Converting neural signals from place codes to rate codes

Jennifer M. Groh

Center for Cognitive Neuroscience and Department of Psychological and Brain Sciences,
6207 Moore Hall, Rm. 356, Dartmouth, Hanover, NH 03755, USA

Abstract. The nervous system uses two basic types of formats for encoding information. The parameters of many sensory (and some premotor) signals are represented by the pattern of activity among an array of neurons each of which is optimally responsive to a different parameter value. This type of code is commonly referred to as a place code. Motor commands, in contrast, use rate coding: the desired force of a muscle is specified as a monotonic function of the aggregate rate of discharge across all of its motor neurons. Generating movements based on sensory information often requires converting signals from a place code to a rate code. In this paper I discuss three possible models for how the brain does this.

1 Introduction

Sensory maps or place codes are ubiquitous throughout the brain. For information processing, several features of this style of representation are of critical importance. First, the individual neurons that make up sensory maps respond maximally to different "preferred" values of the sensory parameter being encoded, and their responses decrease if the actual stimulus either exceeds or falls short of that particular favorite parameter value. These non-monotonic response functions dictate the second key feature of sensory maps: the representation of the sensory parameter must be distributed across an array of neurons with different preferred parameter values. The discharge rate of any one neuron is ambiguous – except at the peak of the tuning curve, the same response level corresponds to at least two possible values of the sensory parameter. Thus, only by examining the responses of a population of such receptors is it possible to deduce what the stimulus actually looks, sounds, feels, smells, or tastes like. If these tuned neurons are topographically

Correspondence to: J. M. Groh
(Tel.: + 1-603-6460241, Fax: + 1-603-6461419
e-mail: jennifer.m.groh@dartmouth.edu)

organized according to their preferred parameter values, a given stimulus will evoke activity at a given site in the population, hence the term place code.

The neural representation of motor commands shares some similarities with sensory systems. Each muscle exerts force along a particular direction, and the motor neurons that control those muscles show tuning for these pulling directions. The overall direction of movement is represented by the ratio of activity in different groups of motor neurons controlling muscles with different pulling directions. However, motor commands differ from sensory maps in how the *magnitude* of the force of each muscle group is controlled. To move a body part farther or faster requires a monotonic increase in motor neuron activity. This can occur by increasing the activity level of a given set of motor neurons, by recruiting additional motor neurons, or both. It does not involve activating a completely different set of motor neurons, as is the case for place codes. Because this monotonic discharge rate can be an unambiguous signal of a parameter of interest, this type of code is commonly referred to as a rate code.

Motor commands do not have a monopoly on rate coding: the responses of sensory neurons can also vary as a monotonic function of certain sensory parameters. Visual neurons, for example, are usually tuned for the location of a visual stimulus (the receptive field), but the response can vary monotonically with the intensity of the stimulus. Indeed, the responses of many if not all sensory neurons can be influenced by more than one sensory parameter, and show place coding for some parameters and rate coding for others. I will consider these issues in more detail later, and concentrate for the moment on those individual sensory parameters that are represented through place codes. Guiding movements based on this kind of sensory information requires translation of place-coded sensory signals into rate-coded motor commands.

In this article I will discuss three models for how this place-to-rate transformation may be accomplished by the brain. I will draw heavily on examples involving oculomotor responses to sensory stimuli, but similar issues apply for more complex skeletal movements such as

reaching movements in which the body interacts with objects in space. A preliminary report of this work has been presented elsewhere (Groh 1997).

2 Methods

Simulations were conducted using Matlab (Mathworks, Natick, Mass.). Interneurons and output neurons were simulated as linear threshold units. Weights were assigned in the principled manner described in detail below. Inhibitory synapses were treated either as divisive (the weighted average model) or as multiplication by zero (the summation-saturation model, Koch 1999). The consequences of these assumptions are discussed in detail below.

3 Results

3.1 Model 1: weighted summation

The simplest way to convert place-coded signals into a rate code is to multiply the level of activity (a) of each neuron in the place code by a synaptic weight (w) that represents that neuron's preferred value, and sum the totals.

$$\text{output} = \sum_i w_i a_i \tag{1}$$

This is essentially the same calculation that computers perform when converting a binary number into a voltage level for an analog output channel. A network of neurons can perform this type of weighted summation calculation very easily (Fig. 1a).

This type of network has been proposed previously (e.g., Van Gisbergen et al. 1987; Scudder 1988; Groh and Sparks 1992; Lefevre et al. 1998), and has a certain elegant simplicity. Indeed, graded anatomical projections of the type needed to perform such a computation have been identified in the brain (Moschovakis et al. 1998). However, it also has some obvious problems. One major problem concerns what happens when there are multiple sites of activity in the place code. This situation

might arise naturally when more than one value of a sensory parameter is present. Suppose, for example, that two (or more) visual stimuli are present in the visual
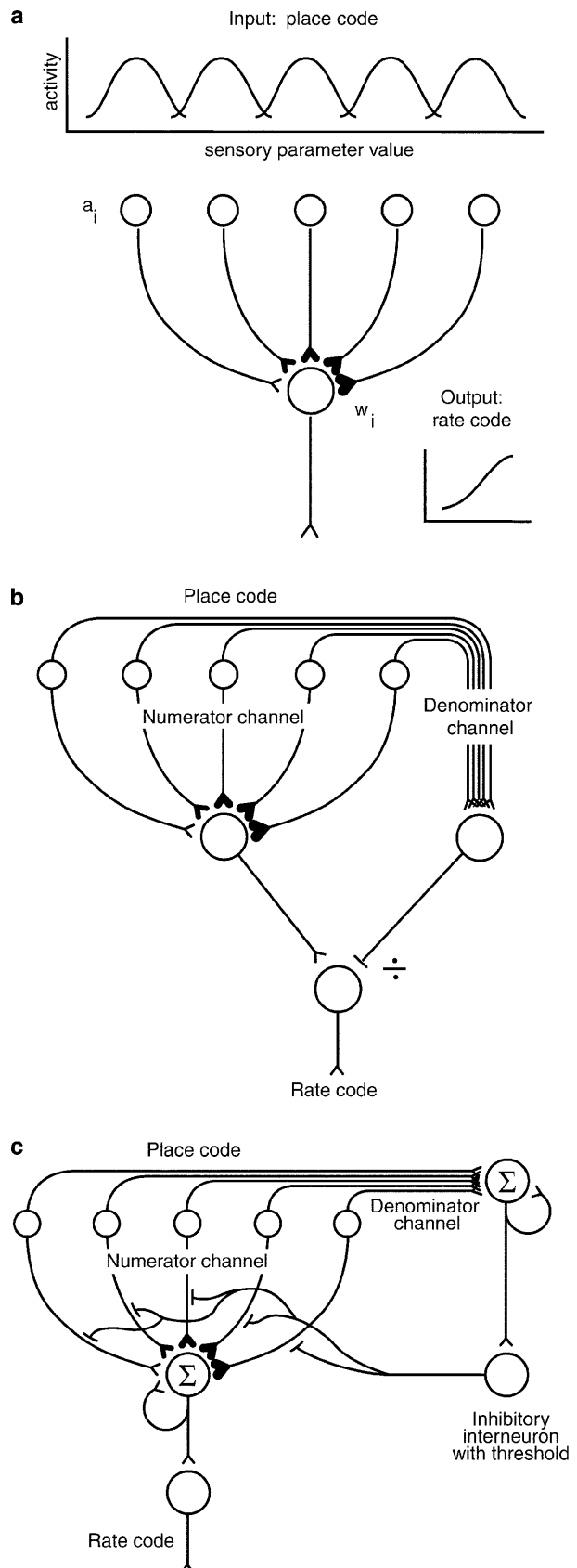

Fig. 1. **a** The weighted summation model for converting signals from a map of tuned neurons into a rate code. Each neuron in the map is tuned for a different parameter value. The synaptic weights (w_i) of the projections onto the rate code unit scale monotonically with the preferred parameter values. The rate code unit calculates the weighted sum of its inputs. **b** The weighted average model. A second set of projections with a uniform pattern of synaptic weights (*denominator channel*) is divided into the output of the first set (*numerator channel*), yielding an overall output that is normalized for the total amount of activity in the map, and corresponds to the average location of activity within the map. **c** The summation-saturation model. The activity in the numerator and denominator channels will charge up until the denominator channel reaches a certain threshold. This triggers an inhibitory neuron, which shuts off the input to the numerator channel. The numerator channel will then ignore any additional activity in the map, but will hold steady at a value that indicates the average location of the activity that occurred up until that point

scene – a situation that is obviously the rule, not the exception. Imagine that these stimuli are located at 10° and 12° to the right of fixation. A rate code can only represent one value at time, so the brain must somehow convert the two sites of activity into one. One option is to select only one of these stimuli for representation as a rate-coded signal, an algorithm known as winner-take-all. The output would correspond to either the 10° or the 12° stimulus. Another alternative would be to represent only the average location of the stimuli as a rate code, producing an output of 11°. But there is little to be gained from calculating the sum of these two values, or 22°, which represents a location far away from either of the actual stimuli. Mounting evidence from behavioral as well as microstimulation and inactivation experiments in a variety of brain areas suggests that the brain either calculates an average (Robinson 1972; Schiller et al. 1979; Findlay 1982; Lee et al. 1988; Groh et al. 1997; Nichols and Newsome 1998) or uses a winner-take-all algorithm to eliminate all but one stimulus value (Salzman and Newsome 1994), but comparatively little evidence for summation alone has been obtained.

An additional closely related problem is that neural responses are generally influenced by more than one factor. For example, as described earlier, neurons in visual areas tend to be sensitive not just to the locations of visual stimuli but also to the contrast of those stimuli relative to other visual stimuli. Suppose the activity levels (a_i) of the input neurons in the neural circuit in Fig. 1a vary as a function of the contrast of the sensory stimulus. The output of the circuit, $\sum w_i a_i$, will therefore also vary as a function of contrast, and a given output level could be produced in more than one way – by a low contrast stimulus at one location or a high contrast stimulus at another.

In short, because both the number of active sites and the level of activity at those sites can vary, a summation mechanism alone would not be sufficient to account for the translation of neural signals from maps to rate codes. Such a mechanism would produce serious errors, and experimental evidence for its existence is lacking.

3.2 Model 2: weighted averaging

An algorithm involving averaging or normalization would be consistent with most experimental findings on this question. Many models involving the read-out of neural maps propose that this is the calculation being performed (for review, see Tweed and Vilis 1990); some also suggest a specific neural architecture that accomplishes this (e.g., Bozis and Moschovakis 1998). How could this computation be performed by neural circuitry? An average differs from a sum only by a normalization factor, so a component capable of performing normalization must be added to the circuit.

$$\text{output} = \frac{\sum_i w_i a_i}{\sum_i a_i} \quad (2)$$

Figure 1b shows a new neural circuit, consisting of the same circuit shown in Fig. 1a with a normalization component added. The original circuit performs the "numerator" portion of the computation, the calculation of a weighted sum $\sum w_i a_i$. The neurons in the place code send a second set of projections that has a uniform pattern of synaptic weights. This second set of projections, the "denominator" portion of the model, calculates the total amount of activity, or $\sum a_i$. This quantity is then divided into the numerator to produce an output corresponding to the average location of activity in the place code (as indicated by the average synaptic weight of the active neurons).

An alternative model that places a normalization process within the place code itself, rather than as part of the read-out, has been proposed by several authors. In this scenario, an inhibitory process involving the lateral connections among the neurons within the sensory map effectively normalizes the pattern of activity *within* the map before it is read-out by any subsequent representations (Van Opstal and Van Gisbergen 1989; Heeger 1992; Snowden and Hammett 1992; Carandini and Heeger 1994; Carandini et al. 1997; see also Bozis and Moschovakis 1998). Under this scheme, mutual inhibitory influences between two competing sites of activity would reduce the level of activity at both, providing the normalization component of the average computation. Models of this type can calculate a weighted average by computing:

$$\text{output} = \sum_i w_i \left(\frac{a_i}{\sum_i a_i} \right) \quad (3)$$

This computation is mathematically equivalent to the one performed by the model described here, but it differs in the order in which the elements of the computation are actually carried out: the activity of each neuron is normalized *before* the weighted sum is computed.

Evidence from microstimulation experiments suggests that lateral inhibition, although it very likely contributes to normalization under certain circumstances, might not be the sole means of performing normalization for the place-to-rate transformation. Suppose that microstimulation within the place code drives individual neurons so strongly that the effects of lateral inhibitory connections are overridden – the stimulated neurons would be "clamped" at a discharge rate related primarily to the stimulation parameters. While it is not known precisely what effect microstimulation has on the stimulated neurons (but see Nowak and Bullier 1998a,b), a variety of experiments have shown that the normalization still occurs, and the output corresponds to the average location of activity. Microstimulation in concert with visual stimulation in the middle temporal visual area produces an output that corresponds to the average site of activity (Groh et al. 1997), as does stimulation at two sites within the superior colliculus (Robinson 1972) or at one site within the superior colliculus and one site within the frontal eye fields (Schiller et al. 1979). Therefore,

internal normalization via lateral inhibition seems unlikely to be the sole form of normalization, at least in the cases where this has been tested.

The downside of conducting the normalization operation in the manner used for model 2, however, is that it places a tremendous computational burden on a small number of critical synapses. Indeed, a single neuron is responsible for dividing $\sum w_i a_i$ by $\sum a_i$, because the operation of division cannot be broken up and distributed across successive stages. Although there might be multiple synapses involved to duplicate the calculation and provide greater accuracy through redundancy, the number of synapses involved in performing this operation would nevertheless probably have to be quite limited if this model is correct. This concern did not apply as severely to the first model because that model relied primarily on addition, which is a commutative operation that can easily be distributed across multiple synapses.

This limitation is worrisome, and it gets worse: the dynamic range of the synapses performing division would also have to be very large. The numerator and denominator channels could both carry a huge range of possible values that would have to be divided accurately. The inhibitory mechanisms that occur at synapses all revolve around ion species that have reversal potentials comparatively near to the resting potential of the neuron. This suggests that the range in which inhibitory interactions would have a divisive nature should be limited (Holt and Koch 1997). As soon as excitatory influences moved the membrane potential substantially away from the resting value, inhibitory influences would tend to have a subtractive nature as well (Koch and Poggio 1987).

3.3 Model 3: summation with saturation

These drawbacks suggest that it would be well worth exploring other means to accomplish this computation circumventing the need to perform precise division at inhibitory synapses. One way to achieve this goal is to substitute an equivalent computation. An alternative method of normalizing is to control how much of the overall activity from the map actually contributes to the computation. If the contributing activity were held constant, further normalization would be unnecessary. When calculating the grades of students in a class, the rank order can be determined by either averaging or summing the scores of each student on each assignment provided they have all performed the same number of assignments. The average and the sum produce an identical ranking since they differ only by a constant that is the same for each student.

Figure 1c shows a model that effectively implements normalization in just this fashion. This model performs the place-to-rate conversion without using the operation of division. Instead, it performs an operation analogous to summation with saturation. As before, the neurons forming the place code have two sets of projections, either weighted according to the location/preferred stimulus value (quasi-numerator channel) or unweighted

(quasi-denominator channel). A local, positive feedback loop causes both the numerator and denominator neurons to integrate their input over time. When the level of activity in the denominator neuron reaches a criterion value, it exceeds the threshold of an inhibitory interneuron. This neuron inhibits the input to the numerator neuron via presynaptic inhibition on the synaptic terminals of the numerator channel projections. Thus, the input to the numerator neuron is terminated when a specified total number of action potentials has been discharged by the neurons in the place code. By ensuring that the total number of action potentials entering the numerator channel is a constant, the circuit eliminates the need for an explicit operation of division. As long as the level of activity in the place code always exceeds the threshold under normal circumstances, variations in the overall level of activity will be ignored. The demands this circuit places on individual synapses are much less severe than they were for model 2, because the operations can be distributed (addition) or do not require great precision (multiplication by zero).

3.4 Simulations, experimental evidence, and predictions

Figure 2a shows a simulation of all three models (Matlab), illustrating the relationship between the
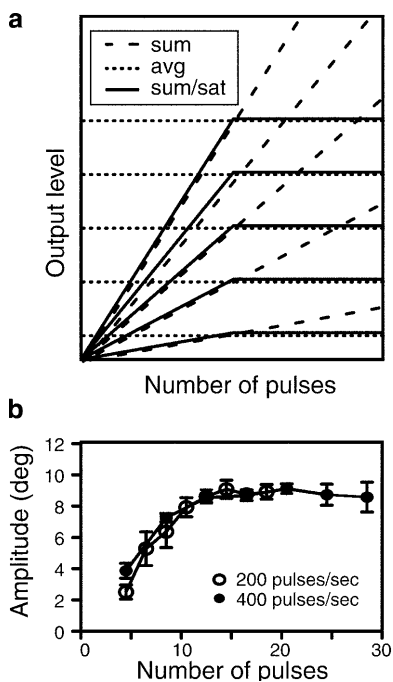

Fig. 2. a Simulation of the summation, averaging, and summation-saturation models. Each curve represents the output value that occurs for "microstimulation" of a unit at one of five sites in the input map as a function of the number of pulses of microstimulation delivered to that site. **b** Comparison with actual microstimulation data from the superior colliculus (Stanford et al. 1996). Microstimulation was conducted at a single site (site number 0202.777) for two different pulse frequencies and for varying durations. The amplitude of the evoked movement initially varies with the number of pulses, then saturates. This behavior is most similar to the summation-saturation model

output and both the location and the amount of activity. Each line represents the output for a single site of activity occurring at one of five different locations in the place code. For the summation model, the output rises at a rate that depends on the site of stimulation. For the averaging model, the output holds steady at a constant level that depends on the site of stimulation. For the summation-saturation model, the output initially rises with the amount of activity, regardless of location. However, the output rises faster for sites specifying larger parameter values, and a plateau occurs when a certain level of input activity has been reached. The level of the asymptote depends on the location – not the amount – of activity in the input layer.

The summation-saturation model provides an attractive explanation for recent experimental findings that the level of activity within a map *can* influence the output value up until some threshold is reached. Microstimulation experiments in the place code of the superior colliculus for saccade vector (Sparks et al. 1976) show that the amplitude of the evoked eye movement scales with strength of microstimulation, but then it saturates at a level corresponding to the location of the stimulating electrode within the map (Fig. 2b; Stanford et al. 1996; see also du Lac and Knudsen 1990; Pare et al. 1994). Various perceptual experiments have also suggested that normalization for visual stimulus contrast may also be incomplete (Stone and Thompson 1992; Thompson et al. 1996; Thompson and Stone 1997; Snowden et al. 1998; but see McKee et al. 1986). Thus, converging lines of evidence support the need for a biologically plausible neural place-to-rate conversion circuit that can simultaneously account for both proper normalization and the failures of normalization that are found experimentally.

The utility of models lies in their ability to provide insight and generate testable experimental predictions. The summation-saturation model proposed above makes a prediction about what should occur when two sites in a place code are stimulated with varying levels of activity. When small amounts of activity are introduced at both sites, this model predicts that the output should resemble a sum of the outputs that would have occurred for the same amount of activity at either site alone. When the total activity levels are increased to the point that the inhibitory interneuron is activated, the output reverts to a value that corresponds to the average location. A simulation of this is shown in Fig. 3 for each of the three models. The results of the simulation of simultaneous stimulation at the two sites show that the summation-saturation model predicts a transition from behavior resembling summation at low levels of activity to averaging at high levels of activity. Thus, two-site microsimulation could be used to distinguish between these models experimentally.

4 Discussion

The translation of signals from a place code to a rate code is not as simple as has sometimes been assumed. In
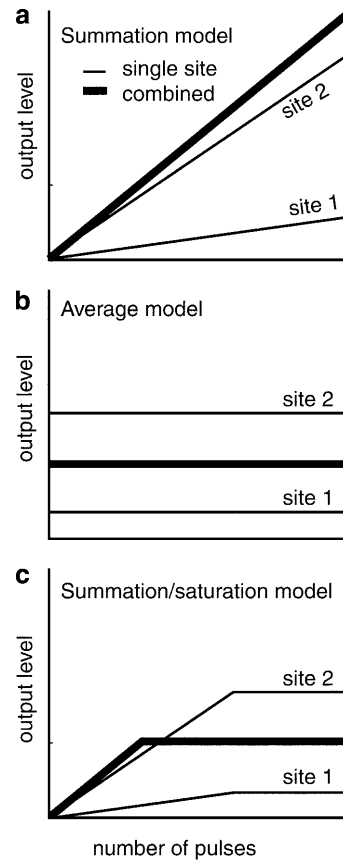

Fig. 3a–c. The predictions of the three models for simultaneous stimulation at two sites with varying levels of activity. The two *light solid lines* show the results of stimulation of each of the models (**a**–**c**) at two sites individually for varying levels of activity. The *heavy solid trace* illustrates the output of each model for simultaneous stimulation at both sites. For simulation of dual-site stimulation, the stimulation parameters (e.g. pulse frequency, number of pulses) for each site were identical to one another

particular, a single weighted projection pattern from units in a place code to a recipient unit will produce a rate-coded output (weighted summation model), but that output will depend not only on the location but also on the amount of activity, and thus does not constitute a true place-to-rate transformation. Some form of normalization is needed, which motivates the design of the averaging and the summation-saturation models. Both employ normalization, but in different fashions. The averaging model calculates a true average, while the summation-saturation model calculates a weighted sum and discards any excess activity present in the place code. The summation-saturation model enjoys somewhat greater biological plausibility, and its pattern of output most closely resembles the results of recent microstimulation experiments in the superior colliculus (du Lac and Knudsen 1990; Pare et al. 1994; Stanford et al. 1996).

It is worth pointing out which aspects of the summation-saturation model are essential and which are useful abstractions that are not integral to its algorithm. Features such as the number of neurons used for the simulation, the precise weighting pattern or threshold levels
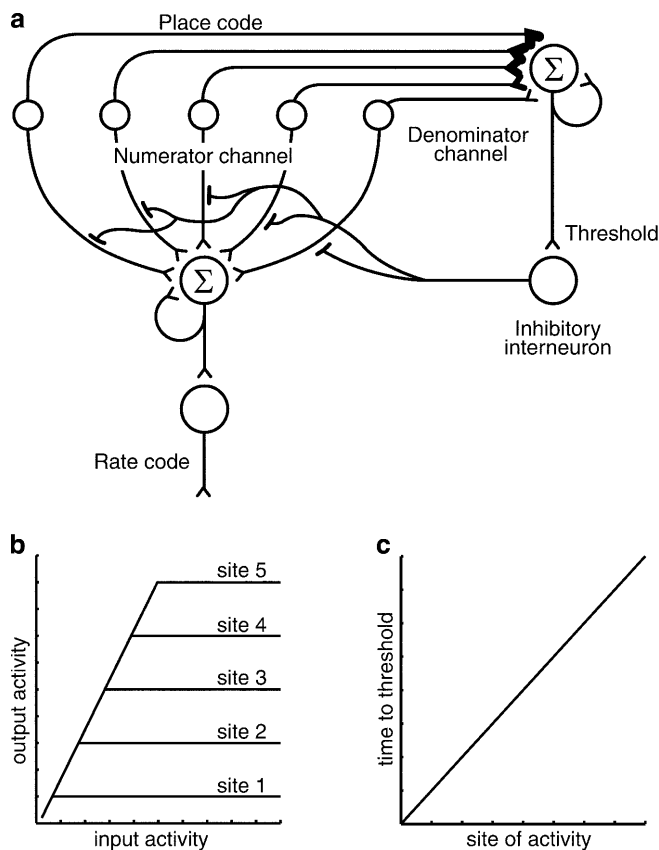
Fig. 4a–c. A variant of the summation-saturation model. **a** The *denominator channel* has a weighting pattern, with input units coding for small parameter values having *stronger* weights than input units coding for large parameter values. The *numerator channel* has a uniform pattern of synaptic weights. **b** Simulation of this model shows that the output initially rises at a uniform rate, regardless of the locus of input activity, but the threshold of the inhibitory interneuron is reached later for sites that represent large parameter values. **c** The relationship between the latency to reach threshold and the site of activity

chosen are, of course, not essential to the model itself since many different combinations of these parameters can produce the same output. The essential features are the two read-out pathways, one that is primarily responsible for ensuring that output is graded according to the location of activity, and another that clips off excess activity to ensure that the level of activity at that location does not unduly influence the output level. However, it is not necessary that these pathways be anatomically distinct in the brain, nor is it even necessary that the graded weights occur in the so-called numerator channel rather than in the denominator channel. The synapses in the denominator channel could be inversely related to the preferred parameter value while the synapses in the numerator channel could be uniform (Fig. 4a). In this variation, the numerator channel will always charge at the same rate, regardless of the location of activity, but the amount of time that elapses before the denominator channel clips off the excess input will vary as a function of the location (Fig. 4b). This variant of the model can provide an attractive explanation for the finding that

saccade latency increases with saccade amplitude (Fig. 4c; White et al. 1962).

The use of integration in the model, although it may not be absolutely essential, is certainly a useful component. Several mechanisms for neural integration have been proposed, ranging from an accumulation of neurotransmitter in synapses over time to positive feedback circuits that feed excitatory activity back on itself, causing the activity to build up over time (Robinson 1989). Although the integration is important to the model, it is not necessary for the operation of integration to be performed perfectly – a leaky neural integrator works perfectly well, provided that the integrators in the numerator and denominator channels decay with approximately the same time constant. A small modification is necessary to the circuit if the integration is leaky – the inhibitory interneuron must inhibit the inputs to both the numerator and the denominator channel integrators. As the denominator channel integrator decays below threshold, the inhibitory interneuron shuts down, allowing both the numerator and denominator channels to recharge momentarily.

Finally, although I have drawn from the primate visual and oculomotor literature in deriving these models, these are by no means the only systems in which signals must be translated from a place to a rate code. Every organism and many sensory systems must perform this operation in order to generate motor commands that are monotonically related to certain sensory parameters. The models presented herein constitute a first step towards elucidating the mechanisms underlying this process, subject to the constraints imposed by experimental evidence from the visual and oculomotor fields. Does the brain actually employ this solution? Only further experimental and theoretical efforts will tell.

References

Bozis A, Moschovakis AK (1998) Neural network simulations of the primate oculomotor system. III. A one-dimensional, one-directional model of the superior colliculus. Biol Cybern 79: 215–230

Carandini M, Heeger DJ (1994) Summation and division by neurons in primate visual cortex. Science 264: 1333–1336

Carandini M, Heeger DJ, Movshon JA (1997) Linearity and normalization in simple cells of the macaque primary visual cortex. J Neurosci 17: 8621–8644

Findlay JM (1982) Global visual processing for saccadic eye movements. Vision Res 22: 1033–1045

Groh JM (1997) A model for transforming signals from a place code to a rate code. Soc Neurosci Abstr 23: 1560

Groh JM, Sparks DL (1992) Two models for transforming auditory signals from head-centered to eye-centered coordinates. Biol Cybern 67: 291–302

Groh JM, Born RT, Newsome WT (1997) How is a sensory map read out? Effects of microstimulation in visual area MT on saccades and smooth pursuit eye movements. J Neurosci 17: 4312–4330

Heeger DJ (1992) Normalization of cell responses in cat striate cortex. Vis Neurosci 9: 181–198

Holt GR, Koch C (1997) Shunting inhibition does not have a divisive effect on firing rates. Neural Comput 9: 1001–1013

Koch C (1999) Biophysics of computation: information processing in single neurons. Oxford University Press, New York

Koch C, Poggio T (1987) Biophysics of computation: neurons, synapses, and membranes. In: Edelman G, Gall WE, Cowan WM (eds) Synaptic function. Wiley, New York, pp 637–698

Lac S du, Knudsen EI (1990) Neural maps of head movement vector and speed in the optic tectum of the barn owl. J Neurophysiol 63: 131–146

Lee C, Rohrer WH, Sparks DL (1988) Population coding of saccadic eye movements by neurons in the superior colliculus. Nature 332: 357–360

Lefevre P, Quaia C, Optican LM (1998) Distributed model of control of saccades by superior colliculus and cerebellum. Neural Netw 11: 1175–1190

McKee S, Silverman G, Nakayama K (1986) Precise velocity discrimination despite random variations in temporal frequency and contrast. Vision Res 26: 609–619

Moschovakis AK, Kitama T, Dalezios Y, Petit J, Brandi AM, Grantyn AA (1998) An anatomical substrate for the spatiotemporal transformation. J Neurosci 18: 10219–10229

Nichols M, Newsome W (1998) Influence of electrical microstimulation in area MT on direction of motion estimates in a direction identification task. Soc Neurosci Abstr 24: 1746

Nowak LG, Bullier J (1998a) Axons, but not cell bodies, are activated by electrical stimulation in cortical gray matter. I. Evidence from chronaxie measurements. Exp Brain Res 118: 477–488

Nowak LG, Bullier J (1998b) Axons, but not cell bodies, are activated by electrical stimulation in cortical gray matter. II. Evidence from selective inactivation of cell bodies and axon initial segments. Exp Brain Res 118: 489–500

Pare M, Crommelinck M, Guitton D (1994) Gaze shifts evoked by stimulation of the superior colliculus in the head-free cat conform to the motor map but also depend on stimulus strength and fixation activity. Exp Brain Res 101: 123–139

Robinson DA (1972) Eye movements evoked by collicular stimulation in the alert monkey. Vision Res 12: 1795–1807

Robinson DA (1989) Integrating with neurons. Annu Rev Neurosci 12: 33–45

Salzman CD, Newsome WT (1994) Neural mechanisms for forming a perceptual decision. Science 264: 231–237

Schiller PH, True SD, Conway JL (1979) Paired stimulation of the frontal eye fields and the superior colliculus of the rhesus monkey. Brain Res 179: 162–164

Scudder CA (1988) A new local feedback model of the saccadic burst generator. J Neurophysiol 59: 1455–1475

Snowden RJ, Hammett ST (1992) Subtractive and divisive adaptation in the human visual system. Nature 355: 248–250

Snowden RJ, Stimpson N, Ruddle RA (1998) Speed perception fogs up as visibility drops. Nature 392: 450

Sparks DL, Holland R, Guthrie BL (1976) Size and distribution of movement fields in the monkey superior colliculus. Brain Res 113: 21–34

Stanford TR, Freedman EG, Sparks DL (1996) Site and parameters of microstimulation: evidence for independent effects on the properties of saccades evoked from the primate superior colliculus. J Neurophysiol 76: 3360–3381

Stone LS, Thompson P (1992) Human speed perception is contrast dependent. Vision Res 32: 1535–1549

Thompson P, Stone LS (1997) Contrast affects flicker and speed perception differently. Vision Res 37: 1255–1260

Thompson P, Stone LS, Swash S (1996) Speed estimates from grating patches are not contrast-normalized. Vision Res 36: 667–674

Tweed DB, Vilis T (1990) The superior colliculus and spatiotemporal translation in the saccadic system. Neural Netw 3: 75–86

Van Gisbergen JAM, Van Opstal AJ, Tax AAM (1987) Collicular ensemble coding of saccades based on vector summation. Neurosci 21: 541–556

Van Opstal AJ, Van Gisbergen JA (1989) A nonlinear model for collicular spatial interactions underlying the metrical properties of electrically elicited saccades. Biol Cybern 60: 171–183

White C, Eason RG, Bartlett NR (1962) Latency and duration of eye movements in the horizontal plane. J Opt Soc Am 52: 210–213