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Effects of synaptic noise on a neuronal pool model with strong excitatory drive and recurrent inhibition

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Abstract

A model originally proposed by Akazawa and Kato (1990) for the spinal cord was adopted as prototypical of a neuronal pool with strong excitatory drive and strong recurrent inhibition. Our simulations of the model have shown that a strong synchronization occurs between the spike trains in the neuronal pool. This happens because the proposed model has a single and strong excitatory drive on the neuronal pool. However, usually a multitude of other randomly occurring synaptic inputs impinge on the neuronal pool and therefore a new investigation was carried out to study the effects of synaptic noise on the network behavior. The synaptic noise decreased the degree of synchronization of the neuronal spike trains but on the other hand caused an unexpected decrease in the mean firing rate of the neuronal pool. A detailed analysis indicated that this phenomenon is due to a combination of two mechanisms: a saturation of the feedback inhibition and a decrease of the synchronization in the neuronal pool with synaptic noise. The synaptic noise caused a more frequent activation of the saturated recurrent inhibitory feedback loop along time, thereby increasing the inhibitory effect on the neuronal pool.

Keywords: Recurrent inhibition; Synaptic noise; Synchronization; Feedback saturation

1. Introduction

Neuronal networks have topological features that are relevant to the several computations they may realize. A few examples are convergence, divergence and feedback inhibition (Shepherd, 1990). The latter, also called recurrent inhibition, is widely found in the central nervous system (Windhorst, 1996) and is the main topic of interest in the present paper. Akazawa and Kato (1990) have presented a partial model of the spinal cord that describes a pool of motoneurons (MN) receiving a strong descending excitatory drive and a strong inhibitory feedback from a pool of Renshaw cells. As their model is one of the few in the literature that includes spiking neurons in the spinal cord it was adopted as a prototype for our studies of neuronal networks

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with recurrent inhibition. Although the model (Akazawa et al., 1989, Akazawa and Kato, 1990) was originally used by the authors to predict mean rate output of MNs and muscle force for different intensities of descending drives our intention was to use it for studying the detailed patterns of discharge of the neurons in the pool in different situations. Since our simulations indicated a strong degree of synchronization between the MNs of the pool it seemed quite relevant to repeat the simulations with added synaptic noise to mimic the effects of the large number of other synaptic inputs to the MNs. As in many papers in the literature, we shall use the term synaptic noise as the membrane potential caused by a large number of randomly occurring postsynaptic potentials (PSPs).

In this paper, the above mentioned model will be used as a prototype of a neuronal pool driven by a strong common source and with a strong recurrent inhibition. Simulation results are presented accompanied by an analysis of the mechanisms behind a rather surprising effect of the injected noise: a decrease in the mean firing rate of the MNs. This is surprising because noise added to isolated neurons causes an increase in their mean firing rate either if they are silent or if they are already firing (Guttman et al., 1977, Buno et al., 1978), something also replicated by many mathematical models of neurons (Lánský and Rospars, 1995).

2. The model and the simulator

The model (Akazawa et al., 1989, Akazawa and Kato, 1990) includes MNs described by extended leaky integrator models driven by a renewal process having intervals distributed according to a truncated Gaussian. This represents the activity of the cortico–motoneuronal pathway (CMN), the truncated-Gaussian leading to a skewed distribution of interspike intervals. The MNs are subjected to recurrent inhibition. The EPSPs and IPSPs on the MNs are graded according to their size, i.e. larger PSPs occur in smaller MNs and vice-versa. There is an absolute refractory period and an exponentially decaying relative refractory period. The recurrent inhibition is simulated by an equivalent Renshaw cell that receives inputs from all MNs and sends its output, without delay, to all MNs. Both the descending drive on the MNs and the inhibitory feedback from the equivalent Renshaw cell are rather strong, e.g. in the smallest MNs, the EPSPs and IPSPs have the same magnitude as the difference between the resting potential and the resting threshold level (in the larger MNs the PSPs were about half of those in the small MNs). The equivalent Renshaw cell model fires a burst of 40 ms duration with an intra-burst firing rate that depends on how many (and which) MNs have fired in a short time interval, but only up to a certain maximum firing rate value. For example, if the maximum firing rate is 500 spikes/s for the equivalent Renshaw cell, then, in the average, the (almost) synchronous firing of 20 MNs is sufficient to saturate its firing rate.

The simulator was developed in C language (Araujo and Kohn, 1996) with graphical outputs to show the neuronal membrane potential as a function of time, the simultaneous discharge activities of sets of MNs as well as the interspike interval histogram of any motoneuron in the network. In the simulations without noise, the exact solutions were used until a threshold crossing was found. In simulations with noise, the time step was 0.1 ms, with exact solutions being used between each time step. The neuronal spike trains were obtained for a 10 s time window.

The synaptic noise was simulated by a zero mean Gaussian lowpass noise input (0–44.0 Hz at -3 dB) which is in accordance with experimental data (Calvin and Stevens, 1968). The synaptic noise was generated independently by simple digital filters for each motoneuron in the pool (Kohn, 1997). The noise standard deviation varied linearly from 3 mV for the larger MN to 5 mV for the smaller MN in the pool.

In all simulations reported here, the network had 60 MNs and a single equivalent recurrent inhibitory cell. The simulated descending drive may also be seen as coming from an equivalent cortical neuron. For the sake of simplicity, we

shall keep in what follows the nomenclature motoneuron pool, motoneurons (MNs), cortico-motoneuronal (CMN) excitatory drive, Renshaw recurrent inhibition. However, the context should be taken as general, as we are in fact modeling and analyzing an arbitrary neuronal network with strong excitatory drive and recurrent inhibition.

3. Simulation results

Our main objective is to analyze the effect of synaptic noise on the mean firing rate of the motoneuron pool for different mean rates of the descending CMN drive. The motoneuron pool mean rate is defined as the mean of the mean firing rates of its MNs. To be able to isolate the contribution of the different aspects of the network, we start with an open loop simulation, where the recurrent inhibition is inoperative. Next, still with an open loop, the inhibitory input to the motoneuron pool has a constant mean rate value similar to that found in the closed loop situation. Finally, in a closed loop situation the inhibitory input to the motoneuron pool is activated by the firings of the MNs themselves. Any simulation set is composed of a noiseless and a noisy run and is presented as such in the figures ahead.

3.1. Without recurrent inhibition

Two cases of open loop simulations were studied. In the first, there was no inhibitory input whatsoever, corresponding to the two upper monotonic increasing lines in Fig. 1 (indicated by '*w/o* Inh'). The lowest of these two lines is the deterministic case (indicated by '*w/o N*') while the upper line is one for which there was additive synaptic noise (indicated by '*w/N*'). As expected, the neuron pool mean rate increases with increasing drive from the CMN descending pathway as well as with the addition of synaptic noise.

Next, a periodic inhibitory train was applied to the motoneuron pool at a fixed rate within the range found in the closed loop situation. This may be thought of as a case in which the inhibitory feedback element was stimulated externally at a constant rate, without receiving any input from the motoneuron pool. The same inhibitory rate was used for the cases without and with synaptic noise. The two corresponding lines in Fig. 1 are the lowermost, labeled '*w*/constant rate Inh'. By comparing the lowermost with the uppermost pairs of lines, it is clear that the MN pool mean rates were lower when constant rate inhibition was applied. More importantly, with constant rate inhibition, the mean rates with synaptic noise were larger than without synaptic noise. The two thick arrows in Fig. 1 indicate the (increasing) effect on output mean rate the addition of synaptic noise in the two conditions.

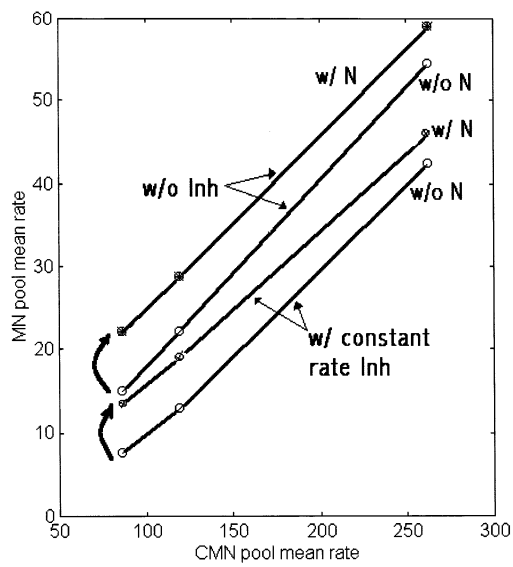

Fig. 1. Motoneuron pool mean rate as a function of the descending drive intensity from the CMN pathway. The upper pair of curves ('*w/o* Inh') correspond to the open loop case without any inhibition. The uppermost curve ('*w/N*') in this pair corresponds to the case where synaptic noise was added to the MNs. The lower pair of curves ('*w*/constant rate Inh') is still for an open loop situation but with a constant rate inhibition acting on the MNs. Again, the lowest curve ('*w/o N*') is for the deterministic case while the upper ('*w/N*') is for synaptic noise added to the MNs. In both cases, the addition of synaptic noise caused an increase in the mean firing rate of the MN pool, as indicated by the two upward pointing thick arrows.

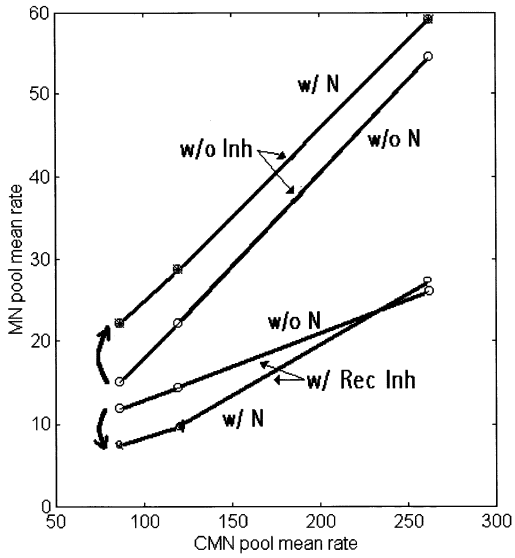

Fig. 2. Motoneuron pool mean rate as a function of the descending drive intensity from the CMN pathway. The upper pair of curves ('*w*/*o* Inh') is a repetition of one pair shown in Fig. 1, in which the feedback loop was open and no inhibition existed on the MN pool. The lower pair of curves ('*w*/Rec Inh') is for the closed loop case, with the lowermost curve ('*w*/*N*') corresponding to the case of synaptic noise added to the motoneuron pool. With an active recurrent inhibition, the MN pool mean rate decreased with added synaptic noise for CMN rates less than ~ 240/s, as indicated by the downward pointing thick arrow.

3.2. With recurrent inhibition

To compare the behavior of the MN pool mean rate with and without recurrent inhibition, the upper pair of curves in Fig. 1 was copied into Fig. 2 as the uppermost pair of curves (marked '*w*/*o* Inh'). The lowermost pair of curves in Fig. 2 (marked '*w*/Rec Inh') indicates the results obtained with recurrent inhibition (i.e. a closed loop topology with negative feedback). Here, the surprising result is that when synaptic noise is added to the MNs, there is a *decrease* in the MN pool rate for CMN mean rates lower than ~ 240/s. This is indicated in the figure by a thick arrow pointing in the downward direction. This property is quite pronounced in the smaller MNs in the network and less so in the largest. For CMN mean rates above ~ 250/s, the motoneuron pool mean rate increases with synaptic noise.

In order to understand what is behind this unexpected result, it is helpful to visualize the spike trains of the MNs and the equivalent Renshaw cell. Fig. 3(a) shows the spike trains corresponding to the simulations without synaptic noise and Fig. 3(b) those with synaptic noise. Each figure shows the discharges of MNs 1–20 and 41–60 followed by those from the CMN and the equivalent Renshaw cell. The latter is seen to be composed of bursts occurring randomly along the time axis, usually with a maximum intra-burst firing rate. The simulations without and with synaptic noise used exactly the same CMN spike train. A high degree of synchronization occurs between the MNs when there is no synaptic noise (Fig. 3(a)). By comparing Fig. 3(a) with 3(b), it can be seen that the synaptic noise decreased the degree of synchronization in the motoneuron pool and that the bursts generated by the recurrent inhibition occurred more densely along the time axis when synaptic noise was present.

4. Mechanisms

If one envisions the system we are studying in terms of a negative feedback system with mean rates as the input (u) and output (y) variables, then a simplistic interpretation of the decrease in the motoneuron pool mean rate when synaptic noise is added could be that it is due to the action of the recurrent inhibition or negative feedback. To see that this is not so, let us imagine a linear system with negative feedback having forward gain G and feedback gain H, as depicted in Fig. 4.

The overall gain between input and output is $G/(1+GH)$, which means that if the input is only from CMN then the output mean rate y will be $[G/(1+GH)]u_{\mathrm{CMN.}}$ On the other hand, with synaptic noise u_{SYN} added at the input, the output mean rate y will be equal to the sum of two terms $[G/(1+GH)]u_{\mathrm{CMN}} + [G/(1+GH)]u_{\mathrm{SYN}}$. This expression shows that the output mean rate may only increase when synaptic noise is added. This last result is based on the reports from the literature, already mentioned in Section 1, that a single neuron subjected to additive noise increases its firing rate. Additionally, the results of our simulations shown in Fig. 1 confirm this quite clearly.

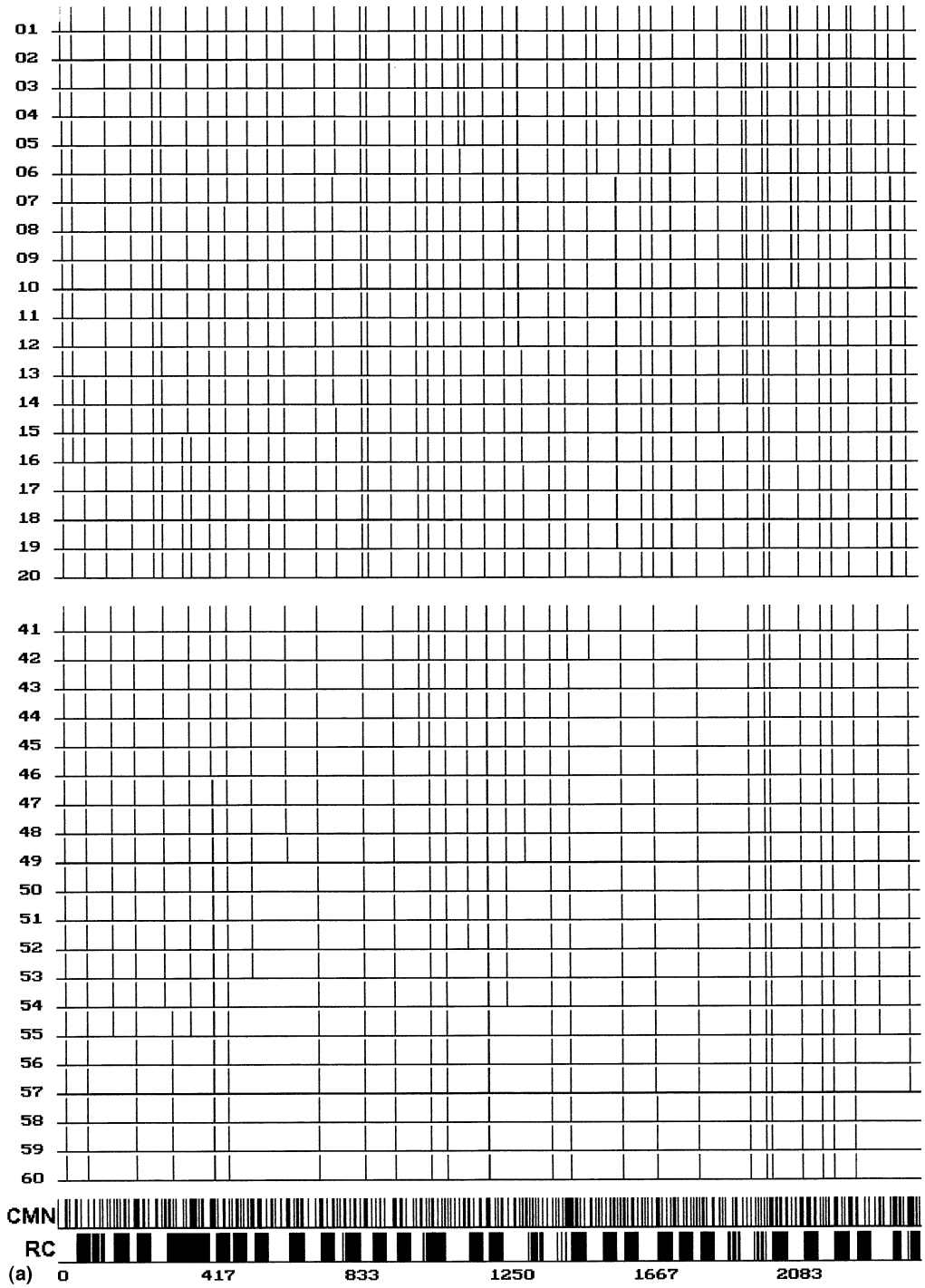

Fig. 3. Spike trains of MNs without (a) and with (b) synaptic noise added. Each figure shows the spike trains of MNs 1–20 and 41–60 (from smallest to largest) as well as those of the CMN and the recurrent inhibition element (indicated as RC). The same CMN spike trains were used for the noiseless and noisy simulations.

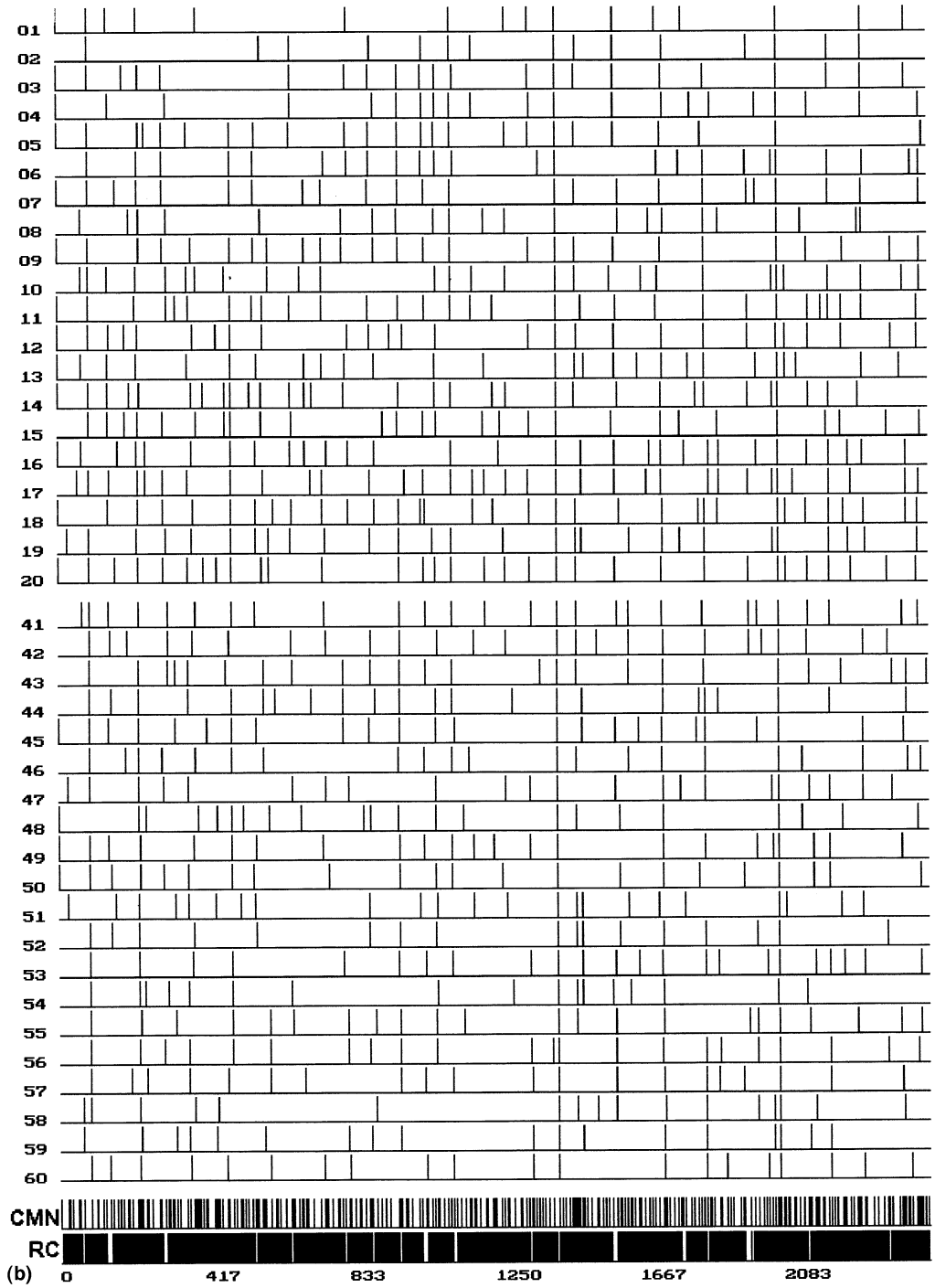

Fig. 3. (*Continued*)

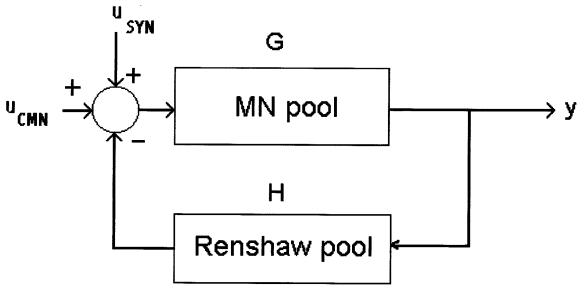

Fig. 4. Simplified feedback loop representation of the neuronal network with recurrent inhibition. All of the variables are mean rates, u_{CMN} and u_{SYN} corresponding to the CMN descending drive and the synaptic noise, respectively. The output variable y is the mean rate of the MN pool.

So what is an alternative explanation? One answer could be that each block is actually a nonlinear system, e.g. exhibiting saturation. However, that does not seem enough to justify the decrease in the output variable y because the nonlinearities (mainly the feedback nonlinearity) should be able to 'feel' that a synaptic noise was added to the previously existing input u_{CMN}, without confounding the added synaptic noise with an increase in u_{CMN}. In other words, it seems quite difficult to find a physiologically reasonable explanation for the phenomenon if one stays with a model based on mean rates (e.g. like the classical artificial neural network models). One fundamental modification required with the model block diagram is that the feedback should not be of the mean rate but of all the spike trains of the MNs in the MN pool. Therefore, one should consider a *vector feedback* (Fig. 5), where the detailed timings of all the motoneuron spike trains are processed by the feedback element.

In creating Fig. 5, we tried to keep some of the features of Fig. 4 in terms of the input mean rate u_{CMN} and the motoneuron pool mean rate y. By setting the CMN descending mean rate u_{CMN}, a train of EPSPs is generated with intervals according to a truncated Gaussian density (Section 2). The motoneuron pool receives this train of EPSPs plus the train of IPSPs coming from the Renshaw pool (or equivalent Renshaw cell). In the case of addition of synaptic noise, this is added to the membrane potentials of the MNs. The double lines in Fig. 5 indicate multiple output variables, basically composing a vector with the spike trains of each motoneuron in the pool. This vector is what is fed back to the Renshaw pool. The dashed block labeled 'mean rate measurement' simply measures the motoneuron pool mean rate to provide an output y similar to that found in Fig. 4, and was included only to provide an output y similar to that found in Fig. 4.

By inspecting carefully Fig. 3(a), we note that the MNs are strongly synchronized and that the equivalent Renshaw cell discharges its bursts (usually at a maximum intra-burst firing rate) preferentially at those time instants when the MNs fire synchronously. When synaptic noise is added to the MNs, these tend to loose some synchrony, with the result that the equivalent Renshaw cell discharges its bursts more frequently, and still at its maximum intra-burst firing rate (because a sufficient number of MNs still end up firing approximately at the same time). If the feedback element discharges more densely along the time axis, it exerts a larger inhibitory action on the MN pool. The interplay of synchronization in the MN pool and saturation in the negative feedback

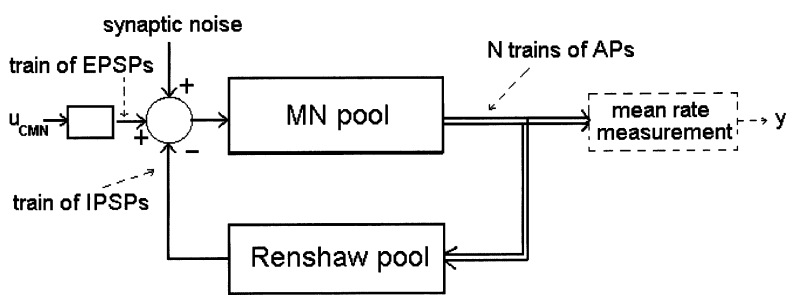

Fig. 5. Feedback loop representation of the neuronal network with recurrent inhibition with an emphasis on the feedback of the vector containing all of the N spike trains of the MNs in the pool.

element (the equivalent Renshaw cell) makes the negative feedback gain nonlinear and increasing with the amount of synaptic noise added at the system's input (the MN pool). From this, it is clear in the block diagram of Fig. 5 that the gain (in terms of mean rates) of the feedback element changes according to the pattern of the incoming spike trains, i.e. according to the specific time evolution of the feedback vector. As the synaptic noise changes the pattern in the vector output from the motoneuron pool this can be sensed by the feedback element. Therefore, in this indirect way, an additive noise at the input may alter the gain of the feedback element. Also, in our case, as the feedback gain increases, the overall gain decreases, as also found in our simulations. The region to the right of abscissa 240/s in Fig. 2 corresponds to the cases where the equivalent Renshaw cell is firing continuously at a frequency equal to its maximum intra-burst rate and hence is equivalent to the lowermost pair of curves in Fig. 1, where the inhibition had a constant rate. Therefore, in both cases, the addition of synaptic noise increases the MN pool mean rate.

5. Discussion

Perturbations of several origins (e.g. synaptic noise) on nervous systems have been studied for a long time (Segundo et al., 1994). Sometimes they may yield effects that are probably quite helpful for the nervous system such as fidelity improvement and increase in sensitivity, while at other times they may increase the level of complexity of the necessary computations. That seems to be the case in the neuronal network that we analyzed, whether its output is decoded by coincidence detection or by mean firing rate. In the former case, the effect of synaptic noise from unrelated sources is to decrease the probability of coincidences because the degree of synchronization in the MN pool decreases (Fig. 3(b)). If rate coding is used, for a low intensity of the main descending drive (CMN) there is a *decrease* in the neuronal pool mean rate with added synaptic noise (i.e. an inhibition) but an increase for a higher intensity of the descending drive (Fig. 2). In some settings, this phenomenon would pose computational difficulties for the nervous system to figure out what is happening or what it should do. For example, in the context of motor output, different levels of synaptic noise (originating from other descending pathways and from a multitude of afferents) would require different responses from the motor cortex to achieve the same muscular activation. More specifically, in a task where a decrease in muscle force is desired, starting from a condition of low synaptic noise, the occurrence of a higher level of synaptic noise (arising in a statistically independent way) would, in some cases, require an *increase* in the cortical descending drive to decrease the muscle force, while in others it would require a *decrease* in the cortical drive to achieve the same effect. As another example, if the synaptic noise intensity would be a signal to be decoded at a later stage, the network we have studied would have an inverted output for low rates of the strong drive (CMN) but a non-inverted output for higher rates of the strong drive, making the decoding quite complex.

As recurrent inhibition is a common finding in neuronal networks, the conceptual discussions presented here should provide a guideline for animal neurophysiologists, both in the planning of the experiments as well as in the interpretation of the results. Our results also showed the importance of analyzing and modeling the neuronal networks in terms of the detailed spike trains of the involved neurons rather than focusing only on the mean rates of firing. The rich variety of behaviors found in nervous systems usually requires a more complete modeling effort, in which the patterns of discharge of the neurons involved are considered in some detail. The nonlinear dependence that we described of a feedback element on the addition of noise *at the input* is an example of the richness of behaviors a neuronal network model can present.

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