Tuning Curves of Noisy Neuronal Oscillators

Summary:

Both subthreshold oscillations and noise have attracted particular attention in recent years. Most of the work was done with regard to synchronisation in neuronal assemblies or stochastic resonance (SR), respectively [2, 8, 9]. Here, we examine the neuromodulatory properties of such noisy oscillators and demonstrate how their transfer characteristics can be changed depending on the membrane parameters or external stimuli.

Our computer model [3] consists of two sets of simplified sodium and potassium conductances operating at two different membrane potentials and on two different time scales: a Hodgkin/Huxley-type spike encoder is represented by rapid, high-voltage activating sodium and potassium conductance, whereas the subthreshold oscillations result from the interplay of a persistent sodium and a subthreshold potassium conductance. An additional noise term accounts for the influence of membrane noise.

The significance of noise is immediately evident when we compare the effect of current injection in our model under completely deterministic conditions and with stochastic forcing. In agreement with cortical data and previous computer simulations [4, 7], depolarising current induces subthreshold oscillations. However, while the deterministic model switches between distinct electrical states, i.e. spiking or not, addition of noise leads to a continuous transition between subthreshold oscillations and tonic firing where the current strength is encoded in the firing probability of the oscillations. Increasing noise intensity reduces the steepness of the stimulus-reponse function which also redudes the maximum sensitivity. However, the encoding range is broadened which allows the detection of previously subthreshold signals and therefore can be considered as the source of stochastic resonance (SR).

Different modifications of the tuning curves are obtained with alterations of the ionic conductances of the low-threshold currents. For example, an enhanced sodium conductance or a reduced potassium conductance shifts the sigmoidal frequency-current function of the noisy oscillator to lower stimulus intensities without significant changes of the steepness of the curve. This shift of the encoding range is without loss

of maximum sensitivity which, for example, allows adaptation to changed stimulus intensities or synaptic background activity.

Moreover, with reduced potassium conductance, our model accurately mimicks experimental data which we recorded from capsaicin sensitive dorsal root ganglion neurons after treatment with the potassium channel blocker 4-aminopyridine (4-AP). According to the shift of the tuning curve, subthreshold oscillations with occasional spiking already occur where the membrane potential was in a stable resting state before. Any additional stimulus, which previously might have been without effect, can now easily modify the firing probability of the cell. Hence, the same effects which allow adaptation can become rather disastrous under pathophysiological conditions, for example, as a possible source for hypersensitivity or chronic pain..

A third type of tuning curve modification is obtained with changes of the ionic kinetics (activation time constants). These simulation were done with regard to own experimental data from thermally sensitive electroreceptors of sharks [1]. In this case, the most prominent change of the frequency-current curve is a reduced maximum frequency with slower activation kinetics. Only minor changes seem to occur with regard to the steepness or an eventual shift of the curve.

However, remarkable effects can be seen when the frequency curves are not plotted versus the current stimulus but versus the activiation kinetics. First of all, these curves do not show sigmoidal but parabolic shapes corresponding to the well-known frequency-maximum curves of thermosensitive skin receptors. Hence, as a function of the activation kinetics (or temperature scaling), the noisy oscillators exhibit a range of positive as well as a range of negative input-output relations, which means that such neurons cannot only change the sensitivity but even can be adjusted to opposite transfer characteristics - simply depending on the actual operating point.

Maximum curves develop when instead of the oscillation amplitude, as with current injection, the frequency of oscillation is changed which, indeed, is the major effect of the activation kinetics. Increasing oscillation frequency, at first, means increasing firing rate. But the shortening of the oscillations also means an increasing number of skippings which finally reduces the mean firing rate despite, or better, because of further acceleration of the oscillation. This again is a situation where an additional stimulus can exhibit drastic effects. It is easy to understand that only slight enhancement of the oscillation amplitude can essentially increase the probability of spike generation when the oscillations operate close below the spike-triggering

threshold. In contrast, only minor effects will be expected when the spiking probability is already high. As a consequence, the position of the maximum frequency will be shifted to higher values of the activation kinetics. This means that part of the curve with negative slope now attains a positive slope, i.e. the neurons transfer characteristic, in this range, is inversed. Such drastic modifications of neuronal tuning curves have been described many years ago for muscle spindle recordings during combined application of stretch and temperature stimuli [5] and also for the effects of Ca-channel blockers or Ca-chelators on cold receptor activity [6]. Most significant effects can be expected in neuronal circuits in the CNS when an inversed input-ouput relation, for example, can turn a positive feedback loop into a negative one or vice versa.

These modelling studies so far only consider the interaction of not more than two stimuli whereby one of them, for simplicity, always was a current injection which might represent a tonic synaptic input. Despite of these simplifications and the simplifications of the model, tuning curves with exceptional neuromodulatory properties can be obtained which can have significant effects in peripheral sensory transduction and in neuronal information processing in the brain. Considering that noise is an inherent property of biological systems and that subthreshold oscillations have been recorded in many anatomically and functionally very different neurons in the peripheral and central nervous system, one could speculate that this wide distribution is not just by chance but that these neurons have adjusted their operating points to make use of these particular tuning characteristics of noisy neuronal oscillators.

References

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