

Processing of sounds by population spikes in a model of primary auditory cortex - analysis and extensions

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Abstract

This paper analyses and extends a model proposed by Loebel et al. on how iso-frequency columns in the primary auditory cortex (A1) are modelled through a recurrent neural network with short-term synaptic depression. Firstly, we explore the biological foundations of sound perception in humans, to build a solid understanding on which to reproduce the mathematical model. We show the relationship between interconnected columns, in response to frequencies reflecting the tonotopic map in A1 and the different mechanisms that accompany the population of neurons emitting Population Spikes (PS). We reproduce a range of findings from the model, from basic propagation and masking effects through to more complex phenomenon such as frequency tuning curves and processing of complex sounds. Lastly, we present some extensions to Leobel et al.'s model to explain further empirical phenomenon, such as phantom tones, the Fletcher Munson effect, hearing and tinnitus, and the effects of aging on inhibition and sensitivity. The paper concludes with an examination of the robustness of the model to stochastic noise.

Introduction: the biology of human sound perception

The processes involved in human sound perception are complex and require multiple integrated stages, as seen in (Figure 1). Air pressure waves first enter through the outer ear canal and impinge on the ear drum, causing it to vibrate. They are then converted to fluid pressure waves by the bones of the middle ear (ossicles), which cause vibrations in the cochlea, a spiral tube similar in appearance to a snail shell. Vibrations in the cochlea subsequently provide stimulation of hair cells in the basilar membrane, triggering neurotransmitter release which stimulates neurons of the cochlear (spiral) ganglion. The basilar membrane is notably also sensitive to the frequency of sound waves, and is thought to be tonotopic, meaning that frequency responses (the tone of the sound wave) reflect spatial position, with high frequencies maximally stimulating the base, and low frequencies maximally stimulating the apex (innermost part of the coil).

Transmissions from the neurons of the cochlea are thought to project through a host of nuclei all the way to the primary auditory cortex (A1). Crucially for the purposes of the models explored in this paper, neurons in A1 are also thought to be tonotopic, whereby they are spatially arranged in columns that respond preferentially to the same particular frequency (iso-frequency columns). The intensity of sound frequencies (volume) are also crucial in sound perception, as this is thought to be a modulating factor for the magnitude of A1 column excitatory firing responses.

Although the tonotopic organisation of the auditory cortex has been established for 40 years [2], many questions still remain regarding the neural mechanisms and representations underpinning behavioural responses to sounds in A1. Non-linear behaviour shown by A1 neurons when reacting to a

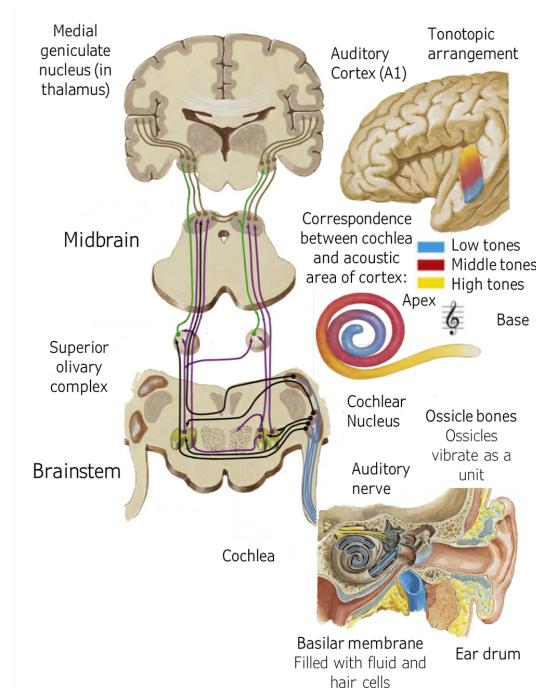


Fig. 1. Ascending and descending pathways from the auditory nerve to the auditory cortex (modified text and merged figures originally from Netter's atlas diagrams [1]).

range of stimuli, have been particularly difficult to adequately explain, including fast and strong initial firing reactions to stimuli, that quickly decrease and appear to lead to adaptation

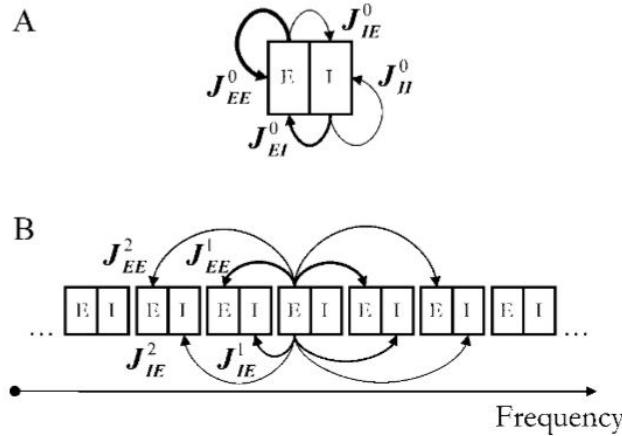


Fig. 2. Interactions between inhibitory and excitatory neurons in a single column (A) as well as the impact of excitatory neuron activity on excitation and inhibition neurons in neighbouring columns (inter-columnar connections) (B). Arrows' width represents the strength of the influence.

after continuous or prolonged activity (phasic response) [3, 4]). Hypotheses explaining aspects of this behaviour include for instance adaptation to mean intensity, though it has been suggested that this is insufficient and can better be explained by short-term synaptic depression as explored by [5].

Synaptic depression refers to the idea that, after firing, neurons have a period where their synaptic transmission resources have been depleted, and therefore must recuperate before being able to respond again to new stimuli. Loebel et al. incorporate this idea in their recurrent neural network model of cortical frequency columns [5], which models the impact of short-term synaptic depression on activation across a cortical column (when large populations of neurons in a column synchronously fire) which they define as a population spike (PS). They also model the interactions between iso-frequency columns by encoding connections between them, which allows exploration of the potential propagation effects (a firing column, exciting near-by columns by its activity), and the neighborhood effect (other columns being sensitive to frequencies which are close to their preferential 'best frequency' i.e. a 40hz column firing a small response to a 50hz frequency).

In this work, we not only reproduce many of the simulations developed by Lobel et al. [5] (Results Sections I, II, III), we also further extend the model with 4 sets of results, exploring phantom tones and the Fletcher Munson effect, hearing damage and the onset of tinnitus, the effect of aging on inhibition and finally the robustness of the model to stochastic effects.

Methods

In order to explain the model, we build it up in steps starting with an explanation of individual neurons, then individual columns, then multiple columns and finally details on the sensory inputs to these columns. The system of ordinary differential equations that determine the complete dynamics of the network, is expressed in equation 1.

Single neurons

Per [5], the model consists of two types of neurons, excitatory and inhibitory that interact with each other along iso-frequency columns following the Wilson and Cowan rate model [6]. Inside each column Q , there are N_E (N_I) number of excitatory (inhibitory) neurons, each of them with a certain activation level E_i^Q (I_l^Q). Just as in real life, energy must come from somewhere, and it is often limited. For this model, each neuron i (l) from the Q -th column, has a set of synaptic resources x_i^Q (y_l^Q), that deplete at a rate U , proportional to the activation level. Once these resources get depleted (Synaptic depression), the neuron temporarily loses the ability to transmit information to its neighbours. The speed at which a neuron reacts is modulated by two time constants (τ , τ_{ref}), while the speed at which the synaptic resources replenish themselves, is modulated by another time constant (τ_{rec}).

Single column

All the neurons of a column are interconnected, so that excitatory neurons can increase the excitatory activity of other neurons in the same column, while inhibitory neurons can reduce excitatory activity. The ratio and interaction between excitatory and inhibitory neuron activity thereby determines the increase or decrease of activity in all neurons in the column. The ratio between excitatory and inhibitory populations is also not symmetric, in the sense that each population (excitatory and inhibitory) has a different weighted *influence* on neighbouring neurons, depending on whether they belong to the same population or not. For instance, excitatory neurons influence other excitatory neurons with a weight J^0_{EE} , and influence inhibitory neurons with a weight J^0_{IE} . Likewise, inhibitory neurons influence other inhibitory neurons with a weight J^0_{II} , and excitatory neurons with a weight J^0_{EI} . Figure 2A shows a graphic representation of these interactions, and the actual values of these and other parameters can be found below in the document.

Multiple column

Influence between neurons is not limited to their own column though. As pictured in Figure 2B, excitatory neurons extend their connections to all neurons up to two columns away from its own (J^1_{EE} , J^2_{EE} , J^1_{IE} , J^2_{IE}), which is designated to model a propagation effect.

External input

The model would not be completed without external (to A1) stimuli, which in this case has two different origins. First, both excitatory and inhibitory neurons perceive a background noise (e^E and e^I respectively) which represents the electric activity of neighbouring brain regions, and follows a uniform distribution between e_{min} and e_{max} as per [5]. Second, sensory information s being sent to the cortex was designated to affect only excitatory neurons.

The sensory information is processed by the physical ear and inner ear in a manner that "distributes" a single pure tone across multiple columns. The pure tone will have the strongest response at a particular column (we call this the column whose best frequency (BF) is that tone). The neighbouring columns will also be sent a stimulus by the ear at a rate that decays

exponentially with the distance from the BF column for that tone. The decayed stimulus, follows equations (2), (3), (4). Briefly, s has a temporal component $\zeta(t)$ which determines how the stimulus varies over time, and a spatial component h which determines the fraction of stimulus at column M 's BF, that neurons at column Q perceive (Equation (2)). The spatial

component h (Equation (3)) follows a decaying exponential curve, with a maximum stimulation A for the column's BF, and a decay modulated by λ_S (Equation (4)). Overall, each neuron i at the Q -th column, receives in a way stimulus directed to all other columns, hence the $\sum_{M=1}^P s_i^{Q,M}$ at Equation (1).

$$\begin{aligned} \tau_E \frac{dE_i^Q}{dt} &= -E_i^Q + (1 - \tau_{\text{ref}}^E E_i^Q) \left[\sum_{R=-2}^2 \frac{|J_{EE}^R|}{N_E} \sum_{j=1}^{N_E} U x_j^{Q+R} E_j^{Q+R} + \frac{J_{EI}}{N_I} \sum_{j=1}^{N_I} U y_j^Q I_j^Q + e_i^{E,Q} + \sum_{M=1}^P s_i^{Q,M} \right]^+ \\ \tau_I \frac{dI_l^Q}{dt} &= -I_l^Q + (1 - \tau_{\text{ref}}^I I_l^Q) \left[\sum_{R=-2}^2 \frac{|J_{IE}^R|}{N_E} \sum_{j=1}^{N_E} E_j^{Q+R} + \frac{J_{II}}{N_I} \sum_{j=1}^{N_I} I_j^Q + e_l^{I,Q} \right]^+ \\ \frac{dx_i^Q}{dt} &= \frac{1 - x_i^Q}{\tau_{\text{rec}}} - U x_i^Q E_i^Q \\ \frac{dy_l^Q}{dt} &= \frac{1 - y_l^Q}{\tau_{\text{rec}}} - U y_l^Q I_l^Q \end{aligned} \quad (1)$$

$$s_i^{Q,M}(t) = \zeta^M(t) h_i^{Q,M} \quad (2)$$

$$h_i^{Q,M} = A e^{-\frac{|Q-M|}{\lambda_S(A)}} \quad (3)$$

$$\lambda_S(A) = \begin{cases} \lambda_C & \text{if } A \leq \alpha \\ \lambda_C + \frac{(A-\alpha)}{\delta} & \text{if } A > \alpha \end{cases} \quad (4)$$

Remarks

It is worth noting an extra couple of points to complete the model's definition as intended by [5]. First, whenever inhibition wins the tug of war, instead of giving an inhibitory input to the neurons, they are given zero input and are left to decay naturally. In equation (1) this is denoted by the $[...]^+$ function, as explained in the equation below.

$$[x]^+ = \max(x, 0) = \begin{cases} x & \text{if } x > 0 \\ 0 & \text{if } x \leq 0 \end{cases} \quad (5)$$

Second, only excitatory neurons with spontaneous activation receive sensory stimulus, $E_i^Q(0) \leq 0 \implies s_i^{Q,M} = 0$, where $E_i^Q(0)$ is the activity of the i -th excitatory neuron in column Q at time $t = 0$. Excitatory background activity determines the column's sensitivity to sensory stimuli.

Original parameters used per [5]

$$\begin{aligned} N_E, N_I &= 100, P = 15, & e_{N_E}^E, e_{N_I}^I &= 10 \text{Hz} \\ J_{EE}^0 &= 6, & J_{EE}^1 &= 0.045, & J_{EE}^2 &= 0.015 \\ J_{IE}^0 &= 0.5, & J_{IE}^1 &= 0.035, & J_{IE}^2 &= 0.015 \\ J_{EI}^0 &= -4, & J_{II}^0 &= -0.5, & \tau_{\text{rec}} &= 0.8 \text{s} \\ \delta_{\text{left}}, \delta_{\text{right}} &= 5, U = 0.5, & \tau_{\text{ref}}^E, \tau_{\text{ref}}^I &= 0.003 \text{s} \\ \lambda_C &= 0.25, & \alpha &= 2, & \tau_E, \tau_I &= 0.001 \text{s}. \end{aligned}$$

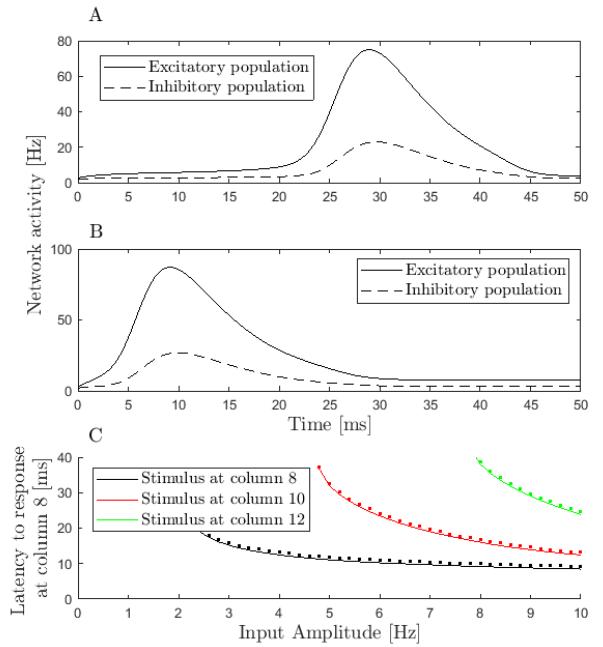


Fig. 3. Temporal co-tuning of excitation and inhibition. A) Response of column 8 to a weak stimulus at its BF. B) Response of column 8 to a strong stimulus at its BF. C) Delay in column's 8 PS as a function of the stimulus amplitude (x axis) and frequency (colour), i.e. applying column 10 and 12's BF. In each case, we are interested in the onset of excitatory (continuous lines) and inhibitory (dotted lines) PS at column 8. The inhibitory response consistently follows the excitatory response for each tone amplitude with a 1ms delay.

Results

Part I - basic effects

We begin by displaying results showing the four major phenomenon of the model: single column activity between excitatory and inhibitory neurons (inhibitory effect), sound

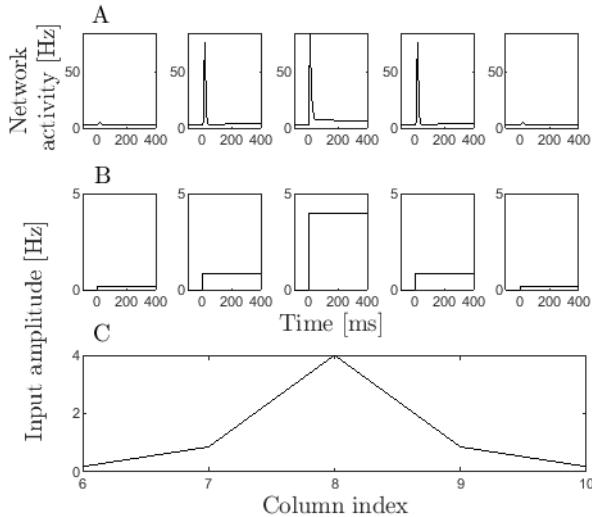


Fig. 4. Response of the model to a sustained pure tone input. The network is stimulated for 400 ms with a sensory input corresponding to column's 8 best frequency. A) Network response to the stimulus at each of the columns. Network activity at each column is calculated as the mean activity of the excitatory neurons along the column ($1/N_E \sum_{i=1}^{N_E} E_i^Q(t)$). B) temporal representation of the stimulus, that each of the columns receives. C) Spatial spread of the stimulus across columns.

spreading (neighborhood effect), cascades (propagation effect) and recovery dynamics (synaptic depression effect).

Excitatory and inhibitory behavior of a single column

Figure 3 shows the population behaviour of a column (i.e. the mean activity in that column) in reaction to an input stimulus. It should be specified that while the results are obtained by modelling the full network (i.e. all columns, interconnected), for the sake of exposition we focus on the reaction of a single column (column 8).

Figure 3A,B show the time taken for onset of excitatory and inhibitory Population Spike (PS) - the synchronous firing of large neuronal populations - based on the strength of the input, where a stronger input leads to faster appearance of the PS. Importantly, note that the onset delay of the inhibitory response is fixed to a few milliseconds after the excitatory response. Figure 3C reinforces this idea by varying the amplitude and frequency of the stimulus applied, showing an influence of both, on how quickly the excitatory neurons react (solid lines), but in each case the subsequent delay to the inhibitory response (dots) is fixed at around 1 ms.

Collectively Figures 3A,B,C therefore show that the inhibitory response which could be considered the self-regulatory activity within the columns is in some sense “fixed”, as the response largely stays the same in all three conditions. This suggests that the inhibitory response does not specifically encode information about incoming frequency or amplitude, which is conceptually useful for our understanding of the model.

Distributed sounds (neighborhood effects)

Figure 4 illustrates the basic behavior of a tone being distributed across multiple columns (neighborhood effect).

In this example, a pure tone is applied at column 8's BF. As per the biological mechanisms in the introduction, the tone is

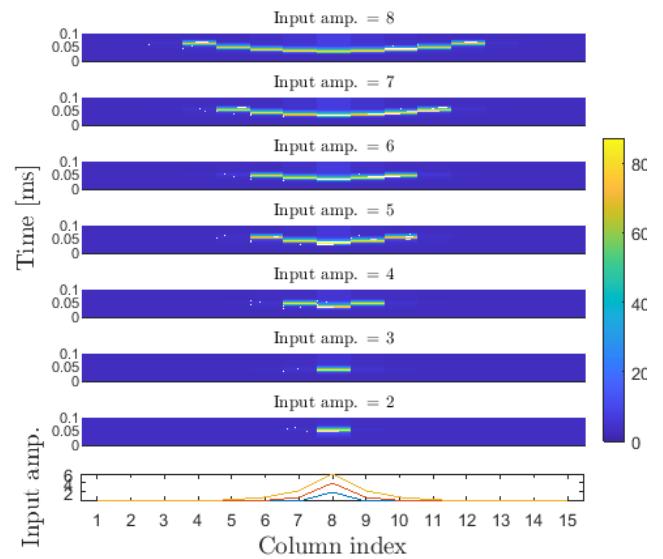


Fig. 5. Localisation of PS induced activity. Top graphs show how the population spike spreads across columns for various stimuli amplitudes at column 8. The stronger the stimulus, the further the PS spreads, due to the inter-column excitation. The bottom graph shows spatial distribution of the stimuli along columns, when the system is induced a sensory input at column 8's BF.

processed by the instrumentation of the outer and inner ear, and passed to the auditory cortex. The column whose best frequency matches the tone (in this case column 8) receives the strongest neural signal, but neighbouring columns in the tonotopic map also receive a stimulus, in a manner that decays exponentially with distance (see Methods - External input for details). The resulting signal that is sent to the A1 is illustrated in Figure 4C. Since the applied tone persists for 400 ms, the panel B shows the temporal profile of the received sensory input at each column over the experiment.

Finally, Figure 4A demonstrates how the model reacts to this stimulus. Column 8, receiving a strong input of its best frequency, presents a PS nearly instantly. The neighbouring columns receive a decayed signal, but are also able to generate PS after a minuscule decay. The next layer of columns do not spike.

This helps demonstrate the neighbourhood effect where input sounds are distributed along tonotopic gradients. Of course, another factor that causes neighbouring columns to present PS is the stimulus from excitatory neurons from one column to its neighbours, leading us to the propagation effect.

Inter-columnar cascades (propagation effects)

Figure 5 displays the idea of propagation across interconnected columns, when the PS activity for the initial central column is sufficiently large. Across the sequence of experiments (from bottom to top), the amplitude of a tone applied at column 8's BF increases, resulting in larger and larger cascades.

In contrast to simply the neighborhood effect we see that excitation in individual columns is spread across adjacent columns, whereby we not only see increased spiking for

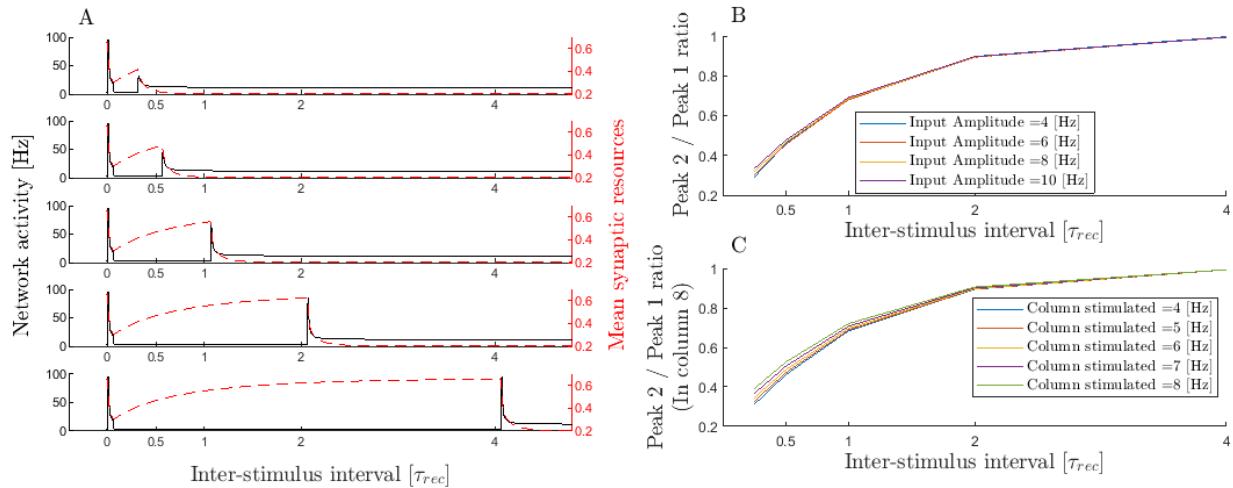


Fig. 6. Forward masking. Column 8's response to two identical stimuli of same duration (50 ms) but varying inter-stimulus interval (ISI). The first stimulus depletes the network from synaptic resources, creating a refractory period in which the second stimulus cannot generate a response of same strength. A) Trace of neural activity over time. B) Ratio between second and first response at column 8, when we vary the input amplitude and frequency. Time scales are written proportional to τ_{rec} , highlighting that the recovery period of synaptic resources is the critical factor determining the effect of the masking.

peripheral columns that receive stimulus from the original firing column, we also see feedback effects for the original middle column.

Recovery dynamics (synaptic depression effects)

Figure 6 exhibits the recovery dynamics of the model by supplying two sequential inputs with a varying time between them. As we increase the timing between stimulus (inter-stimulus interval or ISI), the network can spike more strongly at the second peak. This is because the synaptic resources of the neurons are expended by the PS, and the time delay allows the resources to recover. The depleted secondary response is also referred to as *forward masking*.

The ratio between the peak of the second and first response recovers back to full strength (i.e. ratio = 1) as the time between the stimulus increases. This pattern holds regardless of the input amplitude and frequency (the latter denoted by stimulating the corresponding column of that frequency - in all cases we are examining the response at column 8) (Figure 6B,C).

Results part II - interaction effects

So far, we have demonstrated some of the basic features of the model. We now consider how some of these features can interact.

Interaction effects between depression and cascades

In Figure 7A we see the response of interconnected columns to a pure tone after a prior stimulus (masker), for different recovery times provided. This allows an insight into the potential impact of synaptic depression, whereby the response of the entire network at $\tau_{rec}/8$ after the masker (0.1 s in this case) for instance is very weak due to depleted synaptic resources. However we see as recovery time increases activity also increases, until sufficient recovery is available that we see a full spike and cascade response.

It is worth highlighting this recovery is not just due to the recovery of the neurons in isolation allowing them to spike again. When the columns have just been exhausted, they cannot *pass on* a signal from i.e. their left-hand neighbour to the right-hand neighbour, dampening the cascade (like a line of dominoes with a missing few pieces in between).

Figure 7B provides another visual on this phenomenon through the use of frequency-tuning curves (FTCs). The FTC shows how loud a tone applied at a given column's BF needs to be to activate a population spike at column 8. In other words, the V shape figure, represents column 8 sensitivity to stimuli at other columns' -and its own- BF. It is clear that, after receiving a masker stimulus, the column's sensitivity to a second stimulus temporarily decreases (The figure drifts upwards, as the column needs higher amplitudes to show response), but then settles back to the initial curve.

Results part III - more complex effects

We finally consider a set of results from the paper that consider more complex variations on the inputs or parameters.

Encoding complex sensory inputs

So far, we have considered experiments with *pure tones* (i.e. only a single frequency was provided as input, though this input is spread over a number of neurons). In reality, we experience a complex mixture of frequencies. Figure 8 displays a complex encoded sound on the left hand side, and on the right shows the corresponding population spike activity responses. We see here that in complex tone sequences, though individual tones may be identical to each other, suppression effects due to prior tone activity can lead to different results (where spiking is impossible due to insufficient recovery), which supports the role of synaptic depression in explaining complex non-linear empirical results [7].

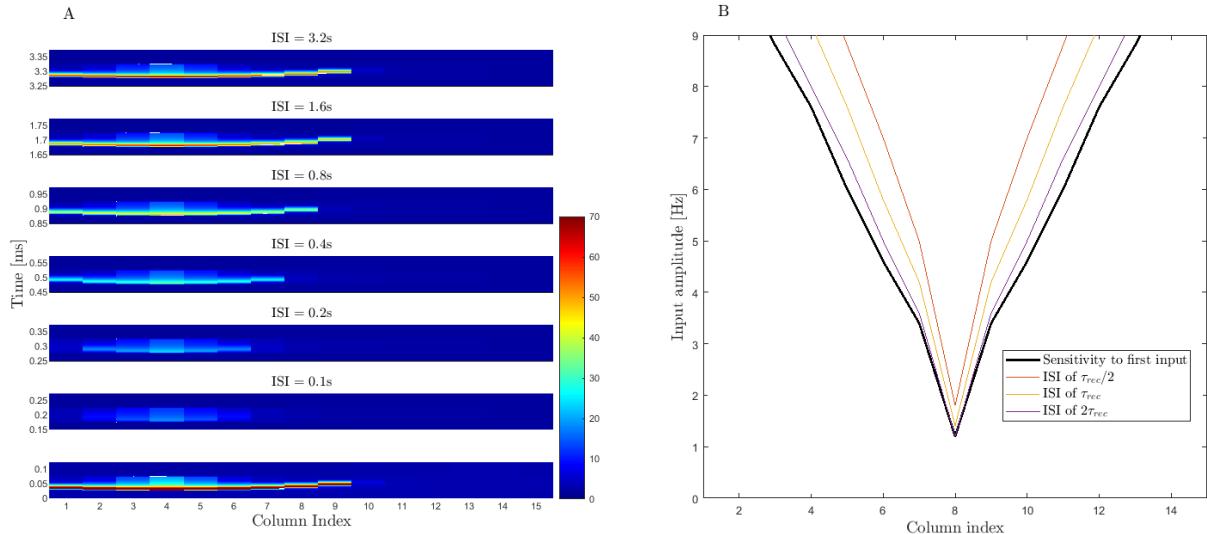


Fig. 7. A) Showcases a sequence of experiments. The bottom row shows the cascade response of the cortex to an initial tone. The rows above it show how the cortex responds to the identical tone, when it is provided at increasing delays after the first tone. The dynamics show the cascade recovers over time. B) Frequency tuning curve perspective on this phenomenon (see main text for a detailed explanation of how to read these).

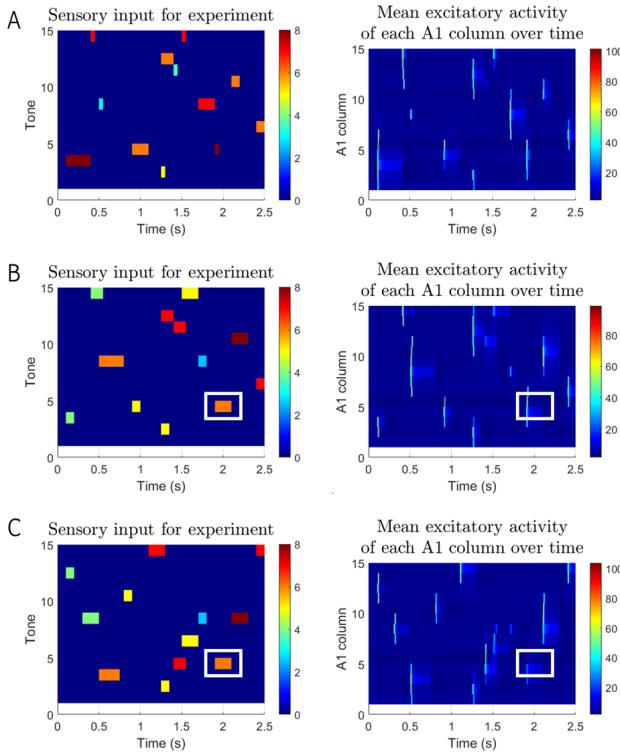


Fig. 8. Illustration of encoding of complex sounds through population spikes. The left-hand images visualise the input sounds, where the frequency of the input is on the y-axis (corresponding to the column whose best frequency is that tone), and time is on the x-axis. The colour illustrates the strength of the tone. The right-hand side show the population responses at each of the corresponding columns over the same time period. The white squares draw attention to the orange tone which is the same in Figures B and C, but leads to different population spike activity, whereby only B shows a population spike. The only differences between these two conditions is the differences in the amplitude and duration of the prior tones.

How variations in parameters affect auditory sensitivity

In Figure 9 simulations indicate how four alterations to the model differentially affect the amplitude required to see PS behaviour (as encoded by the FTCs; see previous section for details on how to interpret these).

Figure 9A, supports the importance of inter-columnar connections where propagation effects reduce the amount of stimulus amplitude required for firing. The propagation effect allows for excitatory stimulation from the original best frequency tone to cascade to the two left and right columns of the initial columns which heightens their stimulus input and lowers the amount of external input required to see a response.

Figure 9B, indicates the effect of asymmetry in the distribution of input sounds by the peripheral hearing instrumentation (i.e. cochlea, etc). This is parameterised by δ_{left} , which determines the decay rate of the sound distribution around the best frequency in left and right directions. While δ_{right} stays fixed, δ_{left} is increased, meaning sound decays more quickly along the left, and as a result we can see that a larger stimulus input is required at the right-hand columns to 8 to trigger a response from 8.

Figure 9C, displays the role of recurrent inhibition in the model, whereby reduced recurrent inhibition (meaning reducing inhibitory connections' strength) lowers the required input amplitude for spiking behaviour. This aligns well with the suppressing effects of the inhibitory neurons, as proposed by the model. When inhibitory activity is lower, less of an input is required to induce a spike at each column.

Figure 9D, displays the potential role of background input on the amplitude required for the column to have PS. In the original simulation [5], increased background input lead to an increased amplitude required for columns to fire. This could be hypothesised as increased background noise leading to generally more 'tired' or 'lazy' neurons (i.e. synaptic resources being wasted in activation to noise rather than sensory stimulus), which require more input to fire. However, in our recreated simulation, the behaviour is reversed

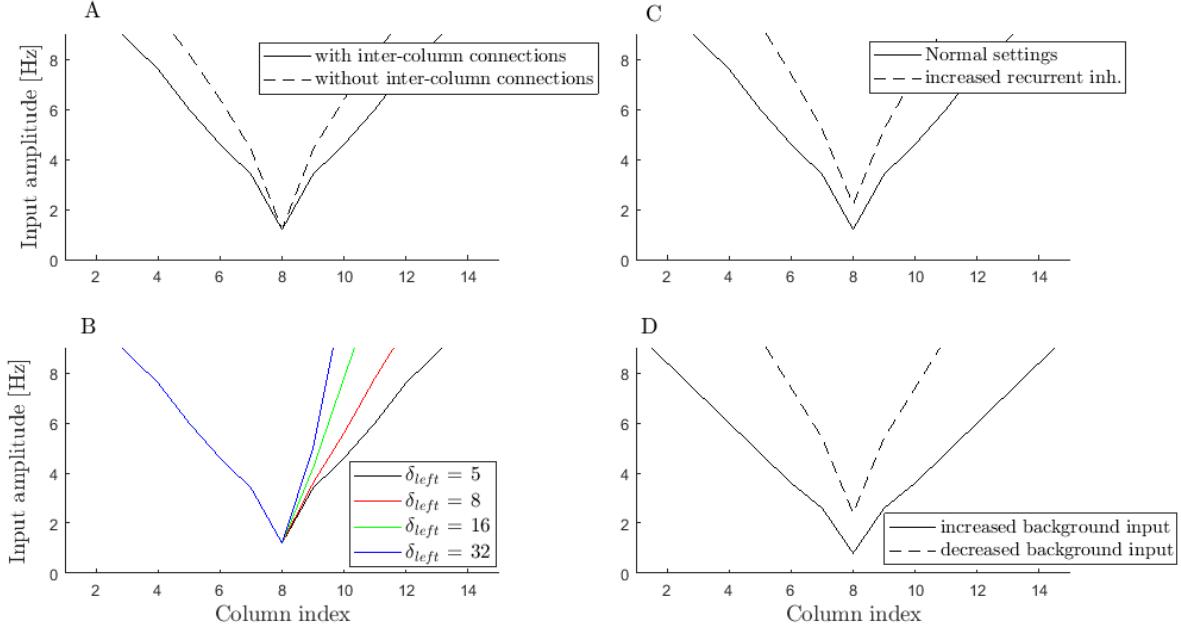


Fig. 9. Frequency tuning curves (FTC) for column 8. Each panel shows the sensitivity of column 8 to sensory inputs at other columns while varying several parameters of the model. Each line represents the minimum amplitude needed to generate a population spike (PS) at column 8 with the given parameters. See the main text for an analysis of each of these results.

whereby increased background noise actually leads to a reduced amplitude required to generate PS, meaning more background noise makes it easier for columns to reach the PS threshold. In Extension 4, we show that the discrepancy may be explained by computational differences when modelling the stochastic behaviour of background noise.

Extensions

So far, we have reproduced a number of the main results in the original analysis by Loebel et al. [5]. These results show how the model recreates important elements of observed auditory behaviour, from fundamental dynamics such as inhibition and cascades, through to interaction outcomes such as masking, and more complex outcomes such as the reaction to complex sounds and variations in parameters.

In this final section, we go further and extend the model to explain a number of other interesting and complex observed psychoacoustic phenomena. We consider phantom tones and the Fletcher Munson effects, the interplay between hearing loss and tinnitus, and the effects of aging and loss of inhibition in the brain.

While the model does a good job of corroborating these empirical phenomena, it is worth highlighting some shortcomings of the model, in particular its sensitivity to stochastic effects. We include at the end a technical analysis of how stochastic effects can lead to discrepancies in the model results.

Extension 1: Phantom sound and Fletcher Munson

Phantom sound perception

Phantom perception is the perception of tones which do not accurately correspond to the original signal. Currently explanations for this effect remain unsatisfactory [8].

In Figure 10, we offer a potential explanation of phantom sound perception as a by product of cascading propagation effects. We show that a high and low tone triggered at the same time can cause a middle tone to be triggered due to the crashing of the two cascades into each other in the middle. This would give rise to a *phantom tone* phenomena described empirically.

Furthermore, the model provides a natural experimental framework to test this hypothesis: if a real second tone is applied where the phantom tone was heard, the phantom tone will suppress the second tone (a *phantom deafness* effect).

The Fletcher Munson Effect

The phantom tone experiment points towards a more general phenomenon we might expect in this kind of intercolumn structure: tones in the middle will be triggered more often due to cascades from high (low) tones propagating down (up), as well as the *echo* effect where cascades from either direction of a middle tone will travel back to the original column. This would give rise to a perception that middle tones are heard more prominently than high or low tones.

In fact, this is a well-known psycho-acoustic phenomenon called the Fletcher Munson effect [9, 10]. In Figure 11, we test this in more detail by providing a uniformly distributed (among columns and time) input to the network, where each column is triggered 10 times with the same loudness and duration at different random points (so as to avoid any effects of a structured or synchronised sound input). We can see that even though all columns received the same level of auditory input,

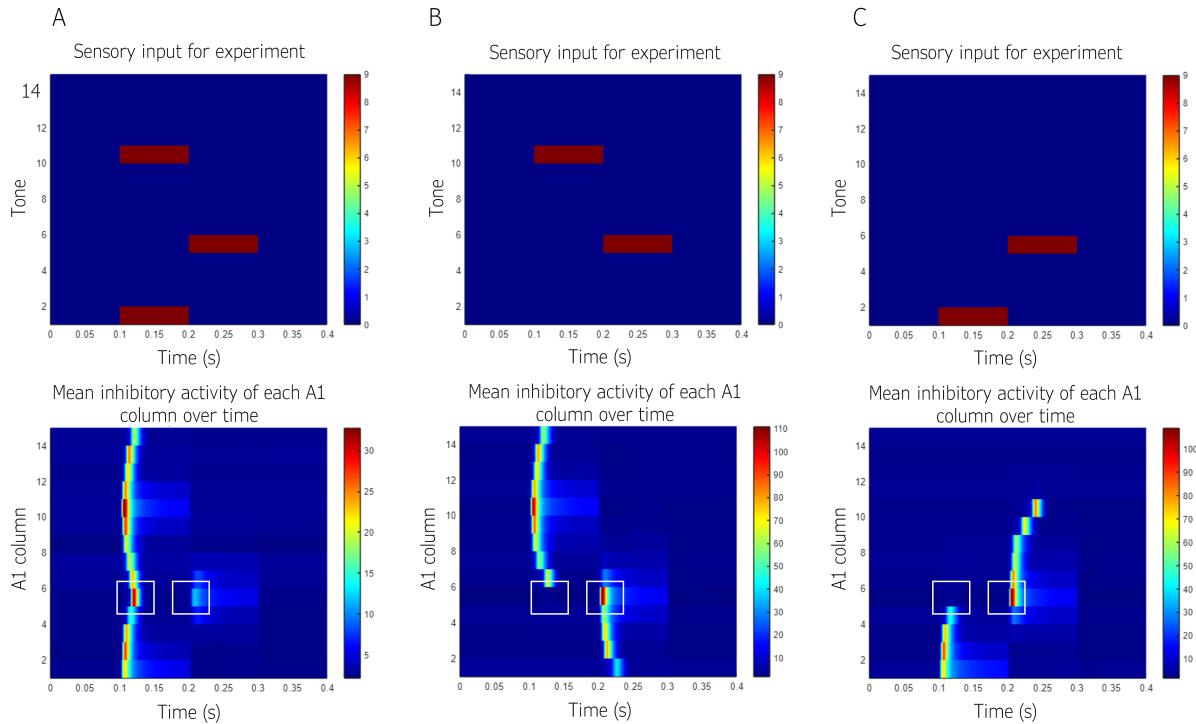


Fig. 10. (A) We see the phantom notes effect where 1) the cascading effect of the first two tones firing simultaneously produce a *phantom tone* i.e. it does not reflect any sensory input, but rather the effect of both columns propagating to the middle leading to increased firing in the center column that is sufficient to lead to a spike that would not be there otherwise. 2) The previous tone acts as a masker, suppressing firing for an actual tone that happens shortly after (*phantom deafness*). This means that due to the cascading effects a subject can think they have heard a tone that did not exist, but then due to suppression be unable to hear the actual real same tone shortly afterwards. (B) and (C) confirms that this effect is not seen when we only have one tone i.e. we do not have two tones propagating to the middle, and therefore since we do not see phantom firing we also do not have suppression of firing for the tone between 0.2 and 0.3 seconds.

the average activity of the middle columns is considerably higher due to the cascade overlaps we described earlier.

Of course, it's worth pointing out that the best explanation for the Fletcher Munson effect points to the sensitivity of the physical ear (i.e. cochlea, etc) to different frequencies rather than resorting to neuronal explanations. This result merely suggests that there may be a neuronal explanation to these phenomenon also.

Extension 2: Hearing loss, Tinnitus and Tonotopic Reorganisation

Tinnitus context

Tinnitus is the perceptual experience of hearing noise in the absence of an objectively real external stimulus, which may come in the form of the perception of sounds such as a ringing or buzzing in the ears [11]. Tinnitus is often associated with hearing loss due to damage to the cochlea [12], which may lead to *negative plasticity* which is defined as maladaptive changes to the tonotopic organisation of the auditory pathway that leads to an amplification of firing activity which is incorrectly interpreted as sound [13, 14]. One hypothesis therefore is that after hearing damage, the auditory cortex 're-wires' the tonotopic map to compensate for signal loss (In terms of the model, values of J_{EE}^1 and J_{EE}^2 are modified), but overshoots, leading to a ringing effect ("central gain model") [15].

Modelling hearing loss, re-organisation and tinnitus

In order to model the effects of hearing loss, subsequent re-organisation and the onset of Tinnitus we consider the following sequence of 6 experiments shown in Figure 12.

For Figures 12 A-D, we show how an auditory system reacts to the same pure tone applied to the BF of column 8, applied for 50 ms. The only difference is the extent of damage to the hearing system, and the extent of tonotopic re-organisation. While in a healthy hearing system the ear and inner ear are able to distribute a pure tone across a range of frequencies to send as inputs to the respective BF column, we model the damaged hearing as an interference with this process resulting in the failure to transmit certain signals (these are illustrated as pink blocks in the bottom panel showing how the processed pure tone is transmitted to the A1). This could rise for example due to the physical hairs being damaged in the basilar membrane meaning that certain frequency responses are not triggered. In response to the physical damage, the auditory cortex might re-organise. The re-organisation is illustrated in the middle panel as a network diagram, where each column is shown as a node distributed along a tonotopic gradient, and connections between columns as lines of varying thickness. Re-organisation results in new edges or thicker edges being shown. Finally, we are interested in the excitatory response of the auditory cortex in the top panel.

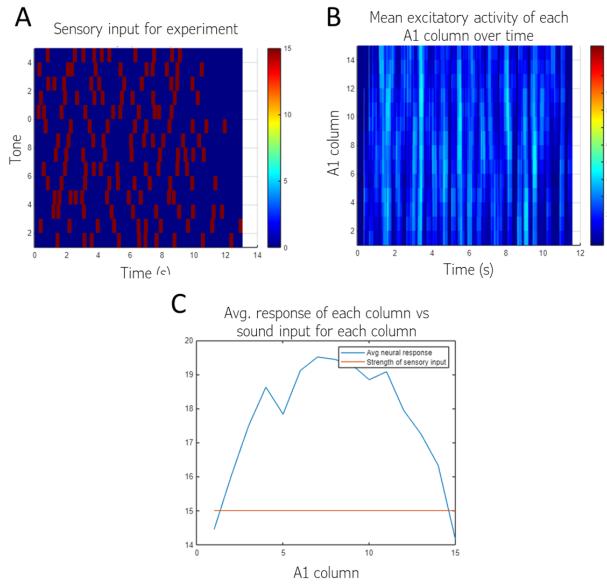


Fig. 11. In order to demonstrate the perception of medium tones sounding louder due to enhanced propagation in the middle columns, white noise is sent in the form of 10 beeps of the same loudness and length to all the columns in a random order. By the excitatory activation (Figure B), the middle columns seems to be more activated, but one can make this clear by taking the average activation for all the columns (Figure C). Even though they all receive the same input sounds, the middle columns clearly are activated more strongly.

Experiment A: Baseline reaction. Without any hearing damage, the pure tone input is distributed evenly either side of the best frequency column (column 8) without any interference, as per Equation 2. The resulting cascade is symmetric.

Experiment B: Minor hearing damage. This is modelled by the fact that no signal is sent by the physical processing to column 10, leading to a gap in the distributed sensory signal. To be clear, there is no damage to the auditory cortex. The only thing that changes is how this input is distributed to other frequencies by the physical hearing instruments. The pink bar highlights the lack of frequency sent by the ear when damaged. As a result, in the middle figure, the cascade is broken, and the A1 does not have the original response we saw in the healthy system. The symmetry is gone.

Experiment C: Minor plasticity. It is thought that when hearing loss occurs, the tonotopic map re-organises to work around the physical loss and reproduce the signal [16].

In order to simulate this, we strengthened the intercolumn excitatory weights only between column 9 and its immediate neighbours, doubling it from $J_{EE}^1 = 0.045$ to $J_{\text{rewire}}^1 = 0.09$ (highlighted in the green box). We note that there might also be an increase in for example the inhibitory intercolumn weights, but since we are just providing an illustration here we do not introduce that complexity. As a result of the re-organisation, the cascade is recovered.

Experiment D: Compounding effects. However, what if the hearing loss worsens over time? In this experiment, we model high damage as the inability of the ear to distribute any high frequency tones to the A1. We allow for the re-organisation to occur exactly as the previous experiment (i.e. keeping the same weight - one could think of this as a sequence of re-organisation unfolding over time as the subject's hearing

progressively declines). In each instance, the re-organisation would have been sufficient for the simple cascade recovery as in the previous experiment, but in aggregate they start to reinforce each other more than was originally anticipated.

As a result, a triggering medium tone can cause a chain reaction which triggers *all* the columns. For the subject, this would effectively mean that small middle or low tones can trigger high pitched ringing - which effectively simulates tinnitus.

Experiment E and F: Spontaneous activation. While the previous experiments show how high frequency tinnitus-like symptoms could be triggered by small mid-frequency external tones. An interesting question is whether the re-organisation can ever be sufficient to produce completely spontaneous population spiking (i.e. in the absence of any external input altogether). In this pair of experiments we demonstrate this is possible in theory but requires re-weighting at an order of magnitude higher than before.

In Experiment E we rewire columns of broken BFs to their neighbours with weight 2 and their two-step neighbours with weight 1. If we do this, we see that they start triggering themselves with no input stimulus at all. This is because of a residual build up of activation from the over-connected columns slowly reinforcing each other and leading to population spikes and cascades.

In Experiment F we provide slightly lower weights but more connections. We re-wire columns with broken BFs to each other with a weight drawn uniformly from 0 to 1. This results in spontaneous population spikes as before, but less frequently.

Our set of results from Experiments A - F, not only helps us illustrate the effects of hearing loss and the re-organisation of the tonotopic map, they provide a plausible explanation as to the emergence of tinnitus in the auditory cortex, and how it worsens with more profound hearing loss. For the first few experiments we chose re-weighting at the same order of magnitude as the parameters in the original A1 model, and were able to realistically recreate tinnitus as a response to mild background noise. For the latter experiments, we have chosen some perhaps unrealistic parameters to demonstrate completely spontaneous tinnitus (i.e. continuous ringing with no input trigger). We hope future work can explore physiologically realistic parameters that could lead to the same spontaneous effects.

Extension 3: Reduced inhibition in the elderly and the effects it has on hearing

Gamma-aminobutyric acid (GABA) is the main inhibitory neurotransmitter, and its key task is to reduce neuronal excitability in the nervous system. In a study conducted by Dobri S.G.J and Ross B [17], the level of GABA in the auditory cortex was measured in young and old adults, in order to investigate if there are any possible trends between GABA levels and the performance of the auditory cortex. There is evidence to suggest that GABA levels decrease with increasing age in humans [18, 19] and also in animals [20].

It is common for elderly people to experience hearing loss, mainly occurring for higher frequencies [21] and they can also struggle with speech perception in the presence of background noise [22]. A theory, suggested by Martin and Jerger [23], describes how age-related alterations in the auditory cortex can be partly responsible for the deficiency of the brain in representing speech in background noise. One of the

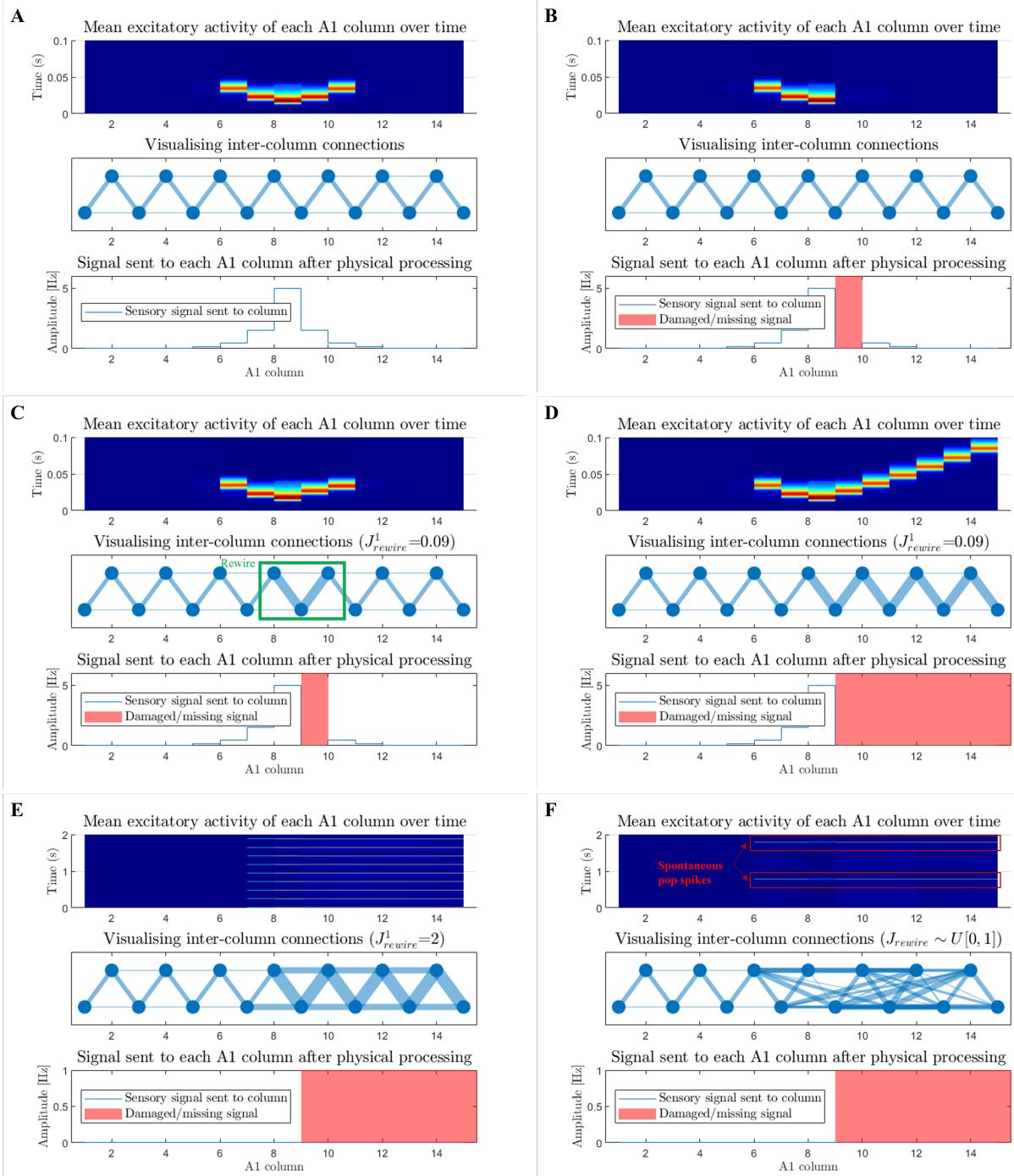


Fig. 12. Illustration of hearing damage, tonotopic reorganisation and resulting tinnitus. For Figures A-D, a single pure tone of amplitude 5 Hz was sent at the best frequency of column 8 for 50ms. In each figure, we see three rows. The bottom row shows how the pure tone, once processed by the physical ear and inner ear, is distributed as a signal for each of the columns. If there is any damage in the physical pathway that means that some frequencies are not triggered for response, a pink bar is shown. In the second row, we visualise the inter-column connections as a network. The width of the edges indicate the strength of the excitatory connection (for example the baseline immediate neighbour weight in the (diagonal lines) is $J_{EE}^1 = 0.045$, much more than the baseline second-neighbour weight (straight lines) is $J_{EE}^2 = 0.006$, and reflected in the thickness). The top row shows the excitatory response. In Figure A, there is no damage and a normal symmetric cascade. In Figure B, there is some damage which means the signal for BF of column 9 is not sent, and the cascade is interrupted. In Figure C we re-weight the edge between 9 and its immediate neighbours in response to the damage up to $J_{\text{rewire}}^1 = 0.09$, resulting in the cascade recovery. In Figure D the re-weight is the same, but we add more hearing damage along other frequencies, meaning a single middle frequency pure tone cascades through to high tones. In Figure E, the hearing damage is the same but re-weights but we increase the re-weight between neighbours of columns with damaged BF to be 2 and for two-step neighbours to be 1. This produces spontaneous population spikes in the absence of any sensory input. In Figure F, columns with damaged BF are randomly rewired to each other with weights randomly drawn between 0 and 1. This also results in the absence of any sensory input (the spikes are hard to spot at the time scales, so they are highlighted with red boxes). The final pair of experiments contain weights an order of magnitude larger not to be realistic but merely to demonstrate the possibility of over-connections in response to damage leading to spontaneous population spiking.

fundamental functions of GABA is to regulate neural activity, so a decrease in GABA levels in older adults could develop a weakened inhibitory effect and in turn a hindered ability to regulate neuronal spike timing.

In the experiment, forty-three participants took part, 21 being part of the younger group (ages 19-29 with average age of 24.1) and 22 being part of the older group (ages 69-90, average age of 77.1). They firstly found that the elevation of threshold in pure tone average (a value to measure the average of hearing sensitivity) was 11.2 dB for each decade of life, which is compatible with results from longitudinal studies [24] and also showed that hearing loss associated to age, advances considerably quicker after the age of 60 compared to earlier in life. A threshold shift means that the sensitivity in hearing will decrease, and it becomes more difficult to notice soft sounds; elevated hearing thresholds were also found to be associated with decreased GABA levels.

When looking at speech-in-noise (SIN) loss, they found that it was strongly correlated with the level of GABA in the higher aged group; the participant in the older group with the best performance also had the highest GABA level, showing that higher GABA levels are directly related to better efficiency in SIN perception. SIN loss was also strongly positively correlated with age.

A study done by Lalwani et al.[25] found that GABA levels in the auditory cortex were not corelated with levels in the sensorimotor or visual parts of the brain, showing that changes in GABA levels are specific to individual areas of the brain rather than as a whole.

The trend between GABA levels and hearing impairment was suggested as it being a means to compensate for reduced sensory input from the peripheral auditory system, where the reason inhibition is reduced from the lowered GABA levels, is to make the auditory system more sensitive. This can be seen in Figure 13, where the less inhibitory neurons, the more sensitive the auditory cortex was to input triggers; this is predominantly seen in Panel B, where there was only 1 inhibitory neuron (an extreme representation of impaired hearing) in comparison to 100 (representing a ‘healthy’ auditory system), and most of the columns show excitatory activity. This could be the result of age-related damage to the peripheral auditory system, lowering inhibitory activity, (represented by less inhibitory neurons in our model) and in turn over-compensating in making the auditory system more sensitive to the sensory inputs.

Extension 4: Technical analysis - stochastic effects and model robustness

As described in [5] methods, the input stimulus s only affects excitatory neurons that show spontaneous activation, caused by the background noise e^E and e^I . Given that these background inputs follow a stochastic distribution, all behaviour derived from them, i.e. network’s dynamics, also does. For this reason, it is worth studying the impact of randomness on the model, in terms of the qualitative meaning of its outputs.

Several no-stimulus simulations were run until convergence to a steady state, varying the random seed at each run (Figure 14). At such steady state, the number of excitatory neurons with spontaneous activity ($E_i(0) > 0$) determined the proportion of neurons per column to be stimulated by external input. Results suggest that, on average, half of the excitatory neurons in the network are silent, with some extreme conditions, where either more than 70% or less than 40% of the entire excitatory neurons are active. The impact of this variance

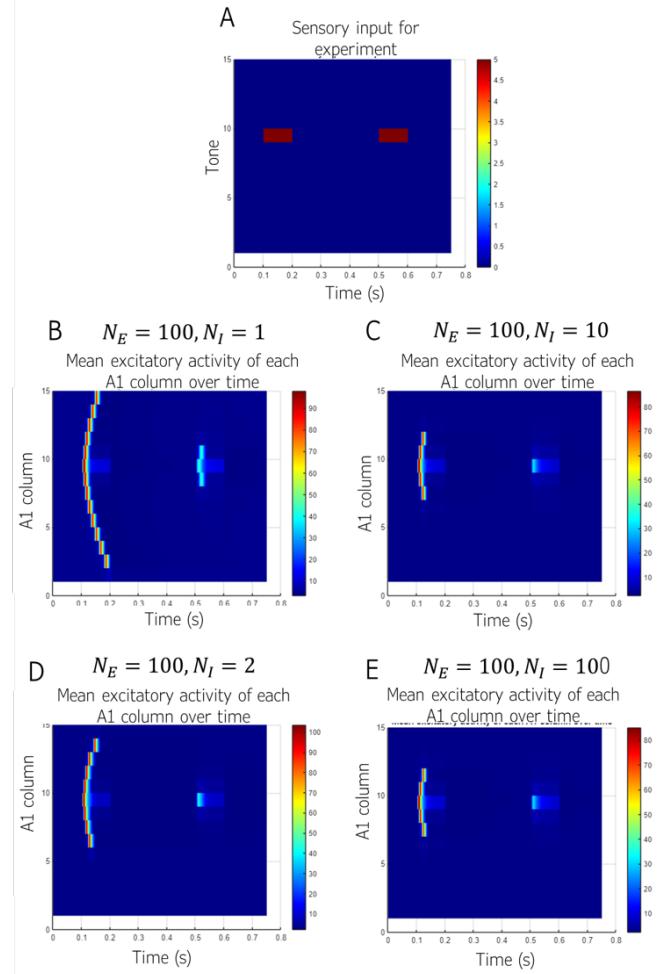


Fig. 13. Effect of reduced inhibitory neurons on sound perception. A) Two sensory input tones at $t = 0.1$ and $t = 0.5$ at column 9, followed by 4 panels showing the mean excitatory activity in the A1 network with differing amounts of inhibitory neurons and a fixed value of 100 excitatory neurons. B) There is a vast cascading propagation effect across most of the columns when there is only 1 inhibitory neuron. As you increase the inhibitory neurons (2 in panel D and 10 in panel C), the cascading effect diminishes. E) A healthy auditory system (as per [5]), where the first tone triggers only a small cascading effect and the second tone has very little effect.

on the networks response to stimulus is yet to be quantified. Figures 15 and 16 show examples of qualitative differences in results caused by this variability.

Additionally, it is worth questioning the biological meaning of giving external input only to the spontaneously active neurons, as per [5]. In the model, background noise represents electric activity in neighbouring brain regions. To imply that this noise somehow turns on and off the ability of A1 to receive external stimulus, might be a useful mathematical shortcut to produce interesting results (See Figure 11 in [5]). Nonetheless, this behaviour may suggests the existence of a complex relationship between A1, thalamus (which gives the stimulus to A1, See Introduction for details), and other brain regions, an idea that needs further analysis to determine the biological relevance of such assumptions.

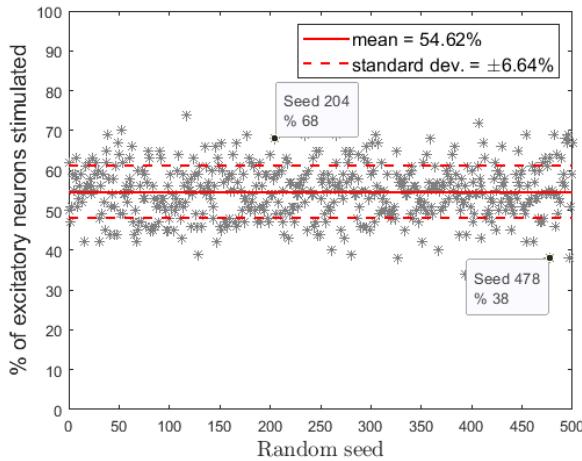


Fig. 14. Variability in the amount of spontaneously active excitatory neurons per column, for different seeds. Results seem to be stable around the mean (54,62%). Nevertheless, these differences can cause qualitatively opposite outputs (e.g. Figure 15, respective percentage of excitatory neurons for the seeds used in that figure, are marked here)

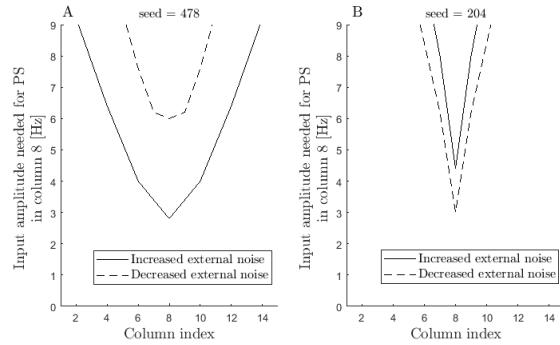


Fig. 15. Re-plot of Figure 9D (Figure 5D in [5]). Different seeds can create opposite outputs. A) column's FTC using a random seed that models low percentage (38%) of spontaneously active excitatory neurons. B) Same experiment than A but with a seed that models high percentage (68%) of spontaneously active excitatory neurons. Further analysis has to be done in order to draw conclusions about the effect that increasing and decreasing external noise has on the network's FTC.

Conclusion

To conclude, through a reconstruction of results from the work by Loebel et al., we are able to verify the findings of synaptic depression, the neighbourhood effect, and propagation; these results display a clear role in explaining behavioural data suggesting the complex behaviour of A1 responses to a range of sound stimuli, which has historically been a process difficult to justify, for example, how there is fast and strong initial firing reactions followed by a quick decrease in response.

The model is built on the central idea that neurons in the same column respond to similar frequencies and that when a sound input is strong enough, this results in Population Spikes (PSs). However, influence between neurons is not restricted to their own column, rather, they lengthen their connections to all neurons up to two columns either side; this is what makes the model able to represent the propagation effect. The model elucidates in a consolidated fashion different properties of neurons in the auditory cortex; these consist of things

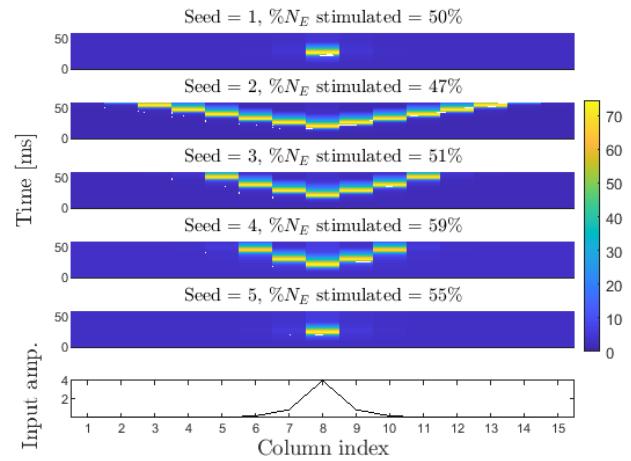


Fig. 16. Variations of the propagation effect for different seeds. Using the same sensory input and only varying the random seed, the network presents widely different cascade effects. The ease with which the PS is spread across columns seems to be independent of the percentage of spontaneously active excitatory neurons. A hypothesis for this behaviour is that, the propagation effect depends more on the total activity of the network at time $t = 0$ ($\sum_{i \in \Omega} E_i^Q(0)$, $\Omega = \{i | E_i^Q(0) > 0\}$), rather than the percentage of spontaneously active neurons. Further analysis is necessary.

such as, the reaction to pure tones under different conditions, the reliance of responses on the time and frequency of two subsequent stimuli and the temporal structure of excitatory and inhibitory inputs to the A1 neurons.

Additionally, we designed further extensions to the model relating to aging, tinnitus and phantom effects, which display the flexibility of the model to simulating a wider range of sound related phenomena in the auditory cortex. Furthermore, it also provides potential novel insights into the mechanisms of tinnitus, for instance, which may improve our understanding of the biological mechanisms behind these maladaptive sound perception outcomes. Moreover, in Extension 4, we explored the model robustness in terms of the stochastic effects; since the model is built with the background inputs following a stochastic distribution, this means dynamics as a whole also do, giving us a cause to investigate the impact of randomness on the model. We also introduced the question of how plausible it is biologically, to only give the external input to the spontaneously active neurons, an idea that perhaps can be examined in the future.

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