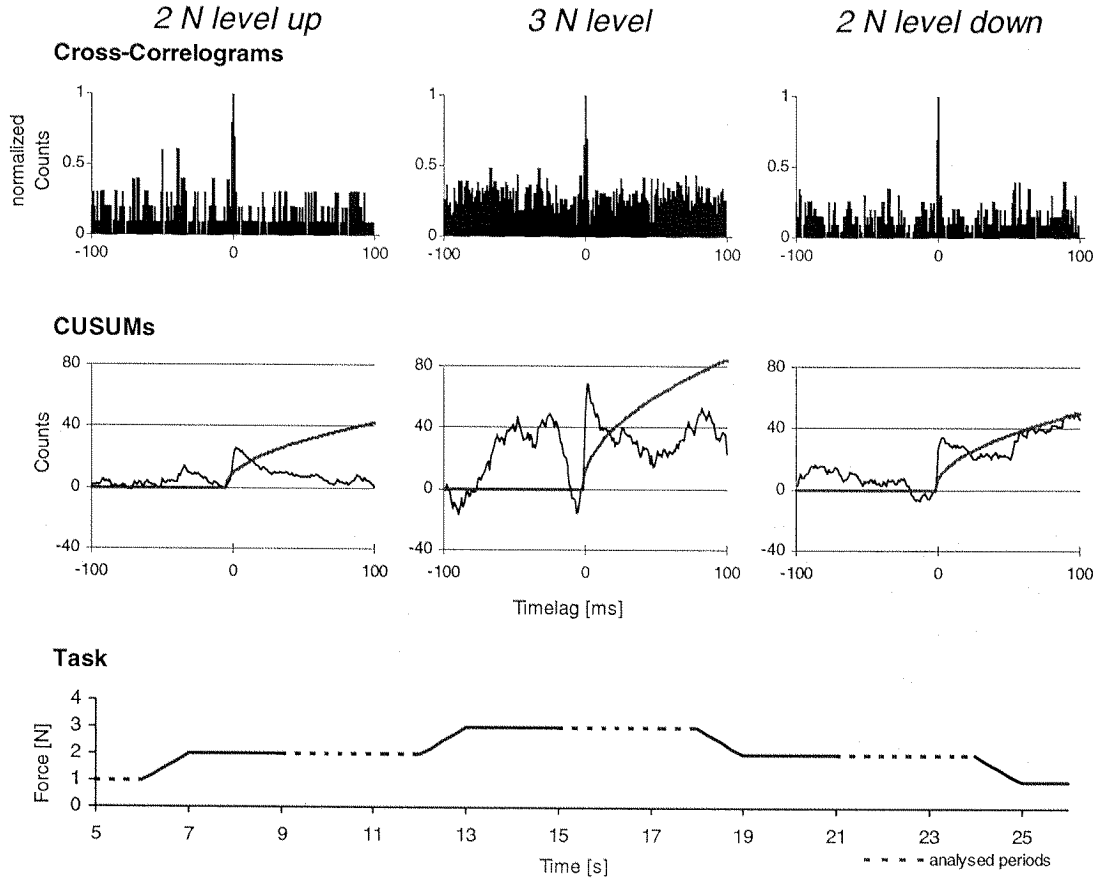


Figure 5-1. Task and cross-correlation analysis - only the three central force levels - "2 N level up", "3 N level", "2 N level down" - are shown. *Top:* Cross-correlograms of two MUs active at the three force levels with a clear central peak indicative of synchronisation. *Centre:* Corresponding CUSUMs with significance limits (parabolic curve). *Bottom:* Target force showing the periods from where the data were obtained for the separate force levels (dashed line).

5.2.2.3 Test D: Twitch Tension

After the performance of Tests A to C, we attempted to describe the MU properties with respect to their contribution to force (twitch tension: F_{TT}) and their contraction time (t_{CT}) in this test. Given these data we wanted to classify the underlying MUs. For this experiment, the subjects were requested to press on the force transducer with a constant force of 2 N during a minimum period of three minutes. Their hands were held in position with the thermoplastic cast as in the other experiments to prevent movement. The thumb and index finger forces - measured by the piezo sensors - were digitised with 2 kHz sampling frequency each, while the EMG activity of the 1DI and AdP muscles

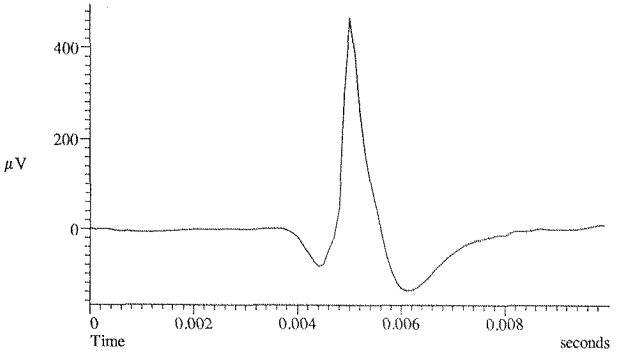
was recorded with needle electrodes at 10 kHz sampling frequency each. The force feedback was given to the subject via the oscilloscope in order to keep the force as constant as possible. The MUs were discriminated off-line with the Spike 2 discrimination program (CED, Cambridge, UK). An example of this discrimination is shown in Figure 5-2 *top*. In a post-processing program, spikes that showed inter-spike intervals of less than 100 ms were rejected. This was done in order to prevent high-frequency activity and subsequently tetanic fusion of the force curves. The inter-potential interval histogram is shown in Figure 5-2 *centre*.

Motor units with less than 100 discriminated spikes were rejected (McMillan et al., 1990). In 19 out of 35 cases of MUs with discharge frequencies of more than 10 Hz the 100 ms boundary was reduced iteratively to less stringent boundaries until a minimal quantity of MU potentials was obtained. The acceptance pulses of these MU potentials were then cross-correlated with the respective force traces - index finger force with index finger MU, thumb force with thumb MU - and the resulting force curves (Figure 5-2 *bottom*) were searched for the first minimum and first subsequent maximum after the acceptance pulse according to E 5-2. The contraction time t_{CT} was defined as the time from occurrence of the spike to the maximum in the force trace.

$$t_{CT} = t(F_{\max}) - t_{Spike}$$
$$t(F_{\max}) > t(F_{\min}) > t_{Spike}$$

E 5-2

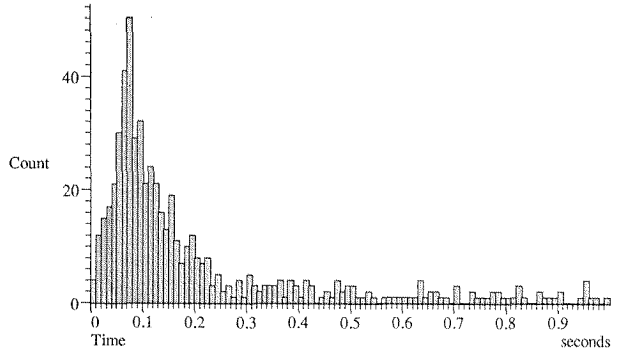
The contraction force (F_{TT}) was gained from the difference of the maximum force and the immediately preceding force minimum.



MU potential template

128 selected spikes from a total of 633 spikes originating in AdP (DH01D.SMR)

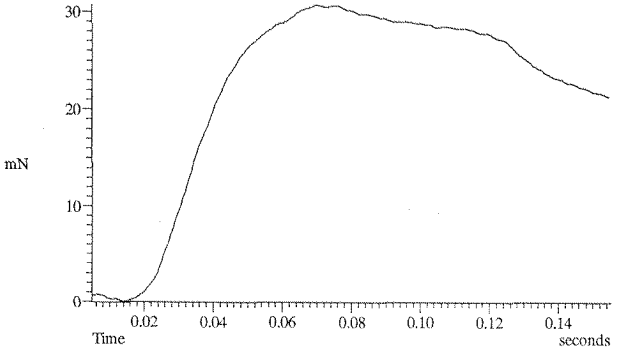
recording time: 390.3 s



Inter-Potential Interval Histogram

mean discharge frequency: 5.1 Hz

modal discharge frequency: 14.0 Hz



Twitch Tension

contraction time t_{CT}: 65 ms

contraction force F_{TT}: 30.6 mN

Figure 5-2. Data output of twitch tension processing. *Top:* The identified MU template from the AdP muscle averaged over 128 MU potentials from a total of 633 detected MU potentials in the record (recording time: 390.3 s). *Centre:* Inter-potential interval histogram of the identified MU template. Mean and modal discharge frequency show a large disparity due to the skewed distribution. *Bottom:* Spike-triggered average of the times of occurrence of the MU potential and the force trace produces the twitch tension. The occurrence time of the MU potential is at time 0. Note the different time scales.

5.2.3 Analysis

Following procedure was performed on the data gained in the Tests A to D. The on-line and off-line single unit records were aligned in time and analysed together. The two strain-gauge force channels and the surface EMG were desampled from 2 kHz to 500 Hz. The data were then transferred to a SUN workstation and split into high frequency force channels (high resolution piezo transducers, 2 kHz), low frequency channels (500 Hz), the spike data and the header information of the LabVIEW files. The spike data was filtered: high-frequency discharges of less than 40 ms inter-spike intervals were discarded. A MU was processed as long as following quality criteria were fulfilled:

[1] IPIH had to be normally distributed with a mode between 60 and 100 ms

[2] if a MU was discriminated both on- and off-line, that record which showed better discrimination, was accepted

[3] a minimum number of 300 spikes per MU

The high frequency force data and the spike trains were reformatted and printed out on the SUN with std/mtd (custom-made data-visualisation program based on the open-source program X-Plot). In Tests A to C, for each of the five stages - either force or MU activity levels - only the last three seconds of the five second holding periods were retained for further analysis, in order to avoid transient effects in MU discharge. In contrast, in Test D the whole recording period up to 3 minutes was used. In the next step a purpose-made C-program (Press et al., 1992) calculated auto- and cross-correlograms of the spike trains and high-resolution force traces, and the IPIH of the spike trains.

The program generated also the CUSUM and significance limits (see above) for the cross-correlograms, calculated the correlation indices, mean discharge frequencies, mean inter-spike intervals and the measures for the cross-correlogram peak such as width and relative height. The correlation data was transferred to a Pentium laptop computer where a macro in Visual Basic for Applications generated the plots of the correlograms.

The cross-correlograms were used to determine synchronisation of MUs under different situations, i.e. during force increase versus decrease, force feedback versus MU activity feedback.

5.2.4 Isometricity

This exploratory experiment was only performed with one test subject. It was used to estimate the movements of the hand that might occur during an experiment, since we claimed that the experiments were performed under isometric conditions. To this goal, we used a VICON three dimensional video system to determine movements during the task. Infrared reflecting markers were stuck on landmark points of the hand: distal phalanx of the thumb (DPh1), metacarpo-phalangeal joint of the thumb (MCP1), the

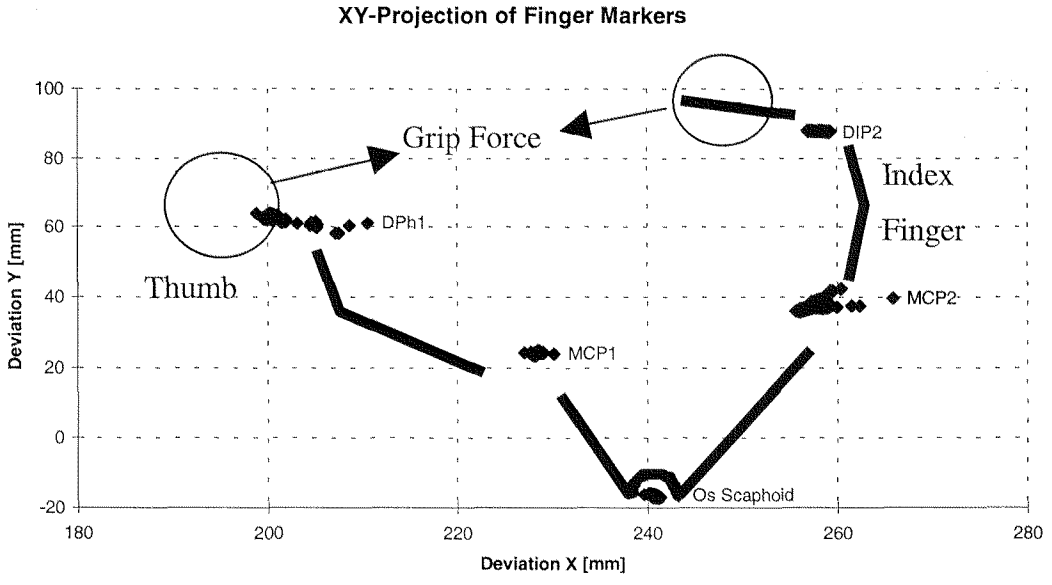


Figure 5-3. Vertical projection of the marker positions on the hand during the task performance onto the horizontal XY plane. Thumb is to the left, index finger is to the right. The two circles symbolise the manipulanda. *Abbreviations:* DPh1, distal phalanx of the thumb; MCP1, metacarpo-phalangeal joint of the thumb; DIP2, distal interphalangeal joint of the index finger; MCP2, metacarpo-phalangeal joint of the index.

scaphoid bone (Os scaphoid), the metacarpo-phalangeal joint of the index finger (MCP2) and the distal inter-phalangeal joint of the index finger (DIP2). Obviously the markers were a considerable distance away from the joint axes. Four infrared cameras were located each at about a distance of 50 cm from the hand such that the cameras were more than 90° away from each other and that no marker was occluded. Figure 5-3 shows the vertical projection of the markers on the hand onto the horizontal plane. The movement of the hand can clearly be seen by the wandering points in the graph. The

cameras digitised the spatial location of markers stuck on the working hand and the manipulandum of the force sensor while the subject performed the task of study 2. The trajectory of the markers was followed over 120 s. From the digitised observations an average and standard deviation of the markers was computed for each marker. The standard deviations of five markers were in the range of one millimetre (statistical error) with a maximal movement of the index metacarpo-phalangeal joint (MCP2) of 5.9 mm (6000 frames at 50 Hz = 120 s). The movements of the other markers were considerably smaller.

5.3 Study 2: Results

5.3.1 Test A-C: Data-set, Validation

In this second study the data of 17 experiments with 12 subjects were used. Eighty-five MUs were discriminated, but only 61 MUs were used for synchronisation analysis, with 28 MUs originating in the AdP muscle and 33 in the 1DI muscle. Eighty-three MU pairs could be obtained of the 61 units. Short-term synchronisation was found in 56 of the 83 MU (67%) pairs, as opposed to 129 out of 235 (IRM + IAM; 55%) pairs in study 1 (significant difference, χ^2-test, $P<0.05$). Figure 5-4 shows the percentage of synchronisation in MU pairs in three groups: all (complete data-set, *left*), synchronisation under force feedback (*centre*) and synchronisation under auditory feedback (*right*); the leftmost column in one group representing always the complete set of the group, while the middle and right column in that group show the respective values of synchrony in the IAM and IRM sub-groups. This scheme is also used in Figure 5-5 and Figure 5-6.

The data-set of the MU pairs was further split up, i.e. the single cross-correlations at each force level were analysed separately, in order to find a more pronounced difference between the two feedback conditions and between IAM or IRM pair. To delimit from the MU pairs with data gained on all five stages, these single cross-correlations are denoted as "cross-correlation pairs". Taken together a total of 213 cross-correlation pairs were investigated and synchronisation was found in 101 (47%; cf. Figure 5-5; study 1: synchrony in 163 of 448 cross-correlograms = 36.3%; significant difference, χ^2-test, $P<0.05$). The strength of synchronisation was based on 101 cross-correlograms with a significant peak. The mean k value was 3.60 ± 2.28, $n = 101$ (for comparison study 1: $k = 2.33\pm0.72$, $n = 163$; significant difference, t-test, $P<0.001$).

In conclusion, the results of this validation show that the synchronisation data gained in study 2 is more frequently and more strongly synchronised than in study 1. One reason is certainly that we confined the sampling of MUs mainly to the AdP and 1DI muscle pair, that showed most synchronised discharges in study 1. Furthermore, in study two we often selected only the most prominent MUs as ARTMUP was no longer available, and thus only the most characteristic MUs were quantified.

5.3.2 Test A: Confirm Findings of Study 1

5.3.2.1 Test A: Intermuscular versus Intramuscular Synchronisation

The 83 MU pairs were split into 33 IAM and 50 IRM MU pairs with occurrence of synchronisation in 27 IAM and 29 IRM MU pairs or 82% and 57%, respectively (Figure 5-4 *left*). This ratio was not significantly different under the two feedback conditions (χ^2-test, $P>0.05$; Figure 5-4 *centre and right*): twenty out of the 27 (74%) IAM MU pairs and 19 of 40 (48%) IRM MU pairs were synchronised under force feedback. Under auditory feedback condition, ten of eleven (91%) IAM and 11 of 23 (48%) IRM MU pairs were synchronised. For comparison of the force feedback condition, study 1 disclosed 78% IAM (n_{iam} = 69) and 45% IRM (n_{irm} = 166) synchronisation. The two IAM and IRM ratios of study 1 are not significantly different from the respective percentages of synchronisation in force feedback MU pairs of this study (χ^2-test, $P>0.05$).

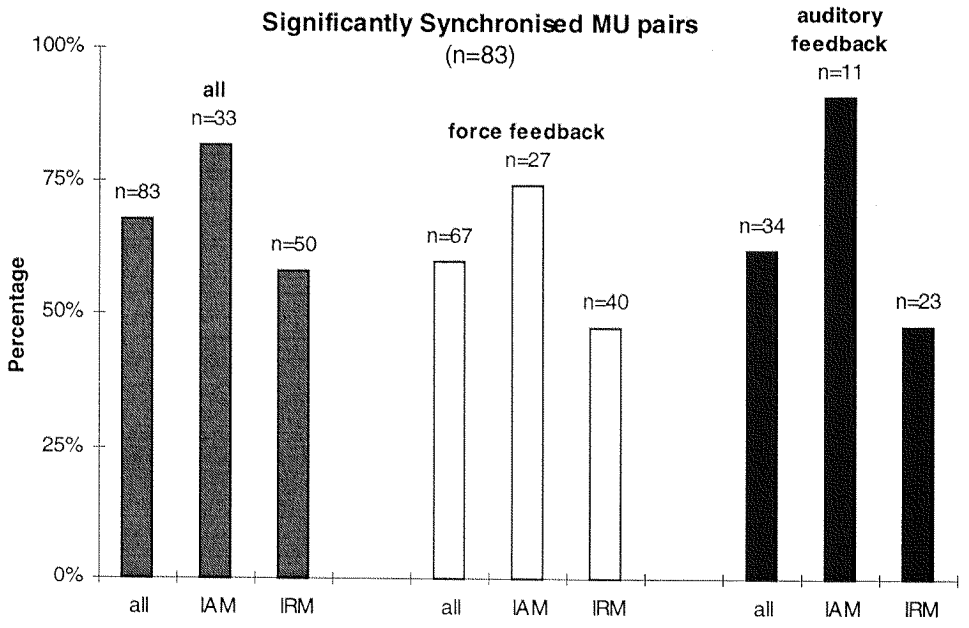


Figure 5-4. Percentage of significantly synchronised MU pairs depending the feedback condition. *Left:* Complete data-set; *centre:* force-feedback group; *right:* auditory feedback group. These groups are further split into the intramuscular (IAM) and intermuscular (IRM) sub-groups. A clear prevalence of short-term synchronisation can be seen in the IAM pairs as opposed to the IRM pairs.

For the *single cross-correlations*, a higher degree in occurrence of synchronisation for the 54 out of 80 IAM than for the 47 out of 133 IRM pairs was observed (68% vs. 35%; χ^2-test, $P<0.001$, Figure 5-5 *left*). Again separated into the two feedback conditions, force feedback showed 35 out of 55 (64%) IAM cross-correlograms with a significant peak and 29 out of 71 (41%) significant IRM cross-correlograms, whereas under auditory feedback 19 out of 25 (76%) IAM and 18 out of 62 (29%) IRM cross-correlograms with significant peak were found. The difference between IAM and IRM pairs is significant for the force feedback condition (χ^2-test, $P<0.05$) and the auditory feedback condition (χ^2-test, $P<0.001$). For comparison, study 1 showed synchrony in 57% of the IAM cross-correlation pairs (n_{iam} = 136) and 28% for the IRM pairs (n_{irm} = 312) under force feedback, only. The difference is not significant for the IAM pairs, significant for the IRM pairs (χ^2-test, $P<0.05$).

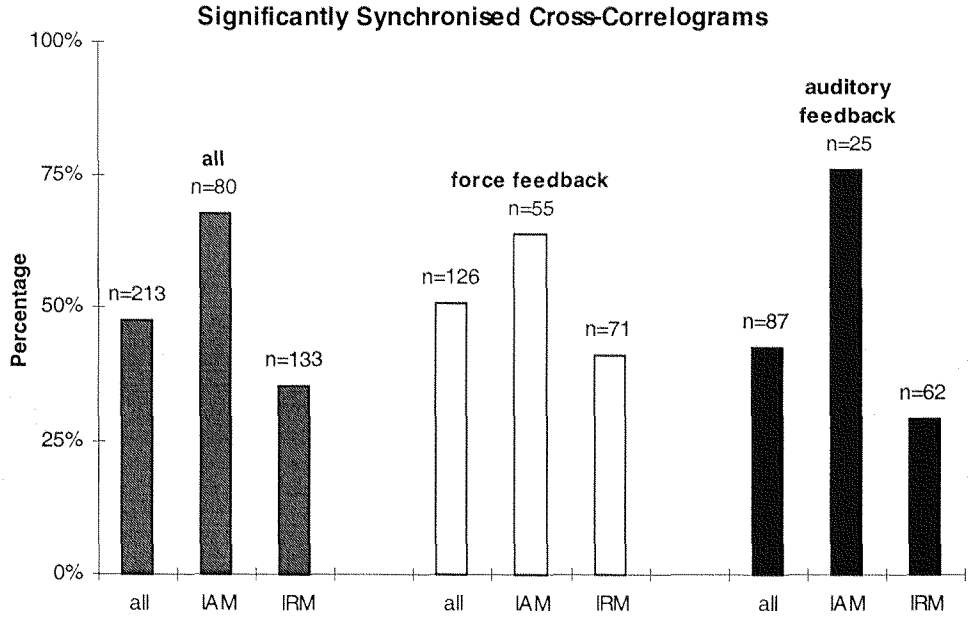


Figure 5-5. Overview of occurrence of synchronisation on the five stages for the complete data-set (*left*), the force feedback group (*centre*) and the auditory feedback group (*right*). Each cross-correlogram was considered regardless of the cross-correlograms on the stages. Synchronisation is occurring more often in IAM MU pairs.

With regard to the strength of synchronisation an average index k of 4.50±2.74 was obtained for the synchronised IAM MU pairs, while the IRM pairs had an index k of 2.58±0.83 (n_{IAM} = 54; n_{IRM} = 47). This result was statistically not significantly different (pair-wise t-test for independent random samples, see Figure 5-6 *left*). In study 1 we had

an average k value of 2.49±0.88 (n = 77) for IAM and 2.19±0.50 (n = 86) for IRM pairs. Both values were significantly different (t-test, P<0.001).

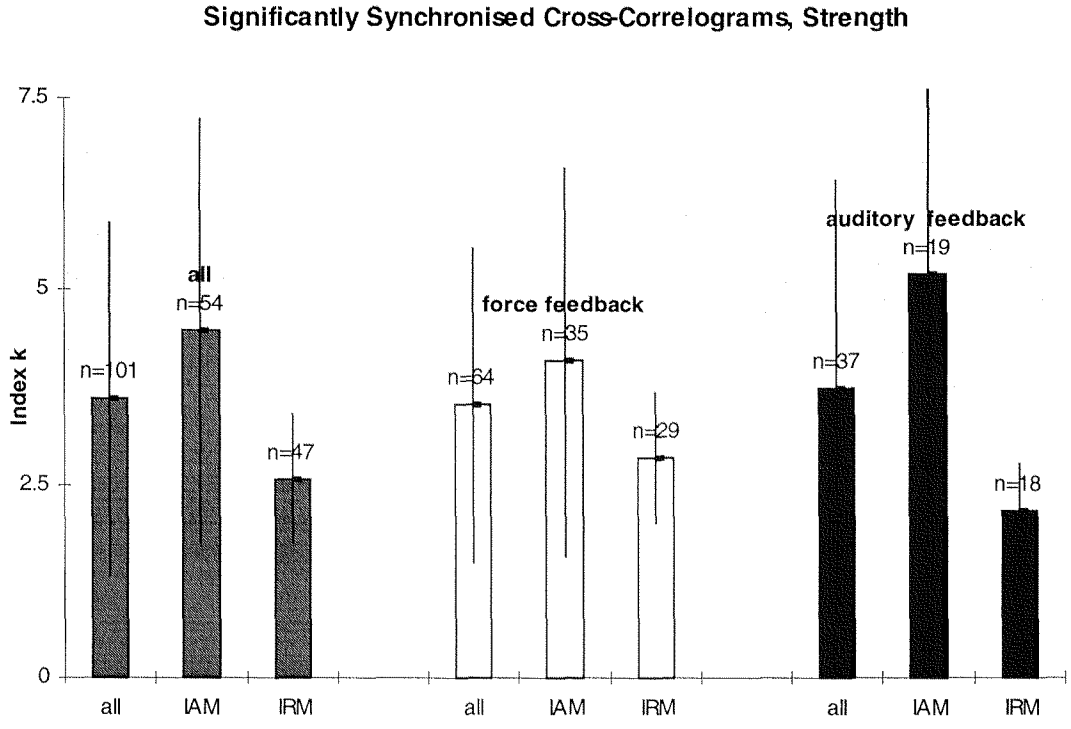


Figure 5-6. Histogram of synchronisation strength as quantified by the index k. Synchronisation under force feedback and auditory feedback differs only for the intermuscular MU pairs (IRM, one-sided t-test, P<0.01) while synchronisation of intramuscular pairs (IAM) show no significant difference.

5.3.2.2 Test A: Synchronisation in Relation to Recruitment

As in the first study we investigated whether there was a relationship of synchronisation to recruitment. In this data-set the MU pairs were checked for synchronisation on all stages where both MUs were active, i.e. first, second and third synchronisation of a MU pair on the increase leg of the task were taken into account, regardless of the feedback condition. This means that 19 MU pairs were counted twice, since they were active both in the force feedback (n_{ffb} = 63) and the auditory feedback (n_{afb} = 34) paradigm during force or activity increase. Before taking the MU pairs tested in the force and auditory feedback as one population, a test of homogeneity was performed to see whether the two groups originated in different populations. Given the estimated χ^2-value, the null hypothesis that both samples were drawn from the same population could not be

rejected and therefore the two groups could be analysed together (comparison of two independent empirical distributions of frequency data: χ^2-test, $P>0.05$). Four MU pairs were active only during the force decrease phase of the paradigm and were, therefore, exempted from this investigation, resulting in a total of 97 MU pairs. Furthermore, as some of the MU pairs got recruited at the stages 2 or 3, i.e. at the 2 or 3 N level or at 13 or 18 Hz firing frequency of the feedback MU, the data-sets for the "synchronisation one stage above recruitment" and "synchronisation two stages above recruitment" were reduced in number from 97 to 53 and 20, respectively (X = 0, X = 1, X = 2, in Figure 5-7 to Figure 5-9).

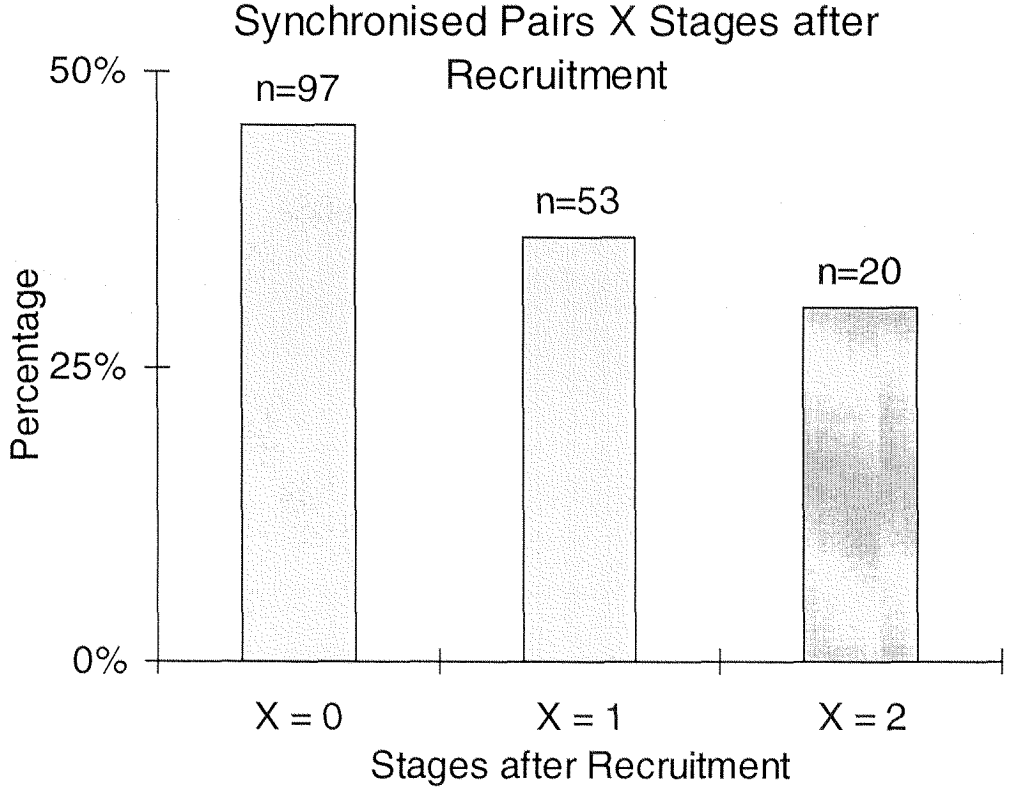


Figure 5-7. Percentage of synchronised pairs over 3 stages in respect to recruitment level (see text). The reduction in synchronisation is not significant.

Just at the stage when both MUs in a pair got recruited, 44 out of the 97 pairs (45%) show synchronisation, at one stage above that 19 of the 53 pairs (36%) were synchronised and at two stages above 30% (6/20 MU pairs) were synchronised (Figure 5-7). This trend, however, proved insignificant (testing a kx2 table for trend: The share of linear regression in the overall variation: χ^2-test, $P>0.05$).

In addition, synchronisation strength was checked in the above mentioned pairs in regard to first occurrence of synchrony (Figure 5-8). Even though the strength became weaker with increasing distance to recruitment this was not significant either: averaged index k_0: 3.72±2.00, n = 44; index k_1: 3.28±2.52, n = 19; index k_2: 3.16±2.38, n = 6 (testing for the presence of correlation: t-test). Again, before pooling the data, the k indices of the force and auditory feedback cross-correlograms were tested for homogeneity and the two populations were found to be similar (comparison of several means by analysis of variance: F-test, P>0.05).

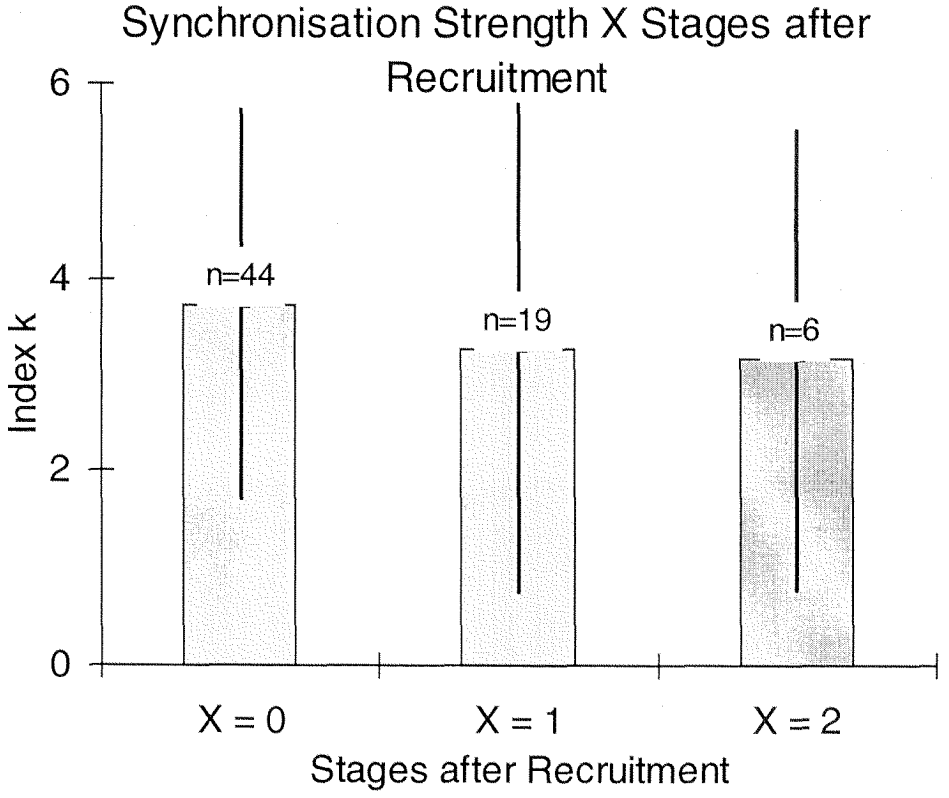


Figure 5-8. Strength of synchronisation in MU pairs over 3 stages in respect to synchronisation level. No significant trend can be found.

We then reduced the data-set to check at which stage the first time synchronisation in a MU pair occurred. In each of the MU pairs we considered only the cross-correlograms where synchronisation occurred for the first time, thus a data-set of 54 MU pairs remained for this analysis. Here, it turned out clearly that a MU pair was preferentially synchronised just at the level of recruitment with 44 pairs being synchronised the first

time at recruitment level, 9 pairs at one level above and finally only one pair at two levels above recruitment. This was the case for the whole population and the sub-populations with force feedback and auditory MU feedback (Figure 5-9).

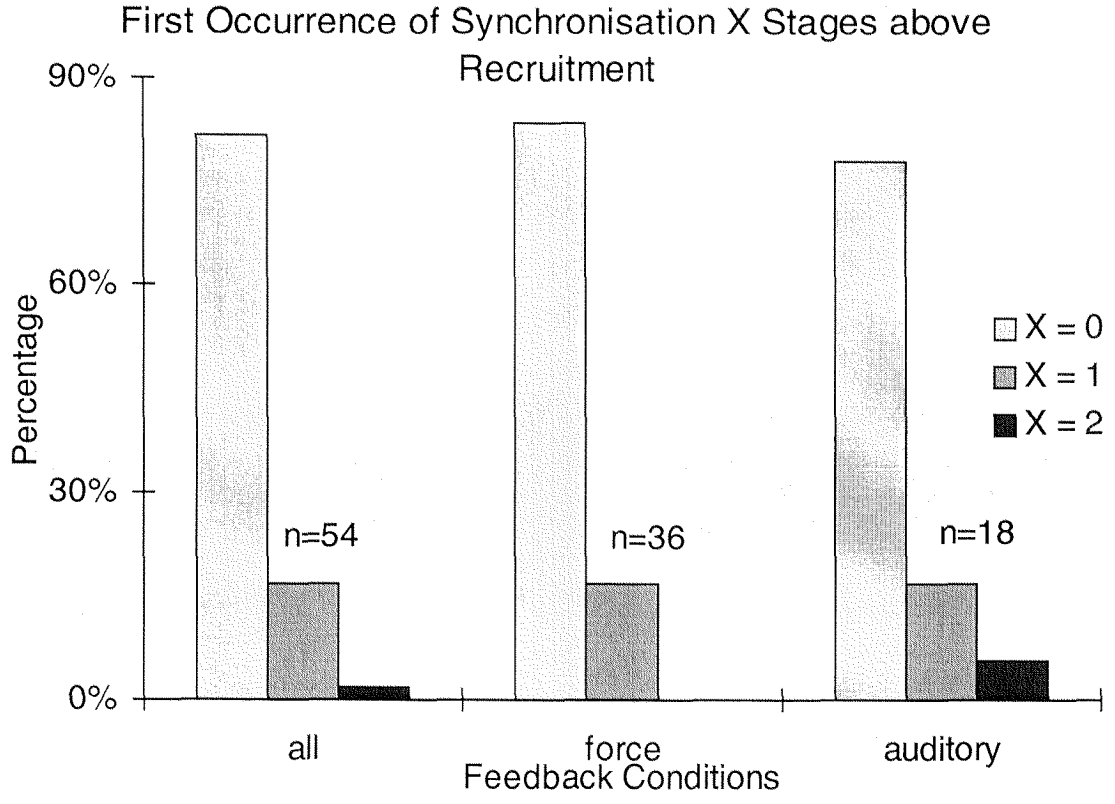


Figure 5-9. First occurrence of synchronisation with regard to the recruitment level of two MUs in a pair. First column in a group shows first synchronisation at recruitment; second column in a group: first synchronisation at a level above recruitment; third column: first synchronisation at two levels above recruitment. Under all feedback conditions, first synchronisation tends to occur just a the recruitment level.

5.3.2.3 Test A: Influence of Firing Frequency on Synchronisation

In order to detect a relationship between the firing frequency of the MU pairs and their synchronisation state, we plotted the histogram of the frequency distribution and built the cumulative sum of this distribution for synchronised (Figure 5-10 *top*) and non-synchronised (Figure 5-10 *bottom*) pairs in a cross-correlation. From the 213 cross-correlograms we gained the mean frequency data of the 426 MUs, whereof 202 were assigned to the synchronised class, and 224 to the non-synchronised class. The

distributions differed significantly at the 0.1% significance level (*t*-test) with a mean frequency of 13.6 Hz for the synchronised MUs vs. 14.5 Hz for the non-synchronised pairs. The difference of the cumulative sums is plotted in Figure 5-11.

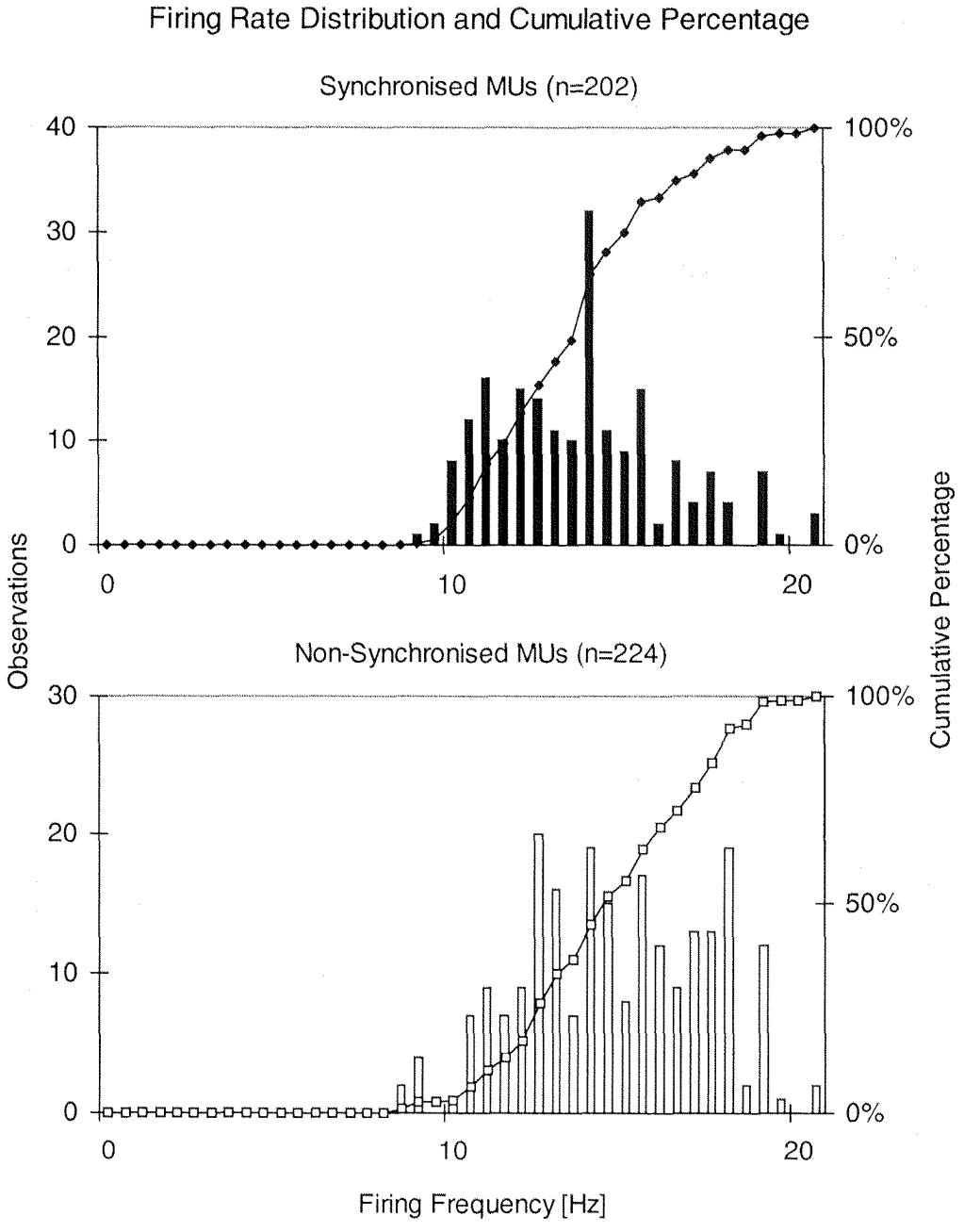


Figure 5-10. Histogram and cumulative sum of MU firing frequencies grouped in cross-correlograms of synchronised pairs (*top*) and non-synchronised pairs (*bottom*). The non-synchronised pairs show a significantly higher discharge rate than synchronised pairs.

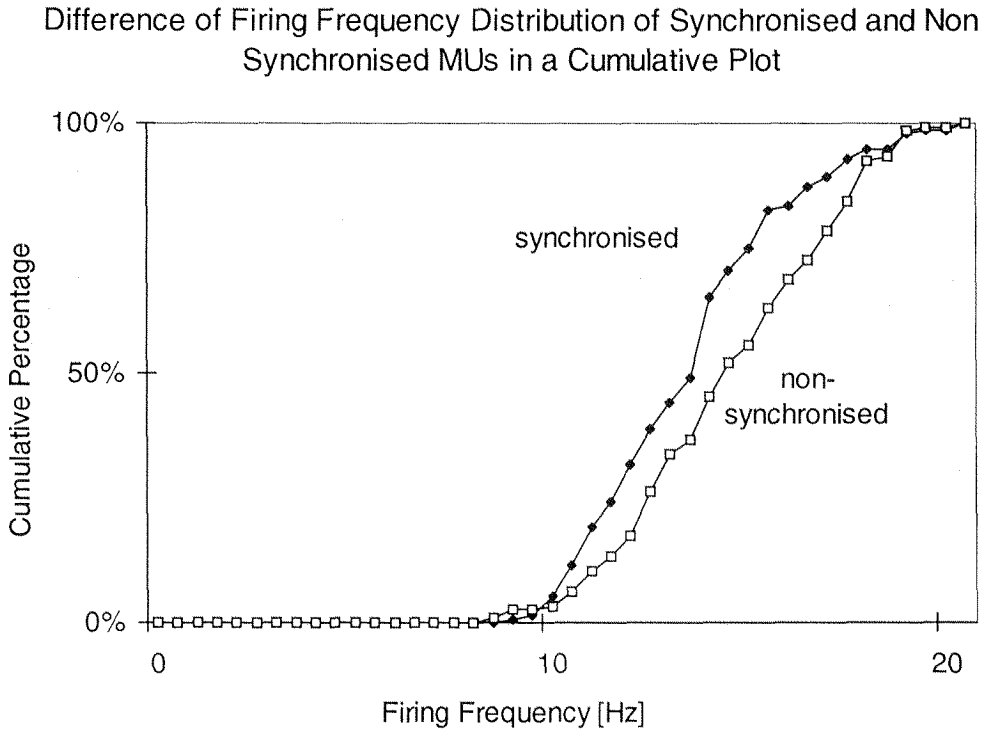


Figure 5-11. Comparison of the cumulative plots of firing frequency distributions displayed in Figure 5-10.

5.3.2.4 Test A: Summary

In Test A we tried to reproduce the findings we had obtained in study 1. Basically, the percentage of total synchronisation found in 83 MU pairs with 67% was higher than the 55% of study 1. In addition, the synchronisation strength in this study was also higher than that of study 1. The level of synchronisation in IAM as opposed to IRM pairs with 82% and 57%, respectively - the two percentages not being statistically different -, was also above the range of the 78% and 45% found in study 1. The influence of recruitment on MU synchronisation was checked. A higher rate and stronger synchronisation could be found, but both values were statistically not significant. However, we could show that MUs that tend to get synchronised are preferentially for the first time so just at the level of recruitment. Finally, we could show that MUs fire at lower discharge frequencies, when they are synchronised with others.

5.3.3 Test B: Force Increase and Decrease

The experimental subjects reported that force decrease to a specific level was much harder to achieve than force increase to the respective level. We, therefore, first investigated the mean firing rate distribution during the performance of the test over the five force/activity stages of single MUs. For this analysis 85 MUs were used. Figure 5-12 shows the mean firing rate distributions (average ± standard deviation) of the AdP and 1DI MUs during the performance of the force and auditory feedback paradigm.

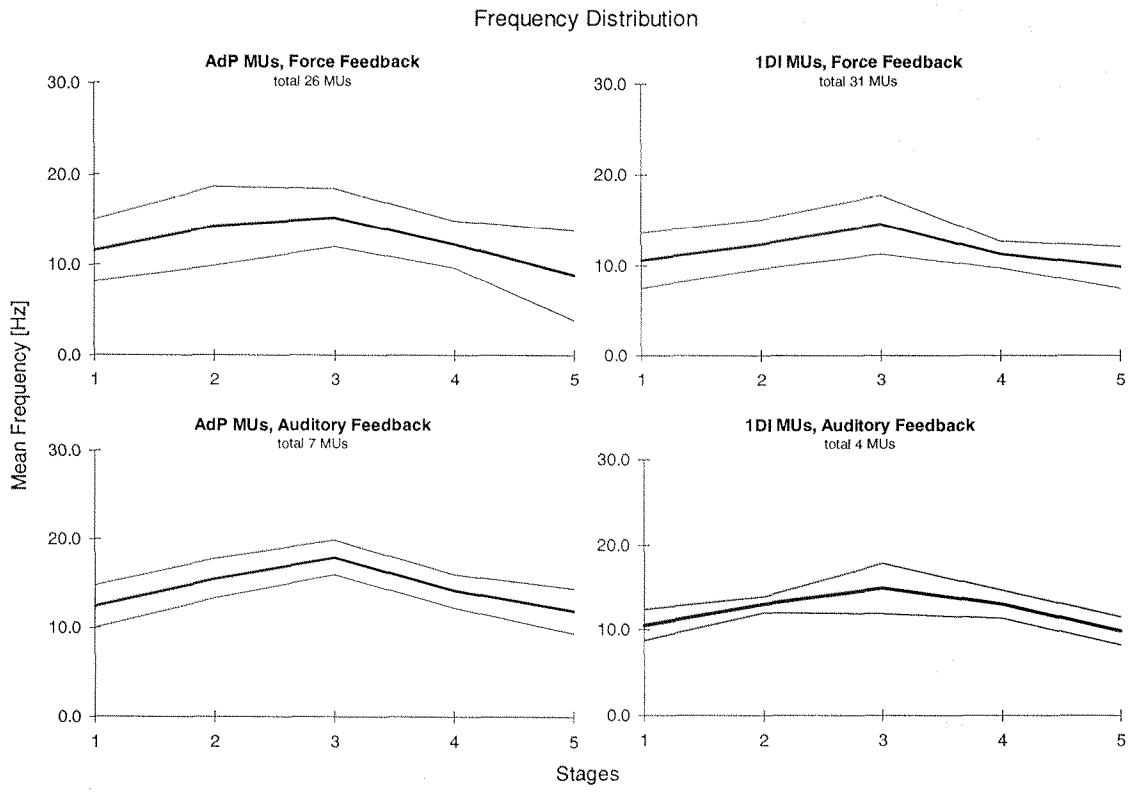


Figure 5-12. Mean firing frequency distribution of MUs of AdP (*left*) and 1DI (*right*) population. The *top row* shows the distribution under force feedback with a much larger scatter in the frequency and also a skew, i.e. higher frequency in the force increase leg vs. lower frequency during force decrease. In the *bottom row* under auditory feedback less scatter and almost symmetrical frequency distribution can be seen. *Heavy lines*: average; *thin lines*: ± standard deviation.

For the total population of the 85 MUs, the mean firing frequency was higher in the upward leg when compared to the downward leg (*t*-test, $P<0.05$, 11.5±3.1 Hz vs. 10.2±3.5 Hz, first versus fifth stage; 13.7±3.5 Hz vs. 12.5±2.5 Hz second versus fourth stage). When comparing the scatter in frequency at the stages between the force/activity increase and force/activity decrease phase following results were found: in the AdP

muscles the scatter at stage 2 was significantly different from stage 4, while similar at stages 1 and 5. For the 1DI muscle the scatter was significantly different at stages 1 and 5, as opposed to stage 2 and 4 were it was similar (comparison of two empirically determined variances of normally distributed populations: F-test, $P<0.05$; not shown). Comparing the scatter in frequency between force feedback and auditory MU feedback in Figure 5-12 showed a significant difference at stage 2 and 5 for the AdP and stage 2 for the 1DI (F-test, $P<0.05$).

In a second step we hypothesised that the cortical influence is enhanced during the controlled release phase, and that this should manifest itself in an increase in synchronisation occurrence and strength.

Twenty-five MU pairs gained in the force and auditory feedback paradigm - whereof one pair was present in both paradigms and therefore counted twice - were active both during the rising and declining phase of the trials. This yielded a total of 33 valid cross-correlation pairs (recruitment levels not always at the first level for the various pairs). We investigated - by pair-wise comparison of the two respective cross-correlograms (stages 1 and 5, stages 2 and 4, respectively) in a MU pair - whether synchronisation occurred in both the rising and declining phase (*balanced*), only during the rising (*increase*), only during the declining phase (*decrease*), or in none (*no sync*). Twelve cross-correlation pairs were *balanced* and twelve were not synchronised at all. Seven *decrease* cross-correlation pairs were found as opposed to two *increase* pairs. The *balanced* pairs were most strongly synchronised (index $k_{bal} = 3.44\pm1.80$, $n = 12$) as opposed to the *increase* or *decrease* pairs (index $k_{incr} = 2.35\pm1.00$, $n = 2$; index $k_{decr} = 2.11\pm0.50$, $n = 7$, respectively). Figure 5-13 shows the distribution of synchronisation strength during force increase and decrease for the three groups. Pairs that are members of the *increase* group are located on the abscissa, pairs belonging to the *decrease* group are on the ordinate. The *balanced* group is situated in the first quadrant. The higher occurrence of *decrease* synchronisation as opposed to *increase* synchronisation corroborates our expectation, that synchrony occurs more frequently in the more difficult part of the task. However, there is no concomitant significant difference in the strength of synchronisation.

Further observations shall be noted: first, all seven *decrease* MU pairs were gained in the auditory feedback condition; second, the vast majority of *no sync* MU pairs consisted of IRM pairs (11 of 12 cross-correlation pairs). Third, in contrast to the results shown above, the set of force feedback cross-correlation pairs showed a better synchronisation of the MUs than the auditory MU feedback cross-correlation pairs. Forth, the MU pairs in Figure 5-13 that had large synchronisation indices originated from the IAM group.

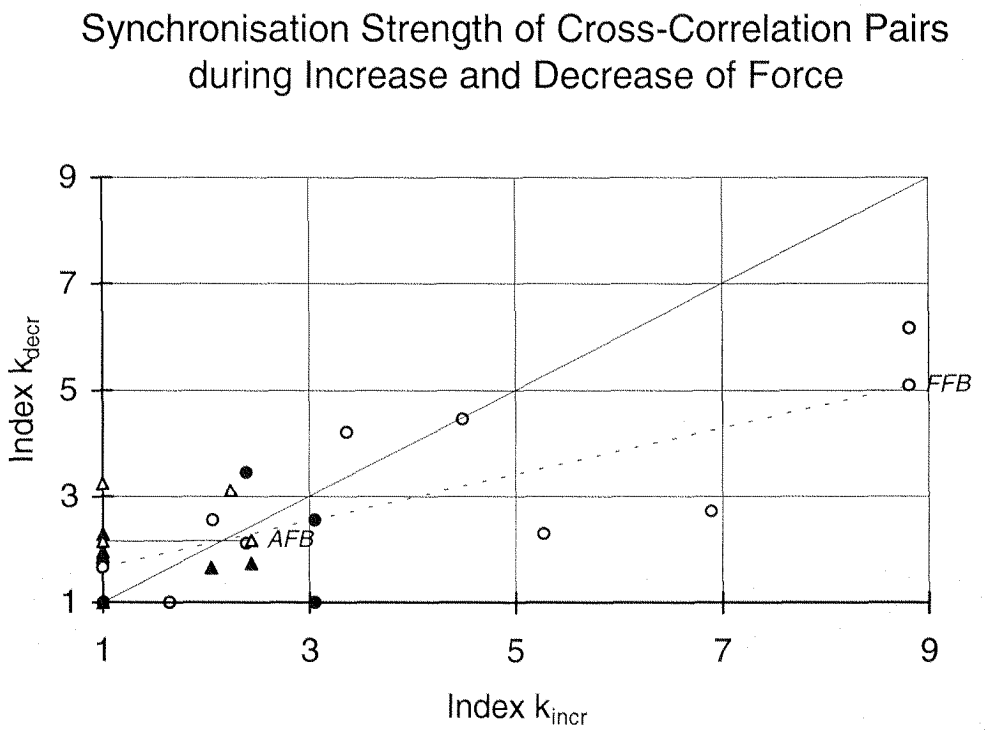


Figure 5-13 Scatter plot of synchronisation strength in 17 cross-correlogram pairs during the force increase and decrease legs. *Increase* cross-correlation pairs have an index $k_{incr} > 1$ and an index $k_{decr} = 1$; *decrease* cross-correlation pairs have an index $k_{incr} = 1$ and an index $k_{decr} > 1$; for *balanced* pairs both indices are larger than 1. Regression lines show the correlation of the force feedback (FFB) and auditory MU feedback (AFB) conditions. Circles: synchronised FFB MU pairs. Triangles: synchronised AFB MU pairs. Full symbols: intermuscular MU pairs; empty symbols: intramuscular pairs. FFB pairs show, in the mean, stronger synchronisation than AFB pairs.

5.3.3.1 Test B: Summary

In Test B we investigated whether increase or decrease of force or MU activity during the trial might have an effect on MU synchronisation. We first noted that the discharge

frequency was higher in the upward leg of the paradigm as opposed to the downward direction of force or activity. The scatter of frequencies was in half of the stages different, in the other half the difference was statistically not significant.

As for synchronisation, the majority of the MU pairs active on both the upward and downward leg of the paradigms showed symmetric behaviour with regard to synchronisation, i.e. they were either synchronised both during force/activity increase and decrease, or they were not at all. Seven cross-correlation pairs showed synchrony in the downward leg as opposed to only two pairs in the upward leg.

5.3.4 Test C: Force versus Auditory Feedback

As shown already above in the analysis of Test B, there was a reduced variability of MU frequency in the auditory feedback paradigm compared to the force feedback paradigm. We were, however, more interested in a possible difference in synchronisation of MUs in the two different paradigms.

In a first step, we approached the data from a global perspective. The MU pairs in the two feedback paradigms were analysed regardless whether they were active in the other paradigm. In the force feedback trials, which were always performed first, 67 pairs were active as opposed to 34 pairs in the auditory feedback condition. It has to be noted that only 18 pairs were present both in the force feedback and auditory feedback condition. The occurrence of synchronisation on at least one stage under these two conditions was comparable (χ^2-test, Figure 5-4, *Force Feedback All and Auditory Feedback All columns*): 40 out of 67 force feedback pairs (60%) vs. 21 out of 34 auditory feedback pairs (62%). These numbers comprise all the MUs that show synchronisation on at least one force or activity stage.

Again, for the single cross-correlations no significant difference in the occurrence of synchronisation could be established between the two feedback condition: synchronisation was found in 64 of the 126 (50.8%) force feedback cross-correlograms versus 37 in the 87 (42.5%) auditory feedback cross-correlograms (χ^2-test, Figure 5-5, *centre and right group*).

Comparing synchronisation strength between force and auditory feedback condition yielded an index k_{ffb} of 3.52±2.03 (n_{ffb} = 64), and an index k_{afb} of 3.73±2.70 (n_{afb} = 47), respectively. This result was statistically not significantly different (pair-wise *t*-test for independent random samples).

In conclusion, from this global perspective, no significant difference in the occurrence of synchronisation could be detected between the two feedback conditions, be it at the MU level (Figure 5-4), or be it for the single cross-correlograms (Figure 5-5). Only when the single cross-correlograms were further split up into IAM and IRM pairs, did the two feedback conditions show a difference in synchronisation strength between the IRM pairs (one sided *t*-test, $P<0.01$; Figure 5-6).

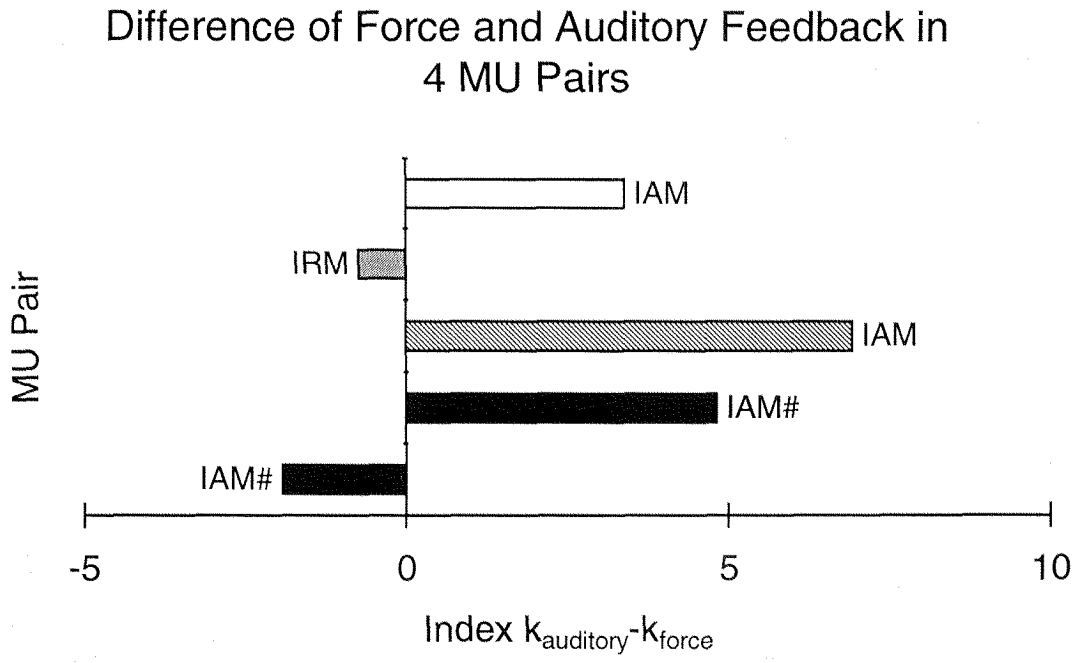


Figure 5-14. Difference in synchronisation strength as quantified by the index *k* between MU pairs that are synchronised both during the force feedback and auditory feedback trials at the same respective stage. A stronger synchronisation is seen for the auditory feedback condition (*t*-test). The lowest two bars (#) originate in the same MU pair for two different stages.

In a second step, we took a closer look at the data-sets. The 18 MU pairs that were active in the two conditions at a given force level and at the corresponding activity level, i.e. cross-correlation were compared. Two of the MU pairs had to be discarded since they were not active on the same respective stages. From the remaining 16 MU pairs 20 corresponding cross-correlation pairs could be gained. Eight cross-correlation pairs with no synchrony in neither of the paradigms were disclosed. Furthermore, there were three pairs with synchrony during force feedback but asynchronous firing under activity feedback, and four pairs with synchrony under activity feedback but asynchronous firing under force feedback. Only five cross-correlation pairs from four MU pairs - one MU pair with two, the remaining three pairs with one cross-correlogram - could be found, that were active and synchronised in both feedback conditions at the corresponding force and activity stage. Looking at this sample of five paired cross-correlograms it was found that, on average, these MUs were more strongly synchronised in the auditory feedback conditions (paired *t*-test, $P<0.05$, Figure 5-14).

5.3.4.1 Test C: Summary

In Test C we tried to determine whether the nature of feedback played a role in MU synchronisation. MU pairs that were active in the force feedback were compared against pairs active in the auditory feedback paradigm. In a first global overview, no difference between the two feedback conditions could be made out, neither for the MU pairs, nor for the cross-correlogram pairs, nor for synchronisation strength. The only significant difference that could be uncovered, was that of synchronisation strength between IRM MU cross-correlations in the two paradigms.

Those 16 MU pairs that were active under both paradigms at the same respective level were then scrutinised. It turned out that only five cross-correlograms could be gained. These pairs showed in three cases stronger synchrony under auditory feedback condition. The two remaining pairs with stronger synchrony in the force feedback paradigm were only slightly stronger in this very condition.

5.3.5 Test D: Twitch Tension

The twitch tension and contraction time of 33 MUs gained in this study were determined using the spike-triggered averaging method (Desmedt and Godaux, 1977; Thomas et al., 1990). Seventeen AdP MUs and 16 1DI units were analysed. With the spike recognition program (Spike 2, CED, Cambridge, UK) up to four MUs in a record could be discriminated. Figure 5-15 shows the result of the discrimination in one channel of a 1DI EMG. In this example two MUs have been identified whose template, IPIH and twitch tension are illustrated.

17 AdP MUs	mean±STD	min	max
Frequency [Hz]	13.8±3.0	9.0	20.0
Contraction Time [ms]	60.6±13.5	29.0	82.0
Contraction Force [mN]	13.3±11.8	0.8	41.2
16 1DI MUs			
Frequency [Hz]	12.8±3.4	8.0	17.0
Contraction Time [ms]	54.8±19.5	16.0	88.0
Contraction Force [mN]	9.8±8.7	1.1	26.7

Table 5-1. MUs characterised by firing frequency, contraction time and force. There is no difference between the two sub-populations.

The discharge frequency of the discriminated MUs ranged between 8 and 20 Hz. The average and standard deviation for the AdP MUs was 13.8±3.0 Hz, for the 1DI MUs 12.8±3.4 ms (see Table 5-1). The contraction time was in the range of 16 and 125 ms with a mean of 60.6±13.5 ms for AdP, and 54.8±19.5 ms for 1DI. The twitch force varied between 0.8 and 41.2 mN. The mean twitch tension for the AdP was with 13.3±11.8 mN not significantly larger than the 1DI twitch tension of 9.8±8.7 mN (*t*-test; cf. Table 5-1). According to the theory of fatiguing and fatigue-resistant MUs we expected to find MUs with short contraction time and large contraction force and vice versa. We plotted the contraction time vs. contraction force (Figure 5-16), but did not find any significant relationship between the two parameters for the whole sample. Only the 1DI MUs showed a significant relationship ($r = 0.51$, $n = 16$, $P<0.05$). There was a

significant relationship between the reciprocal value of firing frequency and the twitch tension of all MUs (*Pearson-correlation:* $P<0.05$), i.e. the longer the inter-potential interval of the MUs the higher the contraction force.

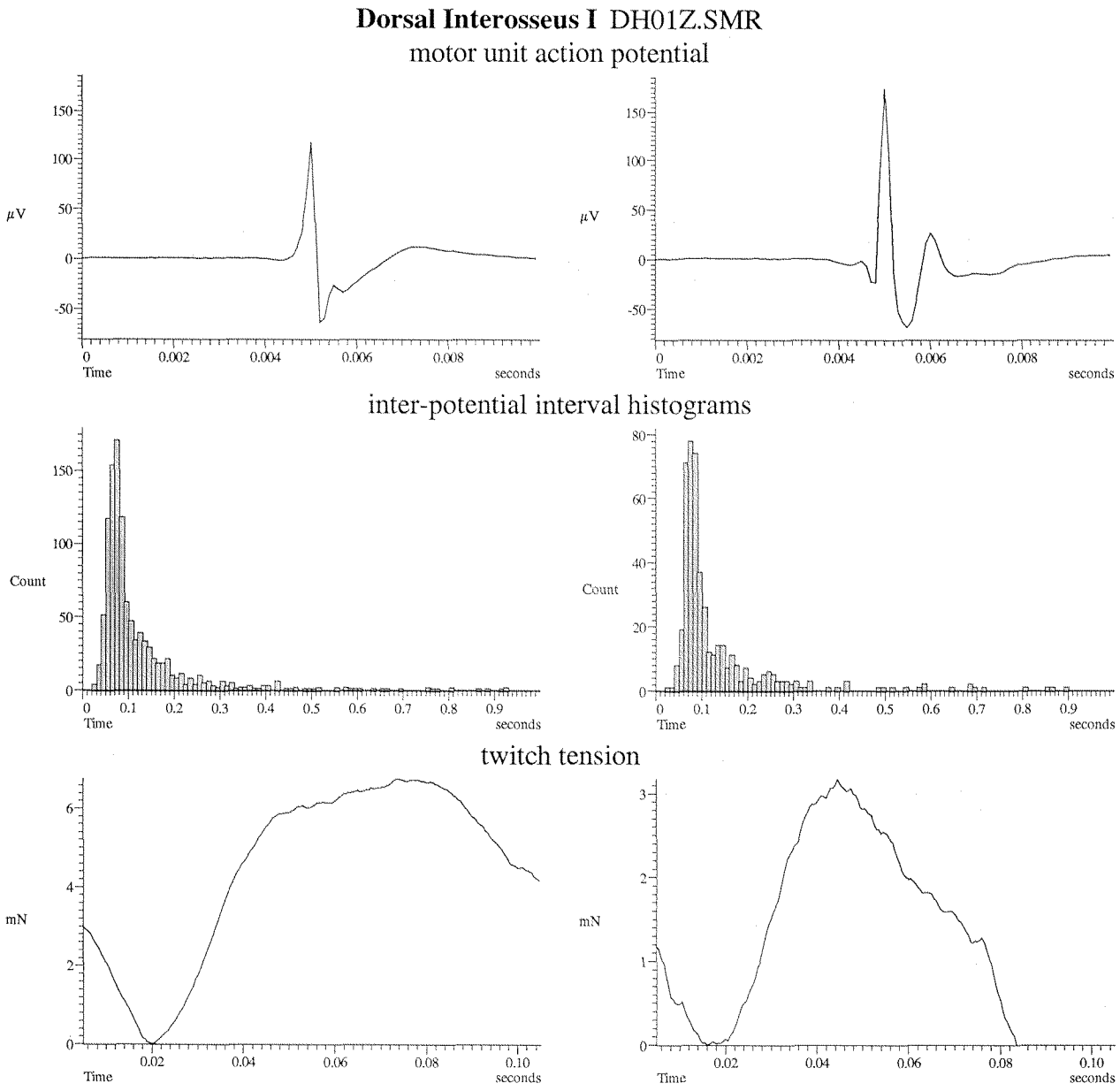


Figure 5-15. Twitch tension of two 1DI MUs discriminated in the same record. The recording length was 424 s. *Left from top to bottom:* MU action potential template generated from 527 potentials; the inter-potential interval-histogram with a modal value of 14 Hz; the force trace shows a contraction time of 69 ms and a contraction force of 6.8 mN. *Right from top to bottom:* Second MU template generated from 308 potentials; the IPIH shows a modal value for the discharge frequency of 14 Hz; the contraction time is 39 ms and the force 3.2 mN.

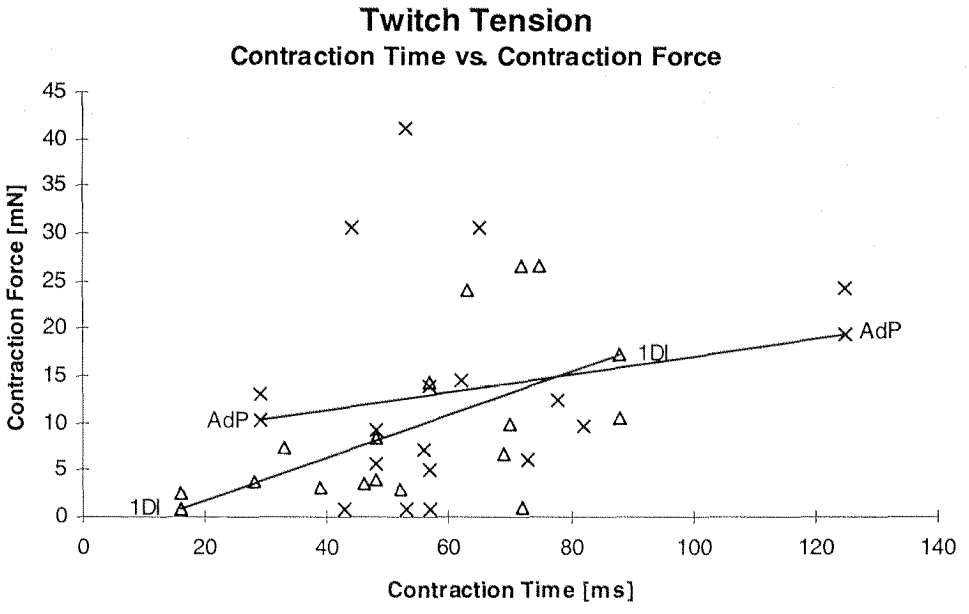


Figure 5-16. Scatter plot of contraction time vs. contraction force of 16 1DI (*triangles*) and 17 AdP (*asterisks*) MUs. Also shown are the regression lines of contraction time vs. contraction force for the AdP and 1DI MUs. Only the 1DI MUs have a significant relationship between contraction time and force ($r = 0.51$, $P<0.05$, $n = 16$).

No significant relationship between contraction time and reciprocal firing frequency was disclosed, in other words we expected to find that MUs with shorter contraction times would discharge at higher frequency, which was not the case.

5.3.5.1 Test D: Summary

In Test D, we characterised the MUs with regard to discharge frequency, contraction time and twitch tension, or contraction force. Discharges frequencies varied between 8 and 20 Hz, with a mean of 13.3 Hz. The mean contraction time measured was 57.0 ms, here the range was relatively large with a minimum of 16 ms and a maximum of 88 ms. The contraction force was, on average, 12.8 mN for the AdP and 9.8 mN for the 1DI MUs. No statistically significant differences could be discerned between the MUs of the two muscles. We then tried to disclose relationships between the three measures, however, we could just find that 1DI muscles with short contraction times tended to produce small contraction forces.

5.4 Study 2: Discussion

5.4.1 Methodological Considerations

5.4.1.1 Set-Up and Task

With a new set-up we reacted to the short-comings of the first experimental set-up. A new force transducer was built which measured the resultant force from 0 to 5 N with a resolution down to 0.5 mN force (cf. Appendix B). Furthermore, given the fact that the manipulanda were free floating at the finger tips, no forces were required to maintain the position of the force transducer. The possibility to feed MU activity back to the subject was added (cf. Appendix A). The experimental task was adjusted such that either force or activity had to be increased *and* decreased in a controlled manner over the force levels 0, 1, 2, 3, 2, 1, 0 N or frequency levels 0, 8, 13, 18, 13, 8, 0 Hz, respectively. The holding time on each level was extended from 3 s to 5 s duration and 25 trials both under force and activity feedback had to be performed resulting in recording periods of about 40 minutes. The amplitude of force was taken from the previous experiments (Maier and Hepp-Reymond, 1995a) while the frequency levels were chosen such that the discharge rate were in the physiological range (e.g. Monster and Chan, 1977) and comparable force levels as in study 1 were generated. However, for some MUs the 18 Hz discharge rate required excessive force and the frequency level was not always reached. In these cases the subjects tried to maintain the highest possible discharge rates.

5.4.1.2 ARTMUP

With the experience gathered with ARTMUP - hardware and resolution limitations, short recording periods, limited access - discrimination of two MUs was now performed on-line by hand, while additional MUs were gained off-line from data stored on DAT tapes. This procedure resulted in some cases in double discrimination of the same MU. Precautions were taken, that these double discriminations were identified: the template of the on-line discriminated MU potential was sketched for later visual comparison with off-line discriminate MU potentials. Furthermore, the cross-correlograms that resembled auto-correlograms (very narrow and high peaks) were sorted out. Only the MU that showed better discrimination (smooth auto-correlogram and inter-potential interval

histogram) was retained. As with ARTMUP, to characterise the MUs only the time points of spike occurrence were stored of the EMG signal.

Due to the recruitment and inactivation of the MUs and long recording periods only few MUs could be followed during the whole length of the experiment. The analysis thus had to put up with MUs that were either active in one or the other task but seldom active during both experimental tasks.

5.4.1.3 Twitch Tension

The twitch tension data-acquisition and analysis was performed on a PC equipped with a CED Spike 2 system. MUs were automatically discriminated from the multi-unit EMG and the spike-triggered averaging algorithm generated the twitch tension. Since this experiment was performed after the force and activity increase/decrease experiment, only 33 MUs could be analysed in this way. Furthermore, acceptance criteria for MUs were incorporated such as 100 spike counts (McMillan et al., 1990) and discharge rates lower than 10 Hz (Calancie and Bawa, 1986; Nordstrom et al., 1989).

5.4.1.4 Isometricity

For study 1 video recordings confirmed the isometricity of the hand during the task performance up to 3 N force. We wanted to see whether with a 3D video system it was possible to quantify also the vertical deviation of the hand during the performance of the experiment. However, taking into account that the spatial resolution of the VICON system used is in the range of millimetres (systematic error) for the distance between cameras and object (around 50 cm) and that the acquisition system is very sensitive to light disturbances, the estimation of the total error (root mean square of statistical error and systematic error) is thus in the range of the resolution of the system. The order of magnitude of the finger movement in the experiment to be expected is also in the range of millimetres as can be determined macroscopically. Therefore, this study was confined to one exploratory experimental run. The data gained in this run showed some major deviations at the distal phalanx of the thumb and at the metacarpo-phalangeal joint of the index finger. Especially the displacement of the thumb distal phalanx is attributed to changes of configuration in the thumb - the marker is placed on the manipulandum at approximately 2 cm off the axis of the thumb. On the other hand, the marker on the

metacarpo-phalangeal joint of the index finger was located directly on the joint axis, and thus, witnessed a considerable deviation from its original position during the task performance. Whether this deviation has any influence on the moment arms of the 1DI muscle is debatable, since the muscle runs in a parallel plane to the rotation for the precision grip at this joint and therefore does not experience a significant change in muscle length due to the deviation described.

5.4.2 Test A: Confirm Findings of Study 1

The results of study 2 differ from study 1 such that in the former stronger and more frequent temporal coupling was found. There are several reasons that might account for this difference: the muscle sample was now confined to those two muscles that showed the largest database in the previous study: AdP and 1DI, both muscles being innervated by the same peripheral nerve, the n. ulnaris. In study 1, synchronisation was found in 40 out of 61 AdP-1DI, AdP-AdP and 1DI-1DI pairs which is almost identical as the 67% in this study. Furthermore, the AdP-1DI muscle pairs are close functional synergists in the present task. This is in contrast to the functional heterogeneity of muscles investigated in study 1. Further important factors that might have improved the data quality are the longer recording periods as well as the more stringent criterion for the spike count. These criteria were defined with the experience gained in study 1: any one MU had to show a spike count in excess of 300 on any given level to be retained for further processing. With the increased number of data points the signal-to-noise ratio was also reduced. When making a literature survey on the degrees of MU synchronisation (cf. study 1) it can be found that the percentage of synchronised discharge from finger MUs can vary from 51% (Semmler and Nordstrom, 1995) up to 100% (Bremner et al., 1991a). These numbers were gained in experiments that strictly controlled the discharge of the MUs under investigation over lengthy periods of several minutes, that were not possible in our experimental set-up. Fatigue, however, was excluded from contributing to increased synchronisation by Nordstrom et al. (1990) and Schmied et al. (1993). Nevertheless, Bremner et al. (1991b) mentioned that the amount of synchronisation can vary from minute to minute of a long recording (their Figure 1), but they also noted that there does not appear to be a trend or periodicity in the variation of this synchronisation over time. Furthermore, inter-individual variability of synchronisation is mentioned in

several reports (e.g. 70% to 82% as reported by Schmied et al., 1993; differing synchronisation strength reported by Bremner et al., 1991b), Maier and Hepp-Reymond (1995b) also mentioned inter-experimental variability in the same subject: "...only 41% of the total number of coupled muscle pairs showed stable synergies within individuals...". The conclusion that can be drawn from this wide range of data is that synchronisation is present in a majority of muscles of the arm and hand, but is fluctuating over time.

With regard to synchronisation being linked to recruitment a first look revealed no evidence for this linkage, both frequency of occurrence and strength of synchronisation were decreasing but not statistically significantly - in contrast to study 1 where the decreasing frequency was statistically significant. Only when identifying the level of first synchronisation, it turned out that this was the case mainly at the stage of recruitment.

5.4.3 Test B: Force Increase and Decrease

We searched for an explanation for the more difficult force control in the decreasing leg of the paradigm. It has been shown that MUs can be activated differently during force increase or decrease (e.g. de-recruitment at lower force levels than recruitment: Howell et al., 1995). The results presented here showed first that at force increase the discharge frequencies of the MUs were higher. Furthermore, in half of the cases the frequency scatter was also larger during force increase. Given the repeated trials, the relatively low force levels and the trend of firing rates over time as described in study 1, we think this is not a consequence of fatigue, were discharge frequency can decline by 50-70% in muscle electrical activity during maximal voluntary contraction (Bigland-Ritchie et al., 1983).

Although a relative majority of the MUs active during force/activity increase and decrease was synchronised during both phases, more MUs showed synchrony in the decrease phase. This is in parallel to a reduced scatter of discharge frequencies during this phase. The fact that all seven decrease MU pairs were gained in the auditory feedback condition is even more notable, since it required more attention (though not measurable, only subjective) to maintain the required discharge frequency.

Furthermore, Johansson and Westling (1987) described the "magnet phenomenon" which occurred during the slow release of grip, i.e. when the subjects were asked to very slowly separate their fingers while holding an object in the air, they often felt as if their fingers adhered to the object. The slow release of grip force may trigger slip responses from afferent units, responsible for the automatic regulation of the balance between the grip force and the load force, as the skin area of the finger pads in contact with the manipulandum is declining and thus elicit slip reflexes. These very reflexes may have contributed to the observed synchronisation of MU pairs in the spinal cord during the decrease of MU activity. Johansson and Westling identified tactile receptors as FA I, FA II and SA I receptor units exhibiting a pronounced dynamic sensitivity. In the accompanying paper Westling and Johansson (1987) reported that FA I receptor units showed a vigorous burst response at the release of grip, followed in intensity and number by SA I units. Responses to grip force increase were seen at about the same levels as these release responses, however, the former were reported to be usually weaker.

In conclusion, the reported findings - lower discharge rates with less scatter but increased synchronisation at force/activity decrease may result from strongly connected reflex loops that impinge on the MUs in the spine. Furthermore, these very reflexes may also explain the subjective difficulties of the subjects to reduce force within the given limits, since the automatic regulation is acting in opposition to the voluntary drive to the MUs. These findings speak in favour of a strong synchronising source that is not cortical, but is active only under very specific conditions of the motor task.

5.4.4 Test C: Force versus Auditory Feedback

With the two feedback conditions, we wanted to show that experiments that rely on auditory feedback for the subjects may be biased towards synchronous discharge of MUs. While Maier and Hepp-Reymond (1995b) showed a disappointingly low number of muscle synchronisation (27%), we reported from a sub-set of this data-set (study 1) 45 - 78% MU synchronisation. In these experiments the subjects were asked to apply isometric grip force onto a force transducer with the hand in precision grip configuration. An experimental sweep consisted of three different force levels of three second holding duration. The force levels were not tied to any predefined discharge

frequency. Neither the subjects nor the experimenters were aware of the discharge frequency or synchronous discharge of MUs.

Other groups reported percentages of MU synchronisation that reached from 45 - 100% (cf. study 1, Table 4-5), which was astonishingly high when compared to our data. However, these percentages cannot be compared directly since several crucial constraints are different: e.g. Bremner et al. (1991a) listed percentages of MU synchrony between 68 and 100%. We claim that their test set-up might have favoured synchronous discharge of MUs: first they instructed their subjects to maintain isometric contraction of the muscle along its optimum plane of action so that the two measured MUs fired continuously at around 10 impulses per second. Second, they provided the subjects with auditory and visual feedback of both unprocessed EMG signals together with a continuous display of the instantaneous firing rates of the two individual MUs. Furthermore, they emphasised to the subjects to keep both MUs firing continuously throughout each experimental run. This resulted in recordings from 3 to 10 minutes of continuous MU discharge with a very high percentage of MU synchronisation.

On the other hand, Schmied et al. (1993) showed that the degree of synchronisation could be altered voluntarily towards synchrony or asynchrony, provided the adequate feedback (auditory feedback: clicks when synchronous discharge occurred) was returned to the subjects and that the subjects had sufficient training to adapt to the new feedback situation and experimental requirements.

Coming back to our data, we found only a limited difference in the two feedback conditions, both with regard to occurrence frequency and strength of synchronisation. Only four MU pairs were found that had synchronisation on the same respective levels of the force feedback and the auditory feedback condition. Here we could show that - at least for these four MU pairs - synchronisation was much stronger during auditory feedback. However, our test set-up had following short-comings to test the hypothesis in the whole depth: we could only return auditory ("clicks") and visual frequency feedback of one MU at one time due to hardware limitations (only one moment rate-meter available). Nevertheless, the discharge time point of the second MU could be shown on the oscilloscope monitor. Here an auditory feedback of the second MU would have facilitated the task tremendously. Furthermore, given the experimentally imposed

increase and decrease of discharge frequency some of the MUs got lost during the performance of the experiment, reducing the yield of data. Finally, the subjects were aware of fatigue building up in their hand muscles, although the force levels were comparable with the force feedback condition experiment. We think that the reason for the fatigue is the sub-optimal direction of force measurement, in that the subjects decreased the compliance of the fingers by co-contracting antagonist muscles together with increasing the grip force, thus reaching a much higher activation level in the investigated muscle.

Nevertheless, given the findings of Schmied et al. (1993) and showing in our experiment that the discharge of MUs can be controlled within narrow boundaries it is very likely that a subject with adequate feedback will start to synchronise the discharge of two MUs once he or she is advised to discharge two MUs during a longer period at approximately the same frequency. This speaks for a more central or rather cortical origin of MU synchronisation, since in the auditory feedback task the activity of the MUs is specifically and voluntarily controlled as opposed to the force feedback, where the grip force *per se,* resulting from the contribution of a variety of muscles and their MUs, is the measure that is regulated.

5.4.5 Test D: Twitch Tension

Most investigations, including this one, recorded MU twitch tension in human muscles by measuring force in a direction which is not specific to the MU, i.e. not the axial pulling direction. Therefore only relative conclusions can be drawn with regard to the MUs types in one muscle. A lot of the discussion about twitch tension is concerning spike-triggered averaging and its short comings to faithfully describe the force output. Only a few investigations have been performed attempting in humans *in vivo* to single out a MU and to measure its twitch tension (Westling et al., 1990, Thomas et al., 1990). This group managed to measure the twitch force of MUs radially to the thumb axis after intraneural motor-axon stimulation. Their twitch forces ranged from 3 to 34 mN, the contraction times from 35 to 80 ms, interestingly not differing significantly from the data we gained in our limited set which measured the twitch force in only one dimension. Thus we tried to find a correlation between contraction time and twitch force. We plotted the contraction time vs. the force (Figure 5-16), but did not detect - as

Thomas et al. (1990) - any significant relationship between the two parameters for the whole sample, i.e. with the continuous distribution of contraction time and twitch force values we could not classify the MUs into *fast-fatiguing*, *fast-fatigue resistant* or *slow* MUs. Furthermore, only the 1DI MUs showed a significant relationship of contraction time to twitch force ($r = 0.51$, $n = 16$). It has to be noted, though, that the regression lines we gained are in contradiction to the theory gained in cat MUs, according to which fast MUs generate large twitches. What may be the reason for such a discrepancy of our data against the generally accepted theory? One issue is certainly the measurement of force. In our experimental set-up we measure the force in a direction which is not aligned to the main axis of the various muscles, let alone the specific MUs under investigation. Especially with the AdP which has a fan-like structure in the palm of the hand it is difficult to determine the optimal pulling direction of the muscle. The second issue is the spike-triggered averaging technique which may bring some bias into the results. While the original theory of the size principle is based on direct measurement of just one muscle in the hindlimb of the cat with a clearly isolated neurone innervating the respective muscle, i.e. the input and the output were easily identified and directly measured, we based our analysis on input and output data that originate in a much noisier environment and this data had to be statistically evaluated. Finally, the limited number of discharges may also have diminished the quality of the results thereby generating contraction time and twitch force values that show large variations.

On the other hand, it is imaginable that the size principle may not have such a high importance in the small muscles of the hand. These muscles are mainly involved in transient actions, they do not have to contribute to weight bearing of other body parts. As already shown in study 1, the intrinsic muscles of the hand are much more involved in the modulation of muscle force, whereas the extrinsic muscles in the forearm contribute to the base level of force. It may thus be that the size principle is distributed topographically over the intrinsic and extrinsic hand muscles, in that the faster and fatiguable muscles are located in the hand itself, while the fatigue-resistant muscles are located in the forearm. Functionally this makes even more sense, since in the power grip, where large forces over longer duration are required, mainly muscles of the forearm are involved. The variations in contraction time and twitch force seen in our data sample would then show up only a limited range of these values. Longer

contraction times and smaller twitch forces are then expected to be found in the forearm muscles.

In summary, we described the MUs with regard to contraction time and twitch force. The obtained values were in the range of values reported earlier. However, no significant relationship of contraction time, twitch force or discharge frequency could be uncovered that would foster the theory of the size principle. Attempts to classify the two sets of MUs were unsuccessful first because of the small sample size, 1DI and AdP MUs had to be regarded separately due to disparate measuring direction and muscle pulling direction with regard to muscle action, and second because of the uncharacteristic distribution of the contraction time, twitch force and discharge rate. Thomas et al. (1991) did not manage to find any sensible classification with a much more elaborated stimulation paradigm and measurement apparatus, either. We proposed a possible explanation for this dilemma in that the size principle is applicable with the different types of MUs distributed topographically over the intrinsic and extrinsic hand muscles.

5.5 Study 2: Summary

Study 2 was split up in four investigations. Test A was performed to validate the data generated in study 1, i.e. overall, intra- and intermuscular synchronisation, and influence of recruitment on synchronisation. The amount of synchrony on the whole MU pool, for the IAM and IRM pairs was *stronger* and *more frequent* to that described in study 1 due to choosing that muscle pair sample in study 2 which showed highest occurrence rate of synchrony in study 1. These two muscles are close functional synergist in the required task and they are both innervated by the same nerve. Further, we could show that MUs tend to get synchronised preferentially at recruitment. And finally, our data indicate that MUs fire at lower discharge frequencies, when they are synchronised with each other. With Test B we attempted to find out, whether the MU pairs co-operated differently under varying loading regimens, e.g. grip force or activity *increase* in contrast to grip force or activity *decrease*. We first noted that the discharge frequencies were higher and more scattered during force and activity increase as opposed to decrease. With regard to synchronisation, the majority of the MU pairs that were active on both the upward and downward leg of the paradigms, showed symmetric behaviour, i.e. they were either synchronised both during force/activity increase and decrease, or they were not synchronised at all. Seven cross-correlation pairs showed synchrony in the downward leg as opposed to only two pairs that showed synchrony in the upward leg. In Test C we tried to determine, whether the nature of the feedback played a role in MU synchronisation. To this end we confronted the subjects with two different feedback conditions in a similar paradigm. In the first condition they received the force output as feedback signal, in the second they received the instantaneous frequency of one MU. In a first global overview, no difference between the two feedback conditions could be made out. Only by going into detail, five cross-correlogram pairs with synchronisation in both feedback conditions turned up. These pairs showed in three cases considerably stronger synchrony under auditory feedback condition. The two remaining pairs had only slightly stronger synchrony under force feedback. In Test D we characterised 33 MUs with regard to their contraction force, contraction time and discharge rate. We correlated these measures, but could find just one significant relationship between them, i.e. we could show that in the 1DI muscle short contraction times of the MUs produced small contraction forces. We proposed that the size principle might be still applicable,

however, with the large MUs located in the extrinsic muscles of the forearm and the small MUs in the intrinsic muscles of the hand.

6 Study 3: The Influence of Cortical Drive

Parts of this chapter have been published in NeuroReport (Huesler et al., 1998, Task Dependence of Muscle Synchronization in Human Hand Muscles).

6.1 Goal

This experimental series was performed to determine whether the task *per se*, i.e. the type of grip, had any influence on the activation of muscles and muscle groups and under which experimental condition (grip type, force increase/decrease, high/low force) the putative cortical drive was strongest. We asked six subjects to perform the force feedback task first with the precision grip and second with the power grip (fist-like grip with the flexion of all fingers against the palm). During the experimental performance, we applied trans-cranial magnetic stimuli (TMS) to the motor cortex of the subjects, in order to detect a putatively stronger contribution of the cortico-motoneuronal system in the precision grip than the power grip.

6.2 Study 3: Means and Methods

6.2.1 Experimental Set-Up

The set-up was basically the same as in the previous experimental series except for some simplifications in the task. There were only three force steps (1.5, 3, 1.5 N) each lasting approximately eight seconds. Each sweep was followed by a resting period of ten seconds with no force applied. During pseudo-randomly chosen force steps three magnetic stimuli (Dantec Magnetic Stimulator MagPro or MagStim Quadro Pulse Model 500, circular coil, Ø13 cm) with 1.5 s intervals were administered to the finger representation of the contralateral motor cortex totalling in 210 stimuli during an experiment. The best stimulus location was determined prior to the experiment with the subject flexing his right index finger lightly (around 1 N) against the force transducer and around 50% stimulator power. The starting point on the head for this search was both 2 cm lateral and anterior to the point determined by the nasion/inion line and the peri-auricular line. The stimulation threshold power was determined as that power at which a muscle response (EMG) in the 1DI muscle could be elicited each time approximately 20 ms after the stimulus was triggered (Meyer et al., 1992). On the

Dantec MagPro, stimulus power was on average 40% of maximal output power, on the MagStim Quadro Pulse around 36%. Ninety percent of this power threshold was used for stimulation during the experiment. After determination of location and stimulus power the coil was rigidly fixed with a corset so that the coil position relative to the head was kept constant during the whole experiment (Schubert et al., 1997).

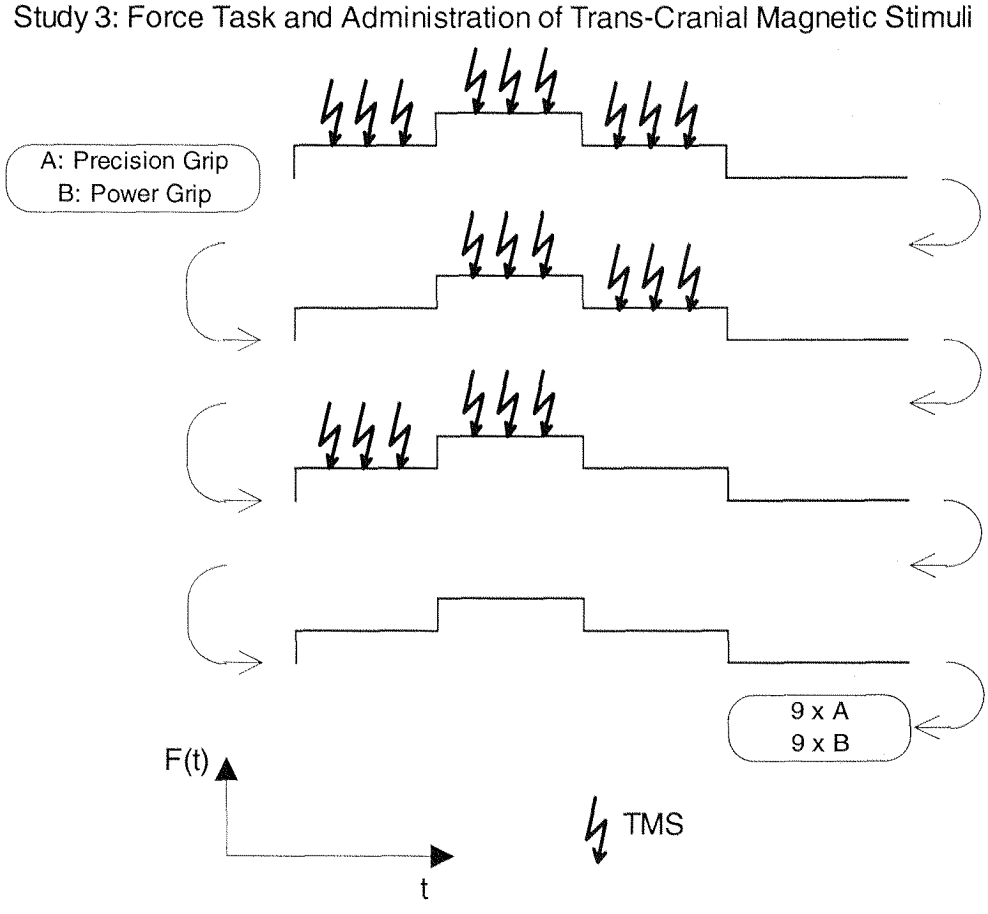


Figure 6-1. Force task and administration of trans-cranial magnetic stimuli (TMS). For each task (precision or power grip) the four force traces have to be repeated ten times. The time points of administering the TMS (arrows) are shown schematically.

6.2.2 Experimental Task

Similar to the previous experiments, six subjects had to perform a visuo-motor step-tracking task matching applied grip force to a given target signal. After force resetting, application of surface electrodes on the selected muscles (AdP, 1DI, FPL, FDS) and determination of location and power of the TMS the tasks were performed, once with the hand in the precision grip configuration and once in power grip configuration. With

each of the two hand configurations ten times four force-increase/decrease cycles had to be performed for the precision and for the power grip (first cycle: three stimuli on each level; second cycle: three stimuli on the 3 N and 1.5 N (down) level; third cycle: three stimuli on 1.5 (up) and 3 N level; fourth cycle: no stimulus; cf. Figure 6-1). After the subject had finished the precision grip experiment, the precision grip manipulanda (rings) were carefully exchanged for bars (width 10 mm, length 100 mm, attached in the middle to the force transducer), so that the subjects could use all fingers for the power grip. Force calibration, TMS power and location were again verified before the start of the power grip experiment. All data were monitored, recorded (sampling frequency, 2 kHz; notch, 50 Hz; bandpass surface EMG, 3 - 600 Hz; bandpass intramuscular EMG, 3 Hz - 1 kHz; surface EMG desampled to 500 Hz) and digitised on-line (National Instruments LabVIEW). In contrast to the previous study, the MUs were discriminated and digitised off-line.

6.2.3 Analysis

The data were processed as in the previous experiments, i.e. the data were compressed, transferred to a SUN workstation and analysed with purpose-written C-programs. Again, the data were grouped into three epochs according to the three force steps "1.5 N up", "3 N", and "1.5 N down". The data of the first 1.5 s of each epoch and segments of 75 ms after a magnetic stimulus were discarded to avoid transients and stimulus artefacts. In addition to the IPIH, the auto- and cross-correlations, their equivalent in the frequency domain, i.e. the power spectra and the coherence were calculated. The power spectral density displays the frequency spectrum of a certain signal, the coherence estimation displays the frequency of interaction in two signal processes, while the cross-correlation displays better the latency of two interacting signals. These calculations were done using the Welch method (Welch 1967). The fast-fourier transform algorithm was written in C language according to Stearns and David (1993). Auto- and cross-correlation were normalised to a value of ±1. For the cross-correlogram peak to be considered significant it had to fulfil following condition:

$$\left| y_{peak} \right| \geq 3.09\sigma + \overline{y_{testrange}}$$

E 6-1

where y_{peak} is the largest peak value, σ is the standard deviation, and $\overline{y_{testrange}}$ is the average of the cross-correlation values generated over a period of -200 to -100 ms prior and +100 to +200 ms after timelag 0 ms. The statistical confidence limits for the cross-correlograms of the MU data were determined according to Davey et al. (1986).

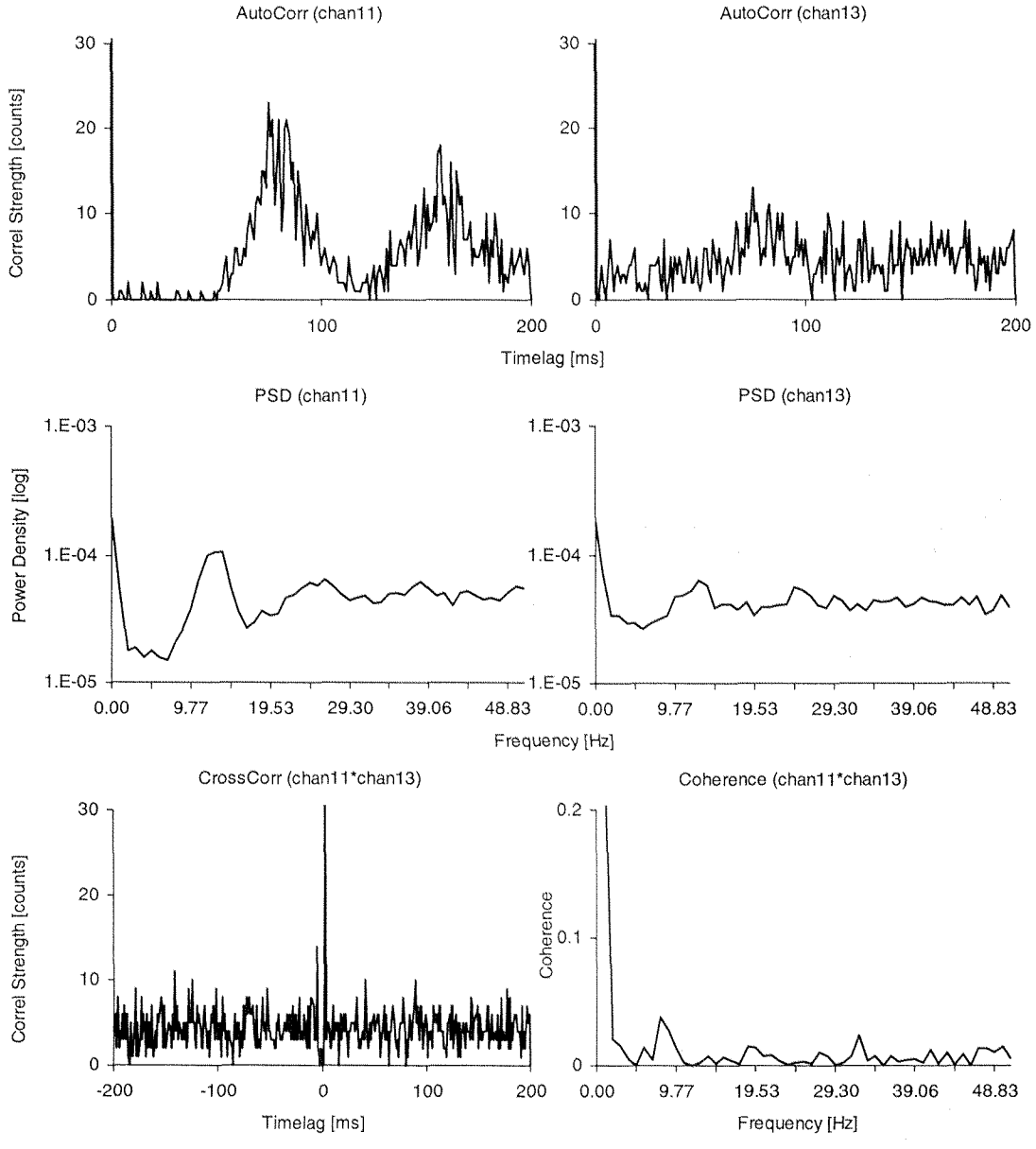


Figure 6-2. Analysis of a pair of 1DI MUs at 1.5 N force level with TMS. *Top:* Auto-correlograms of the two MUs. The left MU shows clear periodicity in firing while the right one is discharging less regularly. *Middle:* Power spectral density estimation (PSD) of the two MUs. Again the MU on the left shows a clear peak at 13.1 Hz discharge frequency, while the MU on the right has a much less pronounced peak at 13.3 Hz. *Bottom left:* Cross-correlogram of the two MUs displays a clear synchronisation peak at 3 ms timelag, while the coherence diagram (*bottom right*) shows only a little coherence peak at 7.8 Hz.

The cross spectral density $f_{NM}(\lambda)$ of processes N and M at frequency λ is defined as

$$f_{NM}(\lambda) = \frac{1}{2\pi} \int_{-\infty}^{\infty} q_{NM}(u) e^{-i\lambda u} du \quad , \qquad \text{E 6-2}$$

the power spectral density as

$$f_{NN}(\lambda) = \frac{P_N}{2\pi} + \frac{1}{2\pi} \int_{-\infty}^{\infty} q_{NN}(u) e^{-i\lambda u} du \qquad \text{E 6-3}$$

and the coherence as

$$\left|R_{NM}(\lambda)\right|^2 = \frac{\left|f_{NM}(\lambda)\right|^2}{f_{NN}(\lambda) f_{MM}(\lambda)} \qquad \text{E 6-4}$$

We checked for whole muscle synchronisation during precision and power grip and tried to determine the influence of TMS on the synchronisation.

6.3 Study 3: Results

6.3.1 Single Unit Test

This test was performed only for the precision grip task. A total of 11 MU pairs were tested with and without TMS. Five pairs, one IRM and four IAM pairs, showed short-term synchronisation on at least one force level. In trials with TMS synchronisation was found in these five pairs. In trials without stimulation synchronisation occurred in only two of the five pairs. In contrast to these findings, the strength of synchronisation (index *k*) was higher for the non-stimulated (*k*: 7.82±0.82, n = 5) than for the stimulated (*k*: 4.07±2.56, n = 5) trials. The two indices were significantly different (*t*-test, $P<0.01$). Figure 6-2 displays as an the example with a 1DI MU pair the analysis that was performed with all MU pairs. This MU pair shows clear synchronisation around time 0 s with a index k = 7.27. In the coherence function a small significant peak at 7.8 Hz can be discerned. This peak lies lower than the peaks in the power spectra with 10 to 15 Hz maxima.

6.3.2 Multi-Unit Test

The multi-unit experiment yielded for the two tasks 48 muscle pairs between the AdP, 1DI, FDS, FPL muscles that were cross-correlated on each force level separately,

resulting in 144 cross-correlograms and coherence functions for each task, respectively. Thus, differences in muscle synchronisation between the two motor tasks could be investigated for the multi-unit level. Figure 6-3 shows the distribution of synchronisation for the precision and the power grip at the three force levels.

When considering all trials irrespective of the stimulation, a significantly more frequent synchronisation was observed between muscles during the power grip than during the precision grip (175 of 216 vs. 143 of 216, respectively; χ^2-test, $P<0.05$). During the trials with TMS this difference diminished and remained statistically significant only for the 3 N force level, i.e. the highest force level. This effect was mainly due to a slight increase in the number of synchronised muscle pairs in the precision grip. A further important finding was that the strength of the synchronisation was generally higher for the power grip than for the precision grip.

6.4 Study 3: Discussion

6.4.1 Methodological Considerations

The experimental set-up was basically the same as for Study 2. The task was simplified to 1.5, 3.0, 1.5, 0.0 N force steps with 8 s duration for the grip conformations: precision and power grip. Intramuscular EMG recording was attempted with special-made wire electrodes (Basmajian and Stecko, 1962), but discontinued since stable recording could seldom be maintained over the two grip experiments. The MU potentials identified in the precision grip task were often no longer present in the power grip task.

Magnetic stimulation had to be performed with two different machines due to availability reasons. The motor reactions to the stimuli of the two machines did not show any significant difference.

6.4.2 Influence of Cortical Drive

The main finding of study 3 is that synchronisation between hand muscles occurred more frequently and was stronger in the power than in the precision grip regardless of magnetic stimulation. At the global muscle level, TMS did not increase this synchronisation significantly. This lack of effect could be explained by the weak TMS power applied, eliciting mostly I-waves that reach the motoneurones with longer

latencies than D-waves (Meyer, 1992). On the other hand, TMS induced a slight general increase of synchronisation between muscles in the precision grip. This observation corresponds with the increased occurrence of synchronisation at the MU level under TMS shown presently. We assume that, even though the stimulus was reduced below threshold, still a macroscopic area on the motor cortex was stimulated, thus generating a synchrony in the cortico-motoneuronal output and consequently in various target muscles.

In comparison to the power grip, the precision grip requires a tighter central control of the finger muscles in order to keep the grip configuration stable. Less activation of the 1DI has previously been shown during the power grip when compared to individuated finger movement (Datta et al., 1989). In another study involving several grip tasks (Flament et al., 1993) TMS consistently elicited stronger EMG responses in the 1DI for the pincer, (i.e. precision) grip than for power grip or index finger abduction. According to these latter investigators the more complex the task, the more important was the contribution of cortico-motoneuronal cells to the activation of single muscles. This was previously documented in the monkey with motorcortical neurones being more active during a precision grip task than during power grip (Muir and Lemon, 1983; Buys et al., 1986). Our finding of a stronger effect of TMS in synchronising muscles during more complex tasks highlights the major contribution of the cortico-motoneuronal system in the control of independent finger movements (Lemon, 1993; Lawrence and Kuypers, 1968). The increased cortical activation induced by TMS during the performance of the precision grip task (Baker et al., 1995) may, as a possible consequence, have enhanced muscle synchronisation. This synchronisation, however, remains smaller than that seen during the power grip. Our basic finding of less synchronisation between muscles during the precision grip supports the view that more complex grip tasks rely on a more specific connectivity from the brain. In contrast, in the power grip the finger muscles are activated in concert and can therefore be addressed by less differentiated signals.

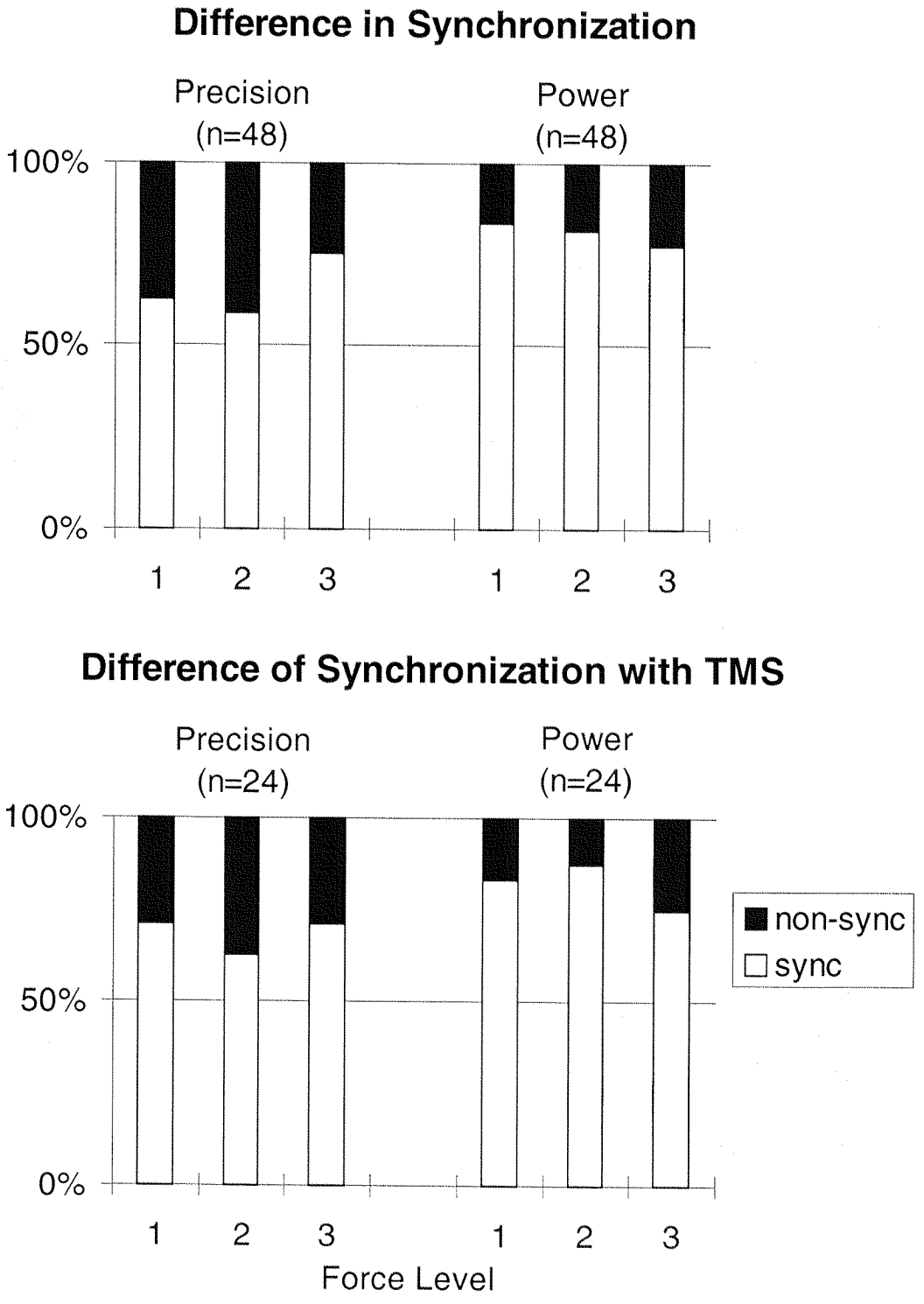


Figure 6-3. Percentage of multi-unit synchronisation in the precision and the power grip for each force level. *Top*: all pairs with and without TMS. *Bottom*: trials with TMS. Force level 1: 1.5 N up; force level 2: 3 N; force level 3: 1.5 N down.

Thus, to achieve a power grip no compliance control of the single muscles is required. Basically, the control signal which is sent to the muscles is only addressed to the flexor muscles of the forearm to achieve power grip force. This can, of course, be achieved by neurones residing in the motor cortex that are relatively limited in number and areal spread and which have strong divergent connections to the respective flexor muscles. Furthermore, it is assumed that this pathway has a strong connectivity also with a reflex response originating in the palm of the hand, given the infant gripping reflex, where the power grip is exerted as soon as a stimulus is placed in the palm of the infant hand. Finally, sensory information seems to be of limited importance to achieve a stable grip. The result of all these points is that any subliminal activation of the motor cortex neurones would, therefore, add no additional synchronisation to the command signal to the MUs.

In the precision grip, a much bigger set of muscles and motoneurones are involved to achieve a stable and delicate grip, which has to be acquired during infancy. Furthermore, the primate precision grip with an opposable thumb is appearing relatively late in evolution. Furthermore, many more afferent pathways are involved to keep the precision grip stable, which may be achieved by feedback loops that connect to the cortico-motoneuronal pathway somewhere between the motor axon of the output motoneurones in the ventral horn of the spine - through axo-axonal synapses - and the motor cortex. Thus, given the many more inputs that change and adjust the original motorcortical command, it is to be expected that a TMS-facilitated command signal from the motor cortex will result in an elevated level of synchrony at the MU level. As a consequence of this additional drive, it can be hypothesised that the afferent signals will loose in weight and the equilibrium of feed-forward and feedback signals will be destroyed, and that the grip will become unstable during the short period where the TMS-facilitated command signal is effective.

6.5 Study 3: Summary

Magnetic stimulation had a stronger effect during the precision grip than during power grip. In the single unit analysis MU synchronisation could predominantly be found during the stimulus trials. Muscle synchronisation was found to be enhanced during the power grip as compared to the precision grip.

The present study demonstrates a remarkable difference in the synchronised activation of finger muscles during different grip configurations. For cruder movements more global neural activation patterns can be found while for intricate and fine movements a fractionation of the patterns can be demonstrated. These findings together with the observed increase of synchronous muscle activation under TMS in precision grip speak in favour of the importance of the cortico-motoneuronal system for complex tasks.

7 Discussion

7.1 Overview

The control of the human hand poses many questions. The large number of muscles, ligaments and bones as well as the mechanical non-linearities and indeterminancies (degrees-of-freedom problem) contribute to a system that may, on the one hand, be versatile in daily life but, on the other hand, still today eludes our complete understanding as to how the hand may be controlled. Several hypotheses have been put forward to answer this question and ideas proposed how the automatic usage of the hand may be acquired during infancy. One of these hypotheses deals with the coupling of muscular groups (Lee, 1984), grouping together several functional entities and thus reducing the number of control parameters in order to alleviate the task of the central controller, the CNS. We have set out in order to find evidence that such temporal coupling of muscles and their MUs occurs in the human hand and that it is indeed used in controlling the manipulative actions of the hand during the two fundamental grips, the precision grip and the power grip (Napier, 1956, 1960; Landsmeer, 1962). The goals of this work were to detect and quantify synchronisation in MUs of the hand muscles and find instances of increased synchronisation probability. With the results we wanted to show under what circumstances - experimental, anatomical, physiological, task-dependence - the increased synchronisation occurred and extrapolate onto the control strategies for muscles of the fingers. By systematically varying the parameters such as force or activity levels, feedback conditions and tasks, we showed that this temporal coupling is present within and between muscles, predominantly just at recruitment with relatively low discharge frequencies of the MUs. We could find more MUs that were synchronised during force release, than during force increase, but with a large portion of MU pairs being synchronised during both phases. At a first glance, feedback condition did not seem to make a difference in MU synchronisation, however, three MU could be shown, where auditory feedback resulted in an increased amount of synchronisation. Finally, with the help of magnetic stimulation we tried to elucidate the influence of the cortical drive to motor control in the hand during the performance of a power grip and a precision grip task. Significantly more and stronger muscle synchronisation was detected during the power grip task as opposed to a precision grip task without TMS.

With TMS this difference diminished. Finally, MUs were more often but more weakly synchronised with TMS than without.

7.2 Functional Relevance of Synchronisation

What is the functional importance of synchronisation? We have shown that synchronisation occurs at variable degrees in pairs of MUs of different hand muscles and within the same muscle. However, except for the time of recruitment, where it is most robust, time points of synchronised discharges are dispersed over time during the task execution in a seemingly sparse and arbitrary manner as was also reported by Dengler et al. (1984). It has to be kept in mind that too high a degree of synchronisation in a motoneuronal pool, e.g. as in long-term synchronisation with a particular discharge frequency due to servoloop activity (Freund, 1983) or synchronisation of the input to the MUs (Logigian et al., 1988), can be detrimental and lead to instability and tremor. In a natural task such as the precision grip, where synchronisation might be used to reduce the complexity of an over-determined biomechanical system, we expected, if this were the case, to find higher levels of synchrony. Contrary to this expectation, we report, especially in the intermuscular MU pairs, not only less synchronisation but also less stable synchronisation, when compared to tasks with a single degree of freedom and optimised feedback conditions as reported elsewhere. This is in contrast to the notion that synergy, as displayed by MU synchrony, is a means for the CNS to reduce an excess in biomechanical degrees of freedom. Some points need to be considered: first, our data indicate that synchrony depends in part on the MU properties, as shown in more detail by Schmied et al. (1994), i.e. different levels of synchrony, both in strength and rate of occurrence, depending on the location in preferred and non-preferred arm, as well as depending on 'fast' or 'slow' MUs. This means that synchrony has a peripheral determinant. Second, the measurement of the peak widths showed a large range from the shortest to longest peak. While, on average, the peaks reported here were shorter (6 -7 ms) than in most other studies, longer peak durations up to 20 ms found here, still suggest that inputs of last-order branched axons (narrow peaks) as well as presynaptically synchronised inputs (broader peaks) contribute to overall synchrony. Kirkwood (1979) suggested specific neuronal connectivities to describe the different forms of synchronisation peaks. The relative contribution of these processes and connections is unknown. The anatomical last-order branching pattern is task-

independent and by necessity produces MU synchrony simply as a by-product of the divergent anatomical connections of branched axons that are used to co-activate functional groups of muscles. Consequently, this arrangement provides some MU synchrony, but is itself without obvious functional relevance.

In contrast, a functional, task-dependent synergy, as shown in study 3, effectively needs to be generated at the presynaptic level, e.g. by the selection of the appropriate cortico-motoneuronal pool. Indeed, a 15-30 Hz coherence between oscillatory motor cortex activity and EMG has been demonstrated in humans (Conway et al., 1995; Salenius et al., 1996) as well as in the monkey (Baker et al., 1997). This coherence showed a task-dependent modulation and was particularly dominant during steady-state co-contraction in precision grip (Kilner et al., 1999), but was absent during transitions. The stronger synchronisation of the MU pairs with auditory feedback as shown in study 2 also speaks in favour of cortical influence contributing to 'task-dependent' synchrony at the MU level. Finally, the difference of MU synchrony between power and precision grip indicates that the control of the MUs can be adjusted for functionally differing requirements. Intricate and individuated movements or force applications necessitate a fractionated pattern in the command signal, hence less synchrony, while crude movements or force applications put up with a relatively coarse activation patterns which allow little differentiation between the various MUs involved in the motor task. Compatible with the above observations and the instability of synchrony, despite a continuous demand on control and an invariant performance, the findings seem to suggest, that non-synchronous means of control exist and might even have functional significance in that they allow the individuation of finger movement and prevent oscillations or tremor due to synchronised discharge of muscles. Whether one mode of control - synchrony vs. asynchrony - predominates over the other in particular tasks, whether they operate concurrently or mutually exclusive, remains to be determined.

7.3 Review and Outlook

This subchapter deals with the experience gained in the performance of this piece of work and recommendations for the future. In the first part I deal with the methodology, in a second part functional issues are addressed.

7.3.1 Methodology

The task as well as the time discrete analysis of the data proved to be very cumbersome mainly because, the task required MUs to be recruited and inactivated over long periods. This made it difficult to follow a representative sample of MUs over longer periods since the MU potentials changed shape over time due to movement of the electrode with regard to the electrical source and due to MUs being turned off completely and new MUs being recruited instead, hinting towards changes in strategy as was also demonstrated by Maier and Hepp-Reymond (1995a). They showed in their Fig. 3 that a muscle could be completely turned off while the force production remained invariant. Another aspect, the repeated interruptions during the imposed resting periods, further diminished the amount of 'countable' events. "Did the identified potentials originate in the same MU or did they come from a different ones?" was a critical question, since MUs recorded from further away from the needle had rather uncharacteristic potential shapes and narrowly resembled each other. These two problems were especially troublesome, since we wanted to follow the paired activity of two or more MUs over longer periods. This short-coming evoked the strongest criticism against the studies performed. A more straight-forward strategy is the recording and comparison of paired multi-unit EMGs, also with view of comparing single-unit and multi-unit synchronisation that did not result in any unexpected finding. Except maybe for the enhanced synchronisation during recruitment and the intramuscular activity any other finding could have been obtained by multi-unit EMGs with a significantly reduced work effort and frustration and a significantly improved signal reliability. The "force steps" task might as well be replaced in the future by a slow ramp for static MU characterisation and a sine wave with appropriately chosen frequency, mean level and amplitude such that a given MU is constantly active. In this way also the dynamic properties of a MU can be tested.

The new experimental set-up turned out well. By its modularity it was easily adjustable to all kinds of hand anatomies. The signal of the two sensors in series (strain gauge and piezo sensor) showed a good overlap and never were subject to problems. Given the large force resolution of the piezo sensor, the DMS force transducer could as well have been neglected and all the force signals only be measured with the piezo sensor. A future development would bring the force sensor into one small, freely movable and

light-weight manipulandum that can be held between the two gripping fingers or fingers and palm, thus making the large support obsolete. In this way the influence of wrist, arm and postural movements can be avoided while getting rid of bulky splints and experimental set-ups.

Computer storage capacity, working memory and processor speed was a concern in the beginning and slowed down many work processes, but was resolved by the advent of powerful personal computers and the Internet in the Locomotion Lab. As for MU identification, the ARTMUP system was interesting to work with. The performance of the algorithm was mainly hampered by inadequate computer power at the time and consequently the limitation to records of 15 s duration. To our dismay, the system was no longer available at later stages of this work as the infrastructure was needed for other purposes.

7.3.2 Functional Aspects

The present studies have been confined to static and isometric muscle contraction in the precision and power grip at different levels of MU activity. The extension of this work leads into the realm of dynamic motor tasks, i.e. movements. It has already been shown by several groups that relatively stereotyped movements, such as stance (Nashner, 1977), gait, arm reaching (Lacquaniti and Soechting, 1982), speech (Gracco and Abbs, 1986) - these skills acquired and matured during infancy (Kuhtz-Buschbeck et al., 1999, Hirschfeld and Forssberg, 1994) - require a timely activation of the muscles and MUs inserting into the various segments of the bony kinematic chains in order to allow for intended and predictable task performance and invariant motor output. The activation patterns for these movements may last several seconds as opposed to the temporal resolution of few milliseconds in the presently described MU synchronisation. These large spatio-temporal patterns can no longer be described by short-term synchronisation. These activation patterns may originate in movement templates or central pattern generators in the CNS as is described for gait and respiration but will be modulated by visual or other somatosensory cues, and also by the state, i.e. movement and configuration, of the limb to be activated, such that any principle signal for a given movement may be masked by sensory inputs that are downstream of these pattern generators. This is in close agreement with Bernstein's (1967) conclusion that the

"...motor effect of a central impulse cannot be decided at the centre but is decided entirely at the periphery ..."

The identification of this whole network with the basic motor control laws may be modelled at a rather large scale. Whether the intricacies and all details of the neural interconnections, muscular non-linearities and degrees of freedom of the bones can be identified - just to mention the exorbitant number of neurones and synapses, the density and various modalities of sensory input originating in the palm of the hand and numerous degrees of freedom of the bony and muscular structures - remains to be seen.

7.3.3 Simulations

The insights we have gained in this work may be implemented in the near future into the design of anthropomorphic robot hands. In contrast to the robot end effectors with technical background, this new anthropomorphic robot hand with biological background would feature a redundant design with regard to its actuators in that many more actuators with varying sizes would be present, maybe even with sizes down to the nano-scale, mimicking large and small MUs with different twitch forces and contraction times. Furthermore, these actuators would have specific drive characteristics corresponding to the *fast-fatiguing, fast fatigue-resistant* and *slow* MUs. Next, at the level of the biological muscles additional non-linearities are present such as rate-, excursion- and movement direction-dependent behaviour. Then the size principle needs to be taken care of. All these behaviours as well as the coupling of several joints by poly-articular muscles will need to be properly modelled. Probably a class of MUs can be programmed with a set of variables describing all the above mentioned characteristics. By assigning the variables values or functions that follow the anatomical and physiological constraints, it might be possible to first generate sensible physiological input-output relationships for the MUs. When this has been achieved a muscle as a sum of differing MUs can be generated. Finally, with regard to kinematical design the small muscles for the agility would have to be placed in the hand and finger themselves, while the large actuators that are required for high forces would have to be placed in the forearm.

The sensory apparatus would need to come up with the integration of several types of sensors to match the large variety of human afferent neurones in the hand, where various

receptive modalities and sub-modalities are present, such as vibration, skin-stretch, skin-indentations, heat, pressure, muscle strain and stress, to name just a few.

Probably the biggest challenge would lie in the control algorithms: implementing a control strategy that copes with the redundant design and that would make use of a massive barrage of information originating from thousands of sensors and actuators at very small dimensions. Starting with the implementation of the size principle might already alleviate the problem of addressing the appropriate actuators. The next issue to tackle would then be, how to make use of synergies and synchronisation in the actuators. Task-dependent rules may lead to synergistic activation and force output.

A further challenge for a physical model would be the large difference of dimensions from the nano-scale up to millimetres and centimetres range over seven orders of magnitude. In simulations this issue is not expected to pose large difficulties.

The anatomy can nowadays be obtained by computer tomographical methods with ease as has, for example, been shown recently in the museum of natural history of the University of Zurich and the Institute for Machine Tools and Manufacturing at the ETH with the remake of a paw of a now extinct animal.

The goal of such a simulation would be to demonstrate that with a redundant system, tailor-made sensors, actuators and, last but not least, control strategies a dexterity can be achieved that is matching the light weight design, the agility and versatility of the human hand. This may well lead one day to hand prostheses that can be directly connected to neurones of the arm via a computer chip and then replace the missing original hand by 100%. The first mile stone, however, will be to demonstrate that with such a model a stable precision grip can be achieved with isometric forces exerted between the thumb and index finger of the bio-robot hand. Moreover, such a model may contribute to the design of light-weight robots with low energy consumption and high versatility. Given today's availability of computational power it is to be expected that such a simulation is feasible and should be endeavoured.

8 Conclusion

Muscular synergies in the human hand were the subject of this work. We showed that in the two basic grips, the precision and power grip, intra- and intermuscular MU synchronisation in finger and hand muscles is present, though waxing and waning. The power grip, being a more cruder grip form with regard to muscle individuation, showed a significantly higher degree of synchronisation than the precision grip. We characterised the rate and strength of synchronisation under different feedback conditions - force and auditory feedback were fed back to the subject - and different tasks - force increase and decrease, power and precision grip. We could show that MU recruitment and force release seemed to generate favourable conditions for synchronisation, no clear difference in synchronisation levels were found for the different feedback conditions and force increase or decrease. Trans-cranial magnetic stimulation of the motor cortex was used to highlight the neuronal connectivity from the cortex to the single MUs and prompted increased muscle synchronisation after the stimulus with the hand in the precision grip configuration, but not power grip configuration. Finally, synchronisation was traced back to putative sources such as task-dependent inputs from higher centres as well as last-order branching axons.

It is proposed to endeavour the computational simulation of such a biological hand. Models exist already that simulate the behaviour of neurones and even swimming lampreys (Grillner et al., 1995), the next step would be to take this simulation one step higher and try to implement the human hand. Furthermore enough information is today available on the physiology, biochemistry and anatomy of MUs and sensors for their modelling. Such a model may lead to a new generation of end-effectors on robots and prosthetic hands that are both light-weight, energy efficient and versatile.

9 Bibliography

[1] Adams L, Datta AK, Guz A (1989) Synchronization of Motor Unit Firing during Different Respiratory and Postural Tasks in Human Sternocleidomastoid Muscle. J Physiol 413:213-231

[2] Adrian ED, Bronk DW (1929) The Discharge of Impulses in Motor Nerve Fibres. Part II. The Frequency of Discharge in Reflex and Voluntary Contractions. J Physiol 67:119-151

[3] Alexander GE, Crutcher MD (1990a) Functional Architecture of Basal Ganglia Circuits: Neural Substrates of Parallel Processing. TINS 13:266-271

[4] Alexander GE, Crutcher MD (1990b) Preparation for Movement: Neural Representation of Intended Direction in Three Motor Areas of the Monkey. J Neurophysiol 64:133-150

[5] Alexander GE, Crutcher MD (1990c) Movement-Related Neuronal Activity Selectively Coding Either Direction of Muscle Pattern in Three Motor Areas of the Monkey. J Neurophysiol 64:151-163

[6] Allum JHJ, Hepp-Reymond M-C, Gysin R (1982) Cross-Correlation Analysis of Interneuronal Connectivity in the Motor Cortex of the Monkey. Brain Res 231:325-334

[7] Andersen P, Sears TA (1964) The Mechanical Properties and Innervation of Fast and Slow Motor Units in the Intercostal Muscles of the Cat. J Physiol 173:114-129.

[8] Baker JR, Bremner FD, Cole K, Stephens JA (1988) Short-Term Synchronization of Intrinsic Hand Muscle Motor Units in a 'Deafferented' Man. J Physiol 396:155P

[9] Baker SN, Olivier E, Lemon RN (1995) Task-Related Variation in Corticospinal Output Evoked by Transcranial Magnetic Stimulation in the Macaque Monkey. J Physiol 488:759-801.

[10] Baker SN, Olivier E, Lemon RN (1997) Coherent Oscillations in Monkey Motor Cortex and Hand Muscle EMG Show Task-Dependent Modulation. J Physiol 501:225-241

[11] Barbas H, Pandya DN (1987) Architecture and Frontal Cortical Connections of the Premotor Cortex (area 6) in the Rhesus Monkey. J Comp Neurology 256:211-228

[12] Basmajian JV, Stecko G (1962) A New Bipolar Electrode for Electromyography. J Appl Physiol 17:849

[13] Bekey GA, Tomovic R, Zeljkovic I (1990) Control Architecture for the Belgrade USC-Hand. Dextrous Robot Hands, Springer Verlag, 1990

[14] Bernstein N (1967) The Co-ordination and Regulation of Movements. Pergamon Press, Oxford, London

[15] Bigland-Ritchie BR, Johansson R, Lippold OCJ, Woods JJ (1983) Contractile Speed and EMG Changes during Fatigue of Sustained Maximal Voluntary Contractions. J Neurophysiol 50:313-324

[16] Bigland-Ritchie BR, Dawson NJ, Johansson RS, Lippold OCJ (1986) Reflex Origin for the Slowing of Motoneurone Firing Rates in Fatigue of Human Voluntary Contractions. J Physiol 379:451-459

[17] Bloedel JR (1994) Functional Heterogeneity with Structural Homogeneity: How Does the Cerebellum Operate? In: Cordo P, Harnad S (eds.) Movement Control. Cambridge University Press, 64-76.

[18] van Bolhuis BM, Medendorp WP, Gielen CCAM (1997) Motor Unit Behaviour in Human Arm Flexor Muscles during Sinusoidal Isometric Contractions and Movements. Exp Brain Res 117:120-130

[19] Bremner FD, Baker JR (1990) The Effect of Muscle Vibration on the Synchronization of Motor Unit Firing during Isometric Contraction in Man. J Physiol 429:36P

[20] Bremner FD, Baker JR, Stephens JA (1991a) Correlation between the Discharges of Motor Units Recorded from the Same and from Different Finger Muscles in Man. J Physiol 432:355-380

[21] Bremner FD, Baker JR, Stephens JA (1991b) Variation in the Degree of Synchronization Exhibited by Motor Units Lying in Different Finger Muscles in Man. J Physiol 432:381-399

[22] Bremner FD, Baker JR, Stephens JA (1991c) Effect of Task on the Degree of Synchronization of Intrinsic Hand Muscle Motor Units in Man. J Neurophysiol 66:2072-2083

[23] Brillinger DR (1988) The 1983 WALD Memorial Lectures: Some Statistical Methods for Random Process Data from Seismology and Neurophysiology. Annals of Statistics 16(1):1-54

[24] Brinkman C (1984) Supplementary Motor Area of the Monkey's Cerebral Cortex: Short- and Long-Term Deficits after Unilateral Ablation and the Effects of Subsequent Callosal Section. J Neurosci 4:918-929

[25] Brodmann K (1909) Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues. Leipzig J.A. Barth

[26] Brooks VB, Thach WT (1981) Cerebellar Control of Posture and Movement, in V.B. Brooks (ed.) Handbook of Physiology, sect. 1, vol. 2, part 2, Williams and Wilkins, Baltimore, 887-945

[27] Buchanan TS, Almdale DPJ, Lewis JL, Rymer WZ (1986) Characteristics of Synergic Relations during Isometric Contractions of Human Elbow Muscles. J Neurophysiol 56:1225-1241

[28] Buchanan TS, Rovai GP, Rymer WZ (1989) Strategies for Muscle Activation during Isometric Torque Generation at the Human Elbow. J Neurophysiol 62:1201-1212

[29] Buchthal F, Guld Chr, Rosenfalck P (1957) Multielectrode Study of the Territory of a Motor Unit. Acta Physiol Scand 39:83-104

[30] Buchthal F, Schmalbruch M (1980) Motor Unit of Mammalian Muscle. Physiol Rev, 60:90-142

[31] Burke RE (1981) Motor Units: Anatomy, Physiology, and Functional Organization. In (ed.) Brooks VB: Handbook of Physiology - The Nervous System. Chap. 10, 345-422. American Physiolog Soc, Bethesda MD.

[32] Buys EJ, Lemon RN, Mantel GWH, Muir RB (1986) Selective Facilitation of Different Hand Muscles by Single Corticospinal Neurones in the Conscious Monkey. J Physiol 381:529-549

[33] Calancie B, Bawa P (1986) Limitations of the Spike-Triggered Averaging Technique. Muscle & Nerve, 9:78-83

[34] Campbell AW (1905) Histological Studies on the Localization of Cerebral Function. Cambridge Univ. Press

[35] Carr LJ, Harrison LM, Stephens JA (1994) Evidence for Bilateral Innervation of Certain Homologous Motoneurone Pools in Man. J Physiol 475:217-227

[36] Chao EYS, An K-N, Cooney WP, Linscheid RL (1989) Biomechanics of the Hand. World Scientific, Singapore.
[37] Christen U, Huesler EJ (1990) Modellierung des menschlichen "Precision Grip", Semesterarbeit am Inst. f. Robotik, ETHZ
[38] Close JR, Kidd CC (1969) The Functions of the Muscles of the Thumb, the Index and the Long Fingers. JBJS 51-A:1601-1620.
[39] Clough JFM, Kernell D, Phillips CG (1968) The Distribution of Monosynaptic Excitation from the Pyramidal Tract and from Primary Spindle Afferents to Motoneurons of the Baboon's Hand and Forearm. J Physiol 198:145-166
[40] Collins DF, Prochazka A (1996) Movement Illusions Evoked by Ensemble Cutaneous Input from the Dorsum of the Human Hand. J Physiol 496:857-871
[41] Conway BA, Halliday DM, Farmer SF, Shahani U, Maas P, Weir AI, Rosenberg JR (1995) Synchronization between Motor Cortex and Spinal Motoneuronal Pool during the Performance of a Maintained Motor Task in Man. J Physiol 489:917-924
[42] Cope TC, Fetz EE, Matsumura M (1987) Cross-Correlation Assessment of Synaptic Strength of Single Ia Fibre Connections with Triceps Surae Motoneurones in Cats. J Physiol 390:161-188
[43] Cordo P, Harnad S (1994) In: Cordo P, Harnad S (eds.) Movement Control, Cambridge Univ. Press
[44] Crameri A (1996) Charakterisierung der Einzelkontraktion von motorischen Einheiten anhand des "Spike-Triggered Averaging", Nebenfacharbeit Sommersemester 1996
[45] Crutcher MD, DeLong MR (1984) Single Cell Studies of the Primate Putamen, Parts 1 and 2. Exp Brain Res 53:233-258
[46] Cutkosky MR (1985) Robotic Grasping and Fine Manipulation. Kluwer Academic Publishers.
[47] Datta AK, Stephens JA (1990) Synchronization of Motor Unit Activity during Voluntary Contraction in Man. J Physiol 422:397-419
[48] Datta AK, Farmer SF, Stephens JA (1991) Central Nervous Pathways Underlying Synchronization of Human Motor Unit Firing Studied during Voluntary Contractions. J Physiol 432:401-425
[49] Davey NJ, Ellaway PH, Stein RB (1986) Statistical Limits for Detecting Change in the Cumulative Sum Derivative of the Peristimulus Time Histogram. J Neurosci Meth 17:153-166
[50] Day BL, Dressler D, Maertens de Noordhout A, Marsden CD, Nakashima K, Rothwell JC, Thompson PD (1989) Electric and Magnetic Stimulation of Human Motor Cortex: Surface EMG and Single Motor Unit Responses. J Physiol 412:449-473
[51] Delagi EF, Perotto A (1980) Anatomic Guide for the Electromyographer (The Limbs). Thomas, Springfield, Ill.
[52] DeLuca CJ, LeFever RS, McCue MP, Xenakis AP (1982) Behaviour of Human Motor Units in Different Muscles during linearly Varying Contractions. J Physiol 329:113-128
[53] DeLuca CJ, LeFever RS, McCue MP, Xenakis AP (1982b) Control Scheme Governing Concurrently Active Human Motor Units During Voluntary Contractions. J Physiol 329:129-142

[54] DeLuca CJ, Mambrito B (1987) Voluntary Control of Motor Units in Human Antagonist Muscles: Coactivation and Reciprocal Activation. J Neurophysiol 58:525-542

[55] DeLuca CJ, Roy AM, Erim Z (1993) Synchronization of Motor Unit Firing in Several Human Muscles. J Neurophysiol 70:2010-2023

[56] Dengler R, Wolf W, Birk P, Struppler A (1984) Synchronous Discharges in Pairs of Steadily Firing Motor Units Tend to Form Clusters. Neurosci Lett 47:167-172

[57] Desmedt JE, Godaux E (1977) Fast Motor Units are not Preferentially Activated in Rapid Voluntary Contractions in Man. Nature 267:717-719

[58] Dettmers C, Fink GR, Lemon RN, Stephan KM, Passingham RE, Silbersweig D, Holmes A, Ridding MC, Brooks DJ, Frackowiak RSJ (1995) Relation between Cerebral Activity and Force in the Motor Areas of the Human Brain. J Neurophysiol 74:802-815

[59] Dietz V, Hillesheimer W, Freund H-J (1974) Correlation between Tremor, Voluntary Contraction, and Firing Pattern of Motor Units in Parkinson's Disease. J Neurolog Neurosurg Psychiat 37:927-937

[60] Dietz V, Bischofberger E, Wita C, Freund H-J (1976) Correlation between the Discharges of Two Simultaneously Recorded Motor Units and Physiological Tremor. EEG Clin Neurophysiol 40:97-105

[61] Edin BB, Johansson N (1995) Skin Strain Patterns Provide Kinaesthetic Information to the Human Central Nervous System. J Physiol 487:243-251

[62] Ellaway PH, Murthy KSK (1985) The Origins and Characteristics of Cross-Correlated Activity between Gamma-Motoneurones in the Cat. Quart J Exp Physiol 70:219-232

[63] Evarts EV (1965) Relation of Discharge Frequency to Conduction Velocity in Pyramidal Tract Neurons. J Neurophysiol 28:216-228

[64] Farmer AK, Swash M, Ingram DA, Stephens JA (1993) Changes in Motor Unit Synchronization Following Central Nervous Lesions in Man. J Physiol 463:83-105

[65] Feneis H (1988) Anatomisches Bildwörterbuch der internationalen Nomenklatur. Thieme: Stuttgart, New York

[66] Fetz EE, Cheney PD (1980) Postspike Facilitation of Forelimb Muscle Activity by Primate Corticomotoneuronal Cells. J Neurophysiol 44:751-772

[67] Fetz EE, Cheney PD, Mewes K, Palmer S (1989) Control of Forelimb Muscle Activity by Populations of Corticomotoneuronal and Rubromotoneuronal Cells. Prog Brain Res 80:437-449

[68] Flament D, Goldsmith P, Buckley CJ, Lemon RN (1993) Task Dependence of Responses in First Dorsal Interosseus Muscle to Magnetic Brain Stimulation in Man. J Physiol 464:361-378

[69] Forssberg H, Eliasson AC, Kinoshita H, Johansson RS, Westling G (1991) Development of Human Precision Grip. I. Basic Coordination of Force. Exp Brain Res 85:451-457

[70] Forssberg H, Kinoshita H, Eliasson AC, Johansson RS, Westling G, Gordon AM (1992) Development of Human Precision Grip. II. Anticipatory Control of Isometric Forces Targeted for Object's Weight. Exp Brain Res 90:393-398

[71] Freund HJ (1983) Motor Unit and Muscle Activity in Voluntary Control. Physiol Rev 63:387-436

[72] Fritsch G, Hitzig E (1870) Ueber die elektrische Erregbarkeit des Grosshirns. Arch. Anat. Physiol. Wiss. Med. 37:300-332
[73] Gentilucci M, Fogassi L, Luppino G, Matelli M, Camarda R, Rizzolatti G (1988) Functional Organization of Inferior Area 6 in the Macaque Monkey: I. Somatotopy and the Control of Proximal Movements. Exp Brain Res 71:475-490
[74] Gibbs J, Harrison LM, Mayston MJ, Stephens JA (1995) Mechanisms Underlying Muscle Synergy Studied in Man. In: Taylor A, Gladden MH, Durbaba R (eds.) Alpha and Gamma Motor Systems. Plenum Press, New York, 466-468
[75] Gielen CCAM, van Bolhuis BM, Theeuwen M (1995) On the Control of Biologically and Kinematically Redundant Manipulators. Human Movement Science 14:487-509
[76] Godschalk M, Lemon RN, Kuypers HGJM, van der Steen J (1985) The Involvement of Monkey Premotor Cortex Neurones in Preparation of Visually Cued Arm Movement. Behav Brain Res 18:143-158
[77] Gracco VL, Abbs JH (1986) Variant and Invariant Characteristics of Speech Movements. Exp Brain Res 65:156-166
[78] Grillner S, Deliagina T, Ekeberg Ö, ElManira A, Hill RH, Lansner A, Orlovsky GN, Wallén P (1995) Neural Networls that Co-ordinate Locomotion and Body Orientation in Lamprey. TINS 18(6):270-279
[79] Haas WF (1989) Methoden der Mustererkennung zur automatischen Zerlegung des Elektromyogramms. Diss ETH Zürich No. 8797
[80] Haas WF, Meyer M (1989) An Automatic Decomposition System for Routine Clinical Examinations in Clinical Research: ARTMUP - Automatic Recognition and Tracking of Motor Unit Potentials. In: Desmedt JE (ed) Clinical Neurophysiological Updates, Vol. 2, Computer-aided Electromyography and Expert Systems. Elsevier, Amsterdam, 67-81
[81] He S-Q, Dum RP, Strick PL (1993) Topographic Organization of Corticospinal Projections from the Frontal Lobe: Motor Areas on the Lateral Surface of the Hemisphere. J Neurosci 13:952-980
[82] He S-Q, Dum RP, Strick PL (1995) Topographic Organization of Corticospinal Projections from the Frontal Lobe: Motor Areas on the Medial Surface of the Hemisphere. J Neurosci 15:3284-3306
[83] Henneman E, Somjen G, Carpenter DO (1965) Functional Significance of Cell Size in Spinal Motoneurons. J Neurophysiol 28:560-580
[84] Hepp-Reymond M-C (1988) Functional Organization of Motor Cortex and Its Participation in Voluntary Movements. In: Seklis HD, Erwin J (eds.) Comparative Primate Biology, Volume 4: Neurosciences, 501-624
[85] Hepp-Reymond M-C, Huesler EJ, Maier MA, Qi H-X (1994) Force-Related Neuronal Activity in Two Regions of the Primate Ventral Premotor Cortex. Can J Physiol Pharmacol 72:571-579
[86] Hepp-Reymond M-C, Huesler EJ, Maier MA (1996) Precision Gip in Humans: Temporal and Spatial Synergies. In: Wing AM, Haggard P, Flanagan JR (eds.) Hand and Brain: The Neurophysiology and Psychology of Hand Movements. Academic Press, San Diego
[87] Hepp-Reymond M-C, Kirkpatrick-Tanner M, Gabernet L, Qi H-X, Weber B (1999) Context-Dependent Force Coding in Motor and Premotor Cortical Areas. Exp Brain Res 128:123-133

[88] Hirschfeld H, Forssberg H (1994) Epigenetic Development of Postural Responses for Sitting During Infancy. Exp Brain Res 97:528-540
[89] Hirzinger G (1999) The DLR Multisensory Articulated Hand, http://www.robotic.dlr.de/HAND
[90] Hogan N (1985) The Mechanics of Multi-Joint Posture and Movement Control. Biol Cybern 52:315-331
[91] Horak FB, Shupert CL, Dietz V, Horstmann G (1994) Vestibular and Somatosensory Contributions to Responses to Head and Body Displacements in Stance. Exp Brain Res 100:93-106
[92] Howell JN, Fuglevand AJ, Walsh ML, Bigland-Ritchie B (1995) Motor Unit Activity during Isometric and Concentric-Eccentric Contractions of the Human First Dorsal Interosseus Muscle. J Neurophysiol, 74:901-904
[93] Huesler EJ, Hepp-Reymond M-C, Dietz V (1998) Task Dependence of Muscle Synchronization in Human Hand Muscles. NeuroReport 9:2167-2170
[94] Huesler EJ, Maier MA, Hepp-Reymond (2000) EMG Activation Patterns during Force Production in Precision Grip. III. Synchronisation of Single Motor Units. Exp Brain Res 134:441-455
[95] Hultborn H, Lindström S, Wigström H (1979) On the Function of Recurrent Inhibition in the Spinal Cord. Exp Brain Res 37:399-403
[96] Hultborn H, Illert M (1991) How is Motor Behavior Reflected in the Organization of Spinal Systems? In: Humphrey DR, Freund H-J (eds.) Motor Control: Concepts and Issues. John Wiley & Sons, 49-73
[97] Jacobson SC, Wood JE, Knutti DF, Biggers KB (1986) The UTAH/MIT Dextrous Hand: Work in Progress, in Pham DT, Heginbotham WB (eds.) Robot Grippers, Springer Verlag, 341-389
[98] Jami L, Murthy KSK, Petit J (1982) Distribution of Physiological Types of Motor Unit in the Cat Peroneus Tertius Muscle. Exp Brain Res 48:177-184
[99] Jami L (1992) Golgi Tendon Organs in Mammalian Skeletal Muscle: Functional Properties and Central Actions. Physiol Rev 72:623-666
[100] Jankowska E, Padel Y, Tanaka R (1975) Projections of Pyramidal Tract Cells to α–Motoneurones Innervating Hind-Limb Muscles in the Monkey. J Physiol 249:637-667
[101] Johansson RS, Westling G (1984) Roles of Glabrous Skin Receptors and Sensorimotor Memory in Automatic Control of Precision Grip when Lifting Rougher or more Slippery Objects. Exp Brain Res 56:550-564
[102] Johansson RS, Westling G (1987) Signals in Tactile Afferents from the Fingers Eliciting Adaptive Motor Responses during Precision Grip. Exp Brain Res 66:141-154
[103] Johansson RS, Westling G (1988a) Coordinated Isometric Muscle Commands Adequately and Erroneously Programmed for the Weight during Lifting Task with Precision Grip. Exp Brain Res 71:59-71
[104] Johansson RS, Westling G (1988b) Programmed and Triggered Actions to Rapid Load Changes during Precision Grip. Exp Brain Res 71:72-86
[105] Johansson RS, Riso R, Häger Ch, Bäckström L (1992a) Somatosensory Control of Precision Grip during Unpredictable Pulling Loads I. Changes in Load Force Amplitude. Exp Brain Res 89:181-191

[106] Johansson RS, Häger Ch, Riso R (1992b) Somatosensory Control of Precision Grip during Unpredictable Pulling Loads II. Changes in Load Force Rate. Exp Brain Res 89:192-203

[107] Johansson RS, Lemon RN, Westling G (1994) Time-Varying Enhancement of Human Cortical Excitability Mediated by Cutaneous Inputs during Precision Grip. J Physiol 481:761-775

[108] Keshner EA, Baker JF, Banovetz J, Peterson BW (1992) Patterns of Neck Muscle Activation in Cats during Reflex and Voluntary Head Movements. Exp Brain Res 88:361-374

[109] Kilner JM, Baker SN, Salenius S, Jousmaki V, Hari R, Lemon RN (1999) Task-Dependent Modulation of 15-30 Hz Coherence Between Rectified EMGs from Human Hand and Forearm Muscles. J Physiol 516:559-570.

[110] Kirkwood PA (1979) On the Use and Interpretation of Cross-Correlation Measurements in the Mammalian Central Nervous System. J Neurosci Meth 1:107-132

[111] Kirkwood PA, Sears TA (1991) Cross-Correlation Analyses of Motoneuron Inputs in a Coordinated Motor Act. In: Krueger J (ed.) Neuronal Cooperativity, Springer Series in Synergetics. Springer Verlag, Berlin, 225-248

[112] Kuhtz-Buschbeck JP, Boczek-Funcke A, Illert M, Joehnk K, Stolze H (1999) Prehension Movements and Motor Development in Children. Exp Brain Res 128:65-68

[113] Kurata K (1993) Premotor Cortex of Monkeys: Set- and Movement-Related Activity Reflecting Amplitude and Direction of Wrist Movements. J Neurophysiol 69:187-200

[114] Landsmeer JMF (1962) Power Grip and Precision Handling. Ann. rheum. Dis. 21:164-169

[115] Lacquaniti F, Soechting JF (1982) Coordination of Arm and Wrist Motion during a Reaching Task. J Neurosci 2: 399-408

[116] Lawrence DG, Kuypers HGJM (1968) The Functional Organization of the Motor System in the Monkey: I. The Effects of Bilateral Pyramidal Lesions. Brain 91:1-14

[117] Lee WA (1984) Neuromotor Synergies as a Basis for Coordinated Intentional Action. J Mot Behav 16:135-170

[118] Lemon RN, Mantel GWH, Muir RM (1986) Corticospinal Facilitation of Hand Muscles during Voluntary Movement in the Conscious Monkey. J Physiol 381:497-527

[119] Lemon RN, Bennett KMB, Werner W (1991) The Cortico-Motor Substrate for Skilled Movements of the Primate Hand. In Requin J, Stelmach GE (ed.s) Tutorials in Motor Neuroscience, Vol. 62:477-495. Kluwer Academic Publishers, The Netherlands

[120] Lemon RN (1993) Cortical Control of the Primate Hand: the G.L. Brown Prize Lecture. Exp Physiol 78:263-301

[121] Liddell EGT, Sherrington CS (1925) Recruitment and some other Factors of Reflex Inhibition. Proc R Soc London Ser. B97:488-518

[122] Logigian EL, Wierzbicka MM, Bruyninckx F, Wiegner AW, Shahahi BT, Young RR (1988) Motor Unit Synchronization in Physiologic, Enhanced Physiologic, and Voluntary Tremor in Man. Ann Neurol 23:242-250

[123] MacPherson JM (1988) Strategies that Simplify the Control of Quadrupedal Stance II. Electromyographic Activity. J Neurophysiol 60:218-231
[124] MacPherson JM (1991) How Flexible are Muscle Synergies? In Humphrey DR, Freund H-J (eds) Motor Control: Concepts and Issues. John Wiley & Sons. 33-47
[125] Maier MA (1992) Control of Force in Precision Grip. An Investigation into the Participation and Coordination of Fifteen Muscles. Ph.D. Thesis Univ. Zurich
[126] Maier MA, Hepp-Reymond M-C (1995a) EMG Activation Patterns during Force Production in Precision Grip: I. Contribution of 15 Finger Muscles to Isometric Force. Exp Brain Res 103:108-122
[127] Maier MA, Hepp-Reymond M-C (1995b) EMG Activation Patterns during Force Production in Precision Grip: II. Muscular Synergies in the Spatial and Temporal Domain. Exp Brain Res 103:123-136
[128] Mason M, Salisbury JK (1985) Robot Hands and the Mechanics of Manipulation. MIT Press, Cambridge Mass.
[129] Matelli M, Camarda R, Glickstein M, Rizzolati G (1986) Afferent and Efferent Projections of the Inferior Area 6 in the Macaque Monkey. J Comp Neurology 251:281-298
[130] Matthews PBC (1996) Relationship of Firing Intervals of Human Motor Units to the Trajectory of Post-Spike After-Hyperpolarization and Synaptic Noise. J Physiol 492:597-628
[131] McMillan AS, Sasaki K, Hannam AG (1990) The Estimation of Motor Unit Twitch Tensions in the Human Masseter Muscle of Spike Triggered Averaging. Muscle & Nerve 13:697-703
[132] Merton PA, Morton HB (1980) Stimulation of the Cerebral Cortex in the Intact Human Subject. Nature 285:227
[133] Meyer B-U (1992) Normwerte: Muskelantworten nach transkranieller Reizung des motorischen Kortex und Reizung der Nervenwurzeln. In Meyer B-U (ed) Magnetstimulation des Nervensystems: Grundlagen und Ergebnisse der klinischen und experimentellen Anwendung. Springer, Berlin Heidelberg New York, 339-371
[134] Milner-Brown HS, Stein RB, Yemm R (1973a) The Contractile Properties of Human Motor Units during Voluntary Isometric Contractions, J Physiol 228:285-306
[135] Milner-Brown HS, Stein RB, Yemm R (1973b) Changes in Firing Rate of Human Motor Units during linearly Changing Voluntary Contractions. J Physiol 230:371-390
[136] Milner-Brown HS, Stein RB, Lee RG (1975) Synchronization of Human Motor Units: Possible Roles of Exercise and Supraspinal Reflexes. EEG Clin Neurophysiol 38:245-254
[137] Monster AW, Chan H (1977) Isometric Force Production by Motor Units of Extensor Digitorum Communis Muscle in Man. J Neurophysiol 40:1432-1443
[138] Moore GP, Segundo JP, Perkel DH, Levitan H (1970) Statistical Signs of Synaptic Interactions in Neurons. Biophys J 10:876-900
[139] Muir RB, Lemon RN (1983) Corticospinal Neurones with a Special Role in the Precision Grip. Brain Research 261:312-316
[140] Napier JR (1956) The Prehensile Movements of the Human Hand. JBJS 38B:902-913

[141] Napier JR (1960) Studies of the Hands of Living Primates. Proc Zoolog Soc London 134:647-657
[142] Nashner LM (1977) Fixed Patterns of Rapid Postural Responses among Leg Muscles during Stance. Exp Brain Res 30:13-24
[143] Nordstrom MA, Miles TS, Veale JL (1989) Effect of Motor Unit Firing Pattern on Twitches Obtained by Spike-Triggered Averaging. Muscle & Nerve 12:556-567
[144] Nordstrom MA, Miles TS, Türker KS (1990) Synchronization of Motor Units in Human Masseter during a Prolonged Isometric Contraction. J Physiol 426:409-421
[145] Nordstrom MA, Fuglevand AJ, Enoka RM (1992) Estimating the Strength of Common Input to Human Motoneurons from the Cross-Correlogram. J Physiol 453:547-574
[146] Penfield W, Rasmussen T (1952) The Cerebral Cortex of Man. MacMillan, New York
[147] Perkel DH, Gerstein GL, Moore GP (1967) Neuronal Spike Trains and Stochastic Point Processes, II. Simultaneous Spike Trains. Biophys J 7:419-440
[148] Porter R, Lemon RN (1993) Corticospinal Function and Voluntary Movement. Monographs of the Physiological Society 45. Oxford Science Publications
[149] Press WH, Teukolsky SA, Vetterling WT, Flannery BP (1992) Numerical Recipes in C: the Art of Scientific Computing. 2nd edition, Cambridge University Press
[150] Qi H-X (1996) The Premotor Cortex: its Contribution to the Control of the Precision Grip in the Monkey. Ph.D. Thesis Univ. Zürich
[151] Ramon y Cajal S (1909) Histologie du système nerveux de l'homme et des vertèbrès, Vol. 1. Maloine, Paris
[152] Ramon y Cajal S (1911) Histologie du système nerveux de l'homme et des vertèbrès, Vol. 1. Maloine, Paris.
[153] Rizzolatti G, Camarda R, Fogassi L, Gentilucci M, Luppino G, Matelli M (1988) Functional Organization of Inferior Area 6 in the Macaque Monkey: II Area F5 and the Control of Distal Movements. Exp Brain Res 71:491-507.
[154] Roland PE, Larsen B, Lassen NA, Skinhøf E (1980) Supplementary Motor Area and Other Cortical Areas in Organization of Voluntary Movements in Man. J Neurophysiol 43:118-136
[155] Romaiguère P, Vedel J-P, Pagni S, Zenatti A (1989) Physiological Properties of the Motor Units of the Wrist Extensor Muscles in Man. Exp Brain Res 78:51-61
[156] Rothwell JC, Thompson PD, Day BL, Boyd S, Marsden CD (1991) Stimulation of the Human Motor Cortex through the Scalp. Exp Physiol 76:159-200
[157] Rothwell JC (1994) Control of Human Voluntary Movement. (2nd edition) Chapman & Hall, London
[158] Rufener EA, Hepp-Reymond M-C (1988) Muscle Coactivation Patterns in the Precision Grip. Adv Biosci 70:169-172
[159] Sachs L (1984) Applied Statistics. (Springer Series in Statistics) Springer Berlin Heidelberg New York
[160] Salenius S, Salmelin R, Neuper C, Pfurtscheller G, Hari R (1996) Human Cortical 40 Hz Rhythm is Closely Related To EMG Rhythmicity. Neurosci Lett 213-75-78
[161] Saltzman E (1979) Levels of Sensorimotor Representation. J Mathematical Psychology, 20:91-163

[162] Sanes JN, Donoghue JP, Thangaraj V, Edelman RR, Warach S (1995) Shared Neural Substrates Controlling Hand Movements in Human Motor Cortex. Science 268:1775-1777

[163] Scherrer JK (1993) Sensorhand für intelligentes Greifen mit Robotern, Diss ETH Zürich No. 10249

[164] Schieber MH (1993) Electromyographic Evidence of Two Functional Subdivisions in the Rhesus Monkey's Flexor Digitorum Profundus. Exp Brain Res 95:251-260

[165] Schieber MH (1995) Muscular Production of Individuated Finger Movements: The Roles of Extrinsic Finger Muscles. J Neurosci 15:284-297

[166] Schmied A, Ivarsson C, Fetz EE (1993) Short-Term Synchronization of Motor Units in Human Extensor Digitorum Communis Muscle: Relation to Contractile Properties and Voluntary Control. Exp Brain Res 97:159-172

[167] Schmied A, Vedel J-P, Pagni S (1994) Human Spinal Lateralization Assessed from Motorneurone Synchronization: Dependence on Handedness and Motor Unit Type. J Physiol 480:369-387

[168] Schubert M, Curt A, Jensen L, Dietz V (1997) Corticospinal Input in Human Gait. Modulation of Magnetically Evoked Motor Responses. Exp Brain Res 115:234-246

[169] Schunk Intec AG, Spann- und Greiftechnik: Product Catalogue Greifsysteme (1998/1999) and (1999)

[170] Sears TA, Stagg D (1976) Short-Term Synchronization of Intercostal Motoneurone Activity. J Physiol 263:357-381

[171] Semmler JG, Nordstrom MA (1995) Influence of Handedness on Motor Unit Discharge Properties and Force Tremor. Exp Brain Res 104:115-125

[172] Shinoda Y, Yokata J-I, Futami T (1981) Divergent Projections of Individual Corticospinal Axons to Motoneurons of Multiple Muscles in the Monkey. Neurosci Lett 23:7-12

[173] Sica REP, McComas AJ (1971) Fast and Slow Twitch Units in a Human Muscle. J Neurol Neurosurg Psychiat 34:113-120

[174] Skoglund S (1956) Anatomical and Physiological Studies of Knee Joint Innervation in the Cat. Acta Physiol Scand 36 (suppl. 124):1-101

[175] Smith AM, Bourbonnais D (1981) Neuronal Activity in Cerebellar Cortex Related to Control of Prehensile Force. J Neurophysiol 45:286-303

[176] Stearns SD, David RA (1993) Signal Processing Algorithms using Fortran and C. Prentice-Hall, Englewood Cliffs, NJ

[177] Thach WT, Perry JG, Kane SA, Goodkin HP (1993) Cerebellar Nuclei: Rapid Alternating Movement, Motor Somatotopy, and a Mechanism for the Control of Muscle Synergy. Rev Neurol (Paris) 149:607-628

[178] Thomas CK, Johansson RS, Westling G, Bigland-Ritchie BR (1990) Twitch Properties of Human Thenar Motor Units Measured in Response to Intraneural Motor-Axon Stimulation. J Neurophysiol 64:1339-1346

[179] Thomas CK, Johansson RS, Bigland-Ritchie B (1991) Attempts to Physiologically Classify Human Thenar Motor Units. J Neurophysiol 65:1501-1508

[180] Vallbo Å, Hagbarth KE (1968) Activity from Skin Mechanoreceptors Recorded Percutaneously in Awake Human Subjects. Exp Neurol 21:270-289.

[181] Vaughan CW, Kirkwood PA (1997) Evidence from Motoneurone Synchronization of Disynaptic Pathways in the Control of Inspiratory Motoneurones in the Cat. J Physiol 503:673-689

[182] Wannier TMJ, Maier MA, Hepp-Reymond M-C (1989) Responses of Motor Cortex Neurons to Visual Stimulation in the Alert Monkey. Neurosci Lett 98:63-68

[183] Wannier TMJ, Maier MA, Hepp-Reymond M-C (1991) Contrasting Properties of Monkey Somatosensory and Motor Cortex Neurons Activated during the Control of Force in Precision Grip. J Neurophysiol 65:572-589

[184] Weinrich M, Wise SP (1982) The Premotor Cortex of the Monkey. J Neurosci 2:1329-1345

[185] Welch PD (1967) The Use of Fast Fourier Transform for the Estimation of Power Spectra: a Method Based on Time Averaging over Short, Modified Periodograms. IEEE Transactions on Audio and Electroacoustics AU-15(2):70-73

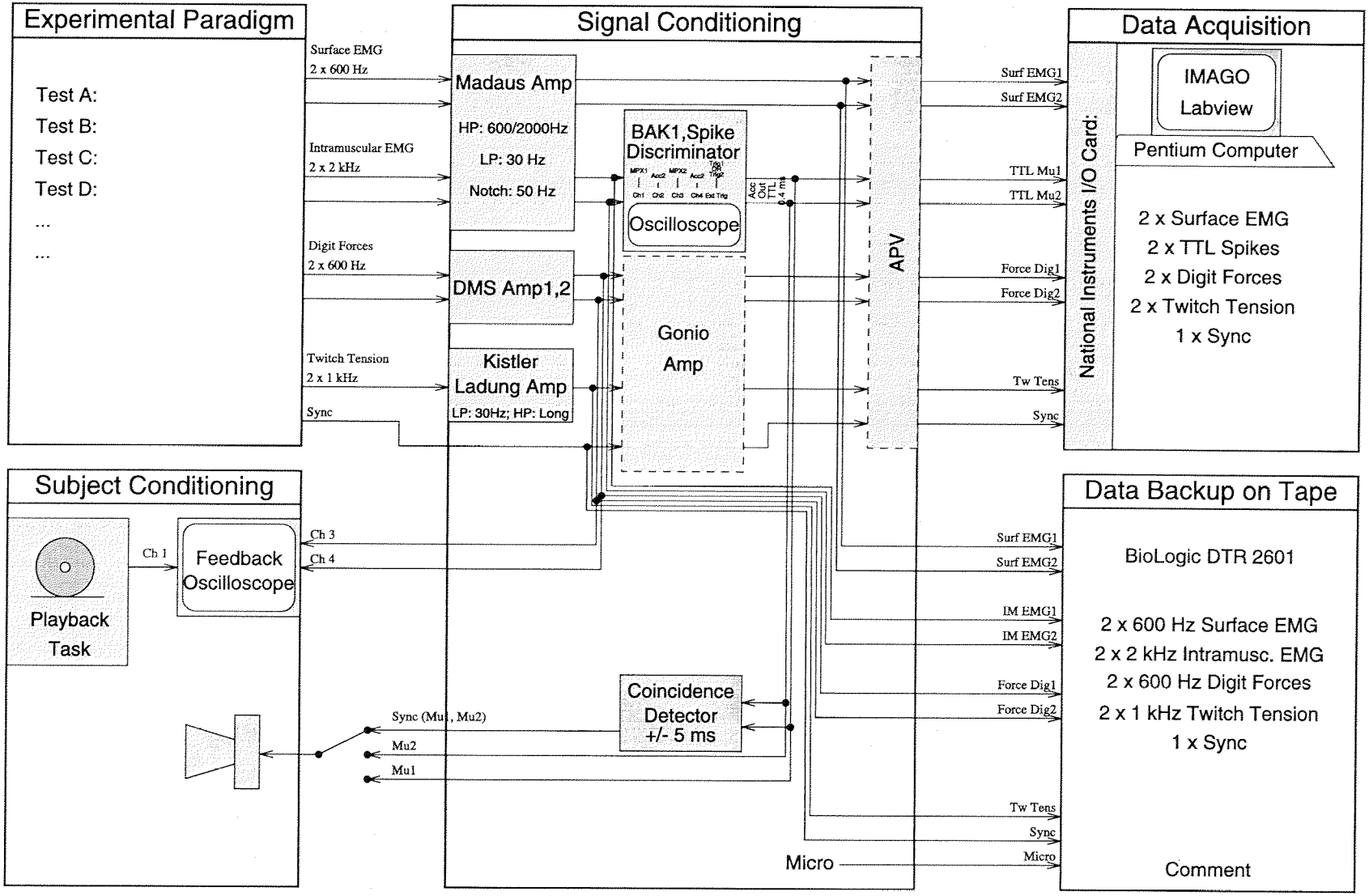
[186] Westling G, Johansson RS (1987) Responses in Glabrous Mechanoreceptors during Precision Grip in Humans. Exp Brain Res 66:128-140

[187] Westling G. Johansson RS, Thomas CK, Bigland-Ritchie B (1990) Measurement of Contractile and Electrical Properties of Single Human Thenar Motor Units in Response to Intraneural Motor-Axon Stimulation. J Neurophysiol 64:1331-1338

[188] Wise SP, Godschalk M (1987) Functional Fractionation of Frontal Fields. TINS 10:449-450

[189] Woelfl K (1995) Planung von Manipulationsvorgängen einer Roboterhand. VDI-Verlag Düsseldorf

Experimental Set-Up: Analysing MU Synchronization



EJH, 04.08.00, exp_setup3.ps

11 Appendix B: Force Transducer for Precision and Power Grip

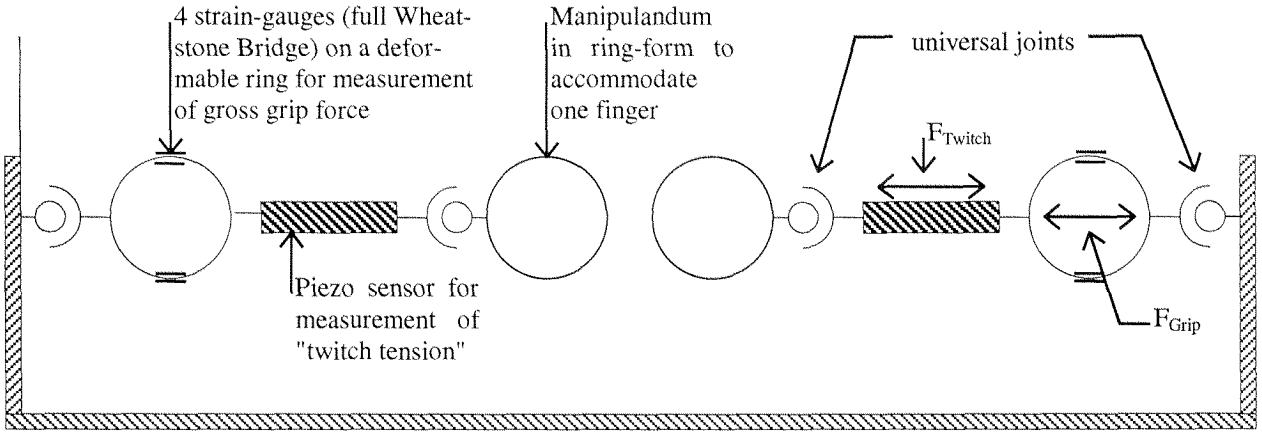
11.1 Requirements

A new force measuring device had to be developed with following requirements:

- measurement of the resultant grip force for the precision grip as well as for the power grip
- possible extension to measuring grip closure (movement of fingers)
- exchangeable manipulanda and adjustable to varying hand and finger sizes
- simple calibration
- 5 orders of magnitude measurement range (0.5 mN - 50 N)

11.2 Working Principle

We chose a design where two sensors were aligned in series for measurement of twitch force (piezo-sensor) and gross grip force (strain gauge sensor) for each finger separately. The device was automatically aligned to grip force direction given the two ball joints at both ends of the measuring handle. Therefore, we had to measure only along the axis of the device ("Pendelstütze").



It can be shown that the stress at the site of the strain gauges is a linear function of the applied force

$$\sigma_x = P\left[\frac{1}{2a^2} + 24 \cdot \frac{R}{a^3}\left(\frac{1}{2} - \frac{1}{\pi}\right)\right]$$

E A2-1

where σ_x is the tensile stress, P is the pulling force, R is the ring diameter and a is the ring thickness and $2a$ is the ring width.

Comparison of linearity between the strain gauge measurement and the piezo sensor with a sinusoidal force curve resulted in correlation coefficients $r > 0.99$.

12 Appendix C: Abbreviations

ARTMUP ..... Automatic Recognition and Tracking or Motor Unit Potentials
CUSUM..... cumulative sum, also *cumsum*
EMG ..... electromyogram, electromyography
IAM ..... intramuscular, within one muscle
IPIH..... inter-potential interval histogram
IRM..... intermuscular, between two muscles
MU..... motor unit
MUP ..... motor unit potential
MVC..... maximal voluntary contraction
TMS..... trans-cranial magnetic stimulation

Synchronization indices
k ..... relative peak amplitude (Sears, Stagg 1976)
k'..... relative peak area (Ellaway, Murthy 1985);
b ..... peak area normalised with total number of trigger plus response spikes (Bremner et al. 1991a)
CIS ..... common input strength: peak area normalised to total recording time (Nordstrom et al. 1992)
mpi ..... mean percent increase above baseline (Cope, Fetz, Matsumura 1987) can directly be derived from the k' index and therefore not used.

Thumb muscles
AbPB ..... Abductor pollicis brevis
AbPL..... Abductor pollicis longus
AdP..... Adductor pollicis
EPB..... Extensor pollicis brevis
EPL..... Extensor pollicis longus
FPB ..... Flexor pollicis brevis
FPL ..... Flexor pollicis longus
OPP..... Opponens pollicis

Index finger muscles
1DI..... First dorsal interosseus
1LUM ..... First lumbricalis
1PI..... First palmar interosseus
EDC ..... Extensor digitorum communis
FDP..... Flexor digitorum profundus
FDS..... Flexor digitorum superficialis

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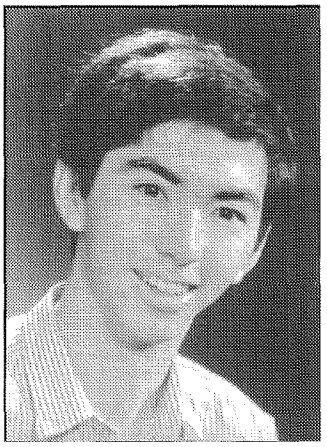
14 Curriculum Vitae



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Aug. 1992 - Sept. 1997	Research Assistant at the Brain Research Institute, Univ. Zürich with Prof. M.-C. Hepp-Reymond
1989	Two Training Stages as Undergraduate in Robotics with Stäubli-Unimation, Switzerland, and at the Mechanical Engineering Laboratory, Tsukuba, Japan

Schooling

1986-1991	Studies in Mechanical Engineering at the ETH Zürich, Majors: Mechanics und Biomed. Engineering
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