TUTORIAL

Temporal coding of sensory information in the brain

Peter A. Cariani

Department of Otology and Laryngology, Harvard Medical School,
Eaton Peabody Laboratory, Massachusetts Eye & Ear Infirmary, 243 Charles St., Boston, MA
02114 USA
e-mail: peter@epl.meei.harvard.edu

Abstract: Physiological and psychophysical evidence for temporal coding of sensory qualities in different modalities is considered. A space of pulse codes is outlined that includes 1) channel-codes (across-neural activation patterns), 2) temporal pattern codes (spike patterns), and 3) spike latency codes (relative spike timings). Temporal codes are codes in which spike timings (rather than spike counts) are critical to informational function. Stimulus-dependent temporal patterning of neural responses can arise extrinsically or intrinsically: through stimulus-driven temporal correlations (phase-locking), response latencies, or characteristic timecourses of activation. Phase-locking is abundant in audition, mechanoception, electroception, proprioception, and vision. In phase-locked systems, temporal differences between sensory surfaces can subserve representations of location, motion, and spatial form that can be analyzed via temporal cross-correlation operations. To phase-locking limits, patterns of all-order interspike intervals that are produced reflect stimulus autocorrelation functions that can subserve representations of form. Stimulus-dependent intrinsic temporal response structure is found in all sensory systems. Characteristic temporal patterns that may encode stimulus qualities can be found in the chemical senses, the cutaneous senses, and some aspects of vision. In some modalities (audition, gustation, color vision, mechanoception, nocioception), particular temporal patterns of electrical stimulation elicit specific sensory qualities.

Keywords: Temporal coding, Phase-locking, Autocorrelation, Interspike interval, Spike latency, Neurocomputation

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1. GENERAL CLASSES OF NEURAL PULSE CODES

The neural coding problem in perception involves the identification of the neural correlates of sensory distinctions [1–8]. Sensory information can be encoded in patterns of neurons that respond (channel codes) or in temporal relations between spikes (temporal codes). Temporal codes can be further subdivided into time-of-arrival codes that rely on relative spike timings across neurons and temporal pattern codes that rely on internal patterns of spikes that are produced (Table 1). Here we review psychophysical and neurophysiological evidence that bears on temporal codes in perception.

Temporal codes utilize stimulus-dependent time structure in neural responses. This time structure can be produced either through phase-locking or intrinsic response characteristics. The simplest time-of-arrival code compares spike arrival times between two neurons to convey the time difference between them, irrespective of the temporal structure internal to each spike train. In contrast, temporal pattern codes utilize this internal time structure to convey information. Temporal pattern codes utilize interspike intervals [1, 8], interval sequences [9], and timecourses of discharge [10, 11] to convey information. Both time-of-arrival and temporal pattern codes permit multiplexing of different kinds of information [10], though time-division [12], frequency-division [13, 14] and code-division [9] schemes. Some evidence for temporal coding exists in virtually every sensory modality [1–5, 7, 15–18]. This review will concentrate on time-of-arrival and temporal pattern codes that arise from both phase-locked and intrinsic temporal response properties of sensory systems.

2. TIME-OF-ARRIVAL CODES IN PHASE-LOCKED SENSORY SYSTEMS

A highly robust cue for stimulus direction is the temporal pattern of activation that it produces across different sensory surfaces. In audition, mechanoception, and electroception, there appear to be common mechanisms that make use of this cue to translate temporal differences into apparent location [3, 15, 16]. In all of these sys-

Table 1 General types of neural codes.

Code class	Response properties	Neural representation/analysis
Channel	Stimulus-driven responses	Characteristic across-neuron activation patterns
Time-of-arrival	Stimulus-locked responses	Temporal crosscorrelation
	Intrinsic responses	Characteristic latency-precedence relations
Temporal pattern	Stimulus-locked responses	Temporal autocorrelation Within neurons (interspike interval patterns) Across neurons (volley patterns)
	Intrinsic responses	Characteristic temporal response pattern

tems, receptors phase-lock to their respective adequate stimuli, such that the temporal structure of the stimulus is faithfully impressed on the timings of spikes produced by primary sensory neurons. By virtue of phase-locking, relative-times-of-arrival of a stimulus at different receptor sites are translated into relative spike latencies in their respective sensory pathways. These relative spike timings are in turn analyzed via neural delay lines and temporal coincidence detectors. This temporal cross-correlation operation appears to be common neurocomputational strategy for many sensory systems across a wide range of phyla.

A classic example is the localization of sounds in the azimuthal plane by means of interaural time differences (ITD). Humans are able to use interaural time differences as small as 20–30 μs to localize sounds. Wavefronts from sound sources not directly in front of an observer arrive at the two ears at different times. They subsequently produce phase-locked spikes in auditory nerve fibers whose relative timings reflect the interaural time differences. In the auditory brainstem, highly secure synapses, tapped delay lines, and neural coincidence detectors in effect implement binaural cross-correlation operations that provide a readout of interaural time delays, and consequently, of azimuth estimates [17, 19, 20]. Units whose discharge rates reflect tuning to particular interaural delays [21] are found at higher stations in the ascending auditory pathway. Central representations of auditory space may also utilize location-dependent temporal response patterns [22] and/or population-latency profiles [23].

A strikingly similar situation can be found in mechanoception, where relative temporal delays (>1 ms) of mechanical stimulation at different skin locations are perceived as differences in apparent location [15]. As in audition, perceived locations move toward the sensory surfaces that lead in time. Mechanoceptors phase-lock to skin deformations and hair displacements, such that their relative timings are impressed on the discharges of neurons at many stations in the somatosensory path-

way [24, 25]. That other sensory systems exhibit comparable behavior suggests that the brain may have a generalized capacity to distinguish fine spike timings (~ 1 ms) [15].

In echolocation systems of bats and cetaceans, acoustic signals are emitted and their reflection patterns are observed. Time delays between emitted signals and their echoes provide information about distances and shapes of objects. In bats, relative times-of-arrival between spikes produced by cries and echoes permit precise estimates of target ranges and shapes that correspond to microsecond time differences [26, 27].

Electroception involves another time-based active sensing strategy [16, 28]. Weakly electric fish produce sinusoidally-varying electrical fields around their bodies that are deformed by the presence of nearby external objects. These deformations alter the relative phases of the electric field at different body locations, which alter the relative latencies of spikes produced in afferent electroceptive pathways. As in the binaural example, these pathways have highly secure, low jitter connections, delay lines, and central coincidence detectors that permit extremely small time-of-arrival differences (here, $<1 \mu$s) to be distinguished.

Visual receptor arrays can also be considered as collections of receptor surfaces. Phase-locking to temporal modulations of luminance produced by moving spatial patterns is ubiquitous in the visual systems of animals [29, 30]. As a consequence of phase-locking, temporal correlations between spikes produced in different visual channels potentially provide a general neurocomputational basis for the representation of visual motion. In the fly visual system, different spike timings in neighboring ommatids are used for detection of motion [7, 31, 32]. This temporal cross-correlation mechanism permits rapid and precise motion from small numbers of incoming spikes to inform flight course corrections in as little as 30 ms [7, 32].

Binocular vision involves cross-correlation of spatio-temporal patterns registered on the two retinas. Introduc-

tion of systematic time delays between the outputs of the two retinas can be produced by placing a neutral density filter over one eye that attenuates luminance and increases the spike latencies in that monocular pathway. When a horizontally moving object is viewed under such circumstances, an illusion of depth, known as the Pulfrich effect [3], is created by the internal temporal disparities produced by the different spike latencies in the two pathways. Provided that at least some spikes are temporally correlated with the movements of object edges across receptive fields [33], then a temporal cross-correlation operation can potentially handle binocular temporal disparities in a manner not unlike ITD processing in binaural hearing.

On the motor side, muscle stretch and joint position receptors phase-lock to muscle movements [34], while vestibular afferents phase-lock to head accelerations. These provide neural representation of the temporal structure of actions: the relative timings of muscle activations and their consequences.

3. TEMPORAL PATTERN CODES IN PHASE-LOCKED RECEPTOR SYSTEMS

To the extent that sensory receptors follow the time structure of their adequate stimuli, that structure is impressed on the discharges of sensory neurons. As we have seen above, comparisons of relative timings across receptors yields information about direction and movement of the stimulus. Pitch, timbre, rhythm, flutter, and tactile texture are examples of sensory qualities that depend on the internal time structure of the stimulus. Temporal patterns of spikes produced by arrays of phase-locking receptors reflect this internal structure and thus provide information about the temporal form of the stimulus.

In the auditory system, functional roles for phase-locked neural timing information in both binaural localization and frequency representation have been well appreciated [6, 35, 36]. Phase-locking of auditory nerve fibers to acoustic stimuli creates time intervals between spikes (interspike intervals) that are directly related to stimulus periodicities. Interval distributions consequently contain spectral information up to the limits of phase-locking (5–10 kHz, depending on species and statistical criterion). Interspike interval representations easily account for the high precision of pure tone frequency discrimination over a wide range of frequencies and sound pressure levels, and for its decline as phase-locking weakens at higher frequencies [7, 35, 37]. Interestingly, minimal human Weber fractions for frequency (0.2% for 1 kHz pure tones = 20 μs difference in period) are comparable to minimal discriminable ITD differences in binaural localization (∼ 20 μs).

The pitches of complex tones also appear to be explicable in terms of interspike intervals. Harmonic complex tones produce pitches at their fundamentals, even in the absence of any spectral energy at the fundamental itself ("the pitch of the missing fundamental"). Many different kinds of stimuli with very different spectral energy distributions can produce the same low, "periodicity" pitches [35, 38, 39]. The most comprehensive and successful neurally-based theories of pitch compute temporal autocorrelations using all-order interspike intervals (*i.e.* between both consecutive and nonconsecutive spikes). J.C.R. Licklider in 1951 outlined a time-delay neural network that operated on phase-locked auditory nerve responses to perform an autocorrelation analysis of interspike intervals in each frequency channel [40]. Three decades later related temporal models for pitch were proposed that summed together interspike intervals across the auditory nerve [35, 39]. These population-based temporal pitch models have been tested in computer simulations [41] and in neurophysiological studies [8, 42, 43].

The major finding of these studies has been that the most common interval present in the auditory nerve at any given time almost invariably corresponds to the pitch that is heard (the few exceptions involve octave shifts). The fraction of pitch-related intervals amongst all others qualitatively corresponds to the strength of the pitch that is heard. Such purely temporal, population-interval representations also account for a number of complex and subtle pitch phenomena: pitches of complexes with "missing fundamentals", pitch equivalence classes (metamery), relative invariance of pitch and pitch salience with sound pressure level, pitches of stimuli having psychophysically-unresolved harmonics, the "nonspectral" pitches of amplitude modulated noise, as well as complex patterns of pitch shift that are heard for inharmonic stimuli. Temporal correlates of many of these effects are also seen in single neuron responses [44] and in human frequency-following responses (FFR) produced by the auditory midbrain [45].

These population-wide distributions of all-order interspike intervals form general-purpose temporal representations that resemble stimulus autocorrelation functions [8], which can serve as time-domain representations of stimulus spectrum. Purely temporal representations of spectral shape and vowel quality are therefore also possible. Auditory nerve fibers phase-lock to frequency components in formant regions, producing related intervals whose respective numbers depend on component intensities. Population-wide interval distributions represent formant patterns through distributions of short intervals (< 4 ms) that are characteristic of the different vowels that produced them [5, 39, 46, 47],

The somatosensory analogue of auditory pitch is the sense of flutter-vibration [3, 15, 24] Discrimination of vibration rates of up to 1 kHz is based on interspike intervals produced through phase-locking of cutaneous afferents [25]. As in audition, complex tactile textures produce spectrally-richer temporal patterns of spikes [48, 49].

Thus, in those sensory systems where spikes are locked to stimulus transients and ongoing periodicities, direct temporal representation of the form of the stimulus is possible. Visual form could potentially be encoded through time intervals between phase-locked spikes produced at different retinal locations. Recent demonstrations that visual forms can be created through short-term spatiotemporal motion correlations that contain no long-term spatial structure suggest some role for temporal correlation structure in perception of visual forms [50].

The eyes are in constant motion, drifting even during fixation, and many central visual neurons discharge with precise latency when contrast gradients (edges) cross their receptive fields [33]. Highest observed precisions of stimulus-driven spike timings in visual systems range from hundreds of microseconds to a few milliseconds [7, 32, 51, 52]. As in many other sensory systems, perceptual discriminations that seen in visual psychophysical tasks are much finer than those permitted by the relatively coarse spatial resolutions of individual receptive fields ("hyperacuity") [3, 7]. However, if the visual system were able to make use of fine spike timing, then these observed spike precisions of 1 millisecond would account for its acuity [53].

Spatial frequency is the visual analogue of acoustic frequency, with sinusoidally modulated gratings being the visual analogues of pure tones. Phase-locking to visual flickers of 50–100 Hz and higher in early stages of visual processing is not uncommon. When such gratings are drifted across receptive fields at constant velocities, their temporal frequency at any given point simply reflects their spatial frequency. Spike timings, as analyzed through post-stimulus time (PST), period, and all-order interval histograms (Fig. 1B), faithfully replicate the temporal structure of the drifting image. As in audition, temporal frequency can thus be accurately estimated from interspike interval statistics. From the distributions in Fig. 1, temporal modulation frequencies of 16 and 32 Hz were estimated to within 1–2% using smoothed peak picking and to 0.1 Hz using best cosine fit. As for harmonic complexes in audition, there is also a "missing" fundamental phenomenon in spatial vision [54] that may be explicable in terms of (spatial) autocorrelations.

Spatial autocorrelation models account for many aspects of visual shape and texture perception [55–57]. Neural autocorrelation mechanisms based on stationary spatial activation patterns [55] and on neural synchronies [56, 57] have been proposed. The latter, spatiotemporal mechanisms move towards a theory of visual form that is based on stimulus-driven, temporally correlated spatial structure.

4. INTRINSIC TEMPORAL PATTERNS FOR ENCODING SENSORY QUALITY

Some sensory qualities, such as distinctions of smell, taste, pain, color, and temperature do not have natural correlates in the internal structure of stimulus waveforms. In sensory systems that subserve such distinctions, there may nevertheless be intrinsic, temporal patterns of neural response that are stimulus-dependent. All sensory receptors and neural populations have impulse- and step-response patterns that reflect timecourses of underlying biophysical, biochemical, and neural processes. Classic examples of such intrinsic response patterns are the different types of tone burst responses (chopping, pausing, buildup, onset) that are seen in the cochlear nucleus.

Early lateral inhibitory interactions also set up temporal precedence relations that can create different relative response latencies for different stimuli. Such across-neuron latency patterns can convey information concerning stimulus quality and intensity [2, 58, 59]. Latency differences can be further magnified by feedforward lateral inhibition [60].

The most striking evidence for temporal coding in the chemical senses is found in the gustatory system. In primary gustatory neurons of the rat, neural responses exhibit tastant-specific temporal discharge patterns (Fig. 2C) [61, 62]. Electrical stimulation of other rats using recorded temporal response patterns elicit orofacial expressions and behaviors that would normally be associated with the respective tastant. When these recorded, naturally-generated temporal patterns used for stimulation are scrambled, or isochronous pulse trains with the same pulse rates are used, no corresponding orofacial expressions and behaviors are produced.

In olfaction, odorant-related time patterns of neural response have been observed in a wide variety of systems [63–67] Historically, efforts to find temporal pattern primitives for smell have been confounded by concentration-dependent changes in temporal response patterns [68] and complex history-dependencies. However, phase-locking to air-intake (sniffing) cycles [69] and emergent synchronized oscillations may provide population-based reference times for latency-pattern [65, 66] and latency-offset codes [70, 71]. Artificial chemical recognition devices that analyze intrinsic temporal response patterns of optical chemosensors have been developed that outperform analyses based on averaged across-
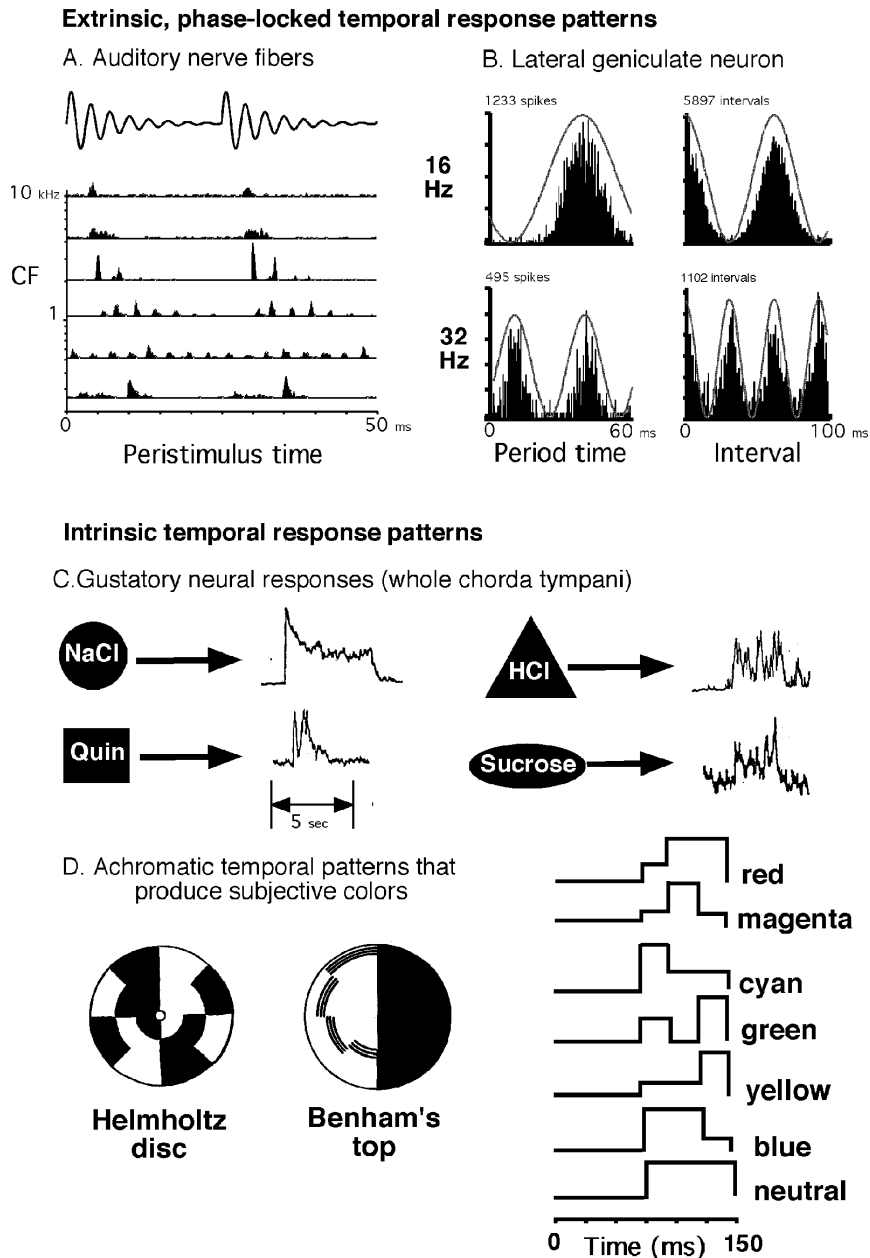
Extrinsic, phase-locked temporal response patterns

A. Auditory nerve fibers

B. Lateral geniculate neuron

Intrinsic temporal response patterns

C. Gustatory neural responses (whole chorda tympani)

D. Achromatic temporal patterns that produce subjective colors

Fig. 1 Extrinsic and intrinsic temporal response patterns. A. Phase-locked responses in six auditory nerve fibers in Dial-anesthetized cat. Plot shows stimulus waveform and post-stimulus time histograms arranged by characteristic frequency (CF) for 100 presentations at 60 dB SPL. B. Phase-locked responses of a typical lateral geniculate parvo cell in anesthetized macaque to 16 and 32 Hz sinusoidal temporal modulations of luminance [83]. Period histograms and all-order interval (autocorrelation) histograms for 25 s of response. Stimulus waveform and autocorrelation have been superimposed (phase-matched). C. Intrinsic response timecourses in the gustatory system to four tastants of different classes: 0.1M NaCl (salty), 0.1M quinine (bitter), 0.1M HCl (sour), 0.5M sucrose (sweet). Waveforms are typical whole-nerve responses recorded from chorda tympani of decerebrate rats (reproduced w. permission) [61]. D. Achromatic temporal patterns that produce subjective colors. Left. Rotating patterns of Helmholtz and Benham. Right: Glow tube luminance patterns and their subjective colors (redrawn) [75].

sensor activation patterns [72].

Intrinsic temporal patterns of neural response potentially encode a number of visual attributes: texture, contrast, pattern, and color. Different patterns of visual stimulation produce different intrinsic time patterns of neural response [10, 13, 14, 73, 74].

Notable are color percepts evoked by temporal flicker. The best known demonstration of these "subjective", "achromatic" "Fechner colors" is the Benham Top (panel D), which generates temporal sequences of changing luminances and edges that correspond to particular colors [75–77]. Glow tubes have also been used to characterize the time patterns that elicit various colors [75]. Related temporal patterns of electrical stimulation of the retina produce correspondingly colored phosphenes [78]. One interpretation is that both temporally-patterned flicker and electrical stimulation extrinsically drive retinal elements to produce temporal discharge patterns that are subsequently interpreted as color signals by central visual stations. These imposed temporal patterns are presumably similar to intrinsic ones that would normally be generated by wavelength-dependent responses in the retina. Wavelength-dependent interspike interval patterns [79] latency patterns, and characteristic time courses of response [10, 14, 73] are seen in different visual systems, although their relation to subjective colors is not clear.

Historically there has been a longstanding debate over whether cutaneous sensations such as pain, touch, warmth, and cold are encoded via labeled lines (neural specificity models) or via pattern codes (channel-temporal-patterns). Interval sequence patterns have been found in thalamic units whose presence coincides with behavioral signs of pain, and whose disruption by means of appropriately patterned electrical stimulation appears to provide analgesia [9].

5. PERCEPTS EVOKED BY TEMPORALLY-PATTERNED ELECTRICAL STIMULI

The ability of a specific temporal pattern of electrical stimulation to evoke a particular sensory quality is strongly suggestive of an underlying temporal code. In a number of cases, temporally-patterned electrical stimuli produce taste [61, 62], color [78], and pain percepts [9], while randomly patterned electrical stimulation controls do not. Since electrical stimulation with gross electrodes nonspecifically drives large ensembles of neurons in the same way, it is difficult to attribute the effect to activation of particular neuronal types.

In phase-locked systems, periodic electrical stimuli produce qualities related to stimulus frequency. Periodic stimulation of the skin evokes sensations akin to flutter-vibration [25]. Electrical stimulation of the cochlea produces distinguishable pitch percepts up to roughly 500–1,000 Hz. Although auditory nerve fibers phase lock well to electrical stimuli of much higher frequencies, the highly abnormal interval patterns that are produced for periodicities above 600 Hz may explain their poor discrimination [80]. The impressive effectiveness of present day cochlear implants in restoring speech reception may be due to the critical role that lower-frequency temporal patterns (< 200 Hz) play in the speech code itself [81, 82].

6. CONCLUSIONS

Stimulus-dependent temporal response structure is found in an astonishingly wide range of sensory systems. Phase-locked responses permit time differences of response to be used as cues for stimulus location that can be analyzed using neural temporal cross-correlation architectures. Phase-locking impresses stimulus time structure on neural responses, providing interval-based representations of the stimulus form that can be analyzed through neural temporal autocorrelation architectures. Intrinsic temporal response patterns produce temporal cues for stimulus properties. Psychoneural correspondences between perceptual qualities and temporal response patterns produced by natural and electrical stimuli suggest that temporal codes may subserve many more perceptual functions than is commonly believed.

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Peter Cariani received his B.S. in Life Sciences from M.I.T. in 1978. As a graduate student he studied under theoretical biologist Howard Pattee in the Department of Systems Science at the State University of New York at Binghamton, receiving his Ph.D. in 1989. His doctoral thesis addressed evolution of new sensing functions and its implications for artificial devices. In 1990 he joined the Eaton Peabody Laboratory of Auditory Physiology as a postdoctoral fellow, and worked with Bertrand Delgutte on the coding of pitch, timbre, musical consonance, and phonetic distinctions in the auditory nerve. Dr. Cariani is currently an Assistant Professor in Otology and Laryngology at Harvard Medical School and a Research Associate at the Eaton Peabody Laboratory. He is currently developing neural timing networks that process temporally-coded patterns. With Dr. Mark Tramo, he is investigating the neural representation of pitch in the auditory cortex.