

### **Sensation-targeted motor control: Every spike counts?**

Focus on: "Whisker movements evoked by stimulation of single motor neurons in the facial nucleus of the rat"

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Traditionally, sensory processing and motor control have been studied separately, reflecting the belief that sensory and motor streams remain independent until linked via cortical "associative" areas. Although this belief no longer dominates neuroscience, the traditional tendency to continue to study sensory processing and motor control separately is not easily overcome. Only after closely examining operation of sensory organs does one realize how important motor control is for sensation. The elegant study of Herfst and Brecht (2008) reveals how accurate sensation-targeted motor control should be in one such system - the vibrissal system.

Even a gross examination of mammalian anatomy reveals that most sensory organs are placed within rich muscular systems. In fact, seeing, touching, smelling, and tasting are enabled by complex modality-specific muscular systems. Detailed examinations of how sensations are acquired in each of these systems have revealed elaborate patterns of sensation-targeted movements of the relevant sensory organs (Ahissar and Arieli 2001; Ahissar and Knutsen 2008; Engbert 2006; Findlay and Brown 2006; Gamzu and Ahissar 2001; Mainland and Sobel 2006; Martinez-Conde et al. 2004; Murakami 2006). How these movement patterns are controlled to achieve accurate sensation is the subject of on-going research in several laboratories.

One important question on this subject concerns the resolution of motor control. The study of Herfst and Brecht (2008) provides a surprising answer – whisker movements induced by single spikes of some motoneurons (MNs) can be as small as 0.1 deg or less, and those of other MNs can be as large as 5 deg or more, with the mean over the sampled population of MNs being 1.8 deg. The existence of such large single-spike evoked movements ("twitches"), which are within the range of whisking amplitudes employed during behavior (Knutsen et al. 2005; Knutsen et al. 2006; Mitchinson et al. 2007; Towal and Hartmann 2006), implies that, when maximal accuracy is required, every spike counts.

Herfst and Brecht used a juxtacellular method (Pinault 1996) to evoke single spikes in individual MNs of the lateral facial nucleus (FN) of the anesthetized rat, and high-resolution video to measure the resulting whisker movements. They found that motor control in this system is based on a labeled-line coding scheme: each neuron is constantly linked to a specific set of movements, and each spike (if isolated in time) constantly, and reliably, evokes a well-defined twitch. The reliability with which each single-spike produced a twitch was extremely high. In their sample, the failure rate was zero, there were no false-alarms (i.e., twitches without spikes), and twitch-to-twitch amplitude variations were low.

Effects of single spikes on muscle force have been studied extensively (Burke 1967; van Eijden and Turkawski 2001), and the time course of single muscle twitches has been repeatedly described in textbooks. However, as far as we know, whether motor systems control the occurrence of single MN spikes has not yet been critically

considered. The findings of Herfst and Brecht allow a quantitative assessment of this question based on their measurements of the resulting whisker angles. Measurements of whisker angles, rather than muscle forces, allow direct comparison of motor and sensory resolutions. Such a comparison is crucial for understanding vibrissal motor control, whose target is sensory acquisition, and which allows accurate sensation via gentle active palpation (Carvell and Simons 1995; Knutsen et al. 2006; Mehta et al. 2007; Ritt et al. 2008; von Heimendahl et al. 2007). In fact, using active gentle palpation, rats can detect left versus right horizontal offsets as small as 1 deg (Knutsen et al. 2006).

How detailed should motor control be to allow 1 deg sensory resolution? In an open-loop system such a question would be meaningless – sensory resolution would only depend on the sensitivity of sensory receptors per a-priori determined motor trajectories. However, active touch is a closed-loop process. During active palpation, rats change whisking amplitudes, velocities, and durations from cycle to cycle, until an accurate perception is achieved (Knutsen et al. 2005; Knutsen et al. 2006; Mehta et al. 2007) or a minimal obstacle impingement is obtained (Mitchinson et al. 2007). In such a closed-loop system, we posit, motor resolution should be at least of the same order as sensory resolution, in order to allow the system to converge on accurate solutions. Indeed, careful tracking of whisker movements reveals whisker movements of a few degrees (at the limit of current tracking noise limitations) that appear to be controlled by the rat during localization (Knutsen et al. 2005; Knutsen et al. 2006; Mehta et al. 2007) and exploration tasks (Mitchinson et al. 2007; Towal and Hartmann 2006). Given the large range of protracting twitch amplitudes (0.12 – 5.6 deg), the identity of activated motor units is crucial. Moreover, for most vibrissal MNs the occurrence of every single spike is crucial. Thus, the vibrissal system must control the firing of these MNs on a unit-by-unit and spike-by-spike basis. An uncontrolled spike might move a whisker beyond the spatial interval to be sensed, inducing a significant sensory error.

Much of our knowledge about the neural basis of motor activation comes from research on skeletal muscles that focuses on force generation in the context of movement-targeted motor control. From these studies, the concept of “motor unit,” was defined as the set of tens to hundreds muscle fibers innervated by a single MN. Several motor unit types, which differ in the muscle fibers they contain, have been identified: slow (type 1), fast fatigue-resistant (type 2A), and fast fatigable (types 2B and 2D). During muscle contraction, motor units are often recruited according to the size principle: smaller before larger (Henneman 1985).

Utilization of the size principle in the FN might eliminate the need to maintain a detailed spike-by-spike control along vibrissal sensory-motor loops. According to one implementation of the size principle, a given input can only activate MNs whose size is smaller than a given threshold. Thus, if all MNs affiliated with a given whisker receive the same input, the resulting movement will be proportional to this input. As the input intensity increases, more (and larger) MNs will be recruited. With such a mechanism, unit-by-unit selection could be implemented, at least to some extent, by the size principle, and movement amplitude (or velocity) could be controlled by the intensity of the common input to FN sub-populations.

Since muscle fibers have only one trick – contraction – additional components in the system have to be recruited in order to return a joint or a whisker to its resting position. In most skeletal muscle systems, movement reversal is achieved via antagonistic arrangement of muscles. In contrast, in the vibrissal system, movement reversal is achieved by a balance between intrinsic muscles (one per whisker), extrinsic muscles (4 per whisker-pad), and passive tissue reactions (Dorfl 1982).

Recently, a remarkable understanding of the intricate control of whisking via the set of intrinsic and extrinsic (3 out of the 4) muscles of the whisker pad has been obtained (Hill et al. 2008). Hill et al found that during typical bouts of whisking in air, one of the extrinsic muscles (the *m. nasalis*) pulls the entire pad forward at the beginning of each whisking cycle, the intrinsic muscles of all whiskers join with a short phase lag and pull the whiskers to their maximal protracted position, and the two caudal extrinsic muscles (the *m. nasolabialis* and *m. maxillolabialis*), join with additional phase lag to initiate whisker retraction. The muscular interplay that occurs during active touch, when whiskers palpate an object, is not yet known. From Herfst and Brecht's study, it is clear that fine position control is possible in both the protraction and retraction directions. However, the high proportion of pad muscles dedicated to protraction, the high proportion of FN neurons "labeled for" protraction (Herfst and Brecht 2008; Klein and Rhoades 1985), and the tenability of protraction to environmental changes (Carvell and Simons 1990), indicate that protraction is the direction most finely controlled by the vibrissal system. This is consistent with the vibrissal system being primarily controlled for sensation, since most encounters with external objects are expected during whisker protraction

The intrinsic whisker musculature is thus the primary target of motor control in the vibrissal system. Unlike skeletal muscles, intrinsic whisker muscles consist almost exclusively of fast contractile, fast fatigable muscle fibers (Jin et al. 2004). So far, the intrinsic muscles have not been shown to contain muscle spindles, and since they are not linked to bony elements, they are not associated with any other proprioceptors. Thus, the control system of these intrinsic muscles differs from that of most skeletal muscles by not having direct proprioceptive feedback to monitor muscle state. Instead, proprioceptive information is sensed by mechanoreceptors in the whisker follicle, and fed back indirectly via "Whisking" sensory neurons (Szwed et al. 2003). Thus, the shortest control loop in the vibrissal system contains at least 3 synapses (Nguyen and Kleinfeld 2005), compared with 2 in most skeletal systems. How this difference affects control efficiency is another open question.

The range of twitch profiles characterized by Herfst and Brecht may serve as a motor alphabet of vibrissal control. The syntax that is used to compose elements of this alphabet into continuous whisking movements is not yet known. However, Herfst and Brecht's limited sample shows that this syntax is not linear in the regime of small amplitudes. In agreement with well documented studies of contraction profiles in skeletal muscles, Herfst and Brecht show that two consequent spikes do not necessarily evoke the sum of their individual movement amplitudes, and that the evoked movement depends on the inter-spike interval (Herfst and Brecht's Fig. 6C,E) (Ding et al. 2000). Understanding of temporal summation, as well as characterization of spatial summation across different motor units, will require further experiments. At the other extreme of the movement amplitude regime, it is also clear that summation of twitches cannot be linear, since as a whisker approaches its maximal protraction angle, the contribution of a given muscle contraction gradually decreases due to increased tissue resistance (Hill et al. 2008) and inability of muscles to contract below a certain length.

Unlike skeletal muscles, intrinsic vibrissal muscles are not attached to bones. Rather, each such muscle is coupled to two adjacent whisker follicles such that its contraction protracts the whiskers attached to both of them (Fig. 1) (Dorfl 1982). So is the target of a single vibrissal motor unit the anterior, posterior, or both whiskers attached to it? Herfst and Brecht show that all 3 are possible. Assuming that most of the protraction twitches are evoked via intrinsic muscles and not via the *m. nasalis* extrinsic muscle, the wide range of anterior/posterior amplitude ratios (0.15 – 4.6) indicates that motor units can primarily affect either the posterior or anterior whisker,

depending, possibly, on their position along the intrinsic muscle (Fig. 1). However, the possibility that single whisker twitches are mediated via extrinsic motor units should not be ruled out. In fact, examples of single-whisker retractions strongly suggest that the specific location of an extrinsic motor unit can be crucial in determining how many whiskers it can affect.

The vibrissal system is not the only system in which single-spike control might be important. For example, in the visual system sensory and motor resolutions also appear to be similar (Ahissar and Arieli 2001), and to be in the order of eye rotations induced by individual MN spikes (Goldberg et al. 1998). Similarly, motor-sensory loops that control gentle grasping (Flanagan et al. 1999; McDonnell et al. 2005) might also utilize single-spike resolution.

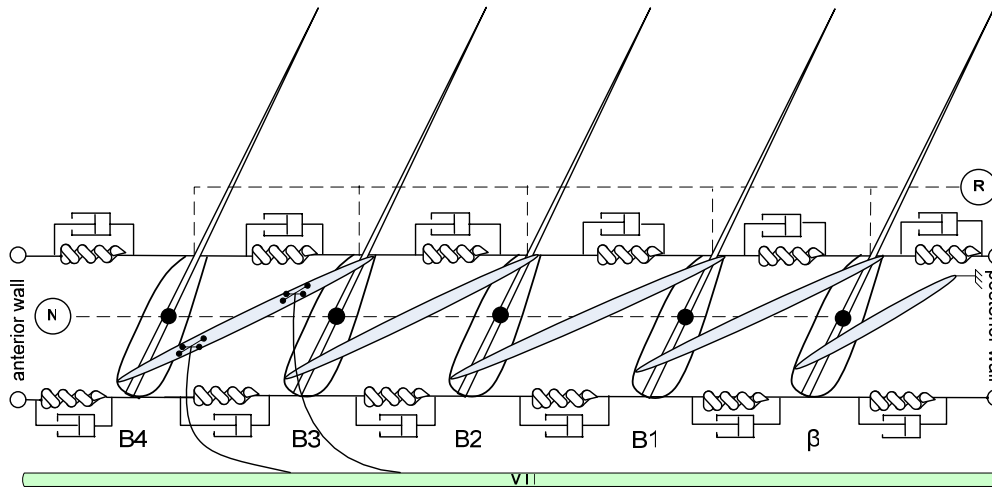
Active sensing is mediated by a complex network of parallel and nested motor-sensory-motor loops (Ahissar and Kleinfeld 2003; Kleinfeld et al. 2006; Kleinfeld et al. 1999). Whereas sensory and motor coding in first-order sensory (Szwed et al. 2003; Szwed et al. 2006) and motor (Herfst and Brecht 2008) neurons of the vibrissal system is relatively simple, coding in higher centers is more intricate (Ferezou et al. 2006; Haiss and Schwarz 2005; von Heimendahl et al. 2007). Consequently, single-cell stimulations in the motor cortex evoke more complex and less reliable whisker movements (Brecht et al. 2004). Nevertheless, the fact that short bursts of single cells in the motor cortex can eventually result in a well-defined whisker movement [and can bias rat behavior when induced in the sensory cortex (Houweling and Brecht 2008)] suggests that the contribution of single spikes, anywhere in the vibrissal system, should not be underrated.

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**Figure 1.** Schematic biomechanical diagram of one row of whiskers. The row includes five follicles (named  $\beta$ , B1-B4), muscles and visco-elastic elements, (springs and dampers) representing the elasticity of the mystacial pad. The whiskers can be moved forward by contraction of the rostral extrinsic muscle *m. nasalis* (N), rotated forward by contraction of the intrinsic muscles (grey ellipses) and retracted by contraction of the caudal extrinsic muscles *m. nasolabialis* and *m. maxillolabialis* (R). Two axons of the motor nerve (VII) are illustrated to demonstrate potential position specificity of motor units (Adapted from Hill et al. 2008 and Dorfl 1985).