Modulated Noisy Biological Dynamics: Three Examples

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Three examples of noisy biological dynamics modulated by a periodic signal are discussed. A minimal neuron model driven by stochastic noise and small periodic force show a firing statistic comparable with stochastic resonance as demonstrated in bistable systems. Similar results are obtained from responses to periodic vibrotactile stimulation on higher-order neuronal units of the somatosensory pathway. Finally, results from a bistable visual perception task exhibiting stochastic resonance are reported.

KEY WORDS: Stochastic resonance; spike generation; mechanoreceptors; spinal cord; somatosensory cortex; visual perception.

1. INTRODUCTION

Appropriate encoding of information is a major task in the nervous system. Mechanisms by which sensory inputs are encoded and eventually decoded in the central nervous system have to take into account the presence of considerable uncorrelated background noise. This noise can be approximated by the ongoing spontaneous neuronal activity. The mean rate of the cellular spontaneous activity varies between regions of the brain and with states of arousal or wakefulness of the animal, yet to date, no concrete function is assigned to this activity.

Recently, in an apparently unrelated context, it has been noticed that the output signal from a noisy bistable system can be modulated in time by applying a weak external periodic forcing.[1, 13] This phenomenon is curious in that an increase in the input noise can result in an improvement in the output signal-to-noise ratio. Since the optimum level of noise at which

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the output of the device becomes coherent with the periodic signal occurs when the two characteristic times, the Kramers time and the period of the signal, are of the same order of magnitude, the phenomenon is known as stochastic resonance. By considering neurons as stochastically driven two-state devices, recent results[4, 10] suggest that in some sensory processes signal encoding might be related to stochastic resonance. In spite of the attractiveness of this theory, no numerical evidence has been collected from realistic mathematical models of neurons. The analysis of previously reported probability density functions of the interspike intervals obtained *in vivo* from auditory and visual sensory neurons seems to agree with the main theoretical arguments. However, there is need for specific experimental observations designed specifically to investigate if stochastic resonance occurs in excitable tissue.

This paper discusses biological dynamics, at three organizational levels, in which noise-induced transitions and periodic modulation are involved. In Section 2 the dynamics of a minimal excitable model with stochastic and periodic forcing is introduced. *In vivo* experiments are reported in Section 3, where encoding of sensory periodic stimuli in different levels of the neuraxis is investigated. Section 4 describes a visual perception task performed on human volunteers, demonstrating some of the properties of stochastic resonance at the level of the integrated output of the conscious brain. Finally, Section 5 offers a biologically oriented discussion of potential areas in which stochastic resonance can help in understanding biological behavior.

2. A SIMPLE TIME-DISCRETE NEURON MODEL

A generic excitable system must be described by at least two state variables: potential and recovery. The minimal time-discrete model equations we study are of the form

$$x_{n+1} = f(x_n, y_n) = x_n^2 \exp(y_n - x_n) + k + z_n$$
$$y_{n+1} = g(y_n, x_n) = ay_n - bx_n + c \tag{1}$$

Equation (1) is a 2-dimensional finite-difference equation, where subscripts stand for the iteration step, x is the state variable related to membrane potential, and y is the second state variable equivalent to a generalized recovery current. z_n represents the external stimulation, and a, b, c are positive parameters $(a, b < 1)$, where a determines the time constant of reactivation, b the rate of inactivation, and c the maximum amplitude of the generalized recovery current (in all the results presented here we use $a = 0.89$, $b = 0.6$, $c = 0.28$, $k = 0.01$). Equation (1) describes the local

dynamics of a single excitable cell at one point in space. The dynamics of Eq. (1) is easily grasped by phase plane analysis. In this simple model it is possible to obtain the nullclines for x and y in closed form:

$$x_{n+1} = x_n = (ay - y + c)/b$$
$$y_{n+1} = y_n = \log(x - k) - 2\log(x) + x$$

(2)

Figure 1 is the graph of Eq. (2). The intersection of both nullclines indicates the singular point, which for the above parameter values is stable. The singular point determine the "quiescent" state of the neuron in the absence of external input. Increasing k in this model has the same effect of a constant bias current being applied to a neuron. For $k \sim 0.029$ an unstable focus appears and at $k \sim 0.03$ a "limit cycle" coexists with an unstable point in the same way as described in other models as well as in *in vitro* experiments.[17]

The model's response to periodic pulsatile stimulation (i.e., $z \neq 0$ for one or more iteration steps, at n multiples of the period, $z = 0$ otherwise) was briefly examined to see its correspondence with the dynamics of periodically perturbed neurons.[12] As stimulus period is decreased (from one stimulus every 45 time steps to one every 10 steps; constant amplitude $z_n = 0.03$), there is a monotonic increase in the $n:m$ ratio, where m is the number of action potentials elicited in each periodic cycle of n applied stimuli (Fig. 2). Examination of the parameter space (stimulus amplitude vs. stimulus period) revealed periodic responses (with isoperiodic regions having $n:m$ structure following Farey's series) for most parameter values;
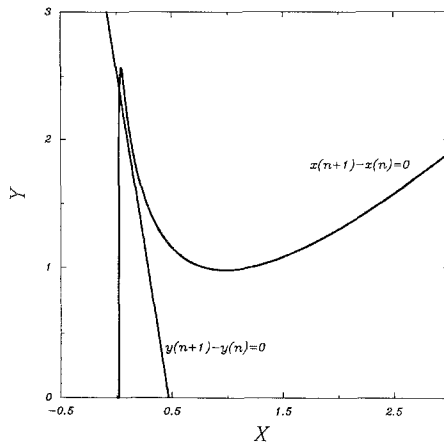

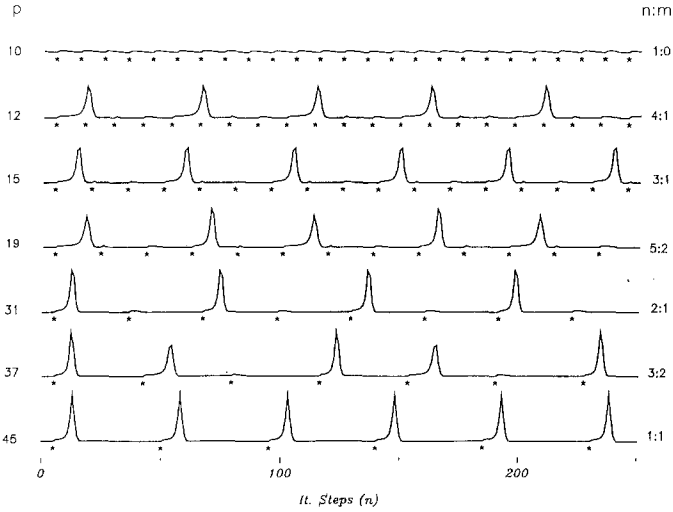Fig. 1.   Nullclines of Eq. (1) for the parameter values indicated in the text.

Fig. 2. Response to periodic pulsatile stimulation of the neuron model of Eq. (1). Forcing z_n is set to 0.03 every p iterations (zero otherwise). Asterisks indicates stimuli. Locked periodic responses are labeled as ratios $n:m$, where m is the number of action potentials ("spikes") contained on a sequence of n stimuli.
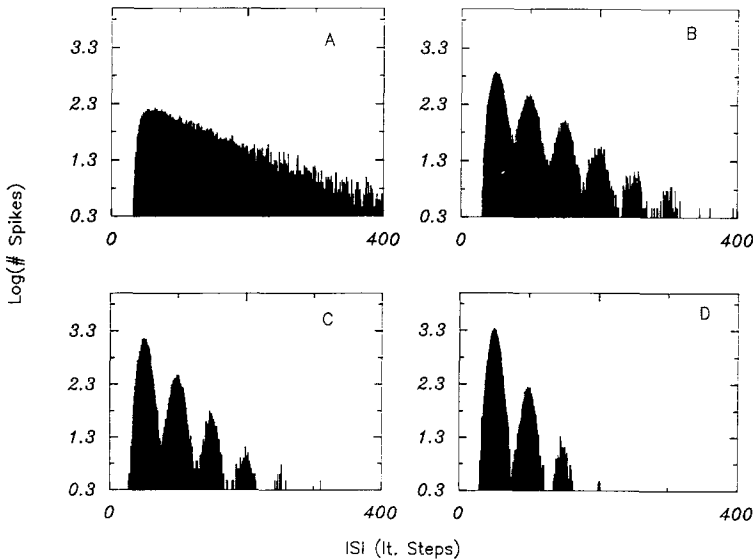

Fig. 3. Interspike interval histogram of the neuron model of Eq. (1) with constant stochastic input (white noise, amplitude 0.12) and different levels of (subthreshold) sinusoidal modulation amplitude (period, 50 iteration steps). (A) No modulation; (B–D) modulation amplitude 0.02, 0.03, and 0.04, respectively.

aperiodic responses are found in small regions. These results agree with those obtained in the squid axon.[12]

When white noise was applied in Eq. (1), the interspike interval histogram (ISIH) of the output spike train had a Poisson distribution (see Fig. 3A). Keeping noise amplitude constant and adding a sinusoidal signal resulted in an exponentially decreasing multipeaked ISIH distribution, where the first peak was at the period of the sinusoidal stimulus and the other peaks were at multiples of the stimulus period. Increasing the amplitude of the sinusoidal signal increased the rate of the exponential envelope (see Figs. 3B–3D). These results are identical to the stochastic resonance properties reported for bistable systems.[10] The first return map of the intervals in one of the above cases (Fig. 3B) is shown in Fig. 4. Notice that this map closely resembles the return maps reported by Siegel[20] for visual cortical cells excited by a flashing bar within its receptive field.

Resonance is also demonstrable by looking at the coherence of the output with the periodic signal for different levels of noise. This is presented in Fig. 5. In this case the input signal amplitude is fixed at a subthreshold value (i.e., unable to induce an action potential) and the ISIH is invest-igated for increasing noise. Of particular interest is the total number of spikes collected during a given fixed time in relation with those intervals equal to the forcing period, both as functions of noise amplitude. In Fig. 5 the total number of counts is plotted in the top panel; those counts with interspike intervals equal to the period of the signal are plotted in the middle panel; and the ratio total counts and counts equal to the forcing
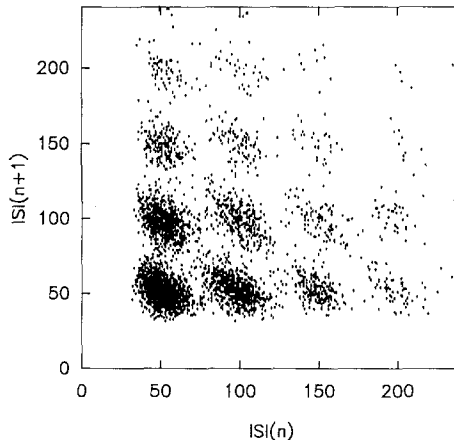

Fig. 4.   Return map of the interspike intervals (ISI) for the data plotted in Fig. 3B.
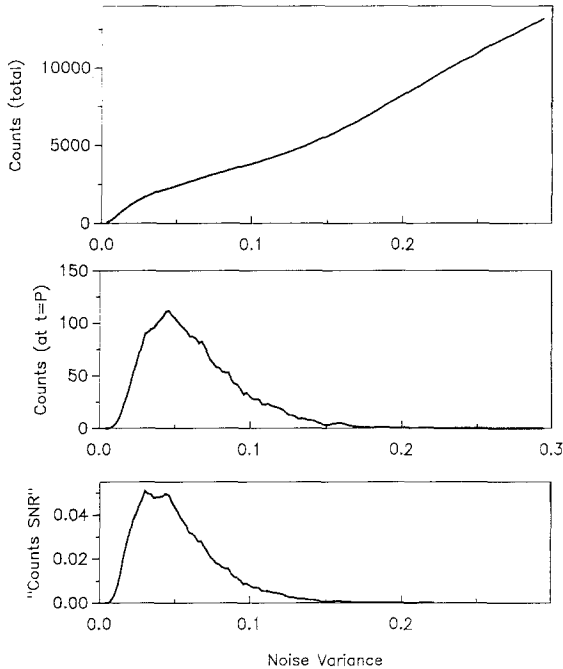
Fig. 5. Coherence of the output with the periodic signal (period, 40 iteration steps; amplitude, 0.015) for increasing levels of noise. Total number of spikes is counted in successive runs of fixed length (10^5 iterations) for different levels of noise (plotted in top panel). Spikes with intervals equal to the period of the modulation are also counted as a measure of output coherence (middle panel). The ratio of the latter to the former is an estimation of the signal-to-noise ratio (bottom panel).

period are plotted in the bottom panel. Notice that number of counts equals zero for zero noise, total counts rises monotonically, and number of counts of intervals equal to the signal period reaches a peak for a given noise variance. The location of this "resonant" peak is dependent on the signal period (other variables fixed), moving to the left for shorter signal periods.

3. RESPONSE PROPERTIES OF SOMATOSENSORY NEURONS

Mechanoreceptor response properties were studied more than 20 years ago. These studies showed that the ISIH of rapidly adapting type primary afferents exhibit multipeaked distributions with envelopes resembling exponential decay when a weak vibratory mechanical stimulus is applied to their receptive fields.[24] Thus, we investigated the dynamics of rapidly

adapting type neurons in the spinal cord dorsal horn and the primary somatosensory cortex of the cat.

Cats were anesthetized with chloralose (80 mg/kg) and maintained by nembutal drip (5 mg/kg per hr). In some animals the primary somatosensory cortex was exposed following a craniectomy and the response properties of units with contralateral hindlimb receptive fields and with rapidly adapting type responses were studied. In other animals the spinal cord dorsal horn of the lumbar enlargement was exposed through a laminectomy and units with ipsilateral receptive fields on the glabrous pads and with rapidly adapting type responses isolated and studied. Spinal cord and cortical single-unit activity was recorded using low-impedance tungsten electrodes (1–5 Mohm). Unit activity was amplified, filtered, both recorded on tape and simultaneously passed through a window discriminator, and the time intervals between spikes stored in a computer. The computer has an on-line display of the ISIH and the peristimulus histogram (for more details see ref. 21). The hindlimb of interest was glued to a stage and the receptive field of isolated units determined by stroking the skin with a brush. The most sensitive spot of the receptive field was stimulated with an electromagnetically driven stylet. This stimulator displaces the stylet (tip diameter 1 mm) by following the amplitude and frequency of a command voltage (linear response DC–150 Hz, amplitude range 0.001–1 mm). The stylet was placed in the receptive field to induce a constant indentation of the skin upon which was superimposed a sinusoidal modulation of various frequencies and amplitudes.

For rapidly adapting type units, the statistic of the ISIH of spinal cord and somatosensory cortical units during vibratory stimulation of their receptive fields showed a multimodal distribution with peak amplitudes decaying exponentially. The rate of decay changed relative to the amplitude of the stimulation. One example, presented in Fig. 6, corresponds to responses recorded from a spinal cord unit during sinusoidal mechanical stimulation (period of stimulus, 190 msec) of the hindlimb receptive field. The ISIHs calculated for consecutive runs at two amplitudes of the vibratory stimuli are shown in Fig. 6 (top panels, 7 and 5 arbitrary amplitude units). The logarithm of the ISIH peaks (located at multiple integers of 190 msec) was plotted for both runs (see Fig. 6, bottom panel). It is seen that both data sets are well defined by a linear regression line ($r = 0.998$ and 0.999) and that the slope, indicating the rate of decay, increased as the stimulus amplitude increased, just as expected if we are in the presence of stochastic resonance.

In the somatosensory cortex the results were basically similar. An example corresponding to activity recorded from the cortex is presented in Fig. 7, where the ISIH and an exponential fitted to the integer multiples of

Ts=0.19 sec
As=7 (AU)
n=661

Ts=0.19 sec
As=5 (AU)
n=601

Count

ISI (sec)

Log(Count)

■ 7 AU { y = 5.9427 - 7.1115x
          R^2 = 0.998

● 5 AU { y = 4.7780 - 4.5355x
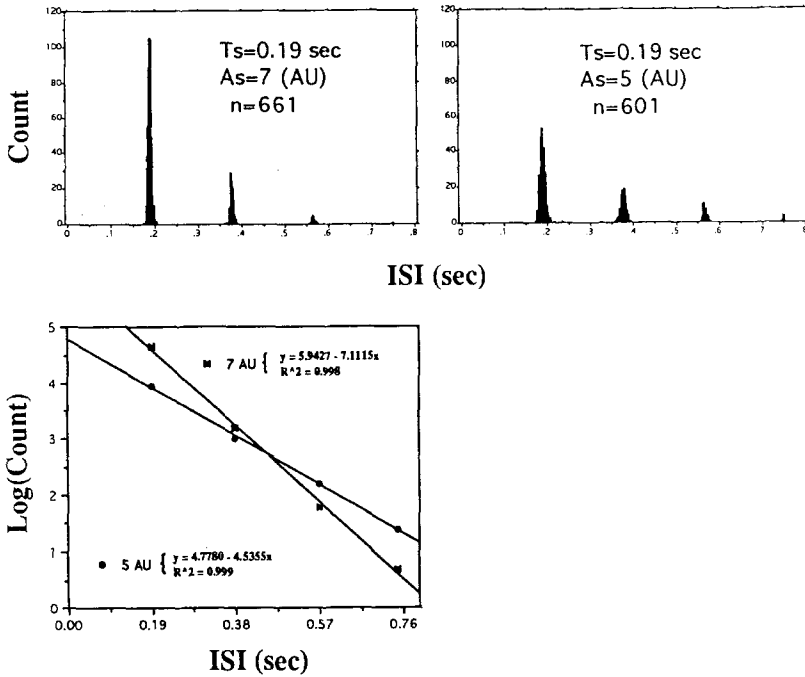   R^2 = 0.999

ISI (sec)

Fig. 6. Interspike interval histograms (top panels) for a neuron in the cat's spinal cord during vibrotactile periodic stimulation of two different amplitudes (7 and 5 arbitrary units). Bottom panel shows the exponential fit of the peak amplitudes in log scale for both cases.
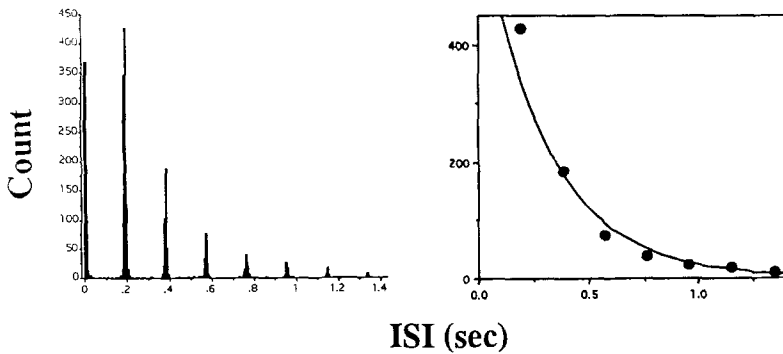
Count

ISI (sec)

Fig. 7. Interspike interval histogram for a neuron in the cat's somatosensory cortex during vibrotactile periodic stimulation. Right panel shows the exponential fit of the peak amplitudes at integer multiples of the driving period.

the driving frequency are plotted. This particular case is shown because there is an additional peak at an interval smaller than the stimulation period. It was found that the presence of this peak depended on the frequency of stimulation, vanishing for values corresponding to the most sensitive frequency of the receptor.

Unlike the auditory primary afferents, which can have spontaneous activity rates of up to 100 Hz, or proprioreceptors, vibrotactile afferents are silent in the absence of somatic stimulation. However, they do exhibit multipeaked responses to small-amplitude sinusoidal stimuli. This implies that the receptor noise is subthreshold and, therefore, tactile primary afferents operate outside the range of stochastic resonance. On the other hand, psychophysical studies in humans show that touch perception threshold decreases when the skin surface temperature is increased.[2] One explanation for this phenomenon would be an increase in receptor noise with temperature, maybe even driving the system into stochastic resonance, which remains to be tested. The spinal cord and cortical units shown above also had no spontaneous activity. However, this is a reflection of the depth of anesthesia, since most central vibrotactile cells display spontaneous activity that can be modulated with states of arousal.

The numerical results in the preceding section as well as the *in vivo* results indicate that neurons are able to exhibit some of the properties of noisy bistable systems. Does this then imply that these higher moment statistical properties of neurons are relevant in information processing in the central nervous system and thus significant for the behavior of the organism? Mean rate or phase-locked responses of neurons have been the mainstay of most neurophysiologic studies. Most coding properties of sensory neurons and motor output commands are understood by the mean rate response of cells, where the background activity is either ignored or subtracted from the response, in the vertebrate brain. However, the ubiquity of noise in the brain is too expensive (in terms of energy demand) to be accepted as just an epiphenomenon.

4. ADDING NOISE AND PERIODIC MODULATION TO HAKEN'S BISTABLE VISUAL PERCEPTION

In stereoscopic vision, the transition from viewing the local elements of an image to perceiving the global picture requires time and exhibits hysteresis; for example, the perception of the Necker cube[25] or of Julesz figures.[9] Although these effects have been described repeatedly,[23] to date there has been no theoretical framework to allow the examination of such phenomena. Here we describe a one-dimensional mapping of visual perception which exhibits stochastic resonance.

Haken[6] briefly described a set of images exhibiting perceptual hysteresis. These images were a sequence of eight hand-drawn images which are meant to represent a smooth transition from a man's face to the body of a woman. Perceptual hysteresis is easily demonstrable using Haken's pictures. Looking at the pictures sequentially in one direction (i.e., starting in the "face") or in the other (i.e., starting with the "woman"), the visual perception switches at different points. However, if the experiment is repeated by the same volunteer several times, some "imperfections" in the original drawing are rapidly learned (as cues), and used by the subject to identify which order corresponds to the image presented. This results in cancellation of the initial detected perceptual hysteresis. To have a smooth transition from women to face, cues have to be removed from Haken's original pictures.

The two extreme images (woman and face) of Haken's original drawings were digitized and reproduced by using in both cases ten continuous lines (see Fig. 8A). Next an algorithm mapped intermediate vectors
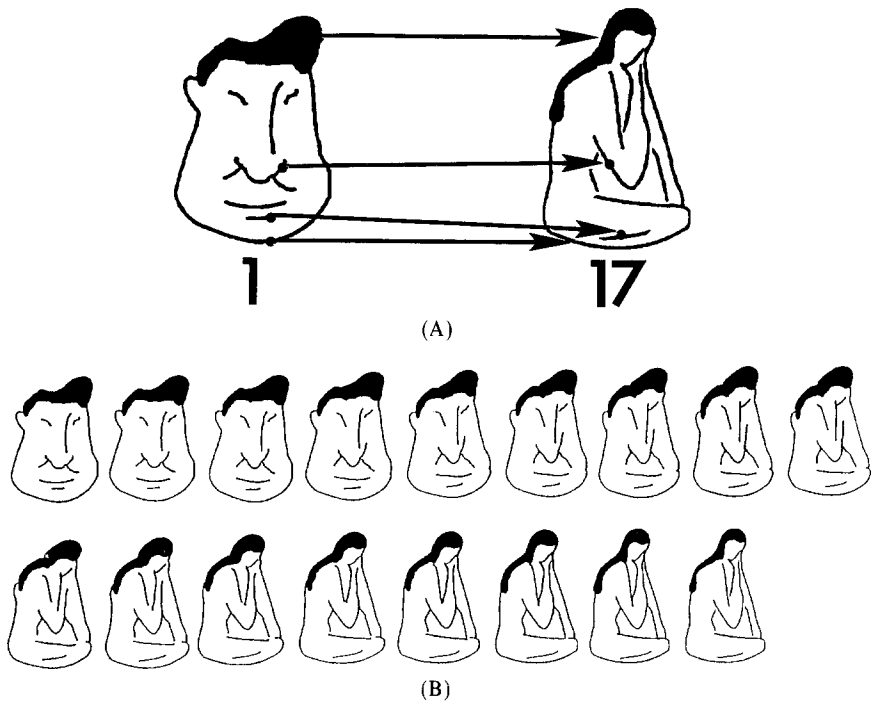

(A)

(B)

Fig. 8. The images used for studying perceptual hysteresis. (A) The two extreme images (woman and face) of Haken's original drawings and the transformation for four elements in the pictures are indicated by arrows. (B) Using the transformation in (A), 17 intermediate images were generated.

for each line with the respective one in the other extreme. In this way 17 pictures were created (Fig. 8B) that give a computerized linear transformation between the extreme images. With this technique imperfections such as abrupt changes, which existed in the original set, were eliminated.

Black and white images were presented sequentially on the computer screen and the subjects were first trained to rank the images from 1 (face in Fig. 8B) to 17 (woman in Fig. 8B). The rate of image presentation was constant in all trials: each image was on for 0.5 sec followed by a blank mask lasting 0.5 sec. The subjects were required to perform the ranking within this 1-sec period. After a brief training period, subjects were able to perform the task comfortably for periods in excess of 30 min.

After the subject familiarization with the images, the 17 images were presented in a random sequence with near uniform distribution. The subject was asked to rank each image. The histogram for the distribution of the images presented is shown in the middle panel of Fig. 9 and the bimodal distribution of the ranking of the images is shown in the bottom panel. This histogram indicates that the subject ranked most images to the two extreme values, corresponding to the well-defined face and woman, and rarely ranked images to the mid values, corresponding to the transitional ambiguous images. The input–output relationship, that is, the image presented vs. the image answered (perceived by the subject), is shown in the top panel of Fig. 9. A linear map (thick lines in top panel of Fig. 9) can approximate the subject input–output data, in that this "perceptual map" contains two stable states and a unstable one.

If the subject's perception of the presented images is indeed reduced to such a bistable map, it should be possible, with the appropriate paradigm, to demonstrate the existence of dynamics similar to noisy modulated bistable systems. For this purpose the perception of the images was studied iteratively: An initial arbitrary image is selected and presented; the subject then ranks this image in the usual manner. The subject's answer is then added to a random number (noise of uniform distribution) and/or a sinusoidal modulation to determine the next image. This image is then presented and ranked by the subject, and so on. The period of the sine wave modulation was relative to the 1-Hz sampling rate (rate of image presentation and ranking). Noise or signal amplitudes are necessarily integers, referred to as image number. Trials lasted up to 30 min, collecting several hundred data points. The statistics of residence times in one of the stable states (face or woman) was then analyzed. A typical result (for the same subject as in Fig. 9) is presented in Fig. 10A, where the histogram of the residence times shows peaks at $p/2$, $3p/2$, and $5p/2$, where p is the modulation period.

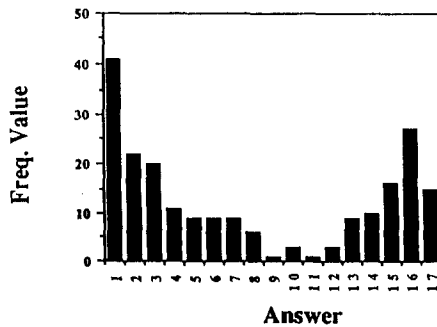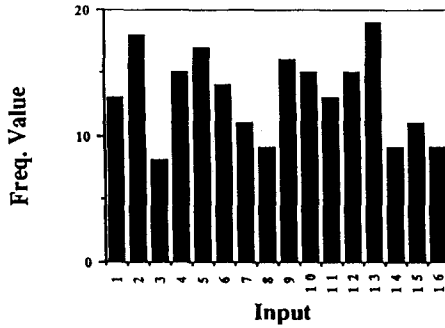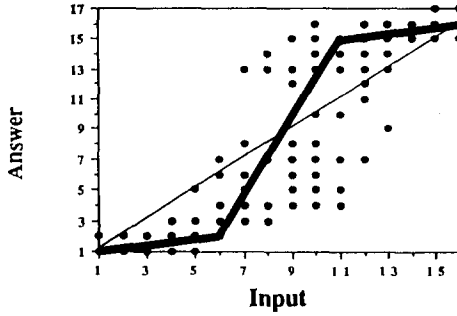Figure 10B shows the effects of increasing noise amplitude (for fixed

Fig. 9. Ranking of the 17 images with random presentation of the pictures in one subject. Top panel shows the input–output relationship (dots are the subject's responses). Superimposed on the responses is a piecewise linear approximation of the input–output relationship (the midportion of the map has a slope >1). Middle panel is the distribution of the images presented (nearly uniform). Bottom panel is the distribution of the output image numbers indicated by the subject (skewed to the two extreme pictures: face and woman).
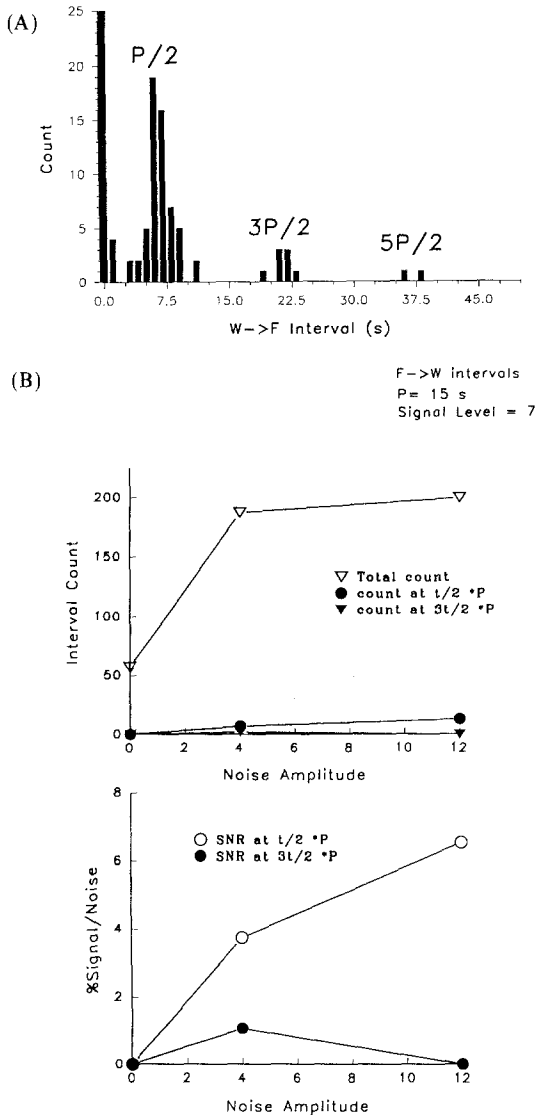
Fig. 10.   Evidence for resonance in the perception of Haken's images when the pictures were presented iteratively with noise and sine modulation. (A) Histogram of residence times in one stable state (transition woman to face, 0.6 noise, 0.4 sine modulation with period 15 sec) has peaks at $p/2$, $3p/2$, and $5p/2$, where p is the modulation period. (B) Increasing noise amplitude increases signal-to-noise ratio. Total number of transitions was counted in successive runs of fixed length (400 sec) for different levels of noise (plotted in top panel, open triangles). Residence times equal to $p/2$ (filled circles) and $3p/2$ (filled triangles) are also counted as a measure of output coherence. The ratios of the transition intervals at the two periods to the total number of transitions are an estimation of the signal-to-noise ratio (bottom graph).

modulation parameters) in the SNR. This ratio was estimated as the number of residence times (in one of the stable states) equal to half of the modulation period, relative to the number of events at other time bins. This ratio increases with increasing noise, reminiscent of stochastic resonance. From the perceptual viewpoint, this result implies a paradoxical improvement of the subject's awareness of the small periodic modulation with increased random presentation of the images.

5. ADDITIONAL COMMENTS AND QUESTIONS

The numerical simulations in Section 2 using a generic excitable model show that direct stimulation of a neuron with a stochastic and periodic signal can induce spike trains with the same statistical properties of noisy bistable systems. Now, what is the chance that such a scenario of noise and periodic signal happens somewhere in the nervous system? In the periphery of the vertebrate nervous system, there is a large diversity of sensory receptors responsive to different energies. In many sensory pathways, there is a dramatic qualitative change in firing properties when we move from the peripheral nervous system centrally. Roughly, the system progressively becomes much noisier. This is mainly due to a tremendous divergence of information, where individual neurons contact many others (synapses onto 1000–100,000 neurons), and since most synaptic contacts are leaky.

In fact, the synaptic leakage of neurotransmitter, or spontaneous release, mainly studied in the neuromuscular junction (i.e., miniature endplate potentials), generally displays Poisson-distributed release intervals.[5] The arrival of a conducted action potential usually triggers a release of neurotransmitter that is a very large multiple of this background noisy release. Thus, in the case of the neuromuscular synapse, the signal (release due to conducted neural activity) is perhaps much larger than the noise (spontaneous leakage), excluding a role for stochastic resonance. However, this picture is not universal for central synapses. Noise in this case is not only restricted to spontaneous release of neurotransmitter(s), but also arises from uncorrelated signals arriving from other neurons, as well as small local ionic fluctuations such as presynaptic intracellular changes in Ca concentration. It is obvious that stochastic resonance in such distributed systems is far more complex than the actual low-dimensional picture we have at the neuromuscular junction.

The appreciation of spike trains as stochastic point processes was formalized in the early 1960s by Gerstein, Perkel, Segundo, Moore, and others.[3, 14, 16, 18] These scientists were among the first to introduce formal measures of higher-order statistics of spike trains, raising the possibility that these higher moments can be important in information transmission.

These investigators also enunciated the advantages of variability in cellular responses in information transmission both at the level of spikes and at the synapse.[15, 19, 22] Since then stimulation of neurons or their receptors by white noise has been used to characterize the systems' transfer functions, linear or nonlinear, in the latter case by computing the Wiener kernels.[11] More recently, connectionist models for neural information transmission have implied an annealing-type role for noise in these networks, implying a similar function for spontaneous activity in the central nervous system.[7,23] In this context, stochastic resonance provides yet another interpretation of background noise, but the utility of the theory remains to be established. For this it is necessary to establish that the background noise in the central nervous system is controlled and systematically modulated during different states of arousal or wakefulness and also that the information transmission under these different states is modified and that this modification is relevant to perception and behavior. These are lofty goals and in our laboratory we have just begun to pursue portions of these objectives.

The single-unit recordings in the spinal cord and cortex both indicate that higher-order neurons share some features of noisy modulated bistable systems. However, the presented data also correspond to an increase in mean firing rate during vibrotactile stimulation. Neurons responsive to vibrotactile stimuli with no change in mean rate have been reported in the primary somatosensory cortex in awake behaving monkeys (ref. 8, see their Fig. 7). These neurons show changes in their phase locking during stimulation without increasing their mean rate. Some of these neurons show correlative changes in their responses to the attentive state of the animal. Using the present theory, it should be possible to determine stimulus amplitudes for a given spontaneous activity rate to demonstrate changes in unit activity with no mean rate change for most neurons showing stochastic resonance. One can then determine whether these stimuli are relevant to perception, given their amplitudes and the robustness of the neuronal responses.

The visual perception task provides a new technique for studying the dynamics of human perception. The main advantage of the procedure is that the volunteers, while performing the task, have no idea as to what the point of it is. Their general reaction is to think of it as a video game where their responses influence the next image they see, without having a clue as to what rules determine the next image. Thus, the sinusoidal wave modulation superimposed on noise is completely masked and the subjects detect it only in a statistical sense. This approach then provides a new strategy that can be used in a variety of psychophysical tests. The specific task we report is closely related to short-term memory and can be applied to classify various short-term memory deficits. Since both the modulation and the sine

wave were forced on the subject externally, we cannot estimate the extent of the "internal" noise that influenced the subjects behavior. However, we have not yet established that this resonance can occur in everyday behavior with the noise generated internally by the subject. But minor changes in the paradigm should enable us to determine the effects of internal noise on the task, which in turn may demonstrate perceptual stochastic resonance. It should be emphasized that the data presented take advantage of the perceptual hysteresis to demonstrate that such perceptions can show stochastic resonance.

The three examples discussed in this paper do show that stochastic resonance can be exhibited at several levels of information processing in the central nervous system. The supposedly functional use of noise in brain function, although very attractive, remains to be established.

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REFERENCES

1. R. Benzi, A. Sutera, and J. Vulpiani, *J. Phys. A* **14**:L453 (1981).
2. S. J. Bolanowski and R. T. Verrillo, Temperature and criterion effects in a somatosensory subsystem: A neurophysiological and psychophysical study, *Am. Physiol. Soc.* **48**:836 (1982).
3. H. L. Bryant and J. P. Segundo, Spike initiation by transmembrane current: A white-noise analysis, *J. Physiol.* **260**:279 (1976).
4. A. Bulsara, E. Jacobs, T. Zhou, F. Moss, and L. Kiss, Stochastic resonance in a single neuron model: Theory and analog simulation, *J. Theor. Biol.* **152**:531 (1991).
5. P. Fatt and B. Katz, Spontaneous subthreshold activity at motor nerve endings, *J. Physiol.* **117**:109 (1952).
6. H. Haken, *Synergetics. An Introduction*, Vol. 1 (Springer-Verlag, Berlin, 1983).
7. G. E. Hinton and T. J. Sejnowski, Learning and relearning in Boltzmann machines, in *Parallel Distributed Processing*, D. E. Rumelhart and J. L. McLelland, eds. (MIT Press, Cambridge, Massachusetts, 1987), p. 282.
8. J. Hyvarinen, A. Poranen, and Y. Jokinen, Influence of attentive behavior on neuronal responses to vibration in primary somatosensory cortex of the monkey, *J. Neurophys.* **43**:870 (1980).
9. B. Julesz, Stereoscopic vision, *Vision Res.* **26**:1601 (1986).
10. A. Longtin, A. Bulsara, and F. Moss, Time interval sequences in bistable systems and the noise-induced transition of information by sensory neurons, *Phys. Rev.* **67**(5):656 (1991).
11. P. Z. Marmarelis and V. Z. Marmarelis, *Analysis of Physiological Systems; The White Noise Approach* (Plenum Press, New York, 1978).

12. G. Matsumoto, N. Takahashi, and Y. Hanyu, Chaos, phase locking and bifurcation in normal squid axons, in *Chaos in Biological Systems*, H. Degn, A. Holden, and L. F. Olsen, eds. (Plenum Press, New York, 1987), p. 143.
13. B. McNamara and K. Wiesenfeld, Theory of stochastic resonance, *Phys. Rev. A* **39**:4854 (1989).
14. G. Moore, D. Perkel, and J. Segundo, Statistical analysis and functional interpretation of neuronal spike data, *Annu. Rev. Physiol.* **28**:493 (1966).
15. D. H. Perkel, Spike trains as carriers of information, in *The Neurosciences. Second Study Program* (1970), p. 587.
16. D. H. Perkel, G. L. Gerstein, and G. P. Moore, Neuronal spike trains and stochastic point processes, *Biophys. J.* **7**:391 (1967).
17. J. Rinzel and G. Ermentrout, Analysis of neural excitability and oscillations, in *Methods in Neuronal Modeling. From Synapses to Networks*, C. Koch and I. Segev, eds. (MIT Press, Cambridge, Massachusetts, 1989), pp. 135–170.
18. R. Rodieck, N. Kiang, and G. Gerstein, Some quantitative methods for the study of spontaneous activity of single neurons, *Biophys. J.* **2**:351 (1962).
19. J. P. Segundo, Communication and coding by nerve cells, in *The Neurosciences. Second Study Program* (1970), p. 596.
20. R. Siegel, Non-linear dynamical system theory and primary visual cortical processing, *Physica D* **42**:385 (1990).
21. M. V. Smith, A. V. Apkarian, and C. J. Hodge, Jr., Somatosensory response properties of contralaterally projecting spinothalamic and nonspinothalamic neurons in the second cervical segment of the cat, *J. Neurophys.* **66**:83–102 (1991).
22. R. B. Stein, The role of spike trains in transmitting and distorting sensory signals, in *The Neurosciences. Second Study Program* (1970), p. 597.
23. J. Szentagothai and M. A. Arbib, Conceptual models of neural organization, (MIT Press, Cambridge, Massachusetts, 1975).
24. W. Talbot, I. Darian-Smith, H. Kornhuber, and V. Mountcastle, The sense of flutter-vibration: Comparison of the human capacity with response patterns of mechano-receptive afferents for the monkey hand, *J. Neurophysiol.* **31**:301 (1968).
25. G. M. Wyburn, R. W. Pickford, and R. J. Hirst, *Human Senses and Perception* (Oliver and Boyd, Edinburgh, 1964).