

01 **Chapter 11**  
02 **The Neural Representation of Kinematics**  
03 **and Dynamics in Multiple Brain Regions:**  
04 **The Use of Force Field Reaching Paradigms**  
05 **in the Primate and Rat**  
06  
07  
08  
09

10 **Joseph T. Francis**  
11

12  
13 **Abstract** In this chapter I will review the past and present motor control  
14 literature with an emphasis on reaching movements. Debate still rages as to  
15 what movement related variables are controlled by the neural motor control  
16 system especially concerning dynamic vs. kinematic variables. There is a rich  
17 history in the motor control literature that has employed monkeys of several  
18 species making reaching movements while holding loaded or robotic manipu-  
19 landum. However, to date very little work has been conducted using the  
20 rat reaching paradigm to investigate the control of dynamics vs. kinematics.  
21 I will review a very simple rat robotic manipulandum paradigm and initial  
22 results from it. This paradigm is presently being expanded from a 1 degree of  
23 freedom system similar to those used in early primate research to a 2 and even  
24 3 degree of freedom version, such as those used with primates and humans  
25 today.  
26

27 **Keywords** Motor learning · brain machine interface · thalamus · somatotopic ·  
28 somatosensory prosthesis  
29

30  
31 **11.1 Introduction**  
32

33 Much of the mammalian nervous system has evolved around a common set of  
34 basic needs, such as obtaining food and evading predators. What elements are  
35 needed to carry out such basic operations by an animal? The animal must be  
36 able to sense the food object, or predator, and be able to reach/grasp or move to  
37 the food, or flee from the predator. Having several senses would certainly be  
38

39 J.T. Francis  
40 Department of Physiology and Pharmacology, State University of New York  
41 Downstate Medical Center, Brooklyn, NY 11203  
42 Program in Neural and Behavioral Science, State University of New York Downstate  
43 Medical Center, Brooklyn, NY 11203  
44 Program in Biomedical Engineering, State University of New York Downstate  
45 Medical Center, Brooklyn, NY 11203  
e-mail: joey199us@gmail.com

01 beneficial to the animal as it could use correlations between the senses to learn  
02 about its environment and its own self generated movement. Even single celled  
03 protozoans, such as paramecium and euglena, have multiple senses such as  
04 chemical sensors (taste/smell), Photo sensors (sight), electric field sensors,  
05 gravitational sensors and mechanical sensors. Animals also need to be able to  
06 move to act on the sensory information, and in general animals learn to make  
07 certain sensory predictions based on their own motor commands. When these  
08 predictions are incorrect learning should takes place.

09 How does our nervous system use this sensory information and execute  
10 movements, and in what form is the information encoded within the neural  
11 substrate? Obviously I will not be able to fully discuss these questions in this  
12 chapter; however, I will attempt to review those aspects that stem from our  
13 sense of proprioception, as it stems from mechanical receptors, the theme of this  
14 book. Specifically, I will focus on the neural representation of dynamics (force  
15 related) and kinematics (position related) neuronal activity, or at least neural  
16 activity that correlates well with these two groups of variables. In addition,  
17 I will be limiting my discussion to primates and the rodent, as well as making  
18 comparisons between these two.

19

20

### 21 ***11.1.1 Reaching Movements***

22

23 I am going to use targeted reaching movements as the basic sensory motor  
24 task for our discussion. Reaching to grasp an object involves a great deal of  
25 neural processing, ranging from the computations that relate external space to  
26 our intrinsic motor apparatus, to sensing the size and compliance of target  
27 objects. The sensory motor control system involves interaction between feed-  
28 forward and feedback signals. The CNS uses visual, proprioceptive and  
29 cutaneous information to make natural reaching movements and to facilitate  
30 motor learning (Polit and Bizzi 1979; Lackner and Dizio 1994; Ghez et al.  
31 1995; Gordon et al. 1995; Sarlegna et al. 2004; Sober and Sabes 2005). More-  
32 over, the sensory motor control system can switch between these sensory  
33 modalities in relation to their reliability and the goals of the task (Sarlegna  
34 et al. 2003; Sober and Sabes 2003; Sarlegna et al. 2004; Scheidt et al. 2005;  
35 Sober and Sabes 2005). Whereas vision can guide the kinematics of move-  
36 ment, it cannot easily detect the loads that must be overcome. The proprio-  
37 ceptive system can detect loads as well as information about the arms position,  
38 velocity and acceleration. However, it has been suggested that the proprio-  
39 ceptive system drifts (Wann and Ibrahim 1992) over time unless it is inter-  
40 mittently reset via visual or tactile input. There is still much debate as to the  
41 cause of proprioceptive drift as well as its extent. The ability of visual input to  
42 ameliorate such drifting and its overall influence on reaching is apparent in  
43 individuals with large fiber neuropathy (Ghez et al. 1995; Gordon et al. 1995).  
44 However, these same individuals make gross errors when vision is occluded. It  
45 is obvious that both vision and proprioception play vital roles in motor

01 control. Thus, reaching movements normally depend on visual, propriocep-  
02 tive as well as and tactile information for humans, and primates in general  
03 (Lackner and Dizio 1994; Graziano 1999).

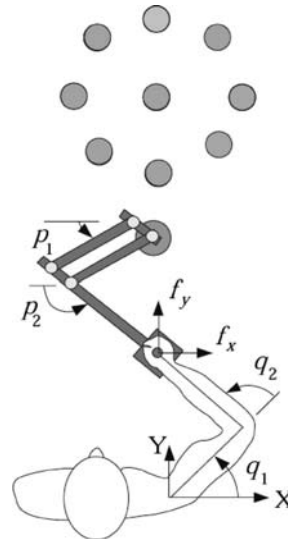
04 For the past several decades neurophysiologists and psychophysicists have  
05 worked to elucidate the control mechanisms employed by the brain and spinal  
06 cord that allow us and other animals to move voluntarily with a great degree of  
07 plasticity. Much of this work has been dedicated to determining which variables  
08 of movement we specifically control. In addition, there has been a great deal of  
09 debate as to what specific brain regions code for which of these variables.  
10 However, many frontoparietal brain regions have been shown to encode  
11 movement related parameters such as the target (Andersen et al. 1985) and  
12 hand (Tillery et al. 1995; Battaglia-Mayer et al. 2000; Graziano et al. 2000;  
13 Buneo et al. 2002; Taylor et al. 2002; Carmena et al. 2003) positions, direction  
14 (Georgopoulos et al. 1982), velocity (Moran and Schwartz 1999b) and force  
15 (Kalaska et al. 1989; Alexander and Crutcher 1990b; Crutcher and Alexander  
16 1990; Li et al. 2001; Scott et al. 2001; Xiao et al. 2006). A more correct statement  
17 would be that correlations have been found between the aforementioned vari-  
18 ables and neural activity. To date there is still heated debate as to whether the  
19 motor cortex and other motor related regions are encoding kinematic, or  
20 dynamic related variables, as well as what coordinate system these regions  
21 use, such as extrinsic vs. intrinsic coordinate systems. Similar types of questions  
22 have been raised regarding information carried in the spinal cord from periph-  
23 eral mechanoreceptors such as muscle spindles and joint receptors (Bosco and  
24 Poppele 2001; Stein et al. 2004).

25 For rodents, such as the rat and mouse, making reaching movements involve  
26 a somewhat different situation than that for primates, as it has been suggested  
27 they use olfaction (Whishaw and Tomie 1989) to locate the target object and  
28 most likely can't see their forepaws within a large region of the forepaw range of  
29 motion. In addition to olfaction, they do have the sense of proprioception, and  
30 whiskers, both on their snout as well as whisker like guard hairs on their wrists.  
31 Traditionally researchers have used human or non-human primates for the  
32 study of targeted reaching movements; however, with the ability to genetically  
33 manipulate mice, the low cost associated with rodent work, and the large  
34 number of animal models based on the rat and mouse there has been a surge  
35 in the use of rodent reaching paradigms. Our understanding of the rodent  
36 motor control system is still lagging that of primates, for instance, we have  
37 only recently identified the major proprioceptive relay nucleus in the rat thalamus,  
38 something that has been long known and studied in the primate (Francis  
39 et al. 2008). Our knowledge on the rat's visual system is also lagging as far as  
40 the functional neurophysiology. There is a good deal of evidence that primates  
41 make their reaching plan in a visual coordinate system, but what about the  
42 rat? Do rats plan reaches in a whisker, olfactory, visual, or some other  
43 coordinate system? This is an open question which we hope to address in the  
44 near future.  
45

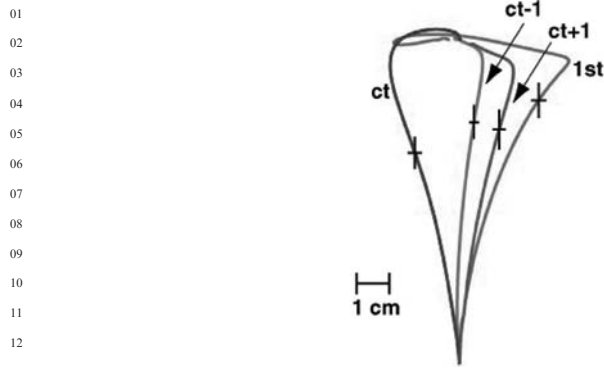
### 11.1.2 The Robotic Manipulandum and the Force Field Paradigm

During a natural reaching movement there is often a large degree of correlation between several movement related variables. If our goal is to determine what movement related variables the different brain regions encode we need to decouple these inherent correlations, and it is for this reason that the loaded and robotic manipulandum have been developed. **Center out reaching paradigm:** In the lower half of Fig. 11.1 is a cartoon of an individual holding onto one type of endpoint robotic manipulandum (bottom) that moves in the horizontal plane. In this widely used paradigm subjects are instructed to make a reaching movement to one of the eight peripheral targets seen at the top of the figure, starting all reaches from the center target. This is the standard center out reaching paradigm. Only one reaching target is cued at a time and may require the subject to wait before a go cue is given to actually make the overt reaching movement. The targets may be projected onto the same plane that the subject is reaching in, or can be represented on a computer monitor placed directly in front of the subject with a visual feedback computer cursor representing the position of the hand. This hand position is read from joint encoders on the manipulandum.

By using robotic systems we can ask questions about both kinematic and dynamic related variables while changing the sensory motor transformations necessary for the subject to complete the task. For instance, one can have the manipulandum produce a velocity dependant curl field, which produces forces tangential to the direction of motion and proportional to the speed, and is complex enough that the subject does not explicitly know what has changed



**Fig. 11.1** A cartoon of the center out reaching paradigm. A subject, *bottom*, holds onto a robotic manipulandum, *top*. Shown are the joint angles for the subject and manipulandum and forces at the handle



**Fig. 11.2** Plotted are the mean reaching trajectories for a group of subjects during the curl field paradigm. During the first fielded movement (1st) the subjects' movements are severely deviated to the right. After learning (ct-1) the movements become straighter indicating the subjects have learned to compensate for the force field. During certain movements the force field was turned off (ct) causing a deviation to the left, that is an error in reaching. This error causes learning to occur, which can be tracked on a trial-by-trial basis, as seen by the difference between ct-1 and ct+1. (Taken from (Thoroughman and Shadmehr 2000) with permission)

(Shadmehr and Mussa-Ivaldi 1994). When first exposed to such a field subject's movements are severely displaced as seen in Fig. 11.2 labeled as 1st. However, after learning (labeled ct-1) the subjects' trajectories become fairly straight as those seen before the force field was turned on. Thus, we now have a situation where the kinematics of the movements are similar, but the forces needed to make the movement are very different. We can also secretly turn the force field off, called a catch trial (ct), as the electric motors of such robotic systems produce no discernable noise for the subjects to use as cues. These ct induce large movement errors and can be used to probe how the sensory motor control system learns on a trial-to-trial basis (Thoroughman and Shadmehr 2000; Donchin et al. 2003; Francis 2007). These robotic systems can also be used to change the mapping between the subjects hand and the visual feedback cursor, as well as combining force and these visual perturbations. In Section 11.3 of this chapter we discuss results from several neurophysiological studies using the robotic manipulandums.

## 11.2 Proprioception

### 11.2.1 Peripheral Mechanoreceptors

Proprioception is defined as the sense of joint position while Kinesthesia is the sense of joint motion. However, often these terms are intermingled and for the

01 purpose of this chapter I will use the term proprioception to indicate the sense  
02 of position and motion of ones body derived from mechanosensitive structures.  
03 In the skin there are six types of mechanoreceptors, Meissner's corpuscles,  
04 Merkel's endings and nerve endings around hair follicles, all of which are pre-  
05 dominantly involved in the sense of touch. In addition, Ruffini endings sense  
06 pressure while Pacinian corpuscles sense vibration. There are also free nerve  
07 endings that sense pain, temperature and touch, for review see (Nolte 2002).  
08 It has been suggested that the skin with these receptors can add to the sense  
09 of proprioception (Moberg 1983) when the skin is deformed due to our own  
10 movement.

11 Although the skin may take part in proprioception, the majority of this  
12 information comes from two types of mechanoreceptors, **Golgi tendon organs**  
13 (**GTOs**) and **muscle spindles** (for great interactive models of both these receptor  
14 types please see Arthur Prochazka's web page, [www.ualberta.ca/~aprochaz/  
15 research\\_interactive\\_receptor\\_model.html](http://www.ualberta.ca/~aprochaz/research_interactive_receptor_model.html)). Golgi tendon organs are located at  
16 the connection between muscles and their tendons. They are comprised of  
17 collagen surrounded by a sheath called a capsule. Inserted into the collagen  
18 matrix are the arborized endings of a 1b afferent sensory nerve fiber. When the  
19 muscle contracts it pulls on the capsule, which causes the collagen to squeeze the  
20 nerve endings, leading to the generation of action potentials. This response is  
21 slowly adapting. In general, one can think of the GTOs as the motor control  
22 systems force feedback receptor, or force transducer. It was once thought that  
23 these receptors only conveyed information when a muscle was stretched to  
24 within its limits, and thus functioned as a warning system. However, this false  
25 interpretation came about due to the fact that when one passively stretching an  
26 entire muscle, such as the biceps, the amount of force across any single muscle  
27 unit and its GTOs is rather small. This is in contrast to when that muscle unit is  
28 actively contracting. Thus, GTOs relay information preferentially about forces  
29 that are actively generated.

30 Just as GTOs are the force transducers of the motor control system we can  
31 think of **muscle spindles** as the motor control system's encoders relaying infor-  
32 mation on position, velocity and acceleration. Briefly, muscle spindles are  
33 comprised of intrafusal (with spindles) muscle fibers, which are connected to  
34 extrafusal (without spindles) muscle fibers that are responsible for generating  
35 force. The central region of the intrafusal fiber is encapsulated within a fluid  
36 filled spindle. Sensory endings make attachments to this non contractile central  
37 region of the intrafusal fibers within the spindle, and are stimulated when the  
38 fiber is stretched that is when the muscle is lengthened. In addition, outside the  
39 spindle region the intrafusal fibers have contractile regions that can be stimu-  
40 lated via the fusimotor system, also called the gamma motor system. This  
41 gamma stimulation adds tension to the spindle and can come in two forms,  
42 static and dynamic activation that can be used to increase the bias or gain of the  
43 spindle.

44 There are two major types of sensory endings innervating the spindles, Ia  
45 (primary) and II (secondary). The Ia afferents are large diameter fast conducting

01 and convey velocity and acceleration information to a larger extent than posi-  
02 tion, which is preferentially conveyed by type II afferents that are smaller and  
03 conduct action potentials at a slower speed. There are three types of intrafusal  
04 fibers within the spindle, nuclear bag 1, which are activated by gamma dynamic  
05 input, nuclear bag 2 (static) and nuclear chain fibers that receive static gamma  
06 activation. The word nuclear refers to the multiple nuclei that these fibers have,  
07 and that either line up parallel to the long axis of the fiber (chain) or group  
08 together (bag).

09 When we use our muscles, such as our biceps during elbow flexion, the  
10 extrafusal fibers of the bicep contract and bring with them the intrafusal fibers.  
11 As stated above, the sensory endings respond when the intrafusal fibers are  
12 stretched, not when shortened as in our example here. However, in this case the  
13 antagonistic muscles (triceps) will be stretched and thus its muscle spindles will  
14 inform the CNS of this. In addition, the gamma system can be used in a manner  
15 called alpha-gamma coactivation. During alpha-gamma coactivation the out-  
16 put of the muscle spindles in the biceps from our example can act as error  
17 detectors. As the extrafusal muscles are activated via the alpha motor system  
18 and they contract. During this contraction the gamma system activates the  
19 contractile region on the intrafusal fibers, keeping them taut at an expected  
20 length, which is the length predicted via the alpha activation. If you happen to  
21 be lifting an object and you underestimated its weight then your biceps would  
22 have contracted less than expected and due to the aforementioned gamma  
23 activity your bicep's muscle spindles will fire indicating this error.

24 A third type of peripheral receptor is simply called a joint receptor. **Joint**  
25 **receptors** are mechanoreceptors located in joint capsules, and it was once  
26 thought they acted as a warning system, signaling the edges of a joints work-  
27 space (Burgess and Clark 1969; Clark and Burgess 1975). Others have argued  
28 that these receptors signal movement, but not position over much of the joints  
29 workspace (Proske et al. 1988). Due to an anatomical oddity it is possible to  
30 disengage the muscles from the last segment of your middle finger (distal  
31 interphalangeal joint) by simply pointing this finger down while pointing your  
32 index, ring and pinky fingers up. Using this hand posture it has been shown that  
33 we can use the information from joint receptors alone for proprioceptive feed-  
34 back; however, our full proprioceptive abilities require the use of our muscle  
35 spindles as well (Ferrell et al. 1987).

### 36 37 38 39 **11.2.2 Central Representations of Proprioception**

40  
41 The representation of proprioceptive information coursing through the spinal  
42 cord, dorsal column nuclei, thalamus, cerebellum, and cerebral cortex have  
43 classically been studied using electrophysiological techniques employing large  
44 electrodes that record EEG (~10,000 neurons) or local field potential (LFP  
45 ~100 neurons) sized neural ensembles, lesioning experiments followed by

01 behavioral testing, and histological analysis. In addition, studies have been  
02 carried out in which tracers have been injection into specific regions within  
03 the CNS in order to elucidate the passage of fiber tracts or neural projections.  
04 After the introduction of the microelectrode in the 1950s it became possible to  
05 record from individual neurons. Advancements in single neuron recordings  
06 from whole animal preparations including the awake behaving animal have  
07 ushered in a new phase of neuroscience. Below I will briefly cover the literature  
08 on the flow of proprioceptive information from the spinal cord to its terminal  
09 cortical and sub-cortical projections.  
10

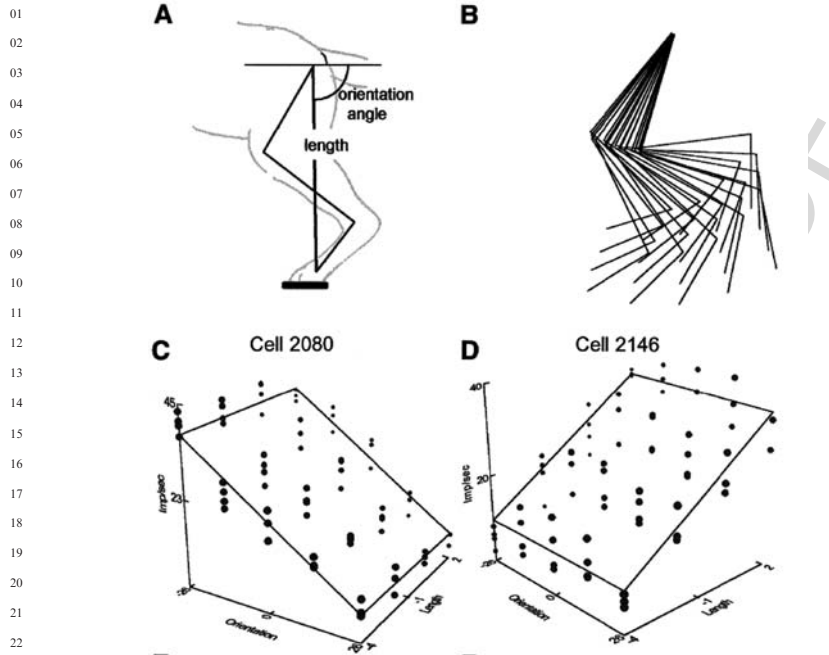
### 11 11.2.2.1 Spinal and Cerebellar

12  
13 Bosco, Poppele and their colleagues have carried out a series of experiments on  
14 the cat dorsal spinocerebellar tract (DSCT), which carries the majority of  
15 proprioceptive information from the peripheral mechanoreceptors of the hin-  
16 dlimbs. The ventral spinocerebellar tract also conveys proprioceptive informa-  
17 tion, but is most likely not as purely sensory showing signs of descending motor  
18 information in the (Lundberg 1971; Lundberg and Weight 1971; Arshavsky  
19 et al. 1972b; Arshavsky et al. 1972a). Proprioceptive information paralleling the  
20 above tracts from the forelimbs is carried via the cuneocerebellar and rostral  
21 spinocerebellar tracts respectively (Grant 1962; Oscarsson and Uddenberg  
22 1964). Bosco and Poppele have suggested that the information from the per-  
23 ipheral receptors are already combined within the spinal cord, and that the  
24 DSCT is carrying a higher level code representing global information about the  
25 limbs rather than simply the length of the muscles, or the angle of the joints.  
26 Specifically, they have suggested that this proprioceptive code is in a polar  
27 coordinate system with the endpoint (foot) represented as a length from the  
28 hip to the paw, and the angle made between the limb axis and the hip Fig. 11.3.

29 The fact that there are only two degrees of freedom in their coordinate  
30 system may have been due to a high degree of coupling among the three joints  
31 of the cat hindlimb, and the fact that its hindlimb's motion is mostly restricted  
32 to a plane. However, in a set of experiments the natural coupling between  
33 the joints was canceled by fixing one joint angle while varying the endpoint  
34 position with a similar conclusion about the endpoint representation (Bosco  
35 and Poppele 2000; Bosco and Poppele 2003). Recent work from this group that  
36 has moved past static paw positions and even into active stepping and has  
37 suggested that the limb length variable is not actually an independent variable,  
38 and encodes limb loading, which they argue is proportional to limb length  
39 under their previously explored passive conditions (Bosco et al. 2005; Bosco  
40 et al. 2006).

41 The aforementioned four spinal tracts give rise to mossy fibers that innervate  
42 the cerebellum, while the olivocerebellar pathway provides climbing fiber  
43 inputs to the cerebellum. These inputs reach the spinocerebellar cortex, consist-  
44 ing of the vermis and intermediate cerebellar cortex, as well as to the inter-  
45 positus nucleus. The cerebellar cortical representation of this information and





24 **Fig. 11.3** (A) The polar coordinate scheme with the hip as the origin. (B) The range of 20 foot  
25 positions used to test the neural representation from the DSCT. (C) and (D) represent  
26 the activity from two DSCT neurons. The  $x$  axis is the length, the  $y$  axis the orientation and the  $z$   
27 axis the neurons firing rate. (taken from (Bosco and Poppele 2001) with permission)

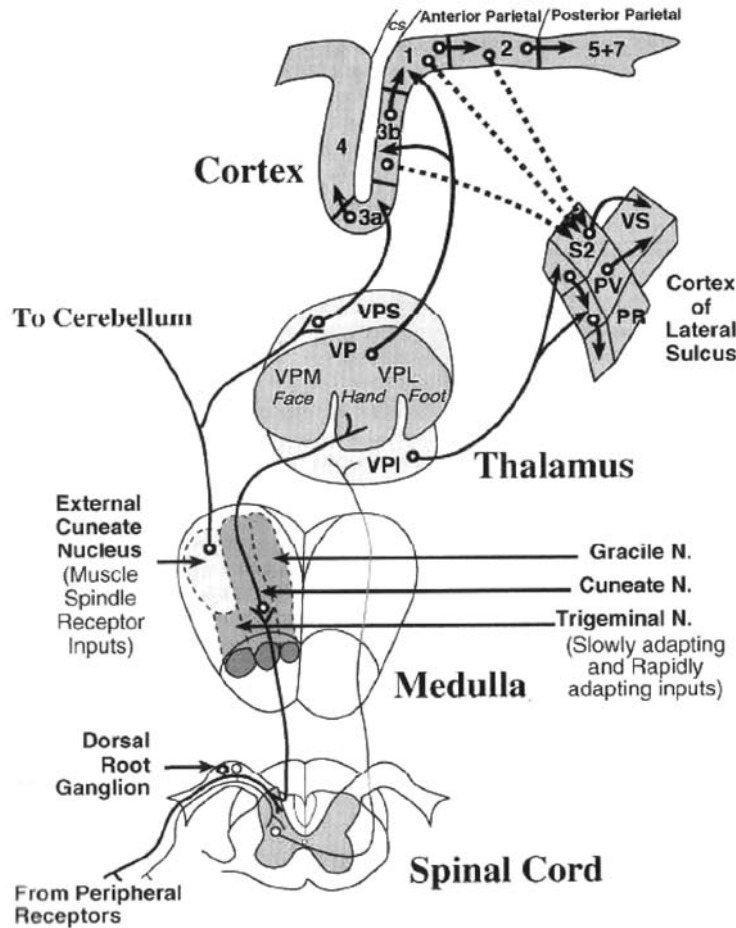
28 somatosensory information in general, is in a fractured form, and there is no  
29 clean somatotopy. As it has been suggested that the information in the spino-  
30 cerebellar tracts is already coding high level information, past a single joint or  
31 muscle, it should be no surprise that such global limb information is also found  
32 in the cerebellum, representing both position and velocity (Casabona et al.  
33 2004). However, the cerebellar representation of limb position dose not seem  
34 to be as strong as that seen in the DSCT (Casabona et al. 2003). Interesting is  
35 the fact that this positional representation is anisotropic (Valle et al. 2007),  
36 which was been described in primate motor (Kettner et al. 1988) and somato-  
37 sensory cortex (Tillery et al. 1996) as well.

40 **11.2.2.2 Thalamic and Cortical Representation of Proprioception**

41  
42 The adjoining figure (Fig. 11.4) by Jon Kaas et al. illustrates nicely the connec-  
43 tions form the spinal cord up to the cortex involved in somatosensation (Kaas  
44 et al. 2002). As seen in the figure, information from peripheral receptors ascends  
45 the spinal cord in two major pathways, the dorsal column system and the

01  
02  
03  
04  
05  
06  
07  
08  
09  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45

The Organization of the Somatosensory System in Primates



**Fig. 11.4** Diagram of the flow of information from the peripheral mechanoreceptors to the cortex. (taken from (Kaas et al. 2002) with permission)

spinothalamic systems. In the monkey the information from these two systems is segregated between the main somatosensory thalamic relay nuclei, such that the spinothalamic information is carried to the ventral posterior inferior (VPI) nucleus as well as the VMpo (Craig and Zhang 2006), while information from the dorsal column nuclei (DCN) project to the ventral posterior VP (comprised of the VPL and VPM). A majority of information from muscle spindles carried to the DCN terminate in separate nuclei, such as the external cuneate nucleus

01 for the forelimb, than that of the cutaneous receptors, which send their major  
02 projections to the cuneate and gracile nucleus.

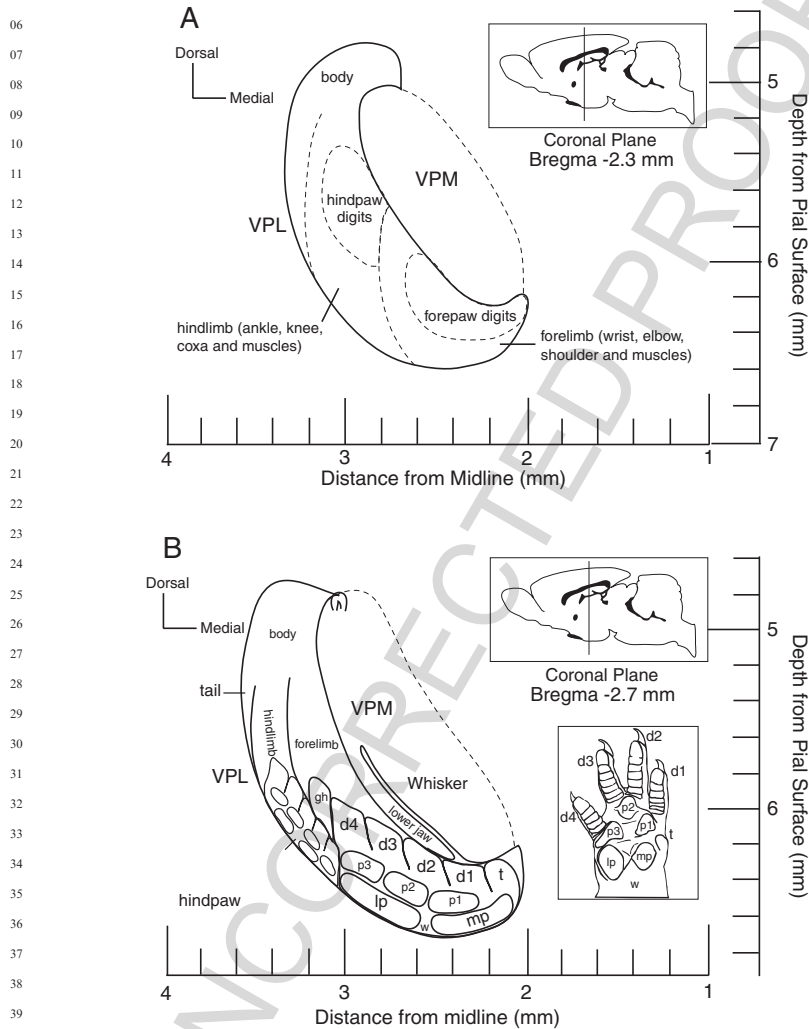
03 The VP has a well defined somatotopy in mammals (Kaas 2007) with the  
04 hand and foot occupying a disproportionately large volume, as compared to the  
05 rest of the body (Angel and Clarke 1975; Wilson et al. 1999). There are cell poor  
06 septa separating the face, hand and foot representations (Welker 1973; Kaas  
07 et al. 2002). The VP receives as its primary type of sensory input, from the DCN,  
08 both rapidly adapting (RA) and slowly adapting (SA) information, coming  
09 from these two main groups of receptors in the skin. The information from  
10 these two groups of receptors reportedly synapse on separate populations of VP  
11 neurons (Dykes et al. 1981), thus with future advances in micro and even nano  
12 electrode technologies, one may be able to differentially stimulate these two  
13 populations for use in a somatosensory neuroprosthesis (Rozenboym et al.  
14 2005; Rozenboym et al. 2006). The use of nano electrodes may not be necessary  
15 in the human, as a focal stroke in the VPL has been shown to specifically impair  
16 static, but not dynamic touch (Timmermann et al. 2000). This data suggests that  
17 the SA and RA information is conveyed by separate portions of the VPL. Such  
18 modality specific losses have also been shown for proprioception in humans  
19 (Sacco et al. 1987).

20 The VP projects strongly to LAYER IV of 3b, which is considered to be the  
21 homologue of S1 in non-primate mammals (Kaas 1983). Receptive fields in area  
22 3b are smaller than in the other somatosensory areas (areas 1, 2, S2, PV), as  
23 would be expected of the primary somatosensory cortex (S1). The VP also  
24 projects to area 1, predominantly above layer IV. Area 1 receives a major  
25 layer IV projection from 3b. Thus, it is possible that VP plays a modulatory  
26 role in area 1, while being the source of excitation in 3b. This architecture implies  
27 a serial order of information processing primarily from VP to 3b and onto area 1.  
28 This apparent serial order of information flow continues onto area 2, which  
29 receives input from area 1, but not directly from VP. Area 2 receives its main  
30 input from area 1 as well as from the VPS, which is the main relay nucleus for  
31 proprioceptive information in the monkey. Area 2 may be involved in form  
32 recognition by combining cutaneous and proprioceptive information for hapsis.

33 The VPI along with the VMpo appear to be the major thalamic recipients of  
34 lamina I projections in the macaque (Craig et al. 1994; Craig 2006), whereas the  
35 caudal VPL is in the rat (Gauriau and Bernard 2004). It has been proposed that  
36 the VMpo is a specific relay nucleus for pain and temperature information. The  
37 VPI is the primary thalamic input to S2 and PV, and projects to the superficial  
38 cortical layers (Krubitzer and Kaas 1992). This VPI input seems to have a  
39 modulatory role rather than directly activating S2 and PV. In fact, if one lesions  
40 areas 3a and 3b there appears to be no cutaneous excitation of area 1, S2 or PV  
41 (Garraghty et al. 1990a; Garraghty et al. 1990b). We will see later in this chapter  
42 that this type of obvious serial order processing doesn't seem to occur in the  
43 sensory motor areas during movement planning and execution.

44 Until recently, the rat homolog of the VPS had not been identified, which is  
45 surprising given the wide spread use of the rat as an animal model. We have now

01 mapped out a region in the rostral VPL of the rat that responds preferentially to  
 02 joint manipulation and muscle palpation (Francis et al. 2008). This region  
 03 contains large cutaneous receptive fields on the paws as well (see Fig. 11.5A).  
 04 Just caudal to this region of the rat thalamus is an area of the VPL that has small  
 05



**Fig. 11.5** A cartoon of somatotopy of the rat VPL in the coronal plane. (A) Bregma  $-2.3$  mm corresponding to the rVPL, and (B) Bregma  $-2.7$  mm corresponding to the mVPL. Insets in the upper right of (A) and (B) depict the position of the plane related to the whole rat brain. Inset in the lower right of (B) depicts the rat right forepaw: lp, lateral pad; mp, medial pad; w, wrist. The depth readings are in reference to the highest point of the pial surface, which is about  $0.4$  mm below Bregma. (Taken from (Francis et al. 2008) with permission)

01 cutaneous receptive fields and an exaggerated representation of the fore and  
02 hind paws (see Fig. 11.5B). This region corresponds to the primate VPL, and we  
03 have termed it the middle VPL (mVPL) in the rat (Francis et al. 2008). Caudal  
04 to the mVPL is the cVPL (caudal VPL), which has large cutaneous receptive  
05 fields, and may be the rat homolog of the primate VPI/VMpo.  
06  
07

### 08 **11.3 Neural Representation of Kinematics vs. Dynamics**

09

10 Does the motor control system use extrinsic (hand position) or intrinsic (joint/  
11 muscle based) coordinates, and is it controlling kinematics (position) or  
12 dynamics (force) related variables. These questions have been fiercely debated  
13 for some time now (Georgopoulos et al. 1982; Georgopoulos et al. 1983; Scott  
14 and Kalaska 1995; Crammond and Kalaska 1996; Taira et al. 1996; Ashe 1997;  
15 Scott and Kalaska 1997; Scott et al. 1997; Sergio and Kalaska 1997; Ajemian  
16 et al. 2000; Todorov 2000; Ajemian et al. 2001; Reina et al. 2001; Sergio and  
17 Kalaska 2003; Sergio et al. 2005) (for review see Shadmehr and Wise). In  
18 general, it seems that certain brain regions tend toward kinematics and others  
19 toward dynamics, and even within a brain region a given neurons representa-  
20 tion may appear to shift. In this section I will present some key results and  
21 experiments related to this debate from the primate and rat literature.  
22

23 Let's start with the spinal cord and muscles and discuss some of their proper-  
24 ties and control abilities before we move up the nervous system to the brain.  
25 Muscles have both active contractile properties as well as passive elastic proper-  
26 ties, like a spring, it requires more force to lengthen, or shorten it as you get  
27 further away from its preferred length. As a simple example consider the arm  
28 configuration of the subject in Fig. 11.1, and assume that we have the subjects  
29 arm supported via a sling so they don't have to counter gravity. Their relaxed  
30 arm will wish to come to rest at some position that is governed by the passive  
31 spring like properties of the muscles, assuming there are no external forces  
32 acting on the arm. You could call this the arms preferred (or zero effort)  
33 equilibrium position. Thus, if they wish to move their hand to another location  
34 and keep it there they need to produce enough force via their muscles to over-  
35 come the inertia of their arm as well as overcoming the passive spring like  
36 properties of the muscles that resist movement away from their preferred  
37 length. This latter component leads to the need for a tonic neural signal  
38 activating the muscles to keep them at this new equilibrium position.

39 In 1966, Feldman conducted a set of experiments in which he had subjects  
40 hold their arm with a given elbow angle and tested what forces the subjects  
41 generated at their hand when he tried to move their arm slightly (Feldman  
42 1966). What he found was that the subjects were unknowingly producing  
43 restoring forces that resisted this imperceptible movement. This was taken as  
44 evidence of an equilibrium point that was set presumably via the brain and  
45 instantiated via the spinal cord and the muscles and mechanical receptors. It

01 was theorized that movements could be produced by shifting this equilibrium  
02 point from where the hand was to some target position. This does not tell us,  
03 however, what the motor control system is actually controlling. Is the equili-  
04 brium position in muscle/force space, or is it in kinematic space, whether that be  
05 joint, or extrinsic.

### 08 **11.3.1 Wrist Movements**

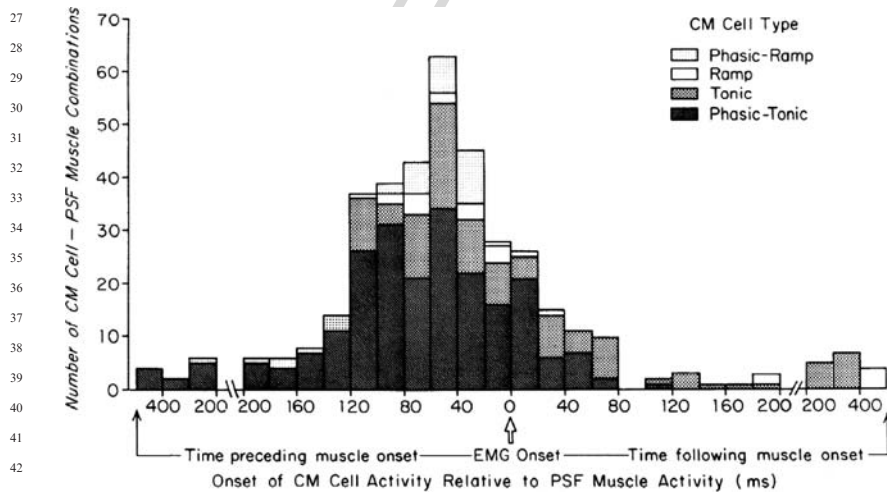
10 Over the past half century neurophysiological motor control studies in the  
11 primate have traveled from the wrist and finger movements, up to the elbow  
12 and finally to the shoulder and reach and grasp movements. Below I have  
13 grouped pertinent papers addressing the control of force and position into the  
14 wrist, elbow and whole arm categories.

15 In 1968 Edward Evarts presented a series of historic papers utilizing a motor  
16 control paradigm where monkeys made wrist movements cued via a light to the  
17 right or left while encountering constant assistive, resistive, or null torques via a  
18 manipulandum (Evarts 1965; Evarts 1966; Evarts 1968). Evarts used electrical  
19 stimulation in the medulary pyramids in order to determine if the motor cortical  
20 cells he was recording from were pyramidal tract neurons (PTNs) or not.  
21 In this series of papers Evarts describes the relation between conduction velo-  
22 cities in PTNs and their recruitment and firing tendencies, with fast conducting  
23 PTNs exhibiting phasic increases in activity during movement, while slowly  
24 conducting PTNs were active even during posture and could have both  
25 increases and decreases in activity during movement. These results point to  
26 the possible separation between the control of posture and movement (Kurtzer  
27 et al. 2005), which is still an active area of research. In this earliest work that  
28 specifically addresses the dynamics (force) vs. kinematics (position) representa-  
29 tion in the motor cortex; Evarts suggests that it is the magnitude of the force  
30 that is best accounted for in M1. In a follow up paper Evarts looked at PTN  
31 activity during a postural task, which is identical to the one he previously used,  
32 but now the monkey had to resist movement of its wrist while experiencing the  
33 different load conditions. Again, the results pointed to the control of force via  
34 the motor cortex (Evarts 1969), were many PTNs changed their activity in  
35 relation to the change in force per unit time  $dF/dt$ . Evarts also noted that the  
36 motor cortex receives input from proprioceptors via Ia afferents that convey  
37 information from the nuclear bag fibers of the muscle spindles. Thus, it is  
38 conceivable that some of the information represented in the motor cortex is in  
39 fact related to muscle lengths and not simply to force. This representation could  
40 include both feedforward sensory expectations via the gamma motor system, as  
41 well as feedback via the Ia afferent system. This is not to imply that the motor  
42 cortex has the leading role in these proprioceptive neural capacities. Another  
43 point that Evarts recognized was the fact that the monkey had to hold the  
44 handle and this would lead to different combinations of force needed by the  
45

01 fingers, or thumb depending on what direction the handle was to be moved.  
 02 Such confounding aspects are common in much of the motor control literature.

03 In 1980 Paul Cheney and Eberhard Fetz published an influential paper  
 04 describing the activity patterns of putative corticomotoneurons (CM) in  
 05 the motor cortex. These neurons demonstrated postspike facilitation (PSF)  
 06 of the rectified electromyography (EMG) activity. Thus, unlike the PTNs (see  
 07 above), which could have had targets other than the muscles, or even the spine,  
 08 these CM cells are chosen based on a relation with the EMG data, this technique  
 09 is called spike triggered averaging. It should not be surprising that these CM cells,  
 10 that were selected due to their spike triggered average relation to the EMG, were  
 11 found to always be active during the production of a torque in the cells preferred  
 12 direction (direction the cell is most response in). It was noted that there were four  
 13 main firing patterns in the CM cells, which are labeled and their numbers shown  
 14 in Fig. 11.6 taken from (Cheney and Fetz 1980). According to the authors the CM  
 15 activity was similar between isometric and auxotonic conditions, indicating that  
 16 the CMs are most related to the torque trajectory, rather than the displacement,  
 17 or its derivatives. They also noted that the two phasic categories (phasic-tonic  
 18 and phasic-ramp) of CMs began to fire significantly earlier (-71 and -63 ms,  
 19 respectively) than the ramp and tonic CMs did (+5 and +101 ms, respec-  
 20 tively). Again this separation may represent the neural control for active  
 21 changes in force output, which are generally associated with movement, and  
 22 postural forces, or an equilibrium point. In this case the equilibrium point  
 23 need not be in positional space, but rather in torque output.

24 These authors found that the relation between the change in torque and CM  
 25 firing rate was steeper for wrist extension than for flexion, and that in general  
 26



44 **Fig. 11.6** Distribution of the onset of corticomotoneuronal (CM) activity with respect to post  
 45 spike facilitated muscle activity. (Taken from (Cheney and Fetz 1980) with permission)

01 when the torque was increased the CMs would increase their rate rather than  
02 new CMs being recruited at higher torque levels. Put another way, very few CM  
03 cells had a torque threshold that was larger than zero for at least some tonic  
04 activity. Others have suggested that there is an extensive representation in M1  
05 around the zero torque, and for the lower torque range, and that the slope of the  
06 relation between M1 neural firing and torque change is steepest at the low  
07 torque range, at least for the wrist (Werner et al. 1991). Werner and colleagues  
08 even suggest that there may be different roles for M1 and the pre-motor cortex  
09 in controlling fine vs. gross forces, as they found the PM cells to represent  
10 torque at a larger range and these neurons had a steeper force/firing rate  
11 relation at higher torques (for force review see (Ashe 1997)).

12 An early debate in motor control that the above work helped settle had to do  
13 with whether the motor cortex controls individual muscles or groups of mus-  
14 cles. Anatomical evidence has indicated that neurons in the motor cortex  
15 innervate multiple motor pools (Shinoda et al. 1981), indicating it controls  
16 groups of muscles and not just one, further support of this idea came from  
17 the above electrophysiological experiments (Cheney and Fetz 1980; Maier et al.  
18 1993), were it was found that the spikes from one motor cortical cell influenced  
19 several muscles, and these muscles often worked together.

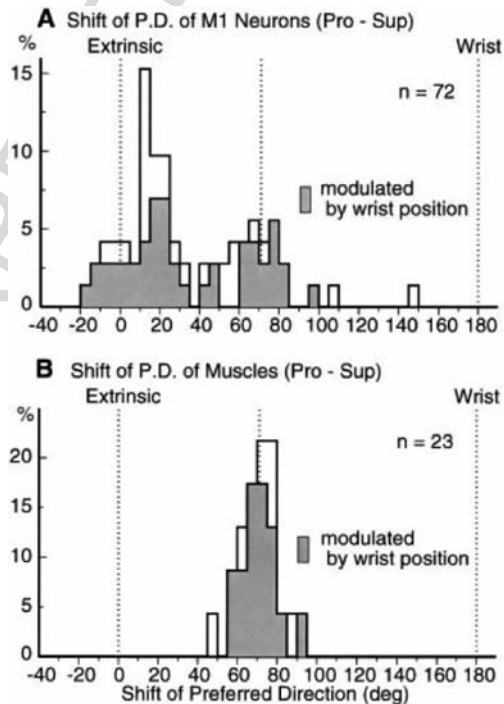
20 In 1983 Humphrey and Reed showed that monkeys would use stiffness, or  
21 compliance control, for high frequency alternating torques on the wrist.  
22 Whereas they would use reciprocal activation patters at lower frequencies.  
23 There where two distinct cell populations in M1 for this joint stiffness and  
24 forward model type control. Below are results from another set of wrist experi-  
25 ments where distinct cell populations were found to represent specific move-  
26 ment related variables, however, this is most likely due to the specifics of each of  
27 these different experimental paradigms as well as the methods used for choosing  
28 cells etc. . .

29 In 1994 Alexa Riehle et al. addressed the issue of controlling force and the  
30 extent of wrist movements (Riehle et al. 1994). In this work they utilized a  
31 paradigm in which partial or no information about the upcoming movement  
32 could be given during a delay period in order to determine the influence this  
33 information had on motor planning and execution. Specifically, they would cue  
34 information about the upcoming movements force or extent. It had been pre-  
35 viously demonstrated that these two variables could be independently controlled,  
36 along with movement direction and extent (Rosenbaum 1980), direction and  
37 force (MacKay and Bonnet 1990), as well as movement direction and duration  
38 (Vidal et al. 1991). Thus, one should be able to find a neural correlate of these,  
39 and indeed there are such correlates (Riehle et al. 1994; Riehle and Requin 1995),  
40 and the neural representation of these two variables differs from brain region to  
41 region, as well as during the evolution of the motor plan and execution. For  
42 extent and force these authors found two populations of neurons, one relating  
43 only to extent and the other only to force with most of the premovement changes  
44 occurring in the pre-motor cortex. These authors suggest that the motor control  
45 system programs extent and force in a serial manner, while direction and extent



01 are planned in either in a fixed order, or in parallel, as determined via reaction  
 02 times using the above task. It may not be surprising that two distinct neural  
 03 populations could be found representing either movement direction or movement  
 04 force. However, unlike some of the previous work it seemed that more neurons  
 05 changed their activity in relation to direction rather than force. It was noted that  
 06 “the number of purely direction-related neurons increased, whereas the number  
 07 of purely force-related neurons decreased from S1 to PA, then to M1 and finally  
 08 to PM.” (Riehle and Requin 1995). Here S1 is the primary somatosensory cortex,  
 09 PA the parietal cortex and PM the premotor cortex.

10 More recently a group of researchers attempted to further our understanding  
 11 on such wrist control by dissociating several possible variables of motor control,  
 12 such as the muscle activity, the direction of the wrist movement and the direction  
 13 of movement of the visually controlled computer cursor (Kakei et al. 1999).  
 14 Unlike the Evarts work, these wrist movements were to eight spatial targets in  
 15 a 2D plane (center out paradigm), not simply to the right or left. In addition, the  
 16 monkey grasped the manipulandum in one of three forearm positions, pronated,  
 17 supinated, or between the two, which corresponds to having the hand with the  
 18 thumb pointing up. The distribution of change in the preferred direction of motor  
 19 cortical cells, and for the muscles is shown in Fig. 11.7, were the preferred  
 20  
 21  
 22



23  
 24  
 25  
 26  
 27  
 28  
 29  
 30  
 31  
 32  
 33  
 34  
 35  
 36  
 37  
 38  
 39 **Fig. 11.7** Distribution of the  
 40 shift in preferred directions  
 41 of M1 neurons (A) and  
 42 Muscles (B) between a  
 43 pronated and supinated  
 44 wrist position (see text).  
 45 (Taken from (Kakei et al.  
 1999) with permission)

01 direction is the direction in which the cell or muscle fires most. It can be seen from  
02 this figure that the distribution in M1 appears to be bimodal, while that of the  
03 muscles is between an extrinsic and wrist centered reference frame, as the differ-  
04 ence between the pronated and supinated positions was 180 degree. The authors  
05 state that the cortical representation strongly represents both muscle-like and  
06 direction of the wrist in space regardless of the muscle activation patterns.

07 This work has been expanded recently using a very similar task while recording  
08 from M1 as well as the spinal cord interneurons (Yanai et al. 2008). In this work  
09 the monkeys made isometric wrist torques to visual targets utilizing the center out  
10 paradigm, but without wrist movement, just isometric torque. The wrist torques  
11 generated in the Yanai work were slower (mean, 670 ms) than the movements in  
12 the Kakei work (movement time < 200 ms). Also, the muscle activation patterns  
13 were less complex during the isometric paradigm as compared to the Kakei work.  
14 These differences may have lead to Yanai et al. stating that they didn't see the  
15 same bimodal distribution of M1 neural activity as that seen in the Kakei work,  
16 although they did see a consistent shift in the cortical PDs with rotation of the  
17 wrist. They noticed a bimodal distribution in the spinal interneurons and inter-  
18 preted their results such that the motor cortex is operating in an intermediate  
19 reference frame between extrinsic and muscle like frames, while the spinal inter-  
20 neurons are already representing a muscle based reference frame. They suggest  
21 that cortico-spinal interactions are involved in the coordinate transformation  
22 between the M1 intermediate frame and the spinal muscle-like frame.

23  
24

### 25 ***11.3.2 Finger and Elbow Movements***

26  
27 A truly amazing finding was published in 1971 by Fetz and Finocchio utilizing  
28 elbow movements and isometric muscle contractions in the primate (Fetz and  
29 Finocchio 1971). These researchers determined that the monkeys could learn to  
30 control the firing patterns of individual motor cortical neurons if they were  
31 provided with auditory or visual feedback on the neurons rate of activity. The  
32 animals were rewarded for increasing the activity of the neuron, which would  
33 normally be associated with the activation of the biceps. However, with training  
34 the monkeys could dissociate the muscle contraction from the increased firing  
35 of the neuron. The opposite dissociation that is neural suppression while con-  
36 tracting the biceps was incomplete, but still noteworthy. These results are  
37 important for two reasons. The first, as pointed out by the authors, is that  
38 temporal correlations between neural firing and movement related variables,  
39 such as EMG, do not prove that there is a causal relation between the two, as  
40 this relation could be controlled by the monkeys. The second reason has to do  
41 with the brain machine interface. This work indicates that the individual has the  
42 ability to change their neural output from the motor control system, and thus  
43 the user of a brain machine interface may be able to control the system even if  
44 the translation of neural activity to say robotic motion is less than perfect.  
45

01 Let's take a look back at the equilibrium point hypothesis using elbow  
02 movement in the monkey. Polit and Bizzi trained monkeys to make elbow  
03 movements in the horizontal plane to visual targets without vision of their  
04 arms (Polit and Bizzi 1979). The monkeys sat in a primate chair with their  
05 right forearm placed in a splint, which was then attached to a one degree of  
06 freedom robotic manipulandum that could move in the horizontal plane. This  
07 manipulandum was used to track the monkeys elbow angle to determine the  
08 precision of his pointing. After the monkeys mastered this pointing task they  
09 were deafferented, that is, the dorsal roots of the spinal cord that receive  
10 proprioceptive and cutaneous input from the arm and hand were surgically  
11 cut (Polit and Bizzi 1979). Even though these monkeys had no somatosensory  
12 feedback from their arms to their spinal cord they could still make these  
13 targeted movements, but only while making movements that they had been  
14 extensively trained on. If the initial arm configuration was different from that  
15 used during training the monkey would make systematic reaching errors. Errors  
16 were also induced if a constant torque was produced by the manipulandum.  
17 However, short pulse torque perturbations just before movement onset did not  
18 fully impair the deafferented animal's ability to make successful movements.  
19 Intact animals had no difficulties compensating for each of the above perturba-  
20 tions. One can interpret these results to mean that the monkeys could use  
21 feedforward control to make well practiced reaching movements, and the  
22 passive properties of the musculoskeletal system are resistant to some perturba-  
23 tion before movement. However, if a constant perturbation interferes with the  
24 feedforward plan sensory feedback information is necessary. These results were  
25 taken as evidence of the equilibrium point hypothesis, and later work by  
26 Giszter, Mussa-Ivaldi and Bizzi demonstrated equilibrium points that could  
27 be produced by stimulating electrically in the frog's spinal cord, thus there may  
28 be a spinal mechanism for maintaining such point (Giszter et al. 1993). More  
29 recently such equilibrium points or postures have been found by using electrical  
30 stimulation of the motor and pre-motor cortex (Graziano et al. 2002).

31 In 1990 Alexander and Crutcher published a series of three papers focused  
32 on M1, SMA and the putamen that addressed the neural representation of the  
33 intended direction of movement, muscle patterns and the visual target of elbow  
34 movements in the primate (Alexander and Crutcher 1990b; Alexander and  
35 Crutcher 1990a; Crutcher and Alexander 1990). In this work the monkey  
36 made visually guided elbow flexions and extensions with and without constant  
37 torque loads. In addition, some experiments dissociated the visual feedback  
38 from the actual arm movement such that they were in opposite directions. As  
39 this was a delayed movement task they could also quantify the number of  
40 neurons from each area that had preparatory activity as well as movement  
41 dependant activity.

42 Alexander and Crutcher found that each of the motor areas tested had  
43 activity during the preparatory period, that is during the motor planning, as  
44 well as during the movement period. The directionally tuned preparatory activ-  
45 ity was either related to the visual information, regardless of the actual arm

01 movement made, which they called target-dependant cells, or they represented  
02 the actual arm movement, in which case they were termed limb-dependent.  
03 There were approximately equal numbers of preparatory target-dependant  
04 cells in the three brain regions, while the SMA had more preparatory limb-  
05 dependent cells (40%) as compared to M1 (15%) and the putamen (9%). Along  
06 with these two types of preparatory neural activity there were also the same two  
07 types of movement related neural activity, which are target-dependant and  
08 limb-dependant activity during the elbow movement time. The majority of  
09 these movement related neurons were limb-dependant with 71% in M1, 65%  
10 in SMA and 14% in the putamen. As the authors point out, these results  
11 indicate that there is a good deal of parallel processing occurring within the  
12 motor control system, and the activation patterns do not support a serial  
13 passing of information from one region to the next. In general, there were  
14 differences in the mean and median peri movement and peri cue activity  
15 between the brain regions, such that the neural activity occurred earlier in the  
16 SMA then M1 and last in the putamen. However, the distributions of neural  
17 activity around the onset of movement for each region spanned both positive  
18 and negative time lags, that is they could be preparatory (motor planning, or  
19 sensory expectation), or sensory/feedback like. Each of these three areas also  
20 had neurons with short latency proprioceptive like responses and muscle like  
21 responses that represented the different torque loads, with these activities being  
22 more prevalent in M1.  
23  
24  
25

### 26 **11.3.3 Whole arm Movements**

28 Over the past two decades and into the present a group of researchers led by, or  
29 former students and post-docs of, Apostolus Georgopoulos have contributed  
30 tremendously to our current options on the motor control system. In **1982**  
31 Georgopoulos et al. reported that the neural activity of about 39% of M1  
32 cells (323 cells out of 606) changed their neural firing in a direction dependant  
33 manner, and that this relationship between the direction of movement and the  
34 cells rate of activity could be accounted for via a cosine function. The beha-  
35 vioral paradigm utilized was a center out reaching task (2D) performed while  
36 the monkeys held the handle of a planar manipulandum. An important idea  
37 that comes out of this work is that the motor cortex has a distribution of  
38 neurons that code for the direction of movement in a smooth manner, with  
39 each cell having a preferred movement direction that it fires most in with this  
40 firing rate dropping off smoothly via a cosine function of the difference between  
41 the current movement direction  $\theta_d$  and the cells preferred direction  $\theta_{pd}$ , such  
42 that  $F(d) = b_o + c_1 \cos(\theta_d - \theta_{pd})$ , where F is the neural firing rate, d the current  
43 direction of motion,  $b_o$  the mean firing rate,  $c_1$  a gain factor and pd stands for  
44 the cells preferred direction (Georgopoulos et al. 1982). Similar neural tuning  
45

01 was subsequently shown when the monkey held its hand in a static posture at  
02 each of the outer targets in the center out paradigm (Georgopoulos et al. 1984).

03 In 1986 this cosine tuning idea was taken to the population level, that is, how  
04 can neurons with broad tuning curves specify accurately a movement to a given  
05 direction in 3D space? A solution to this problem was termed the population  
06 vector (Georgopoulos et al. 1986). In essence what the population vector  
07 formalism states is that each of the directionally selective M1 neurons con-  
08 tributes information about the current movement direction. The information  
09 from all of these cells is summed to form an accurate prediction of the actual  
10 movement direction to be made, or that is being made. The amount of informa-  
11 tion added to the sum by each cell is dependant on that cells preferred direction  
12 and the direction of the movement being planed, or made, following the afore-  
13 mentioned cosine directional tuning. John Kalaska et al. combined the center  
14 out reaching task (Georgopoulos et al. 1982) with a loaded manipulandum that  
15 could pull the monkeys hand/arm in eight different directions. Thus they could  
16 now determine the neural correlations to both movement direction as well as  
17 load direction. They found that shoulder joint related M1 neurons could have  
18 both a preferred movement direction as well as a preferred load direction, which  
19 they called the cells load axis (Kalaska et al. 1989). Almost ten years later  
20 prudd'home and Kalaska presented similar types of neural activity in S1 to  
21 load direction, as noted above for M1, but this S1 activity was less robust in its  
22 response to the loads during the target hold time. Area 5 of the parietal cortex  
23 demonstrated no appreciable load dependant activity (Prud'homme and  
24 Kalaska 1994; Hamel-Paquet et al. 2006).

25 In an effort to determine if arm orientation could influence the neural  
26 representation during reaching movements, Stephen Scott and John Kalaska  
27 had monkeys make these center out reaching movements using either a natural  
28 arm orientation, or an abducted orientation while holding a manipulandum.  
29 They found that a large portion of cells changed their activity from the one  
30 posture to the other, either in their tonic activity, the directional tuning as  
31 reviewed above, or both. These changes were seen during the movement time  
32 as well as during the postural maintenance of the target hold period (Scott and  
33 Kalaska 1995; Scott and Kalaska 1997; Scott et al. 1997). These researchers  
34 showed that during these two different postures the population vector pointed  
35 in different directions, and thus the motor cortex dose not simply represent the  
36 spatial trajectory of the hand, but includes at least some information on the arm  
37 orientation, and from the previously reviewed results, some representation of  
38 force, and proprioception.

39 The above work involved primates grasping and moving a manipulandum  
40 and thus any loads generated via the manipulandum had to be represented at  
41 the handle. To overcome this situation and test the force related neural activity  
42 at the shoulder and elbow during reaching movements Stephen Scott intro-  
43 duced the use of an exoskeletal robotic manipulandum (KINARM). It was  
44 noted that equal numbers of M1 neurons were sensitive to torques applied via  
45 the KINARM to the shoulder, elbow, or both, and most cells were related to

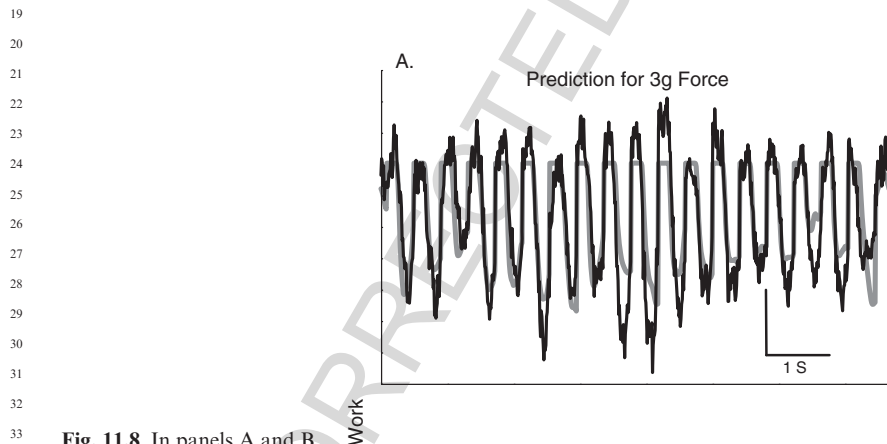
01 flexor torques at one joint and extensor torques at the other. Also, the neural  
02 activity to combined shoulder and elbow torques was predictable based on the  
03 neurons response to the two individual torques via a vector sum (Cabel et al.  
04 2001). A second paper from this group in 2001 showed systematic discrepancies  
05 between the M1 population vector's prediction of hand direction and the actual  
06 hand direction, and that these discrepancies were due to a non-uniform dis-  
07 tribution of preferred directions in the M1 population. Furthermore, the non  
08 uniform distribution could be related to the peak joint power at the shoulder  
09 and elbow.

10 As should be clear by now, researchers are steadily finding new correlations  
11 between movement related variables and neural activity in the motor cortex, as  
12 well as other movement related brain regions in the primate.

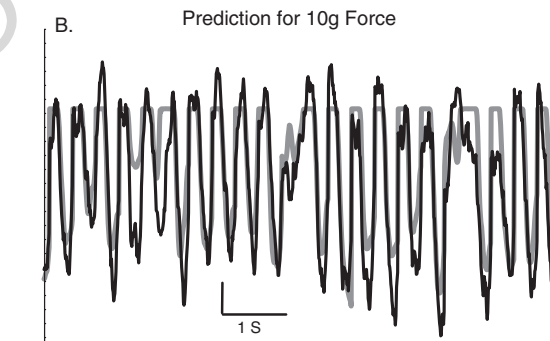
13 As primate research is fairly expensive and it takes a great deal of time and  
14 effort to train monkeys, one might wish to conduct some of this motor control  
15 research on rodents, and indeed much has been done in the realm of reaching  
16 movements (Whishaw and Pellis 1990; Whishaw et al. 1991; Whishaw 1996;  
17 Ballermann et al. 2000; Kargo and Nitz 2003; Kargo and Nitz 2004). However,  
18 most of this work involved rats reaching for food pellets and did not separate  
19 kinematic and dynamic related variables. In a recent set of papers I have  
20 introduced a simple torque manipulandum reaching task for rats (Francis and  
21 Chapin 2004; Francis and Chapin 2006). Unlike previous rat lever paradigms  
22 where the rat can simply step on a lever with its fore paw, this task requires the  
23 rat to actually grasp the manipulandum handle and pull or push it to a specific  
24 target position within a given time window, which they learn to do within an  
25 hour. Once the rats had practiced making reaching movements for a week or so  
26 they were implanted with arrays of recording electrodes in their sensory and  
27 motor cortex as well as the proprioceptive thalamus rVPL (Francis et al. 2008).  
28 I was then able to use the simultaneously recorded neural activity from these  
29 brain regions to predict the time varying position, work and force produced by  
30 the rat at the hand. This work has helped close the gap between a simple rat  
31 model and the primate motor control experiments that I have reviewed. I plan  
32 to take this paradigm into three dimensional movements in the near future.  
33 There are some interesting differences between the rat and the primate, the most  
34 obvious is that we are heavily dependant on our vision for determining targets  
35 of interest and while making reaching movements. However, rats most likely  
36 cannot see their hands in a large portion of their personal workspace. It has  
37 been suggested that rats mainly use olfaction for determining the target of  
38 reaching targets. In my manipulandum task it appears as though the rats are  
39 using both olfaction and to a large extent their whiskers to "see" the handle  
40 within their whisker field. Unlike a the food pellet reaching task for the rat,  
41 which places the food item outside the animals whisker field, the manipulan-  
42 dum on the other hand is in the animals workspace, so if it wishes it can sniff,  
43 lick, bite or grasp the handle. Their first instinct is to bite it, but this can be easily  
44 overcome by only allowing the manipulandum to be moved when they grasp it  
45 with their hand (for details see (Francis and Chapin 2004)).

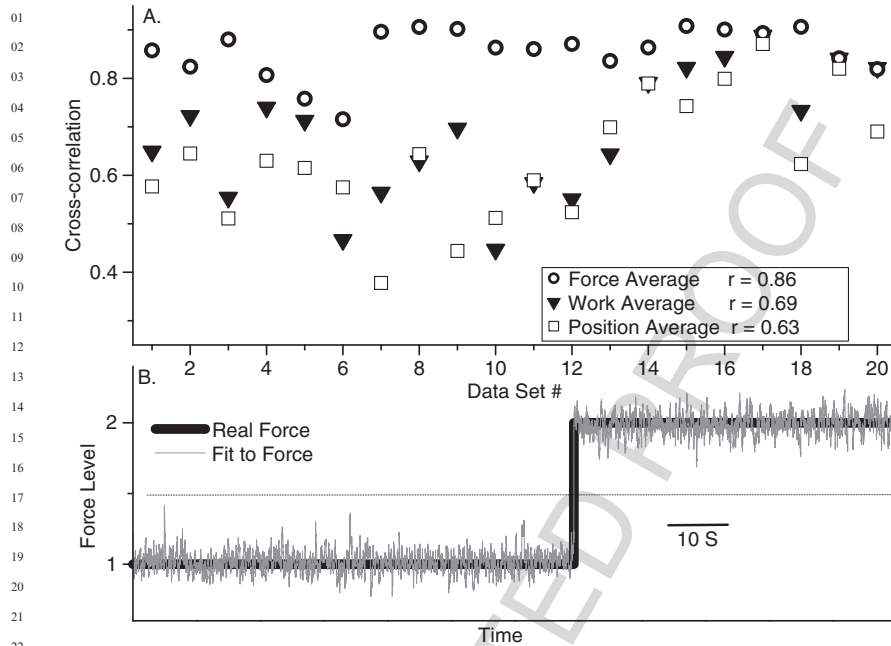
01 An important concept that I have been probing with these rat experi-  
 02 ments, and in companion primate experiments, is the degree of generaliza-  
 03 tion we can determine between reaching movements made in different  
 04 dynamical environments (Donchin et al. 2003; Francis 2007). This work  
 05 will be necessary for developing a neural controlled prosthetic arm, so as  
 06 to allow the user the ability to control their force output when picking up  
 07 novel objects etc. . . I have found that as long as I train my neural decoding  
 08 algorithms on a large enough sampling of force related state space that I can  
 09 then accurately predict the position, work, and force being produced by the  
 10 rat, even if they are working against loads not used for building the decoding  
 11 model. In Fig. 11.8A. I have plotted the variable work (force \* displacement)  
 12 during these rat reaching movements against two different constant loads,  
 13 one of 3 g and the other 10 g, also plotted are the neural predictions of the  
 14 work. Fig. 11.8. B. shows the two different forces used as well as the neural  
 15 prediction of them.

16 In Fig. 11.9A. I have plotted the cross correlation between the neural pre-  
 17 diction of the labeled movement related variable's and the actual variables  
 18 values for each data set from several animals (Francis and Chapin 2006).  
 19



33 **Fig. 11.8** In panels A and B we have plotted the work  
 34 needed to move the  
 35 manipulandum in *gray* and  
 36 the regression model  
 37 prediction from the neural  
 38 data in *black*. Note scale  
 39 differences between A and  
 40 B. The prediction to the  
 41 work variable was  $r = 0.89$   
 42 and  $r = 0.87$  for prediction  
 43 of the position variable (data  
 44 not shown). (From (Francis  
 45 and Chapin 2006) with  
 permission)





**Fig. 11.9** In panel A we have plotted the cross correlation values between each of the three variables of interest's real values and those for the predictions of the models. In panel B we have plotted the real force state produced by the manipulandum as a binomial variable of either 1 or 2 as well as the model's fit to this data. (From (Francis and Chapin 2006) with permission)

Below this plot in Fig. 11.9B is an example of the neural prediction to the force variable during this two force rat reaching paradigm, which was run as a block paradigm. For presentation purposes I have aligned all of the low force time bins to the left and the high force time bins to the right, even though they were presented in random blocks (Francis and Chapin 2006). To date I have had rats work against 6 different force loads in one experimental session, including 2 constant loads, 2 velocity dependant loads and 2 spring-like loads to allow the dissociation between kinematic and dynamic variables with similar results to those presented in Fig. 11.8, which are being prepared for publication. I believe that this experimental strategy should allow us to produce a BMI that gives the user control over both positional and force related variables. We are also starting to use the BMI as an experimental tool to ask questions about the neural representation of movement related variables by allowing the animal direct neural control over different types of variables in order to see which ones they are best at transferring to. The BMI is most likely the next great experimental paradigm that will lead to an explosion of new ideas.



## 11.4 The Brain Machine Interface as a Tool for Motor Control Research

In 1999 a group of researchers led by John Chapin demonstrated that they could record neural ensemble activity, using arrays of microwire electrodes, from the rat sensory-motor cortex, as well as the VL thalamus, and formed a set of mathematical models that would predict the position of a lever being pressed by the rat, which caused a robotic system to deliver a water reward. After the prediction of the models was sound the animal was transitioned to brain control at which time the neural ensemble activity was controlling the robotic motion. After continued practice in brain control mode the animals decreased the number of, or stopped making overt movements, a phenomenon seen by other research teams (Serruya et al. 2002; Carmena et al. 2003). In 2000 a group led by Miguel Nicolelis took the BMI from the rat and implemented it with non-human primates in an open loop paradigm (Wessberg et al. 2000) where they translated neural activity from 3-D reaching movements into 3-D robotic motion. They found very similar results using simple linear models and artificial neural networks, and noted that they needed to continually update their models, otherwise the open loop prediction and robotic control would deteriorate over time.

In 2002 two research teams published results demonstrating that monkeys could use a closed loop BMI, or BMic, in order to control a computer cursor (Serruya et al. 2002; Taylor et al. 2002) in 2 or 3 dimensional reaching movements. There are some important differences between these two papers. The group of Taylor, Helms Tillery and Schwartz used a modified population vector algorithm (Georgopoulos et al. 1986) with the closed loop result of poor initial control by the animals, so much so they found the results were just as good if they started their incrementally updating algorithm with random weights. This may be due to the fact that the population vector formalism makes certain assumptions about just what the sensory-motor cortices are coding (Georgopoulos et al. 1982; Kalaska et al. 1983; Moran and Schwartz 1999a; Schwartz and Moran 1999). However, after the algorithm had time to update they obtained impressive results. The second group of researchers led by John Donoghue did not make assumptions about the neural code, or at least did not use the assumptions made in the population vector algorithm, but rather used a simple linear regression fitting the neural activity to kinematic endpoint variables such as hand position with good results from the beginning of brain control. However, neither group incorporated the control of force related variables, or of an actual robotic system.

In 2003 the group led by Miguel Nicolelis expanded their earlier work with some important additions. Jose Carmena et al. incorporated a reach to grasp task with a robotic system that the monkey could control in a closed loop manner by moving a cursor on a computer screen that coded for the grip force as the size of the cursor, that is it would increase in size with grip strength

01 output. This was the first time that force was explicitly introduced into a BMI  
02 with successful results using simple linear models (Carmena et al. 2003). How-  
03 ever, in this work the animal did not have control over the forces that moved the  
04 robotic system, or cursor. In the above cases the monkeys did not actively  
05 interact with the robotic system either.

06 Recently the group led by Andrew Schwartz has demonstrated that a mon-  
07 key can use an anthropomorphic robotic arm that was positioned at the animals  
08 shoulder, so that it acted like the monkeys own arm, to retrieve food items and  
09 bring them to the monkey's mouth indicating the possibilities of BMic  
10 (Schwartz et al. 2006). Once again the monkey did not have control over the  
11 forces of the robot, but this was the first demonstration of a monkey actually  
12 interacting with a robotic system in order to achieve a natural goal with a BMic.

13 In 2004 we witnessed two highly publicized instantiations of BMIs in  
14 humans. The group led by Miguel Nicolelis used arrays of 32 electrodes that  
15 were driven into the thalamus (VOP/VIM or STN). The subjects then interacted  
16 with a "video game" in which they had to hold a squeeze ball and produce a  
17 given force via squeezing the ball, not that dissimilar to one of the force tasks  
18 performed by the monkeys in the Carmena paper. However, in this work they  
19 could only record a given site for 5 min, do to the fact that this work was done  
20 during DBS implantation surgeries, limiting the amount of data used for fitting  
21 and subsequent time for prediction. This work furthered research that has been  
22 conducted by PR Kennedy who demonstrated the capacity for a BMI/BCI  
23 using a neurotrophic electrode (Kennedy et al. 2000). The group led by John  
24 Donoghue benefited from an electrode array consisting of 100 contact points  
25 that had been developed by Richard Norman's group (Campbell et al. 1989;  
26 Campbell et al. 1990) that has been approved for human implantation. Using  
27 this system the Cyberkinetics company implanted a paralyzed individual who  
28 could use his neural activity to play video games as well as operate a TV and  
29 computer cursor, which has been covered in the popular press. Although this  
30 work did not incorporate robotic motion or dynamics it certainly has pushed  
31 forward the BMI/BCI capacity in humans and hopefully will help perfect the  
32 surgical implantation of such electrode arrays. This work also demonstrates  
33 that the motor areas of a paralyzed individual can still be used to control at least  
34 kinematic variables such as cursor position.

## 35 36 37 38 **11.5 Conclusion and Perspective**

39  
40 As we have seen the neural activity in the movement related brain regions  
41 appear to represent more than one simple variable, with regions around the  
42 central sulcus having both kinematic and dynamic like representations (PMd,  
43 PMv, SMA, M1, 3a, 3b, 1 and 2). The timing of this movement related activity  
44 has different distributions between many of the sensory motor control regions,  
45 however, several of these regions do have some activity before initiation of

01 movement, during movement, and even postural aspects that remain after  
02 movement, such as a direction dependant hysteresis (Prud'homme and Kalaska  
03 1994). In a recent paper it has been suggest that we look for the representation  
04 of spatiotemporal movement related variables, such as preferred pathlets rather  
05 than the preferred direction, or any other instantaneous representation, which  
06 may prove fruitful (Hatsopoulos et al. 2007).

07 Over the past few years we have seen an explosion in the number of publica-  
08 tions on brain machine interfacing (BMI), and it should now be apparent  
09 that such technology can be used to ask fundamental questions about the  
10 sensory motor control system. By giving animals and humans real time neural  
11 control over different movement related variables while having a robotic system  
12 directly move the subjects arm, or simply allowing their neural activity to move  
13 a visual cursor, we may be able to further tease apart just what the different  
14 brain regions are computing during the different stages involved in motor  
15 control. In essence one can think of the BMI as the evolution of the robotic  
16 manipulandum.

17  
18 **Acknowledgments** I would like to thank John Chapin for helpful discussions over the years.  
19 I would also like to acknowledge my funding sources. The national academies Keck futures  
20 initiative #SP09, The New York State Spinal cord injury research program #C0022048, and  
21 the State of New York Downstate medical center Dean's initiative grant.

## 22 23 24 **References**

- 25  
26 Ajemian R, Bullock D, Grossberg S (2000) Kinematic coordinates in which motor cortical  
27 cells encode movement direction. *J Neurophysiol* 84: 2191–2203
- 28 Ajemian R, Bullock D, Grossberg S (2001) A model of movement coordinates in the motor  
29 cortex: posture-dependent changes in the gain and direction of single cell tuning curves.  
30 *Cereb Cortex* 11: 1124–1135
- 31 Alexander GE, Crutcher MD (1990a) Neural representations of the target (goal) of visually  
32 guided arm movements in three motor areas of the monkey. *J Neurophysiol* 64: 164–178
- 33 Alexander GE, Crutcher MD (1990b) Preparation for movement: neural representations of  
34 intended direction in three motor areas of the monkey. *J Neurophysiol* 64: 133–150
- 35 Andersen RA, Essick GK, Siegel RM (1985) Encoding of spatial location by posterior parietal  
36 neurons. *Science* 230: 456–458
- 37 Angel A, Clarke KA (1975) An analysis of the representation of the forelimb in the ventro-  
38 basal thalamic complex of the albino rat. *J Physiol* 249: 399–423
- 39 Arshavsky YI, Berkinblit MB, Fukson OI, Gelfand IM, Orlovsky GN (1972a) Origin of  
40 modulation in neurones of the ventral spinocerebellar tract during locomotion. *Brain Res*  
41 43: 276–279
- 42 Arshavsky YI, Berkinblit MB, Fukson OI, Gelfand IM, Orlovsky GN (1972b) Recordings of  
43 neurones of the dorsal spinocerebellar tract during evoked locomotion. *Brain Res* 43:  
44 272–275
- 45 Ashe J (1997) Force and the motor cortex. *Behav Brain Res* 87: 255–269
- Ballermann M, Tompkins G, Whishaw IQ (2000) Skilled forelimb reaching for pasta guided  
by tactile input in the rat as measured by accuracy, spatial adjustments, and force. *Behav*  
*Brain Res* 109: 49–57

- 01 Battaglia-Mayer A, Ferraina S, Mitsuda T, Marconi B, Genovesio A, Onorati P, Lacquaniti F,  
02 Caminiti R (2000) Early coding of reaching in the parietooccipital cortex. *J Neurophysiol* 83:  
2374–2391
- 03 Bosco G, Eian J, Poppele RE (2005) Kinematic and non-kinematic signals transmitted to the  
04 cat cerebellum during passive treadmill stepping. *Exp Brain Res* 167: 394–403
- 05 Bosco G, Eian J, Poppele RE (2006) Phase-specific sensory representations in spinocerebellar  
06 activity during stepping: evidence for a hybrid kinematic/kinetic framework. *Exp Brain*  
07 *Res* 175: 83–96
- 08 Bosco G, Poppele RE (2000) Reference frames for spinal proprioception: kinematics based or  
kinetics based? *J Neurophysiol* 83: 2946–2955
- 09 Bosco G, Poppele RE (2001) Proprioception from a spinocerebellar perspective. *Physiol Rev*  
10 81: 539–568
- 11 Bosco G, Poppele RE (2003) Modulation of dorsal spinocerebellar responses to limb move-  
12 ment. II. Effect of sensory input. *J Neurophysiol* 90: 3372–3383
- 13 Buneo CA, Jarvis MR, Batista AP, Andersen RA (2002) Direct visuomotor transformations  
for reaching. *Nature* 416: 632–636
- 14 Burgess PR, Clark FJ (1969) Characteristics of knee joint receptors in the cat. *J Physiol* 203:  
15 317–335
- 16 Cabel DW, Cisek P, Scott SH (2001) Neural activity in primary motor cortex related to  
17 mechanical loads applied to the shoulder and elbow during a postural task. *J Neurophysiol*  
18 86: 2102–2108
- 19 Campbell PK, Jones KE, Normann RA (1990) A 100 electrode intracortical array: structural  
variability. *Biomed Sci Instrum* 26: 161–165
- 20 Campbell PK, Normann RA, Horch KW, Stensaas SS (1989) A chronic intracortical elec-  
21 trode array: preliminary results. *J Biomed Mater Res* 23: 245–259
- 22 Carmena JM, Lebedev MA, Crist RE, O’Doherty JE, Santucci DM, Dimitrov DF, Patil PG,  
23 Henriquez CS, Nicolelis MA (2003) Learning to control a brain-machine interface for  
24 reaching and grasping by primates. *PLoS Biol* 1: E42
- 25 Casabona A, Valle MS, Bosco G, Garifoli A, Lombardo SA, Perciavalle V (2003) Anisotropic  
26 representation of forelimb position in the cerebellar cortex and nucleus interpositus of the  
rat. *Brain Res* 972: 127–136
- 27 Casabona A, Valle MS, Bosco G, Perciavalle V (2004) Cerebellar encoding of limb position.  
28 *Cerebellum* 3: 172–177
- 29 Cheney PD, Fetz EE (1980) Functional classes of primate corticomotoneuronal cells and their  
relation to active force. *J Neurophysiol* 44: 773–791
- 30 Clark FJ, Burgess PR (1975) Slowly adapting receptors in cat knee joint: can they signal joint  
31 angle? *J Neurophysiol* 38: 1448–1463
- 32 Craig AD (2006) Retrograde analyses of spinothalamic projections in the macaque monkey:  
33 input to ventral posterior nuclei. *J Comp Neurol* 499: 965–978
- 34 Craig AD, Bushnell MC, Zhang ET, Blomqvist A (1994) A thalamic nucleus specific for pain  
35 and temperature sensation. *Nature* 372: 770–773
- 36 Craig AD, Zhang ET (2006) Retrograde analyses of spinothalamic projections in the macaque  
37 monkey: input to posterolateral thalamus. *J Comp Neurol* 499: 953–964
- 38 Crammond DJ, Kalaska JF (1996) Differential relation of discharge in primary motor cortex  
39 and premotor cortex to movements versus actively maintained postures during a reaching  
task. *Exp Brain Res* 108: 45–61
- 40 Crutcher MD, Alexander GE (1990) Movement-related neuronal activity selectively coding either  
41 direction or muscle pattern in three motor areas of the monkey. *J Neurophysiol* 64: 151–163
- 42 Donchin O, Francis JT, Shadmehr R (2003) Quantifying generalization from trial-by-trial  
43 behavior of adaptive systems that learn with basis functions: theory and experiments in  
human motor control. *J Neurosci* 23: 9032–9045
- 44 Dykes RW, Sur M, Merzenich MM, Kaas JH, Nelson RJ (1981) Regional segregation of  
45 neurons responding to quickly adapting, slowly adapting, deep and Pacinian receptors

11 The Neural Representation of Kinematics and Dynamics in Multiple Brain Regions 243

- 01 within thalamic ventroposterior lateral and ventroposterior inferior nuclei in the squirrel  
02 monkey (*Saimiri sciureus*). *Neuroscience* 6: 1687–1692
- 03 Evarts EV (1965) Relation of Discharge Frequency to Conduction Velocity in Pyramidal  
04 Tract Neurons. *J Neurophysiol* 28: 216–228
- 05 Evarts EV (1966) Pyramidal tract activity associated with a conditioned hand movement in  
06 the monkey. *J Neurophysiol* 29: 1011–1027
- 07 Evarts EV (1968) Relation of pyramidal tract activity to force exerted during voluntary  
08 movement. *J Neurophysiol* 31: 14–27
- 09 Evarts EV (1969) Activity of pyramidal tract neurons during postural fixation. *J Neurophy-*  
10 *siol* 32: 375–385
- 11 Feldman AG (1966) Functional tuning of the nervous system with control of movement or  
12 maintenance of a steady posture-II. COntrollable parameters of the muscles. *Biofizika* 11:  
13 565–578
- 14 Ferrell WR, Gandevia SC, McCloskey DI (1987) The role of joint receptors in human  
15 kinaesthesia when intramuscular receptors cannot contribute. *J Physiol* 386: 63–71
- 16 Fetz EE, Finocchio DV (1971) Operant conditioning of specific patterns of neural and  
17 muscular activity. *Science* 174: 431–435
- 18 Francis JT (2007) Error generalization as a function of velocity and duration: human reaching  
19 movements. *Exp Brain Res*
- 20 **AQ1** Francis JT, Chapin JK (2004) Force field apparatus for investigating movement control in  
21 small animals. *IEEE Trans Biomed Eng* 51: 963–965
- 22 Francis JT, Chapin JK (2006) Neural Ensemble Activity From Multiple Brain Regions  
23 Predicts Kinematic and Dynamic Variables in a Multiple Force Field Reaching Task.  
24 *IEEE Trans Neural Syst Rehabil Eng* 14
- 25 **AQ2** Francis JT, Xu S, Chapin JK (2008) Proprioceptive and Cutaneous Representations of the  
26 Rat Ventral Posterolateral (VPL) Thalamus. *J Neurophysiol*
- 27 **AQ3** Garraghty PE, Florence SL, Kaas JH (1990a) Ablations of areas 3a and 3b of monkey  
28 somatosensory cortex abolish cutaneous responsivity in area 1. *Brain Res* 528: 165–169
- 29 Garraghty PE, Pons TP, Kaas JH (1990b) Ablations of areas 3b (SI proper) and 3a of  
30 somatosensory cortex in marmosets deactivate the second and parietal ventral somato-  
31 sensory areas. *Somatosens Mot Res* 7: 125–135
- 32 Gauriau C, Bernard JF (2004) A comparative reappraisal of projections from the superficial  
33 laminae of the dorsal horn in the rat: The forebrain. *J Comp Neurol* 468: 24–56
- 34 Georgopoulos AP, Caminiti R, Kalaska JF (1984) Static spatial effects in motor cortex and  
35 area 5: quantitative relations in a two-dimensional space. *Exp Brain Res* 54: 446–454
- 36 Georgopoulos AP, Kalaska JF, Caminiti R, Massey JT (1982) On the relations between the  
37 direction of two-dimensional arm movements and cell discharge in primate motor cortex.  
38 *J Neurosci* 2: 1527–1537
- 39 Georgopoulos AP, Kalaska JF, Caminiti R, Massey JT (1983) Interruption of motor cortical  
40 discharge subserving aimed arm movements. *Exp Brain Res* 49: 327–340
- 41 Georgopoulos AP, Schwartz AB, Kettner RE (1986) Neuronal population coding of move-  
42 ment direction. *Science* 233: 1416–1419
- 43 Ghez C, Gordon J, Ghilardi MF (1995) Impairments of reaching movements in patients  
44 without proprioception. II. Effects of visual information on accuracy. *J Neurophysiol* 73:  
45 361–372
- Giszter SF, Mussa-Ivaldi FA, Bizzi E (1993) Convergent force fields organized in the frog's  
spinal cord. *J Neurosci* 13: 467–491
- Gordon J, Ghilardi MF, Ghez C (1995) Impairments of reaching movements in patients  
without proprioception. I. Spatial errors. *J Neurophysiol* 73: 347–360
- Grant G (1962) Projection of the external cuneate nucleus onto the cerebellum in the cat: an  
experimental study using silver methods. *Exp Neurol* 5: 179–195
- Graziano MS (1999) Where is my arm? The relative role of vision and proprioception in the  
neuronal representation of limb position. *Proc Natl Acad Sci USA* 96: 10418–10421

- 01 Graziano MS, Cooke DF, Taylor CS (2000) Coding the location of the arm by sight. *Science*  
02 290: 1782–1786
- 03 Graziano MS, Taylor CS, Moore T (2002) Complex movements evoked by microstimulation  
04 of precentral cortex. *Neuron* 34: 841–851
- 05 Hamel-Paquet C, Sergio LE, Kalaska JF (2006) Parietal area 5 activity does not reflect the  
06 differential time-course of motor output kinetics during arm-reaching and isometric-force  
07 tasks. *J Neurophysiol* 95: 3353–3370
- 08 Hatsopoulos NG, Xu Q, Amit Y (2007) Encoding of movement fragments in the motor  
09 cortex. *J Neurosci* 27: 5105–5114
- 10 Kaas JH (1983) What, if anything, is SI? Organization of first somatosensory area of cortex.  
11 *Physiol Rev* 63: 206–231
- 12 Kaas JH (ed) (2007) *The Evolution of the Dorsal Thalamus in Mammals*. Elsevier
- 13 Kaas JH, Jain N, Qi H (2002) The Organization of the Somatosensory System in Primates. In:  
14 Nelson RJ (ed) *The Somatosensory System Deciphering the brain's own body image*. CRC  
15 press, Boca Raton
- 16 Kakei S, Hoffman DS, Strick PL (1999) Muscle and movement representations in the primary  
17 motor cortex. *Science* 285: 2136–2139
- 18 Kalaska JF, Caminiti R, Georgopoulos AP (1983) Cortical mechanisms related to the direc-  
19 tion of two-dimensional arm movements: relations in parietal area 5 and comparison with  
20 motor cortex. *Exp Brain Res* 51: 247–260
- 21 Kalaska JF, Cohen DA, Hyde ML, Prud'homme M (1989) A comparison of movement  
22 direction-related versus load direction-related activity in primate motor cortex, using a  
23 two-dimensional reaching task. *J Neurosci* 9: 2080–2102
- 24 Kargo WJ, Nitz DA (2003) Early skill learning is expressed through selection and tuning of  
25 cortically represented muscle synergies. *J Neurosci* 23: 11255–11269
- 26 Kargo WJ, Nitz DA (2004) Improvements in the signal-to-noise ratio of motor cortex cells  
27 distinguish early versus late phases of motor skill learning. *J Neurosci* 24: 5560–5569
- 28 Kennedy PR, Bakay RA, Moore MM, Adams K, Goldwithe J (2000) Direct control of a  
29 computer from the human central nervous system. *IEEE Trans Rehabil Eng* 8: 198–202
- 30 Kettner RE, Schwartz AB, Georgopoulos AP (1988) Primate motor cortex and free arm  
31 movements to visual targets in three-dimensional space. III. Positional gradients and  
32 population coding of movement direction from various movement origins. *J Neurosci* 8:  
33 2938–2947
- 34 Krubitzer LA, Kaas JH (1992) The somatosensory thalamus of monkeys: cortical connections  
35 and a redefinition of nuclei in marmosets. *J Comp Neurol* 319: 123–140
- 36 Kurtzer I, Herter TM, Scott SH (2005) Random change in cortical load representation  
37 suggests distinct control of posture and movement. *Nat Neurosci* 8: 498–504
- 38 Lackner JR, Dizio P (1994) Rapid adaptation to Coriolis force perturbations of arm trajec-  
39 tory. *J Neurophysiol* 72: 299–313
- 40 Li CS, Padoa-Schioppa C, Bizzi E (2001) Neuronal correlates of motor performance and  
41 motor learning in the primary motor cortex of monkeys adapting to an external force field.  
42 *Neuron* 30: 593–607
- 43 Lundberg A (1971) Function of the ventral spinocerebellar tract. A new hypothesis. *Exp Brain*  
44 *Res* 12: 317–330
- 45 Lundberg A, Weight F (1971) Functional organization of connexions to the ventral spinocer-  
bellar tract. *Exp Brain Res* 12: 295–316
- MacKay WA, Bonnet M (1990) CNV, stretch reflex and reaction time correlates of prepara-  
tion for movement direction and force. *Electroencephalogr Clin Neurophysiol* 76: 47–62
- Maier MA, Bennett KM, Hepp-Reymond MC, Lemon RN (1993) Contribution of the  
monkey corticomotoneuronal system to the control of force in precision grip. *J Neuro-  
physiol* 69: 772–785
- Moberg E (1983) The role of cutaneous afferents in position sense, kinaesthesia, and motor  
function of the hand. *Brain* 106(Pt 1): 1–19

11 The Neural Representation of Kinematics and Dynamics in Multiple Brain Regions 245

- 01 Moran DW, Schwartz AB (1999a) Motor cortical activity during drawing movements:  
02 population representation during spiral tracing. *J Neurophysiol* 82: 2693–2704
- 03 Moran DW, Schwartz AB (1999b) Motor cortical representation of speed and direction  
04 during reaching. *J Neurophysiol* 82: 2676–2692
- AQ4 04 Nolte J (2002) *The Human Brain an introduction to its functional anatomy*. Mosby
- 05 Oscarsson O, Uddenberg N (1964) Identification of a Spinocerebellar Tract Activated from  
06 Forelimb Afferents in the Cat. *Acta Physiol Scand* 62: 125–136
- 07 Polit A, Bizzi E (1979) Characteristics of motor programs underlying arm movements in  
08 monkeys. *J Neurophysiol* 42: 183–194
- 09 Proske U, Schaible HG, Schmidt RF (1988) Joint receptors and kinaesthesia. *Exp Brain Res*  
10 72: 219–224
- 11 Prud'homme MJ, Kalaska JF (1994) Proprioceptive activity in primate primary somatosen-  
12 sory cortex during active arm reaching movements. *J Neurophysiol* 72: 2280–2301
- 13 Reina GA, Moran DW, Schwartz AB (2001) On the relationship between joint  
14 angular velocity and motor cortical discharge during reaching. *J Neurophysiol* 85:  
15 2576–2589
- 16 Riehle A, MacKay WA, Requin J (1994) Are extent and force independent movement  
17 parameters? Preparation- and movement-related neuronal activity in the monkey cortex.  
18 *Exp Brain Res* 99: 56–74
- 19 Riehle A, Requin J (1995) Neuronal correlates of the specification of movement direction and  
20 force in four cortical areas of the monkey. *Behav Brain Res* 70: 1–13
- 21 Rosenbaum DA (1980) Human movement initiation: specification of arm, direction, and  
22 extent. *J Exp Psychol Gen* 109: 444–474
- 23 Rozenboym AV, Xu S, vonKraus L, Francis JT, Chapin JK (2006) Microstimulation in  
24 somatosensory thalamus elicits naturalistic responses in cortical networks. In: *Society  
25 for Neuroscience, Atlanta, Georgia*
- 26 Rozenboym AV, Xu S, vonKraus L, Semework M, Chapin JK, Francis JT (2005) Neuronal  
27 ensemble representation of cutaneous stimuli in the somatosensory cortex of awake and  
28 anaesthetized macaques. In: *Society for Neuroscience, Washington, DC*
- 29 Sacco RL, Bello JA, Traub R, Brust JC (1987) Selective proprioceptive loss from a thalamic  
30 lacunar stroke. *Stroke* 18: 1160–1163
- 31 Sarlegna F, Blouin J, Bresciani JP, Bourdin C, Vercher JL, Gauthier GM (2003) Target and  
32 hand position information in the online control of goal-directed arm movements. *Exp  
33 Brain Res* 151: 524–535
- 34 Sarlegna F, Blouin J, Vercher JL, Bresciani JP, Bourdin C, Gauthier GM (2004) Online  
35 control of the direction of rapid reaching movements. *Exp Brain Res* 157: 468–471
- 36 Scheidt RA, Conditt MA, Secco EL, Mussa-Ivaldi FA (2005) Interaction of visual and  
37 proprioceptive feedback during adaptation of human reaching movements. *J Neurophy-  
38 siol* 93: 3200–3213
- 39 Schwartz AB, Cui XT, Weber DJ, Moran DW (2006) Brain-controlled interfaces: movement  
40 restoration with neural prosthetics. *Neuron* 52: 205–220
- 41 Schwartz AB, Moran DW (1999) Motor cortical activity during drawing movements: popula-  
42 tion representation during lemniscate tracing. *J Neurophysiol* 82: 2705–2718
- 43 Scott SH, Gribble PL, Graham KM, Cabel DW (2001) Dissociation between hand motion  
44 and population vectors from neural activity in motor cortex. *Nature* 413: 161–165
- 45 Scott SH, Kalaska JF (1995) Changes in motor cortex activity during reaching movements  
with similar hand paths but different arm postures. *J Neurophysiol* 73: 2563–2567
- Scott SH, Kalaska JF (1997) Reaching movements with similar hand paths but different  
arm orientations. I. Activity of individual cells in motor cortex. *J Neurophysiol* 77:  
826–852
- Scott SH, Sergio LE, Kalaska JF (1997) Reaching movements with similar hand paths but  
different arm orientations. II. Activity of individual cells in dorsal premotor cortex and  
parietal area 5. *J Neurophysiol* 78: 2413–2426

- 01 Sergio LE, Hamel-Paquet C, Kalaska JF (2005) Motor cortex neural correlates of output  
02 kinematics and kinetics during isometric-force and arm-reaching tasks. *J Neurophysiol* 94:  
03 2353–2378
- 04 Sergio LE, Kalaska JF (1997) Systematic changes in directional tuning of motor cortex cell  
05 activity with hand location in the workspace during generation of static isometric forces in  
06 constant spatial directions. *J Neurophysiol* 78: 1170–1174
- 07 Sergio LE, Kalaska JF (2003) Systematic changes in motor cortex cell activity with arm  
08 posture during directional isometric force generation. *J Neurophysiol* 89: 212–228
- 09 Serruya MD, Hatsopoulos NG, Paninski L, Fellows MR, Donoghue JP (2002) Instant neural  
10 control of a movement signal. *Nature* 416: 141–142
- 11 Shadmehr R, Mussa-Ivaldi FA (1994) Adaptive representation of dynamics during learning  
12 of a motor task. *J Neurosci* 14: 3208–3224
- 13 Shinoda Y, Yokota J, Futami T (1981) Divergent projection of individual corticospinal axons  
14 to motoneurons of multiple muscles in the monkey. *Neurosci Lett* 23: 7–12
- 15 Sober SJ, Sabes PN (2003) Multisensory integration during motor planning. *J Neurosci* 23:  
16 6982–6992
- 17 Sober SJ, Sabes PN (2005) Flexible strategies for sensory integration during motor planning.  
18 *Nat Neurosci* 8: 490–497
- 19 Stein RB, Weber DJ, Aoyagi Y, Prochazka A, Wagenaar JB, Shoham S, Normann RA (2004)  
20 Coding of position by simultaneously recorded sensory neurones in the cat dorsal root  
21 ganglion. *J Physiol* 560: 883–896
- 22 Taira M, Boline J, Smyrnis N, Georgopoulos AP, Ashe J (1996) On the relations between  
23 single cell activity in the motor cortex and the direction and magnitude of three-dimen-  
24 sional static isometric force. *Exp Brain Res* 109: 367–376
- 25 Taylor DM, Tillery SI, Schwartz AB (2002) Direct cortical control of 3D neuroprosthetic  
26 devices. *Science* 296: 1829–1832
- 27 Thoroughman KA, Shadmehr R (2000) Learning of action through adaptive combination of  
28 motor primitives. [see comments.]. *Nature* 407: 742–747
- 29 Tillery SI, Ebner TJ, Soechting JF (1995) Task dependence of primate arm postures. *Exp*  
30 *Brain Res* 104: 1–11
- 31 Tillery SI, Soechting JF, Ebner TJ (1996) Somatosensory cortical activity in relation to arm  
32 posture: nonuniform spatial tuning. *J Neurophysiol* 76: 2423–2438
- 33 Timmermann L, Ploner M, Freund HJ, Schnitzler A (2000) Separate representations of static  
34 and dynamic touch in human somatosensory thalamus. *Neurology* 54: 2024–2026
- 35 Todorov E (2000) Direct cortical control of muscle activation in voluntary arm movements: a  
36 model. *Nat Neurosci* 3: 391–398
- 37 Valle MS, Casabona A, Bosco G, Perciavalle V (2007) Spatial anisotropy in the encoding of  
38 three-dimensional passive limb position by the spinocerebellum. *Neuroscience* 144: 783–787
- 39 Vidal F, Bonnet M, Macar F (1991) Programming response duration in a precueing reaction  
40 time paradigm. *J Mot Behav* 23: 226–234
- 41 Wann JP, Ibrahim SF (1992) Does limb proprioception drift? *Exp Brain Res* 91: 162–166
- 42 Welker WI (1973) Principles of organization of the ventrobasal complex in mammals. *Brain*  
43 *Behav Evol* 7: 253–336
- 44 Werner W, Bauswein E, Fromm C (1991) Static firing rates of premotor and primary motor  
45 cortical neurons associated with torque and joint position. *Exp Brain Res* 86: 293–302
- 46 Wessberg J, Stambaugh CR, Kralik JD, Beck PD, Laubach M, Chapin JK, Kim J, Biggs SJ,  
47 Srinivasan MA, Nicolelis MA (2000) Real-time prediction of hand trajectory by ensembles  
48 of cortical neurons in primates. *Nature* 408: 361–365
- 49 Whishaw IQ (1996) An endpoint, descriptive, and kinematic comparison of skilled reaching in  
50 mice (*Mus musculus*) with rats (*Rattus norvegicus*). *Behav Brain Res* 78: 101–111
- 51 Whishaw IQ, Pellis SM (1990) The structure of skilled forelimb reaching in the rat: a  
52 proximally driven movement with a single distal rotatory component. *Behav Brain Res*  
53 41: 49–59



11 The Neural Representation of Kinematics and Dynamics in Multiple Brain Regions 247

- 01 Whishaw IQ, Pellis SM, Gorny BP, Pellis VC (1991) The impairments in reaching and the  
02 movements of compensation in rats with motor cortex lesions: an endpoint, videorecord-  
03 ing, and movement notation analysis. *Behav Brain Res* 42: 77–91
- 04 Whishaw IQ, Tomie JA (1989) Olfaction directs skilled forelimb reaching in the rat. *Behav*  
05 *Brain Res* 32: 11–21
- 06 Wilson P, Kitchener PD, Snow PJ (1999) Cutaneous receptive field organization in the ventral  
07 posterior nucleus of the thalamus in the common marmoset. *J Neurophysiol* 82:  
08 1865–1875
- 09 Xiao J, Padoa-Schioppa C, Bizzi E (2006) Neuronal correlates of movement dynamics in the  
10 dorsal and ventral premotor area in the monkey. *Exp Brain Res* 168: 106–119
- 11 Yanai Y, Adamit N, Israel Z, Harel R, Prut Y (2008) Coordinate transformation is first  
12 completed downstream of primary motor cortex. *J Neurosci* 28: 1728–1732
- 13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45
- UNCORRECTED PROOF

01  
02  
03  
04  
05  
06  
07  
08  
09  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45

UNCORRECTED PROOF