Temporal coding of similar tastants in the nucleus of the solitary tract in the rat.

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Introduction

It has been argued that taste quality is encoded by the relative response magnitude across tastants, either in separate groups of tastant-dedicated cells or in the across-neuron pattern of responsiveness produced by various tastants. Recent work in our lab (Di Lorenzo & Victor, J. Neurophysiol., 90: 1418-1431, 2003) has produced evidence that temporal information provides an additional mechanism that may participate in the identification of tastants. This information can be present in the rate envelope of a taste response; in addition, we have found the precise timing of spikes over the course of a taste response to contribute information beyond that contained in the rate envelope.

The present experiment was designed to study 1) whether responses to tastants evoking similar qualities may be distinguished by spike timing and 2) whether the stability of the relative magnitudes of taste responses predicts when temporal coding is present. Preliminary results suggest that rate coding predominates when the response to one stimulus is consistently greater than that to another. However, regardless of whether two tastants evoked similar qualities, spike timing contributed to the overall information in a response when response magnitude varied such that responses to one stimulus were at times larger and at times lower than responses to the other.

Table 1: Summary of All Cells

S = sucrose F = fructose N = NaCl L = LiCl
H = HCl C = citric acid Q = quinine U = urea

	Response Profile spikes/sec					Average 5 sec Response Magnitudes spikes/sec (standard deviation)								
Cell #	Best	S	N	H	Q	S	F	N	L	H	C	Q	U	# of Blocks
1	n/a	n/a	n/a	n/a	n/a	-	-	5.9 (5.8)	2.9 (6.6)	4.4 (2.6)	10.0 (2.7)	-	-	21
2		-0.2	-0.3	0	-0.6	-0.1 (1.1)	0.7 (1.7)	-	-	0.4 (1.5)	0.7 (2.0)	-	-	25
3	Q	0.2	1	0.8	1.4	-	-	8.2 (3.9)	-0.5 (3.2)	-4.1 (3.1)	-2.9 (3.7)	-	-	14
4	H	3.4	1	6.8	2.6	-	-	3.6 (4.2)	3.9 (3.2)	2.4 (3.3)	-0.65 (2.1)	-	-	16
5	Q	-3	-0.6	-0.8	4.4	-	-	6.2 (3.51)	8.95 (1.50)	-0.5 (1.27)	-0.4 (0.67)	-	-	12
6	H	-0.6	-1.6	0.2	-0.8	-	-	1.3 (1.15)	0.5 (0.8)	-	-	0.5 (0.9)	-0.1 (0.6)	10
7	S	1.8	1.7	0.2	-0.7	-	-	0.0 (0.7)	0.2 (0.7)	-	-	0.2 (0.7)	2.1 (1.2)	15
8	N	-0.2	4.8	1.4	0.2	-	-	0.95 (0.9)	0.62 (0.5)	0.6 (0.4)	0.4 (0.9)	-	-	13
9	H	2.4	23	29.2	13.4	-	-	25.6 (1.9)	26.4 (2.3)	28.6 (2.4)	35.5 (2.3)	-	-	11
10	n/a	n/a	n/a	n/a	n/a	-	-	1.8 (2.6)	1.7 (3.0)	0.9 (3.4)	-0.1 (2.2)	-	-	10
11	Q	0.2	1	0.8	1.4	-	-	0.6 (0.4)	0.5 (0.4)	0.9 (0.5)	1.5 (0.6)	-	-	12
12	S	3.8	1	1.4	2	-	-	0.0 (2.0)	1.6 (1.9)	2.1 (2.5)	3.1 (3.0)	-	-	15
13	N	0.6	7.6	7.4	1.4	-	-	12.0 (3.0)	12.4 (1.9)	6.3 (1.3)	7.5 (1.6)	-	-	10
14	N	-0.4	24.5	3.5	3.7	-	-	34.9 (4.6)	37.1 (6.3)	-	-	3.3 (2.0)	1.2 (0.7)	17
15	n/a	35.2	39.4	68.2	-	30.1 (8.5)	21.0 (8.3)	-	-	67.6 (13.1)	-	-	-	12

Surgery and Data Collection

- Fifteen Sprague-Dawley rats (300-500g) were used in this study. Animals were anesthetized (urethane, 1.4 mg/kg, i.p. 25 mg/kg Nembutal i.p.) and prepared for recording in the NTS.
- Etched tungsten microelectrodes were lowered into the NTS until a taste responsive cell responding to two or more tastants was isolated.
- Each trial consisted of 10 sec baseline, 10 sec distilled water rinse, 5 sec tastant, 5 sec pause, and a 20 sec distilled water rinse. The inter-stimulus interval was 2 min. Solutions were passed over the tongue at 5 ml/sec.
- Electrophysiological responses were first recorded to a single presentation of the following tastants: 0.1 M NaCl, 0.01 M HCl, 0.01 M quinine HCl and 0.5 M sucrose. If the cell remained isolated for a sufficient period of time (60-90 minutes) these tastants were presented again.
- The animal was then presented repeatedly with two exemplars each of two taste qualities, depending on the tuning of the cell. The pairs of similar tastants were as follows: 0.01 M HCl and 0.001 M citric acid, 0.5 M sucrose and 0.3 M fructose, 0.1M NaCl and 0.1M LiCl, and 1.0 M urea and 0.01M quinine.
- Taste stimuli were repeated in blocks, such that all four stimuli were presented before a given tastant was repeated. Two exemplars of the same taste quality were never presented consecutively. Blocks were repeated until the unit was lost or isolation degraded.
- Responses were measured as the firing rate during the first 5 sec of stimulus presentation minus the rate of response in the latter 5 sec of water pre-rinse.
- The first two seconds of the taste responses were analyzed for the contribution of spike timing to the overall information they contained.

Cell 13

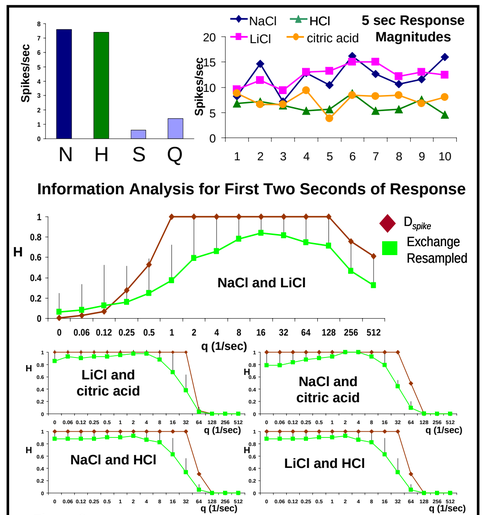

Figure 2: This cell displayed consistently greater responses to salty than to sour tastants. There was considerable overlap between responses to tastants of the same quality, but not dissimilar tastants. Temporal information contributed nearly all the information distinguishing the two salty tastants, while the contribution of firing rate was negligible. Rate coding was sufficient to discriminate between all pairs of salty and sour tastants.

Cell 4

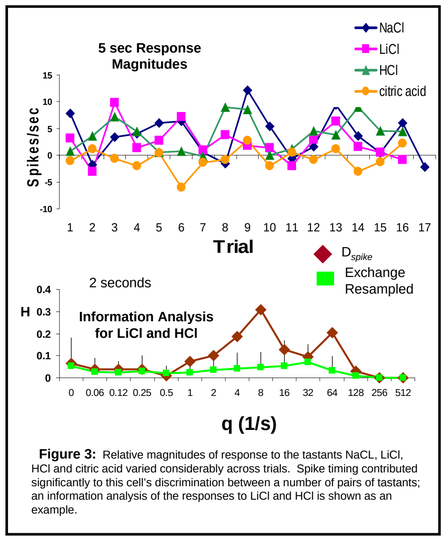

Figure 3: Relative magnitudes of response to the tastants NaCL, LiCl, HCl and citric acid varied considerably across trials. Spike timing contributed significantly to this cell's discrimination between a number of pairs of tastants; an information analysis of the responses to LiCl and HCl is shown as an example.

Summary

1. Electrophysiological responses to taste stimuli were recorded in the NTS of anesthetized rats. Responses to between ten and twenty-five presentations of two pairs of similar tastants, i.e of the same taste quality, were recorded in fifteen cells. When the response profile was recorded, three of these responded best to quinine, three to HCl, two to sucrose, and three to NaCl (Table 1).

2. Responses to repeated presentations of NaCl and LiCl were recorded in thirteen cells. Responses to presentations of HCl and citric acid were recorded in eleven of these cells, and responses to quinine and urea were recorded in three of them. In one cell, responses were recorded to sucrose and fructose, and quinine and urea. In one instance (cell 15), only three tastants were presented: fructose, sucrose, and HCl.

3. Responses to pairs of tastants whose relative response magnitudes remained constant with repetition were less likely to exhibit temporal coding (e.g. Fig. 2).

4. Responses to pairs of tastants whose response magnitudes frequently overlapped across trials often showed a significant contribution of temporal coding to the amount of information distinguishing those responses (Fig. 1, Fig. 2, Fig. 3). This information could be expressed by the precise timing of spikes in a response (Fig. 1, Fig. 3, Fig. 4) or by the time course of response (rate envelope; Fig. 2).

5. Irrespective of whether the tastants involved represent the same taste quality, spike timing may be invoked as a coding mechanism when the rate envelope alone is insufficient to disambiguate taste stimuli.

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Analysis of Temporal Patterns of Response

To characterize the contribution of the temporal structure of a response to the neural code for taste, spike trains were analyzed by the metric space method of Victor and Purpura (1996, 1997).

The analysis derives a family of metrics which measure "distance" (i.e., dissimilarity) between spike trains. Each of these metrics represents the "cost" of transforming one spike train into another by changing a different aspect of the spike trains that are being compared. These include the number of spikes, the precise timing of spikes and the precise sequence of interspike intervals. The simplest of this family of metrics represents the difference in the number of spikes contained in two spike trains associated with two responses. To calculate cost in this case, each spike that is either deleted or added incurs a cost of "1", so that this metric, *Dcount* , is simply the arithmetic difference between the number of spikes in each response.

To measure the difference between two spike trains in terms of the arrangement of spikes in time requires a definition of how close in time two spikes need to occur to be considered equivalent. In the family of metrics described by Victor and Purpura (1996, 1997), the similarity of the timing of spikes, or the sequence of interspike intervals, in two responses is calculated at a variety of levels of precision, measured by a parameter called "*q*." The cost of adding or deleting a spike is set at "1" as in *Dcount* , and, in addition, the cost of moving a spike (or interspike interval) by an amount of time *t* is set at *qt* where *q* is in units of 1/sec. The resulting metric for spike timing is called *Dspike*[*q*]. The corresponding metric for the sequence of interspike intervals is called *Dinterval*[*q*]. For each metric, the information conveyed at various levels of precision (values of *q*) is calculated, and the value of *q* at which information is maximized is obtained. Thus, the relative contribution of spike count, spike timing and the sequence of interspike intervals to the information conveyed by taste responses can be quantified. Importantly, there are several additional analyses that serve as controls for the possibility of spurious results.

Victor, J.D. and Purpura, K.P. (1996) Nature and precision of temporal coding in visual cortex: a metric- space analysis. *J. Neurophysiol.* 76: 1310-26.

Victor, J.D. and Purpura, K.P. (1997) Metric-space analysis of spike trains: theory, algorithms and application. *Network*. 8: 127-164.

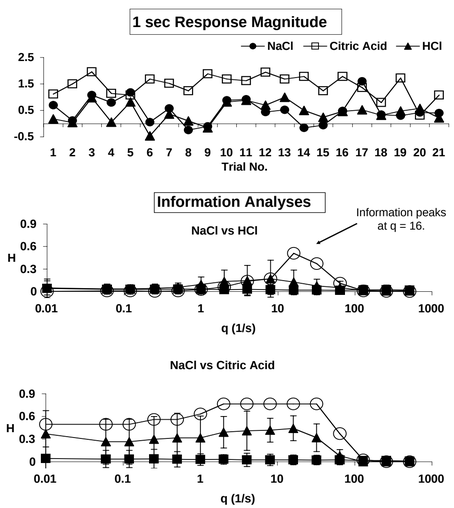

Figure 4: One-second response magnitudes and information analyses from cell 1. In the information analyses, circles represent information contributed by spike timing in the actual data set, triangles represent information contributed in surrogate data sets matching the time-varying rate of the actual data, and squares represent information contributed in surrogate shuffled data sets.

Cell 9

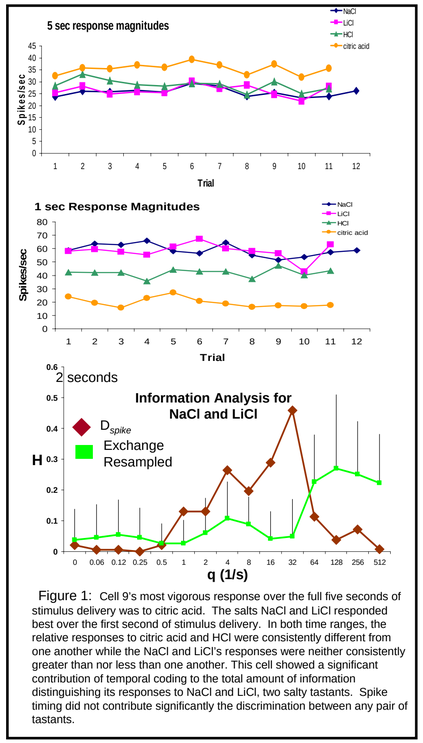

Figure 1: Cell 9's most vigorous response over the full five seconds of stimulus delivery was to citric acid. The salts NaCl and LiCl responded best over the first second of stimulus delivery. In both time ranges, the relative responses to citric acid and HCl were consistently different from one another while the NaCl and LiCl's responses were neither consistently greater than nor less than one another. This cell showed a significant contribution of temporal coding to the total amount of information distinguishing its responses to NaCl and LiCl, two salty tastants. Spike timing did not contribute significantly the discrimination between any pair of tastants.