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The neural code for taste in the brain stem: Response profiles

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Abstract

In the study of the neural code for taste, two theories have dominated the literature: the across neuron pattern (ANP), and the labeled line theories. Both of these theories are based on the observations that taste cells are multisensitive across a variety of different taste stimuli. Given a fixed array of taste stimuli, a cell's particular set of sensitivities defines its response profile. The characteristics of response profiles are the basis of both major theories of coding. In reviewing the literature, it is apparent that response profiles are an expression of a complex interplay of excitatory and inhibitory inputs that derive from cells with a wide variety of sensitivity patterns. These observations suggest that, in the absence of inhibition, taste cells might be potentially responsive to all taste stimuli. Several studies also suggest that response profiles can be influenced by the taste context, defined as the taste stimulus presented just before or simultaneously with another, under which they are recorded. A theory, called dynamic coding, was proposed to account for context dependency of taste response profiles. In this theory, those cells that are unaffected by taste context would provide the signal, i.e., the information-containing portion of the ANP, and those cells whose responses are context dependent would provide noise, i.e., less stimulus specific information. When singular taste stimuli are presented, noise cells would provide amplification of the signal, and when complex mixtures are presented, the responses of the noise cells would be suppressed (depending on the particular combination of tastants), and the ratio of signal to noise would be enhanced.

Keywords: Neural code; Taste; Brain stem; Response profiles

1. Introduction

In the study of the neural code for gustation, there are two major theories that have dominated the literature. These are the across-neuron pattern (ANP) theory and the labeled-line theory. In the ANP theory [27,28,33,63,64,90], the perception of a given tastant is thought to be represented by the pattern of relative firing rates across cells in the system. This theory is based in part on the observation that taste-responsive neurons are most often multisensitive across taste qualities, for example, salty, sour, bitter, and sweet. More importantly, correlation coefficients of ANPs generated by similar tasting stimuli tend to be larger than those generated by dissimilar tastants. In contrast, the labeled-line theory [29–32,37,41,67] maintains that the signal for a given tastant is carried exclusively by a subset of cells that are preferentially tuned to that stimulus quality. This theory emphasizes the observation that, despite the nearly ubiquitous multisensitivity of taste responsive neurons, knowledge of a neuron's "best" stimulus, i.e., the one that produces the most robust response (or in some cases a specific combination of taste stimuli that produce the largest responses [29,30]), allows the prediction of the relative effectiveness of the other stimuli to which the neuron responds. Underscoring the fact that these two theories are not inconsistent, Smith et al. [72] have provided evidence that both mechanisms may be used. These investigators suggested that the ANP among cells in a given stimulus-best category is what may constitute the neural representation for that stimulus.

At the heart of both of these theories of taste coding is the response profile, defined as the relative response rates of a cell across taste stimuli. Most commonly, response profiles are determined by recording the electrophysiological responses to an array of tastants that are presented in individual trials. One of the assumptions that is implicit in both the ANP and the labeled-line theories is that these profiles determine the role that a given cell will play in the neural representation of a taste stimulus. It follows, therefore, that the response profile of a cell should be a stable, or at least predictable, characteristic. Two questions naturally emerge from this assumption: (1) how are these profiles constructed synaptically, and (2) are there any conditions under which a response profile can change?

The answer to the first question, the synaptic construction of response profiles, is critical to a conceptualization of the neural representation of a taste, because the answer may provide clues about how the information about a taste stim-

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ulus is processed as it ascends from tongue to cortex. If cells with one type of response profile, say NaCl best, receive input exclusively from cells with similar response profiles, then a good case could be made for parallel coding channels, each associated with one or a combination of taste qualities. Alternatively, if taste-responsive cells received input from cells with a wide variety of response profile types, then it could be argued that information about taste stimuli is more distributed.

2. Morphology and function of taste cells in the brain stem

In the brain stem of the rodent, there are two neural structures that are involved in processing of information about taste. The first is the nucleus of the solitary tract (NTS), which projects rostrally to the second, the parabrachial nucleus of the pons (PbN). Although most investigators have shown only ipsilateral projections from the NTS upstream, some evidence suggests that the projection may be bilateral [89].

Over the past decade there have been a number of investigations of the anatomy and physiology of the gustatory portion of the NTS in the rodent. Although most of the anatomical descriptions have pertained to the hamster [2,11–15,39,52,73,84–88], analogous studies in the rat [40,43–46,57,65,66,76,77,79,80] have suggested that the NTS in both species is arranged in a similar manner. Incoming fibers from the oropharyngeal cavity arise from the chorda tympani (CT) nerve (part of the facial nerve), the greater superficial petrosal nerve, the glossopharyngeal nerve, and the superior laryngeal nerve [57,58,84,85]. Although the termination fields of these nerves show a distinct topographic segregation, there is considerable overlap [40,52,58,73,77,84]. These primary afferents form excitatory synapses on the distal dendrites and spines of cells in the rostral central and rostral lateral subdivisions of the NTS [84,85]. They terminate in glomeruli in which are located a variety of synaptic relationships. These include both axo-dendritic (possibly inhibitory) and dendro-dendritic connections [84]. Most investigations of the morphological characteristics of neurons in the gustatory NTS have identified three cell types: fusiform (a.k.a. elongate), stellate (a.k.a. multipolar), and ovoid. Fusiform cells have at least two primary dendrites (more recent evidence using reconstruction of Neurocytin-labeled cells suggests that very few NTS cells are actually bipolar [65]) that are preferentially oriented in the mediolateral plane, perpendicular to the solitary tract, and can extend distances of several hundred microns [84,85]. It has been suggested that this arrangement maximizes the opportunity to synapse with a large number of incoming fibers [13,14,84,85]. A more recent analysis of the morphology of NTS cells has defined six cell types, based on a cluster analysis of six morphological features [65,66]. One of these features, cell size, may correlate with immunohistochemical features, i.e., large cells are associated with immunoreactivity to tyrosine hydroxylase [15], and small cells are immunoreactive to GABA [12,45], and may be inhibitory interneurons [85]. A significant proportion of cells in the rostral central and rostral lateral subdivisions of the NTS are responsive to exogenously applied GABA [38,49,70,80]. Evidence that both $GABA_A$ and $GABA_B$ receptors are present has been reported [49]. These observations have fueled speculation that inhibitory processes may be important in the neural processing of gustatory stimuli in the NTS.

From the NTS, the gustatory pathway in the rodent is known to have an obligatory synapse in the PbN [57,58]. Approximately one-third of the taste responsive NTS cells send axons to the PbN [54,59–61]. Anatomical studies have shown that only fusiform and stellate cells send axons to the gustatory portions of the PbN [86]. These cells also receive input from primary gustatory afferents, and are therefore, second-order neurons in the gustatory pathway. In the PbN, taste-responsive cells are found in the medial and lateral subdivisions and scattered among the fibers of the brachium, in the so called “waist” area [11,44]. Two types of cells have been described in the areas that receive afferents from the gustatory portions of the NTS: fusiform and multipolar cells [11,44]. Compared with cells in the NTS, neurons in gustatory subdivisions of the PbN apparently show more elaborate dendritic arborizations that do not extend large distances [11]. Parenthetically, it has recently been suggested that methodological limitations of previous studies may have resulted in an underestimation of the dendritic elaborations of NTS cells in the gustatory recipient zone [65], so that these putative differences between NTS and PbN taste-responsive cells may not be as clear cut as was thought originally.

In recent years, several attempts have been made to relate the morphology of gustatory cells with their physiological characteristics [4,43,44,66]. In a series of investigations of the gustatory region of the NTS, Bradley and his colleagues characterized the biophysical properties of neurons in the gustatory portion of the NTS recorded in an in vitro slice preparation [3,4,43,75,83]. Results showed that these properties were poorly correlated with the morphological characteristics of the cells [43]. The authors suggested that there may be functional categories of cells that cut across anatomically defined cell types. Another strategy to relate morphology to function has been to study patterns of gustatory responsiveness in NTS cells [52,65,66]. Although initial studies failed to find a tight relationship between response profile and morphological categories [43,52], data from a more recent study by Renehan et al. [66] suggest that there may be morphometric characteristics that predict some aspects of gustatory sensitivity [65,66]. For example, these investigators found that more narrowly tuned cells in the NTS, i.e., those that responded to fewer stimuli, had more extensive dendritic branching with more dendritic spines. In addition, they reported that quinine specific cells tended to be smaller and NaCl-specific cells were larger than other cells in their sample.

Although investigations of structure–function relationships in the gustatory system promise to reveal important aspects of the neural processing of taste information, information about the functional circuitry that connects taste responsive neurons may be an essential piece to the puzzle.

3. Origins of response profiles: Functional circuitry in the NTS and PbN

Given the reliance of taste coding theories on the interpretation of response profiles, it is perhaps surprising that so little is known about how they arise in the central nervous system or about the mechanisms by which they can change. Reports about information transfer between structures in the taste system have generally been restricted to comparisons of relative mean response rates [33,68]. This type of data provides no information about the nature of inputs to cells with particular response profiles or how those inputs interact to produce those response profiles.

Two previous investigations have addressed the question of the origin of response profiles in the NTS and PbN [1,91]. In these studies, pairs of units were recorded simultaneously, and the crosscorrelation functions (CCFs) of taste-evoked spike trains were used to infer the existence of common input. In this technique, two simultaneously recorded spike trains, A and B, are recorded. These can be from cells in the same or different structures. The CCF is constructed as a histogram that depicts the number of occurrences of each A-B interval for all spikes. If there is a tendency for A and B to fire coincidentally, there is a peak in this function. If the two are driven by a common input, this peak would center around the zero point. If the two are monosynaptically connected, this peak (or trough for inhibition) would be located at an interval representing the synaptic delay [17,25,34,35,53,55,62].

At the level of the NTS [1], half (11 of 22) of the pairs of neurons showed positive crosscorrelograms, i.e., significant peaks were present. The authors suggested that many of the NaCl-best neurons in the NTS receive convergent and divergent input from NaCl-best first order neurons. This was based on the observations that seven of the 11 crosscorrelation-positive pairs were both NaCl best, and that in five of these the frequency of correlated discharge was highest during NaCl stimulation. In the PbN [91], there were similar findings and conclusions about the NaCl-best neurons: seven of eight crosscorrelation-positive, NaCl-best/NaCl-best neuron pairs showed the highest frequency of correlated discharge during NaCl presentation, suggesting that NaCl-best neurons in the PbN were most often controlled simultaneously by presynaptic NaCl-best neurons.

More recently, we studied the functional inputs to taste-responsive cells in the PbN of anesthetized rats by simultaneously recording taste responses in pairs of units, one in the NTS and the other in the PbN [23,25,26]. Results showed that taste responsive cells in the PbN receive input from NTS cells with response profiles that are both similar and different from their own. Figure 1 illustrates this point. Response profiles from 12 pairs of NTS-PbN units that showed evidence of monosynaptic connectivity are shown. It can be seen that even though some pairs of units share the same best stimulus, PbN units that are narrowly tuned can get input from both narrowly and broadly tuned NTS units. The same is true for broadly tuned PbN units. However, further analyses showed that input from cells with similar response profiles appeared to be more effective, i.e., an NTS spike was more likely to be followed within 3 ms by a PbN spike, when the stimulus was the shared best stimulus. In contrast, input to PbN cells from NTS cells with dissimilar response profiles appeared to be nearly equally effective for all tastants tested. This latter, nonstimulus-selective input was interpreted as a means of providing a general amplifica-

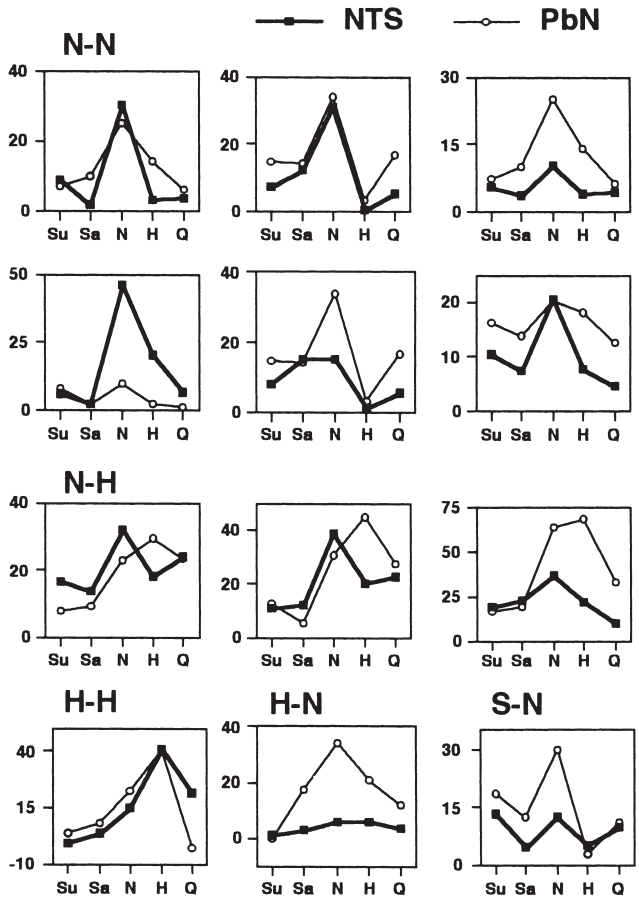

Fig. 1. Response profiles for all pairs of coupled NTS-PbN units in Di Lorenzo and Monroe [25]. Stimulus is shown along the abscissa and response magnitude (spikes per second; average spontaneous activity is subtracted from the response measure) is shown along the ordinate for each pair of units. Labels on top of graphs indicate best stimulus category of the NTS and PbN unit, respectively. Abbreviations are as follows: for stimuli, Su, sucrose; Sa, saccharin; N, NaCl; H, HCl; Q, quinine. For labels, N, NaCl best; H, HCl best; S, sucrose best. Reprinted from Brain Res., 763, P.M. Di Lorenzo and S. Monroe, Transfer of information about taste from the nucleus of the solitary tract to the parabrachial nucleus of the pons, p. 175, 1997, with permission from Elsevier Science.

tion of incoming signals. This type of nonstimulus selective input might in effect flatten the tuning of the PbN cell. Thus, the relative sensitivity of a PbN cell might be the result of a balance of stimulus selective and nonselective inputs.

4. Changes in response profiles: Are they stable?

The question of whether response profiles are reliable (stable) characteristics of cells is important because of its implications for how taste stimuli are represented by the brain. Logically, some aspect(s) of the neural activity that is evoked by a given taste stimulus must be consistent over repeated presentations. This would allow the identification of or the stimulus in the face of changes in variables such as hunger or satiety that may change the behavioral reactions to it. Because changes in response profiles of taste cells would necessarily change the ANP associated with a taste stimulus, i.e., some cells that were highly responsive might become relatively insensitive and vice versa, knowledge of which aspects are labile and which are stable is essential for a full understanding of how information about taste is processed. Furthermore, the question of how labile response profiles could be incorporated into a labeled-line type of coding scheme becomes an important conceptual issue.

In fact, there is a growing literature that supports the idea that response profiles of taste cells are not static characteristics of taste cells, but rather are dependent on the conditions under which tastants are presented. In this context, experimental manipulations such as sodium deprivation [9,10,42, 50,69,74], taste aversion learning [7,51], conditioned preference learning [36] and the level of ovarian hormones [21,22] have all been shown to chronically alter the response profiles of taste-responsive neurons. In general, results of these types of experiment have shown that the changes in the patterns of sensitivity in individual cells result in changes in ANPs that might be predicted based on the associated behavioral effects. So, for example, changes in the sensitivity of NTS cells to sucrose following a conditioned taste aversion to sucrose resulted in ANPs for sucrose that were more similar to those produced by quinine compared with the ANPs for sucrose in untrained animals [7]. These changes in the response profiles persist even after extinction [51].

In addition to long-term changes in response profiles, several studies have demonstrated the ability of taste-sensitive neurons in the brain stem to modify their response profiles within a relatively short time frame. Responses for a given cell to some stimuli, but not others, can be affected by removal of corticofugal input for example [18,24]. These changes can be of such magnitude that the best stimulus of a cell is often altered. Other investigators have shown that the application of amiloride, a sodium channel blocker, to the tongue can selectively alter the sensitivity of NaCl best cells in the NTS to sodium salts [5,37,71].

Because adaptation of the tongue can selectively suppress the response to a particular taste stimulus, changes in response profiles are a natural result. However, besides the obvious deletion of a response to the adapting stimulus, changes in the response to a nonadapting stimulus (defined as “crossadaptation”), can change the order of effectiveness of the remaining stimuli, and in effect, alter the classification of the cell in terms of its best stimulus. For example, recent work from our laboratory has shown that in both the NTS and PbN, adaptation to any representative the four basic taste qualities, for example, NaCl, HCl, quinine, and sucrose, resulted in changes in the order of effectiveness of the remaining stimuli in a substantial proportion (between 12 and 42% of the units tested, depending on the adapting stimulus) of the units ([19]; Di Lorenzo and Lemon, in press; Lemon and Di Lorenzo, in preparation). This effect was not only the result of crossadaptation across taste stimuli, but in many cases it was the consequence of enhanced responses to one stimulus following adaptation of the tongue to another stimulus. Figure 2 illustrates this phenomenon in two cells recorded from the PbN. The cell in Fig. 2A had no significant response to sucrose; however, adaptation to sucrose enhanced the response to quinine. In Fig. 2B, the cell had no response to HCl before adaptation, but a very vigorous and significant response following adaptation to sucrose. Adaptation to all four taste qualities were capable of producing this effect, and in all cases the effect was significant. These data complement results from studies of the effects of GABA antagonists on brain stem taste responses ([70]: discussed below), and suggest the possibility that taste cells in the brain stem are potentially more broadly responsive than they normally appear.

To summarize, data from a number of studies point to the idea that response profiles are not immutable characteristics of taste responsive cells in the brain stem. Instead, there are a number of conditions under which response profiles can change. Moreover, these changes can occur within a relatively short time frame. These observations imply that for any given stimulus, the conditions under which that stimulus is presented can alter its representation in the brain.

5. Changes in response profiles: The role of inhibition

The idea that the response profile of a taste-responsive cell can change leads to the question of what mechanisms might be invoked to accomplish the changes. One of the obvious candidates is the modulation of inhibitory input to the cells.

There are several lines of evidence that attest to the widespread influence of inhibition in the brain stem. For example, results from in vitro electrophysiological studies have suggested that taste-responsive cells in the brain stem are under a tonic inhibitory influence [38,49]. In addition, it has been suggested that taste responses in these areas are a complex interaction of inhibitory and excitatory influences [38,70,83]. Although it has been shown that the infusion of GABA [70] and substance P [16] into taste-responsive areas of the brain stem blocks responses to taste stimuli, the inter-

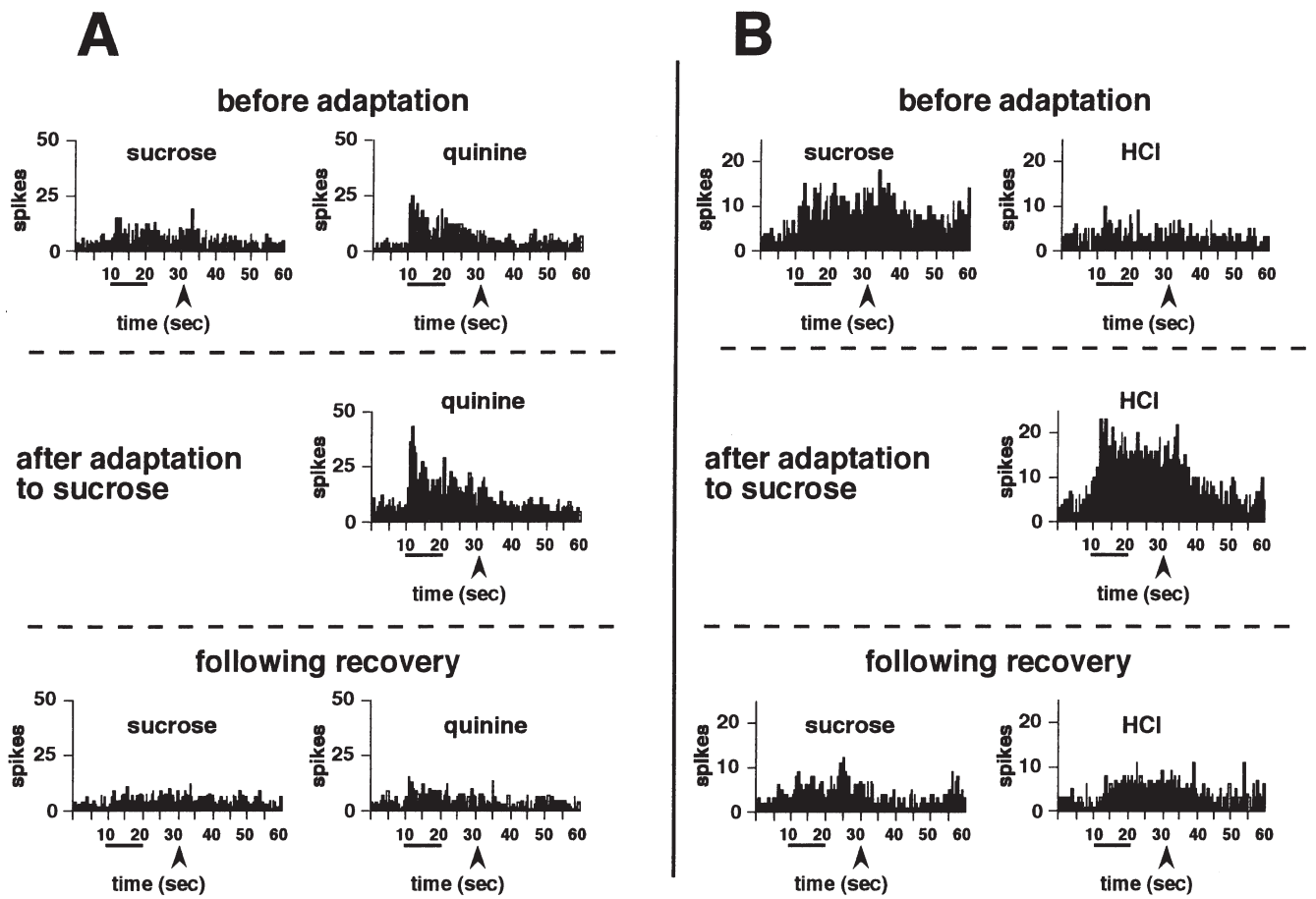

Fig. 2. Taste responses from two cells recorded from the PbN [19]. Adaptation protocol consisted of five consecutive 10-s presentations of the adapting stimulus without intervening water rinses. Test stimuli were tested immediately after adaptation and before any water rinse. Recovery protocol consisted of bathing the tongue with at least 2 min of distilled water. (A) Top: cell showed a significant response to quinine but not to sucrose before adaptation protocol; middle: response to quinine was enhanced by 34% following adaptation to sucrose; bottom: cell showed a significant response to quinine but not to sucrose following recovery from adaptation. (B) Top: cell showed a significant response to sucrose but not to HCl before adaptation protocol; middle: significant response to HCl following adaptation to sucrose; bottom: sucrose and HCl responses following recovery from adaptation. Abscissa shows time in seconds; line below each graph indicates stimulus presentation; arrow indicates onset of distilled water rinse.

action of inhibitory agents with excitatory inputs remains largely unknown. In this context, Grabauskas and Bradley [38] have recently described tetanic potentiation of inhibition in NTS cells in vitro. They suggested that the spike trains evoked by taste stimulation in the intact animal might provide the natural analogue to a tetanic electrical pulse train.

Importantly, Smith and Li [70] have recently reported a study of the effects of manipulations of GABAergic inhibition on taste responses in the hamster NTS. In that study, it was found that the attenuation of inhibitory influences by infusion of bicuculline methiodide (BICM) enhanced response magnitude in 60% of the cells studied. Responses to all taste stimuli that were tested were affected regardless of the best stimulus of the cell. In those cells that were tested with more than one stimulus, the overall effect of BICM infusion was to increase the breadth of responsiveness across tastants. It was, therefore, suggested that the function of inhibitory influence on taste-responsive cells in the NTS was to shape the tuning of response profiles.

6. Dynamic coding of taste in the brain stem

Collectively, the observations cited above support two general points concerning response profiles of taste cells in the brain stem. First, the response profile of a given taste cell is constructed from a variety of inputs. These include excitatory input from some cells with similar response profiles and additional input from cells with response profiles that are dissimilar from their target cells. The diversity of these inputs may convey the potential for broad sensitivity across taste stimuli while widespread inhibitory input may narrow the tuning of taste cells thus determining their relative sensitivity across taste stimuli. Second, there are a number of conditions under which the order of effectiveness of taste stimuli within a given taste cell will change. The impli-

cation of such changes is that a particular taste cell may play different roles in the neural representation of a tastant, depending on the context (conditions) under which a stimulus is presented. Moreover, because these changes can take place within a relatively short time frame, the result may be a dynamic self-organization of the ANP. That is, the ANP for a given taste stimulus may be different depending on the context under which a taste stimulus is presented. As the context changes over time, the ANP may also change.

Context-dependent changes have somewhat different interpretations from the standpoints of the ANP and labeled line theories. If it is true that the ANP evoked by a stimulus conveys stimulus quality (identity), then by definition context-dependent changes in the ANP imply that the perception of stimulus quality also changes. However, if a given context shifts all of the ANPs in an approximately equivalent manner, then the relationship among ANPs may be preserved. In effect, there is only a linear transformation that would retain the discriminability among the various taste stimuli. This is what appears to occur following adaptation to NaCl in the NTS and PbN ([19]: Di Lorenzo and Lemon, in press; Lemon and Di Lorenzo, in preparation). Alternatively, if it is true that there are subsets of cells that are devoted to encoding a single taste quality, then context-dependent changes in the response profile would have different consequences on the code for a given tastant, depending on the role of the cell in representing that tastant. For example, if the response to the best stimulus of a cell were context dependent, then the number of spikes evoked by that stimulus, i.e., the signal for that stimulus, would vary. On the other hand, if there are context-dependent changes in the so-called "side band" responses (responses to stimuli other than a cell's best stimulus), then the level of noise (defined as stimulus-evoked but not stimulus-selective neural activity) in the population response would vary.

To test the hypothesis that ANPs are dynamically context dependent, we have recorded taste responses from cells in the NTS when taste stimuli were presented alone or when they were immediately preceded by another stimulus (DiLorenzo, Lemon, and Reich, in preparation). In those experiments, brief pulses (100 ms), called "prepulses," of taste stimuli were followed by a 1-s water rinse and then a 3-s taste stimulus presentation. Results showed that taste responses in some cells were unaffected by the prepulses but the responses in other cells were changed significantly ([47]: DiLorenzo and Lemon, in preparation). Figure 3 shows examples of both types of cells. Across the sample of taste-responsive cells, these effects produced a change in the ANP associated with a taste stimulus, depending on the prepulse that preceded it [20]. Because the most common effect of a stimulus prepulse was a suppression of the response to the subsequently presented stimulus (although occasional enhancement was also noted), it is possible that prepulses of natural taste stimuli might initiate a recurrent inhibitory process, the end result of which would be to narrow the range of sensitivity of the cell. This would be consistent with the work of Grabauskas and Bradley [38], which showed that tetanic stimulation of the solitary tract at frequencies near those produced by natural tastants could induce a long-lasting potentiation of inhibitory influence on NTS cells.

Because taste responses in some NTS cells were affected by prepulses and others were not, it is possible to distinguish between them functionally and to propose that they serve different roles in the coding process. Considering their stability in the face of changing taste contexts, those cells that were unaffected by taste prepulses can be conceptualized as "signal" cells. Those cells whose response magnitudes sometimes depended on the particular stimulus that preceded it can be thought of as "noise" cells. Thus, when a given stimulus is preceded closely by another, responses of the signal cells will be unaffected, while responses of most of the noise cells will be suppressed. Not surprisingly, signal cells are generally more narrowly tuned than are noise cells. This implies that each response-related spike that they produce will convey more information than a spike in more broadly tuned cell, for example, a noise cell.

In the ANP view, signal cells would anchor the ANP associated with the various taste stimuli to provide the ability to discriminate between them and to represent some stable characteristics. Interpreted from a labeled line viewpoint, spikes evoked in signal cells would straightforwardly encode the various taste stimuli. However, although signal cells are generally more narrowly tuned than others, they remain multisensitive. It is, therefore, possible that the ANP across these signal cells, functionally defined by their independence from context effects, actually carries the representation of a taste stimulus. The idea that the ANP in a subset of cells represents the neural code for taste stimuli is not new, and was first suggested by Smith et al. [72]. The difference between Smith et al.'s [72] conclusions and those presented here are in the determination of which cells are essential for the ANP. Smith et al. defined these cells according to their best stimulus, and here the cells are defined by their stability in the face of different preconditions, regardless of their best stimulus. It is, therefore, possible, for example, that a NaCl-best cell could contribute essential information to the population response to sucrose, because that cell's sucrose response would be reliably the same despite changing taste contexts.

From the standpoint of the ANP theory, the noise cells would provide some jitter to the ANP. However, because of the stability of the signal cells, the relationship of the ANPs to each other would remain relatively constant. Interpreted according to the labeled-line theory, noise cells might amplify or bolster the signal by adding spikes to the population response or, conversely, they might obscure it by adding "background" spikes that contain little information about taste quality. (The assertion that a response conveys little information about taste quality is based on the idea that a cell that responds equally well to two stimuli can communicate nothing about the difference between them. However, it is

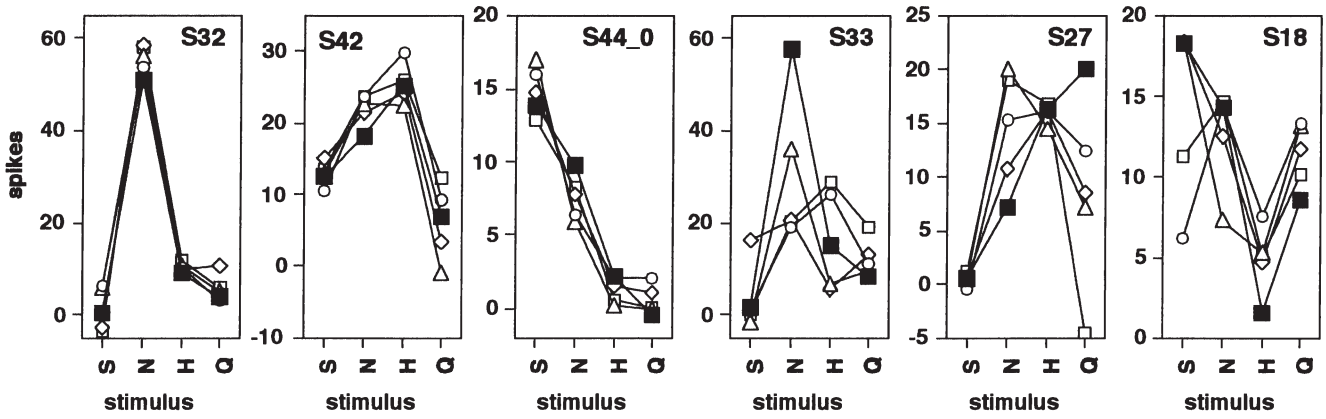

Fig. 3. Response profiles from six NTS units. Stimuli were initially presented individually (filled squares) without a stimulus prepulse. All stimuli were presented again (3 s) in separate trials preceded by a 100 ms pulse of sucrose (open circles), NaCl (open triangles), HCl (open diamonds) or quinine (open squares) followed by 1 s of distilled water. Responses of the three cells on the left were not affected by the prepulses; however, for the three cells on the right, the best stimulus was altered depending on the prepulse that preceded stimulus presentation. Stimuli were presented through separate stainless steel tubes, perforated along their longitudinal axes, that were positioned in the mouth. Liquid in the tubes was pressurized with compressed air; activation of solenoids released stimuli at a flow rate of 5 mL/s. A 100-ms pulse delivered 0.5 mL of fluid to the mouth. Abbreviations are as follows: S, sucrose; N, NaCl; H, HCl; Q, quinine.

entirely possible that these cells might convey information about other aspects of taste stimuli such as nutritive or hedonic value.) These two possibilities are not mutually exclusive. Because noise cells are generally more broadly tuned than signal cells, it is likely that they are providing a nonselective backdrop for the signal cells that adds magnitude to the population response. However, when stimuli are preceded by short taste pulses, responses of most noise cells are suppressed, the consequence of which is that the signal cells then carry proportionately more of the population response. Thus, the ratio of signal to noise is enhanced.

One of the functions of dynamic tuning of response profiles may be to facilitate the analysis of complex mixtures of taste stimuli into their components. The mechanism for this is illustrated in Fig. 4. At the top of the figure, the "responses" of three hypothetical units to two "stimuli" are shown. These are the response profiles of those units. In the middle of Fig. 4, the ANPs associated with stimulus A and stimulus B have been constructed from the response profiles of Units 1–3. At the bottom left of the figure, the ANP that might result from the presentation of a mixture of stimulus A and B without dynamic coding. Here, the response of each unit is taken as the response to the most effective component of the mixture. In the bottom right of the figure, the response to the mixture is shown assuming that the responses of Unit 2 are dynamically tuned. It can be seen that, without dynamic tuning, the ANP for the mixture is nearly flat; that is, all cells are firing at their maximum rate. (If the mixture were even more complex, one can imagine that the population of cells would nearly all be firing at the maximum because such a mixture might contain the most effective stimulus for every cell.) However, with dynamic tuning, those cells that are particularly tuned to either component of the mixture would respond well, while those cells that respond well to both components would be suppressed. The resulting ANP would be customized to the components of the mixture, such that the signal associated with each of the components would occur in a low-noise environment.

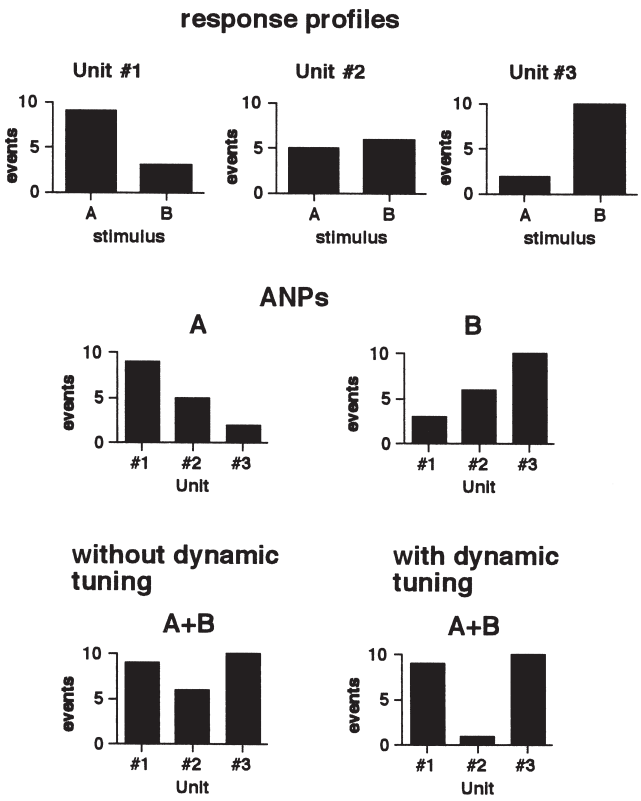

Fig. 4. "Responses" from hypothetical units illustrating the way that dynamical coding might operate in the brain stem. See text for explanation.

The effects of dynamic coding of taste stimuli should be apparent in the electrophysiological responses to mixtures of taste stimuli. For example, cells that showed context dependent taste responses would presumably respond less to a mixture of taste stimuli than to either component presented alone (defined as mixture suppression). These cells would presumably be the noise cells. Other cells would respond to a mixture as they would to the most effective component of the mixture. These would presumable be the signal cells. Unfortunately, there are no data on the responses of single cells in the rat NTS to mixtures, so there are no data available to test these conjectures directly. However, relevant data are available in the hamster and, despite known species differences between the hamster and rat, it is not unreasonable to suggest that the coding mechanisms used in each species would be quite similar. In this context, there are some reports on the responses of hamster PbN cells to mixtures [78,80–82] that are consistent with the dynamic coding scheme. For example, in an early study of the hamster PbN, Travers and Smith [78] reported that 95 of 137 responses to mixtures showed no evidence of mixture suppression. In a more recent series of studies, also of the hamster PbN, Vogt and Smith [80–82] found that at least a third of the cells in each experiment showed no mixture suppression. These cells would thus be considered signal cells, as defined above. The remaining cells showed evidence of mixture suppression to varying degrees, and could therefore be classified as noise cells.

There are several aspects of dynamic coding theory that have been observed in other sensory systems besides gustation. In the olfactory system of the moth, for example, the same odor can evoke different responses from the same neurons, depending on the temporal pattern of odor presentation [8]. The differences between these patterns are an example of context dependency of receptive fields, and are thought to be the result of inhibitory input [8]. Inhibitory interactions in the mammalian olfactory bulb are also involved in the population response to odorants by decreasing the overlap between patterns of output evoked by two different stimuli [48]. This represents a mechanism similar to the one proposed here in the taste system. Context dependency has also been demonstrated in the rat somatosensory system [56]. Specifically, it has been reported that some cells, but not others, in the ventral posterior medial thalamus show time-dependent caudal-to-rostral shifts in the centers of their receptive fields. In effect, these cells are maximally responsive to a particular sequence of spatial stimulation. This suggests that there are two types of cells in this area: some that show context-dependent responses, and others that do not. Similar effects have been reported in the rat somatosensory cortex [6]. There, regular spiking barrel neurons showed inhibition of their receptive fields according to which adjacent whiskers were being stimulated and in which combination. Fast-spiking neurons showed no such surround inhibition. In those cells that showed evidence of inhibitory influences, the inhibition was targeted at responses to the deflection of whiskers at the nonpreferred angles. The authors suggested that, during active touch where many whiskers are stimulated, the overall function of inhibitory interactions was to sharpen the tuning of cortical columns toward encoding the stimulation of a single principal whisker [6].

7. Summary and Conclusions

In the study of neural coding in the gustatory system, two theories have dominated the literature—the ANP, and the labeled-line theories. Although these theories are not mutually exclusive, much of the early literature on taste coding was devoted to experiments designed to distinguish between them. Both of these theories are based on the same set of observations: that taste cells are multisensitive across a variety of different taste stimuli. Given a fixed array of taste stimuli, a cell's particular set of sensitivities defines its response profile. The particular characteristics of response profiles have guided the construction of both major theories of coding. In reviewing the data on the construction and stability of response profiles, it is apparent that this fundamental characteristic of taste-responsive cells is an expression of a complex interplay of excitatory and inhibitory inputs that derive from cells with a wide variety of sensitivity patterns. These observations suggest that, in the absence of inhibition, taste cells might be potentially responsive to all taste stimuli. Several studies also point to the idea that response profiles are not stable characteristics of taste cells, but instead, can be influenced by the taste context, defined as the taste stimulus that was presented just before or simultaneously with another, under which they are recorded. A theory, called dynamic coding, was proposed to account for the usefulness of context dependency of taste response profiles. In this theory, those cells that are unaffected by taste context would provide the signal, i.e., the information-containing portion of the ANP, and those cells whose responses are context dependent would provide noise, i.e., providing less stimulus-specific information. When singular taste stimuli are presented, noise cells would provide amplification of the signal, and when complex mixtures are presented, the responses of the noise cells would be suppressed (depending on the particular combination of tastants) and the ratio of signal to noise would be enhanced.

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