An Investigation into the Role of Cortical Synaptic Depression in Auditory Processing

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Abstract

In comparison with the speed and precision associated with processing in the auditory periphery, the temporal response properties of neurons in primary auditory cortex can appear to be surprisingly sluggish. For example, much of the temporal fine structure is lost, best modulation frequencies are generally low and the effects of forward masking can be detected for a surprisingly long time. What gives rise to these responses and can they be explained by some common mechanism? Intracortical inhibition has been suggested as a likely cause but inhibition does not provide an adequate account, at least in the case of forward masking, which is unaffected by the application of inhibitory antagonists. On the other hand, simple threshold neural models cannot replicate such behaviour without some form of inhibition. The purpose of this investigation was to explore whether depression at thalamocortical synapses could account for these observations. As far as we are aware, the experiments which we have replicated, many of them only recently published, have not previously been modelled, and certainly not all by the same model. Since synaptic depression depends on pre- and not postsynaptic activity, the model also provides a novel account of the effect of subthreshold stimuli.

Introduction

There are many aspects of auditory perception, such as the growth of loudness with duration and the effects of masking, which indicate that the auditory system performs some sort of temporal integration in processing incoming acoustic signals. However, the auditory system is also capable of fine temporal resolution, as evidenced by gap detection, double click discrimination, and also in the short latency and lack of jitter of onset responses in cortex (Viemeister and Plack 1993). This has been termed the resolution-integration paradox, i.e. how is it possible for a system to integrate information over long periods while retaining fine temporal resolution. Most accounts which satisfy the integration criterion use long time constants and therefore fail to behave swiftly enough to explain fine temporal resolution, and vice versa.

The time constants typically associated with sub-cortical processing differ substantially from those in the cortex. In comparison with the speed and precision associated with processing in the auditory periphery, the temporal response properties of neurons primary auditory cortex (AI) can appear to be surprisingly sluggish. For example, in the thalamocortical transformation of incoming signals a great deal of the temporal fine structure is lost (Creutzfeldt et al 1980), best modulation frequencies measured in AI are generally below 15 Hz (Schreiner and Urbas 1988), and the effects of a masker on a probe tone can be detected up to 400 ms after masker offset (Brosch and Schreiner 1997). The focus in this paper is therefore on the temporal response properties observed in AI. As yet there have been no models proposed which can satisfactorily explain the observed behaviour of neurons in AI. Explanations in terms of intracortical inhibitory circuits have been proposed but inhibition does not provide an adequate account, at least in the case of forward masking which is unaffected by the application of a GABA antagonist (Brosch and Schreiner 1997). On the other hand, simple threshold neural models cannot replicate such behaviour without some form of inhibition or by means of very long time constants, which as discussed above, would then prevent the model from satisfying the requirements for good temporal resolution.

Recently it has become apparent that cortical synaptic dynamics may be an important factor affecting the behaviour of biological neurons (Markram et al 1997, Abbott et al 1997, Thomson and Deuchars 1994, Reyes et al 1998). When synapses are repeatedly activated they do not simply respond in the same way to each incoming impulse and synapses may develop a short-term depression or facilitation, depending on the nature of the pre- and postsynaptic cells, and on the characteristics of the particular synapse involved (Thomson and Deuchars 1994, Reyes et al 1998). Within current neural network models synapses are generally modelled as simple gains and it is interesting to consider how models of cortical processing might be enhanced by the inclusion of a richer synaptic model. If synapses are not simply be viewed as passive weighting elements in neuronal circuits, but rather as dynamical systems in their own right, then perhaps many of the response properties observed in AI might be explained in a relatively simple way. To explore this hypothesis, a model of cortical synaptic depression was used to investigate the computational properties of a neuron model that included dynamic synapses. This model

was found to account for a wide range of experimental observations, including those outlined above.

The Dynamic Synapse Model

The dynamic synapse model we use here was presented in (Tsodyks and Markram 1997) and shown to replicate experimental results reported on synaptic depression. In fact, this model of the dynamics of neurotransmitter release had already been proposed much earlier by (Grossberg 1968, 1969), who derived a set of psychological postulates to explain the excitatory transients in transmitter release after a rest period and subsequent synaptic depression, which had been observed experimentally by (Eccles 1964). This synaptic depression model has been further developed and used subsequently by Grossberg in more recent years, for example to explain a number of important perceptual features involving the visual cortex. In the area of auditory modelling, a very similar model was also developed by (Meddis 1986) to describe transduction in cochlear inner hair cells.

The dynamic synapse model characterises the synapse by defining a "resource", e.g. the amount of neurotransmitter in the synapse, a proportion of which can be in one of three states: *available, effective, inactive*. The dynamical behaviour of the proportions of the resource that are in each of these states is determined by a system of three coupled differential equations below. In these we use notation similar to that in (Grossberg 1969).

$$\frac{dx}{dt} = g.y(t).I(t) - \alpha.x(t)$$

$$\frac{dy}{dt} = \beta.w(t) - g.y(t).I(t)$$

$$\frac{dw}{dt} = \alpha.x(t) - \beta.w(t)$$

where $x(t)$ is the amount of *effective* resource, e.g. activated neurotransmitter within the synaptic cleft, as a proportion of the total resource, $y(t)$ is the amount of *available* resource, e.g. free neurotransmitter in the synapse, and $w(t)$ is the amount of *inactive* resource, e.g. neurotransmitter being reprocessed.

The input signal $I(t)$ represents the occurrence of a presynaptic action potential (AP) and is set equal to one at the time of arrival of the AP and for a small period of time δt thereafter, and otherwise is set equal to 0. The constant β determines the rate at which the inactive resource $w(t)$, is released to the pool of available resource on a continuing basis, and α represents the rate at which effective resource $x(t)$ becomes rapidly inactive again. The instantaneous efficacy of the synapse is determined by the variable g, which can be interpreted as the fraction of available resource released as a result of the occurrence of the presynaptic AP. It takes a value in the range zero to one.

The key idea behind the model is that there is a fixed amount K of total resource available at the synapse, a proportion $g.y(t)$ of which is activated in response to presynaptic activity, rapidly becomes inactive, and is then subsequently made available again through reprocessing. Thus, if the synapse is very active the amount of available resource $y(t)$ is rapidly reduced. There must then follow a period during which the synapse can recover in order to respond fully once more. This process appears to replicate the experimentally observed characteristics of synaptic depression, for example as reported in (Markram and Tsodyks 1996, Tsodyks and Markram 1997).

The EPSP at the synapse, $e(t)$, is computed from $x(t)$ using the following equation for the passive membrane mechanism (Tsodyks and Markram 1997):

$$\tau_{EPSP}.\frac{de}{dt} = \gamma.x(t) - e(t)$$

The neuron model used is described by the following system of equations, which has been adapted from a model described in (McGregor 1989):

$$\tau_E \frac{dE}{dt} = -E(t) + V(t) + G_K(t).(E_K - E(t))$$

$$s(t) = 1, \text{ if } E(t) \geq \theta(t), \text{ else } s(t) = 0$$

$$\tau_{G_K} \frac{dG_K}{dt} = -G_K(t) + \eta.s(t)$$

$$\tau_\theta \frac{d\theta}{dt} = -(\theta(t) - \theta_0) + s(t)$$

where, $E(t)$ is the variation of the neuron's membrane potential relative to its resting potential, $V(t)$ is the driving input found by summing all the synaptic EPSPs, $G_K(t)$ is the potassium conductance, divided by the sum of all the voltage-dependent ionic membrane conductances, E_K is the potassium equilibrium potential of the membrane relative to the membrane resting potential, $\theta(t)$ is the firing threshold potential, θ_0 is the resting threshold, $s(t)$ is the variable which denotes firing of the cell, τ_E, τ_{EPSP}, τ_θ, and τ_{GK} are time constants, and γ, χ and η are constant parameters.

Simulation Results

Not all cortical synapses are depressing; for example, synapses between cortical pyramidal neurons and bi-tufted GABAergic interneurons synapses are strongly facilitating (Reyes et al 1998). However, thalamocortical synapses appear to be depressing; they are mediated by non-NMDA

excitatory amino acids, depress rapidly and remain desensitised for some time (Thomson and Deuchars 1994). In the simulations that follow, it can be seen that the response characteristics of the model neuron, when the dynamic synapse model is included turn out to be very similar to that found in primary auditory cortex.

Loss of Temporal Fine Structure

Differences between the response properties of thalamic and cortical neurons were investigated by (Creutzfeldt et al 1980). Activity in thalamic relay cells and subsequent activity in paired pyramidal cells in AI was recorded, and it was found that even when thalamic activity was clearly synchronised to the stimulus up to 200 Hz, the paired cortical cell was unable to follow the details of the signal beyond about 20 Hz. The plots in figure 1 show the response of the model to spike trains generated to resemble typical thalamic activity in response to stimuli of the frequencies indicated. Total activity for 20 presentations is plotted both for the presynaptic spike trains and the model response. The model behaviour resembles that found experimentally. The model responds to details of the stimuli occurring at 10 Hz and to a lesser extent to details at 20 Hz, but for higher stimulus frequencies, the model only responds strongly at the onset of the signal. The reason for this is that at high frequencies successive presynaptic spikes arrive before the synapse has time to recover. This causes a strong depression of the synapse, resulting in the generation of very small postsynaptic EPSPs that are insufficient to raise the cell membrane potential above the firing threshold.

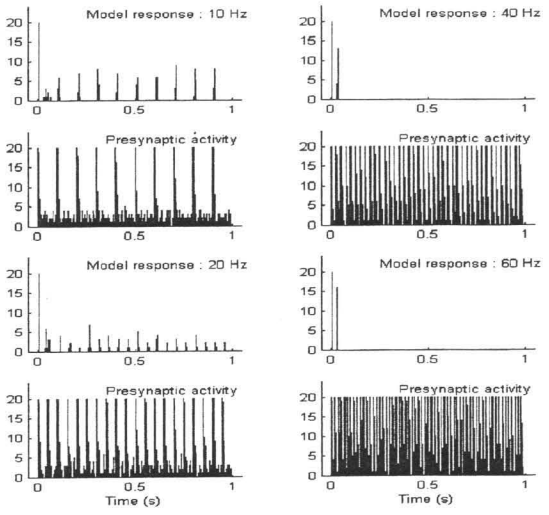

Figure 1. Simulation of the transmission of signals between thalamic relay and cortical pyramidal cells. The model qualitatively replicates the behaviour of paired pyramidal cells in AI, which showed almost no response except at signal onset when stimuli exceeded 20 Hz.

Frequency Response of the Model

The frequency response of the neuron model with a depressing synapse is illustrated in figure 2b. Although the synaptic dynamics were tuned to match those found experimentally in the somatosensory cortex (Markram and Tsodyks 1996), it is interesting to note that the model clearly responds preferentially to frequencies under 10 Hz, as is also found in AI. It seems to be the case that the dynamics of cortical depressing synapses may be quite similar across different cortical areas.

For comparison the response of a neuron model without a depressing synapse is shown in figure 2c. Clearly such a model could not replicate the behaviour observed experimentally without the addition of delayed inhibitory inputs which somehow increase in strength with stimulus frequency. Alternatively, modelling the synapse as a low pass filter but with very low cut-off frequency could result in a similar frequency response, but would fail simultaneously to account for the short response latency found in AI. The benefit of the proposed model is that it can account both for the low pass frequency response and short onset latency.

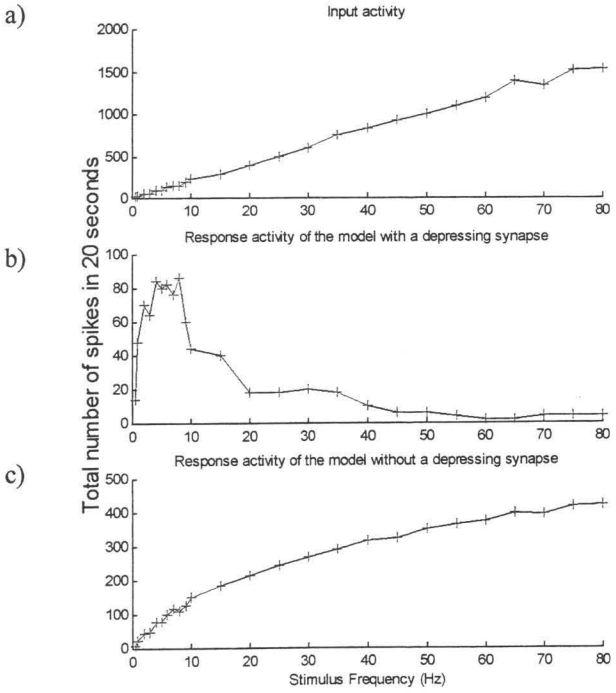

Figure 2. Frequency response of the model. The response of the neuron model with and without a depressing synapse to an incoming spike train of the frequency indicated. Plots show a) total input activity; and the number of times the cell fired during the 20 second period b) with and c) without synaptic depression.

Limitations of the Simulations

For many of the experiments simulated, the nature of the thalamocortical signals is unknown, which makes it difficult to know whether the stimuli used as inputs to the model are realistic. However, the details of the acoustic stimuli used in the experiments are generally well documented and therefore it is desirable to be able to simulate the experiments using similar acoustic stimuli. For this reason a well-documented and tested peripheral model, DSAM (O'Mard, Hewitt and Meddis), was used to generate signals characteristically found in auditory nerve fibre recordings in response to acoustic stimuli. The problem with this approach is that the rest of the subcortical auditory system has not been similarly modelled. Therefore, in the following simulations the output from the peripheral model is reprocessed to ensure that the firing rate remains below about 200 Hz by enforcing a reasonable refractory period. Clearly this ignores the computations which occur in the rest of the auditory system. However, the model can replicate a number of experiments and this would almost certainly be improved upon by more accurately modelling the thalamic-cortical signals. While recognising that this simplification likely to result in a poor approximation of actual thalamic relay cell activity, it is difficult at this stage to do much better, and has the added benefit of making the simulations tractable.

For the remainder of the simulations, the acoustic signals specified are processed by the DSAM model that includes an outer-middle ear transfer function, a gammatone filterbank, and Meddis' inner hair cell model. A simple stochastic spike generator model is used and a convergence of 20 inner hair cells to 1 auditory nerve fibre assumed. The spike trains are then processed to ensure that refractory periods are generally greater than 20 ms. However, when more than one spike occurs simultaneously, as is possible with a combinations of 20 spike trains per channel, then the refractory period is allowed to decrease in proportion to the extent of the coincidence. This has the benefit of not destroying the enhanced onset response generated by the inner hair cells.

Best Modulation Frequencies

Rate modulation transfer functions were extensively investigated by (Schreiner and Urbas 1988), who found that the best modulation frequencies in AI were generally below 15 Hz. More recently very similar normalised rate modulation data was presented (Kilgard and Merzenich 1998). To demonstrate the validity of the modelling approach taken, figure 3 shows a comparison between these experimental results and the response of the model to similar acoustic stimuli, pre-processed in the way described above.

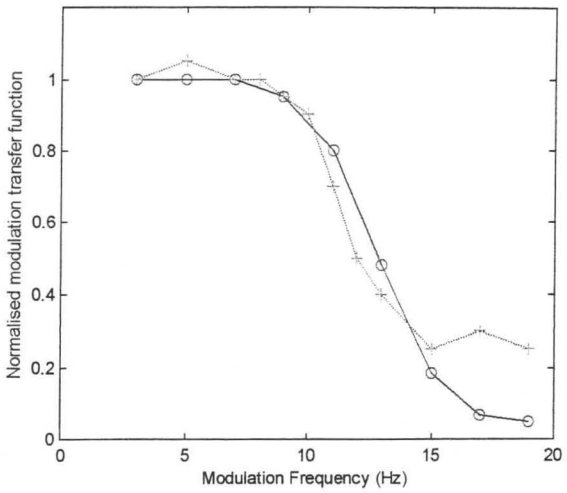

Figure 3. Response to repeated tones at the given repetition rates; model 'o__o' and experimental results '+...+' (Kilgard and Merzenich 1998). Normalised repetition rate transfer functions are found using a stimulus consisting of 6 tones pulses at the repetition rate indicated and then calculating the mean response to the last 5 tones in the sequence divided by the response to the first tone; each tone has a duration of 25ms.

The Time Course of Forward Masking

Although there are undoubtedly a number of factors that contribute to the phenomenon of forward masking, it is clear that the depression of thalamocortical synapses must contribute to the total effect. Explanations for forward masking have also been sought in terms of lateral or forward inhibition. However, it has been shown that masking continues to exist even in the presence of a $GABA_A$ antagonist and therefore even if inhibitory inputs have some part to play they cannot provide a full account (Brosch and Schreiner 1997). Both cortical forward masking and that evidenced behaviourally have been shown to last far longer than explainable in terms of peripheral adaptation (Relkin and Smith 1991). The model clearly provides a mechanism for forward masking, since synapses that have been previously activated require time to replenish their transmitter stores and respond less strongly when depleted. The time course of synaptic recovery appears to be consistent with the time course of cortical forward masking. The tonotopic distribution of masking is also consistent with a model of forward masking in terms of the depression of thalamocortical synapses since it has been shown that masking is closely related to the receptive fields of cortical neurons (Brosch and Schreiner 1997, Calford and Semple 1995). Figure 4 shows the transmitter depletion at synapses across the tonotopic axis in response to masking stimuli at the intensities indicated.

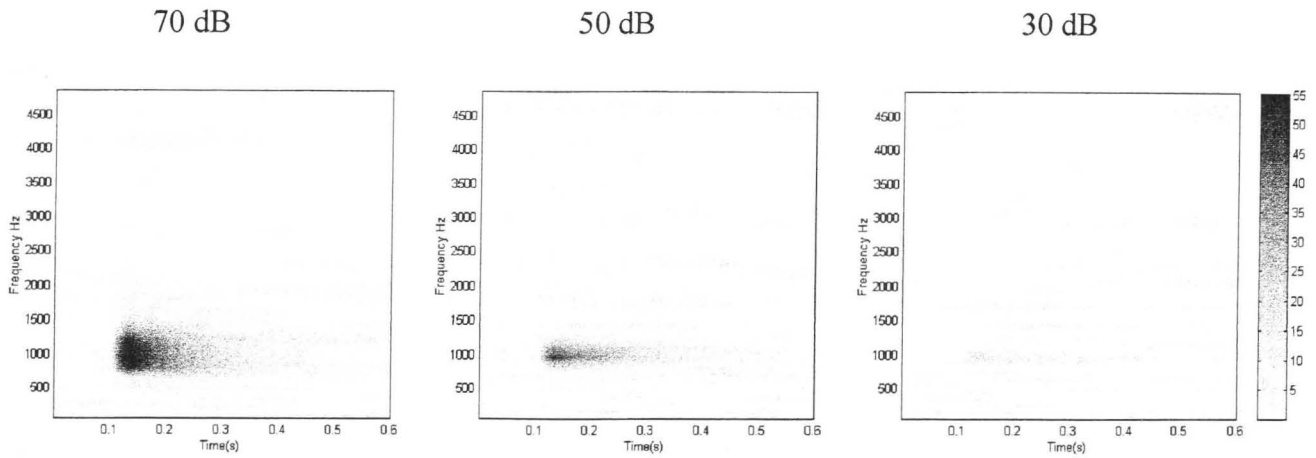

Figure 4. Distribution and time course of transmitter depletion at synapses across the tonotopic axis in response to a 1000 Hz masker of 30 ms duration at the intensities indicated. Greyscale indicates the percentage depletion relative to that at the start of the stimulus. These results are very similar to Brosch and Schreiner's plots of the time course and distribution of masking.

An important aspect of this model is that it demonstrates that cortical forward masking could be dependent on presynaptic rather than postsynaptic activity. This offers a simple explanation for the puzzling experimental observation that masking is sometimes detected even in response to maskers that do not actually activate the target cell (Brosch and Schreiner 1997). If masking is a result of transmitter depletion of thalamocortical synapses, then it would be quite possible for such synapses to become depleted by thalamic activity even though there is insufficient incoming activity to actually cause the cortical cell to fire, which is how the response to the masker was determined. Since these synapses would nevertheless be depleted, the probe tone could therefore be masked by the 'sub-threshold' masker.

The Effect of Masker Duration

In psychophysical experiments it has been shown that the degree of masking is affected by the duration of the masker and masking increases with masker duration (Kidd and Feth 1982). This was also found to be the case by (Brosch and Schreiner 1997) in their recordings in AI. However, the sensitivity to duration was observed even when the AI cell responded only at the onset of the masker, and although the effect of masker duration was noted, it was not suggested how this could occur. The model investigated here suggests a simple explanation, i.e. as long as there is some tonic incoming activity during the masker, then transmitter depletion at the thalamocortical synapses will be related to masker duration. Therefore, if as we hypothesise, the degree of masking is related to the degree of transmitter depletion at thalamocortical synapses, then the sensitivity to masker duration follows.

(Brosch and Schreiner 1997) did not include any detailed results on masker duration, so in figure 5, a comparison between the results in (Kidd and Feth 1982) and the model's response is shown. However, it should be noted that although these results are qualitatively the same, it is not clear how the degree of transmitter depletion in the model can be directly related to the probe threshold shifts plotted by Kidd and Feth.

Disruption of Synchronisation Responses by Subthreshold Stimuli

In a recent paper (Nelken and Yosef 1998), Nelken suggested that his experiments showed a correlate of comodulation masking release. Activity was record in AI in response to noise modulated at 10 Hz, and was found to synchronise to each noise pulse as expected. However, when a very soft, even subthreshold, continuous pure tone with frequency corresponding to the cell's best frequency, was added to the noise, then this synchronisation was disrupted. In contrast, when the pure tone was added to an unmodulated noise then the response to the noise alone was indistinguishable from that to the noise plus tone. Nelken suggested that the cortex might therefore be able to detect masked sounds by means of their disruption of the more powerful masker.

Once again a simple explanation of Nelken's results is suggested by the model, which can easily replicate the experimentally observed behaviour as long as there is some tonic thalamic activity in response to the pure tone. Because the activity in response to the pure tone continues through the silent gaps between the noise pulses, this prevents the recovery of the synapses between noise pulses and so the synchronised response is disrupted. This explanation is also consistent with Nelken's unpublished

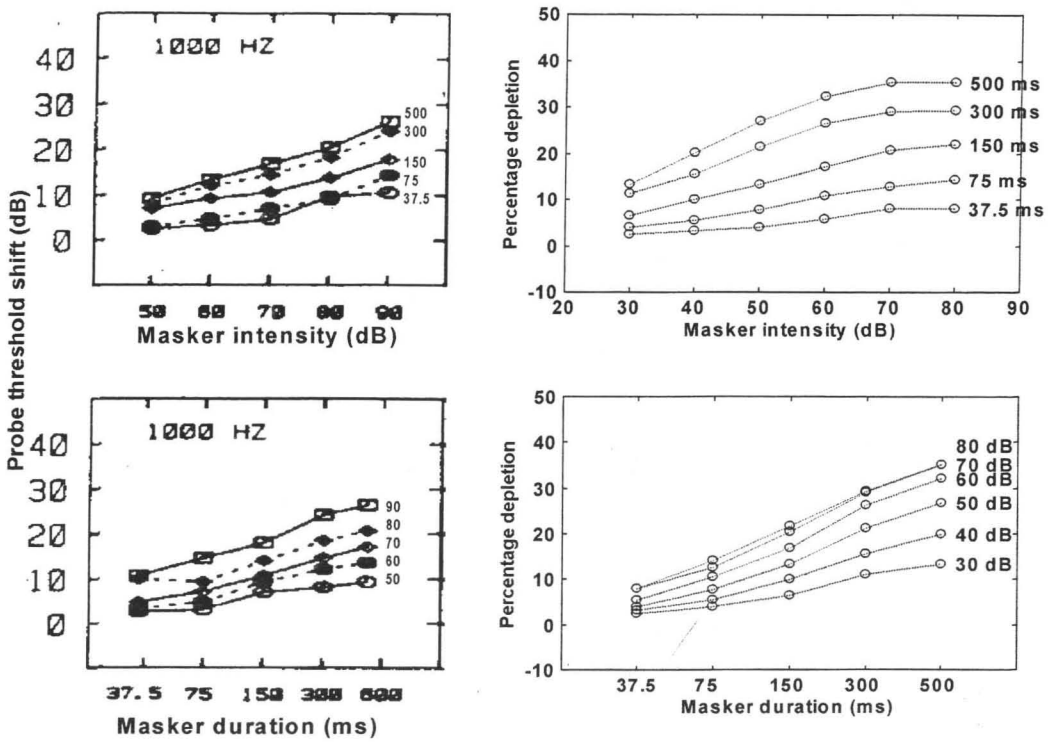

Figure 5. The effect of masker duration. For comparison, experimental results relating masker duration and masker intensity to probe threshold shifts (Kidd and Feth 1982) are shown on the left and the percentage transmitter depletion in the model in response to similar stimuli is plotted on the right.

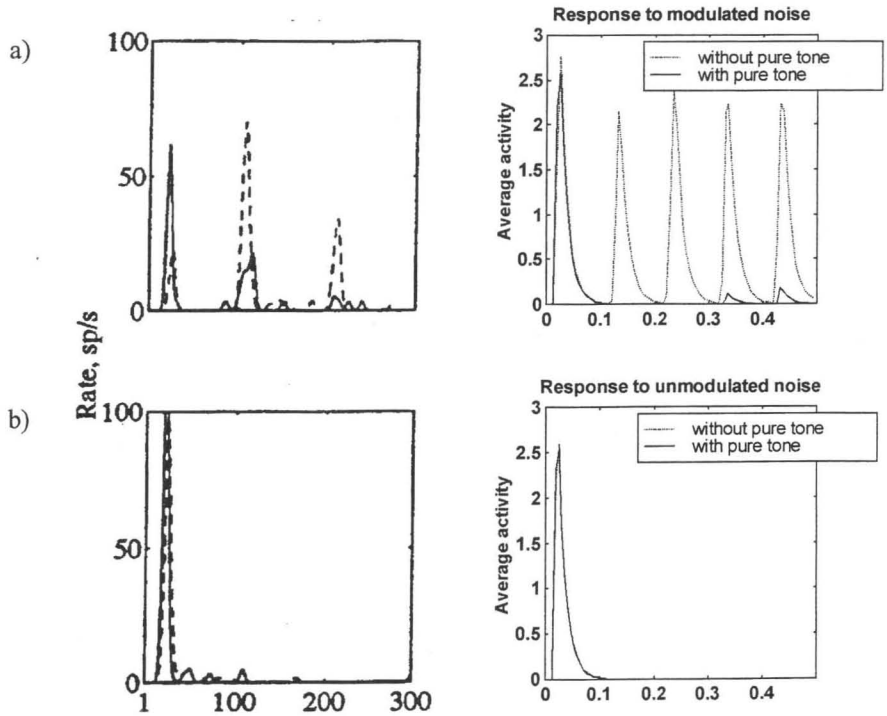

Figure 6. a) Response of neurons in AI (Nelken and Yosef 1998), left column, and the model, right column, to a wideband noise stimulus trapezoidally modulated at 10 Hz, without '---' and with '___' a continuous pure tone. b) Experimental and model responses when the noise is unmodulated.

observations that the synchronised response to the noise alone was far more reliably obtained when the noise was trapezoidally modulated, than when sine wave modulation was used. Figure 6 shows Nelken's experimental results and the model's responses to similar stimuli.

Discussion

In this paper it has been shown how a model neuron which incorporates dynamic synapses responds to a number of different stimuli. The results seem to indicate that synaptic depression at thalamocortical synapses may explain a number of aspects of the response properties of neurons in AI.

The nonlinearity of the dynamic synapse model allows it to behave in many situations like a low pass filter whilst also retaining a fast onset response. In response to repeated stimulation much above 10 Hz, synaptic depletion prevents the cell from responding except at the onset of the stimulus. However, the synaptic dynamics are not slow and after a period of rest the synapse can respond with a large EPSP to the onset of a new stimulus, which can result in a response of short latency. Since the reliability of a depressing synapse also appears to be related to amount of available transmitter (Reyes et al 1998), an aspect not included in this model, this means that after a period of rest such synapses will tend to respond very reliably as well. This is therefore consistent with the generation of onset responses of short latency and with little jitter. Although the cell tends to respond only at the onset of stimuli, important processing can continue to occur in the synapses throughout the duration of the stimulus. This allows the cell to exhibit sensitivity to stimulus duration, even when only active at stimulus onset. In addition, some of the apparent nonlinearities of responses measured in AI, such as the influence of subthreshold stimuli or interactions between different components of a complex stimulus (Nelken and Yosef 1998), could be accounted for in this way.

Since synaptic depression operates at thalamocortical synapses which are the route through which sensory signals must pass in order to get to cortex, it seems likely that the dynamics of depressing synapses have a major role to play in sensory processing. Synaptic depression appears to result in a relatively infrequent sampling of the sensory inputs by cortex, where such information is presumably integrated with ongoing cognitive processes. This bears a remarkable similarity to Viemeister's 'multiple looks' model that was formulated in order to explain temporal processing in auditory perception and to resolve the resolution-integration paradox (Viemeister and Wakefield 1991). In this model, it is envisaged that 'looks' or samples from a short time constant process are stored in memory and can be accessed and processed selectively depending on the task.

The frequency response of the model, illustrated in figure 2b, bears a strong relationship to speech modulation transfer functions, with frequencies around 4 to 6 Hz being the dominant frequency of the envelope of speech signals. Syllables in speech are generally, although not always, distinguished by an amplitude peak preceded and closed by amplitude trough (Jusczyk 1997). Therefore, when the model is stimulated by a speech signal, it has a tendency to fire at the onsets of syllables within the signal. Synaptic depression may therefore give rise to a syllable-like segmentation of speech signals within AI. Such segmentation could occur in parallel across the tonotopic axis, independently within each frequency channel. This suggestion is consistent with the experimentally observed response to species-specific calls of neurons in AI, which tend to fire primarily at the onset of segments or syllables within calls, irrespective of the characteristic frequency of the neuron (Creutzfeldt et al 1980, Wang 1997, Wang et al 1995). One effect this would have is to increase temporal synchrony across the tonotopic axis thereby promoting the grouping of related frequency components of a call. Synchronous activity is likely to be important for the effective transmission of signals to further processing centres which integrate information across frequency channels.

In experiments in which species-specific calls were manipulated (Wang et al 1995), it was also shown that speeding up of slowing down the signal, or reversing it all resulted in reduced responses. We suggest that the reasons for this differ between manipulations and that the behaviour of the model can help to explain these results. In the first case when the signal is slowed down, activity is still generated in response to syllable onsets, but since these occur at a slower rate, the total amount of activity per second decreases. In the second case, when the signal is speeded up, synaptic depression would prevent synchronisation to syllable onsets as effectively as for the control case. Finally, reversing the signal results in a reduced response, not because of a change in timing of the stimulus but because of the change in the nature of the transients in the signal. As shown in experiments on onset latency, sharp transients with abrupt rises are far more effective in generating responses than those with slow rise times (Heil 1997). Reversing the speech signal means that the transients generally become less abrupt and therefore generate reduced activity. It seems reasonable to suppose that communication sounds have evolved to optimise their detection by cortex, and that the communication sounds that are used are those which are most salient within AI. Hence, the similarity between the modulation transfer functions of speech signals and of those measured in auditory cortex. Interestingly, although derived very

differently, the behaviour of the model is very similar to the RASTA filter and which was found to markedly improve speech recognition in noise (Hermansky and Morgan 1994).

Conclusions

By taking synaptic dynamics into account in modelling these experiments, it has been possible to account for a number of previously unexplained results in a fairly straightforward way. On the basis of these investigations it is suggested that the dynamics of thalamocortical synapses may help to explain the temporal integration observed in AI and in auditory perception.

References

Abbott LF, Varela JA, Sen K, Nelson SB, "Synaptic depression and cortical gain control", *Science,* Vol. 275, 220-224, 1997.

Bregman AS. *Auditory scene analysis.* MIT, Cambridge, MA, 1990.

Brosch M, Schreiner CE, "Time course of forward masking tuning curves in cat primary auditory cortex", *J.Neurophys.*, 1997.

Calford MB, Semple MN, "Monaural inhibition in cat auditory cortex", *J. Neurophys.*, 73(5), 1876-1891, 1995.

Creutzfeldt O, Hellweg FC, Schreiner C, "Thalamocortical transformation of responses to complex auditory stimuli", *Exp. Brain Res.*, 39, 7-104, 1980.

Denham SL, "Cortical synaptic depression and auditory perception", in Greenberg S, Slaney M, (ed.s), "*Computational Models of Auditory Function*", NATO ASI series, IOS Press, Amsterdam, in press.

Eccles JC. *The physiology of synapses.* New York: Academic Press, 1964.

Grossberg S, "Some physiological and biochemical consequences of psychological postulates", *Proc. Natl. Acad. Sci, USA,* 60, 758-765, 1968.

Grossberg S, "On the production and release of chemical transmitters and related topics in cellular control", *J. Theor. Biol.,* 22, 325-364, 1969.

Heil P, "Auditory cortical onset responses revisited. I. First-spike timing', *J.Neurophys.*, 2616-2541, 1997.

Hermansky H, Morgan N, "RASTA processing of speech", *IEEE Trans. On Speech and Audio Processing*, 2(4), 578-589, 1994.

Jusczyk PW, "*The discovery of spoken language*",MIT Press, 1997.

Kidd G, Feth LL, "Effects of masker duration in pure-tone forward masking", *J. Acoust. Soc. Am.,* Vol. 72 Num. 5, 1384-1386, 1982.

Kilgard MP, Merzenich MM, "Plasticity of temporal information processing in the primary auditory cortex", *Nature Neuroscience*, 1(8), 727-731, 1998.

McCabe, S. L. and Denham, M. J. (1997), "A model of auditory streaming", *J. Acoust. Soc. Am.,* Vol. 101, No. 3, pp. 1611-1621.

McCabe SL, Denham MJ, "A thalamocortical model of auditory streaming", *Proceedings of the IEEE International Joint Conference on Neural Networks (IJCNN'98),* 1541-1546, IEEE Press: New York, 1998.

McGregor RJ, *Neural and Brain Modelling*, Academic Press, 1989.

Markram H, Lubke J, Frotscher M, Sakmann B, "Regulation of synaptic efficacy by coincidence of postsynaptic APs and EPSPs", *Science,* Vol. 275, 213-215, 1997.

Markram H, Tsodyks M, "Redistribution of synaptic efficacy between neocortical pyramidal neurons", *Nature*, 382, 807-810, 1996.

Meddis R, "Simulation of mechanical to neural transduction in te auditory receptor", *J. Acoust. Soc. Am.,* 79(3), 702-711, 1986.

Nelken I, Yosef OB, "Processing of complex sounds in cat primary auditory cortex ", *Proc. Nato ASI on Computational Hearing*, 19-24, 1998.

O'Mard LP, Hewitt MJ, Meddis R, "DSAM : Development System for Auditory Modelling", http://www.essex.ac.uk/psychology/hearinglab/lutear/home.html

Relkin EM, Smith RL, "Forward masking of the compound action potential: Thresholds for the detection of the N_1 peak", *Hear. Res.,* 53, 131-140, 1991.

Reyes A, Lujan R, Rozov A, Burnashev N, Somogyi P, Sakmann B, "Target-cell-specific facilitation and depression in neocortical circuits", *Nature Neuroscience*, 1(4), 279-285, 1998.

Schreiner CE, Urbas JV, "Representation of amplitude modulation in the auditory cortex of the cat. I. Comparison between cortical fields", *Hear. Res.*, 32, 49-64, 1988.

Thomson AM, Deuchars J, "Temporal and spatial properties of local circuits in neocortex", *TINS*, 17(3), 119-126, 1994.

Tsodyks MV, Markram H, "The neural code between neocortical pyramidal neurons depends on neurotransmitter release probability", *Proc. Natl. Acad. Sci, USA,* 94, 719-723, 1997.

Viemeister NF, Wakefield GH, "Temporal integration and multiple looks", *J. Acoust. Soc. Am.,* 90(2),858-865, 1991.

Viemeister NF, Plack CJ, "Time analysis", in Yost WA, Popper AN, Fay RR (Ed.s), *Human Psychophysics*, 1993.

Wang X, " What is the neural code of species-specific communication sounds in the auditory cortex ?", *Proc. 11th Int. Symp. on Hearing*, Grantham, UK, 456-462, 1997.

Wang X, Merzenich MM, Beitel R, Schreiner CE, "Representation of a species-specific vocalisation in the primary auditory cortex of the common marmoset: Temporal and spectral characteristics", *J.Neurophys.*, 74(6), 2685-2706, 1995.