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Experimental-neuromodeling framework for understanding auditory object processing: integrating data across multiple scales.

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Abstract

In this article, we review a combined experimental-neuromodeling framework for understanding brain function with a specific application to auditory object processing. Within this framework, a model is constructed using the best available experimental data and is used to make predictions. The predictions are verified by conducting specific or directed experiments and the resulting data are matched with the simulated data. The model is refined or tested on new data and generates new predictions. The predictions in turn lead to better-focused experiments. The auditory object processing model was constructed using available neurophysiological and neuroanatomical data from mammalian studies of auditory object processing in the cortex. Auditory objects are brief sounds such as syllables, words, melodic fragments, etc. The model can simultaneously simulate neuronal activity at a columnar level and neuroimaging activity at a systems level while processing frequency-modulated tones in a delayed-match-to-sample task. The simulated neuroimaging activity was quantitatively matched with neuroimaging data obtained from experiments; both the simulations and the experiments used similar tasks, sounds, and other experimental parameters. We then used the model to investigate the neural bases of the auditory continuity illusion, a type of perceptual grouping phenomenon, without changing any of its parameters. Perceptual grouping enables the auditory system to integrate brief, disparate sounds into cohesive perceptual units. The neural mechanisms underlying auditory continuity illusion have not been studied extensively with conventional neuroimaging or electrophysiological techniques. Our modeling results agree with behavioral studies in humans and an electrophysiological study in cats. The results predict a particular set of bottom-up cortical processing mechanisms that implement perceptual grouping, and also attest to the robustness of our model.

Keywords

functional magnetic resonance imaging; fMRI; auditory; speech; hearing; large-scale; neurobiologically realistic

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1. Introduction

Neuroscience is in a “golden age” of discovery. Innovative techniques such as functional magnetic resonance imaging (fMRI) have opened up new avenues of research. This explosion of data advances our knowledge, yet can be overwhelming. We need well-constructed theories that illuminate the data and lead to the determination of universal principles underlying brain function. In particular, we need theories that combine experimental data from multiple levels of inquiry, ranging across neurons, cortical columns, regions, and systems. Computational or mathematical modeling provides a framework for consolidating incommensurate data from multiple studies, reducing multiple data dimensions to a few critical ones, articulating hypotheses explicitly, and generating predictions. Models are not unmoored from data but are constrained and validated by experimental evidence. They give greater focus to experimental design mainly because they provide a construct or language within which to think about and articulate a problem. The predictions of the model are tested by experimental studies. Data from experimental studies are used to validate the model and revise it better account for the new data. Such an “evolving” experimental-neuromodeling framework allows for a resonance between modeling and experiments, leading to better models, better experiments, and ultimately to a better understanding of neuroscience.

There have been several experimental-neuromodeling approaches that investigate brain function, focusing their attention at different levels, from neurons to cortical columns to the level of regions or systems. Our approach differs from the others’ primarily in its focus on functional brain imaging data and the need to reconcile these with neuronal and behavioral data. In this article, we illustrate this combined brain imaging-neuromodeling approach in understanding brain function using our own work related to auditory processing. We constructed a large-scale neurobiologically realistic neural network model (Husain et al., 2004) of auditory object processing. Auditory objects are meaningful sounds such as words, syllables, melodic fragments, chords, bird calls, etc. (Griffiths and Warren, 2004; Kubovy and Van Valkenburg, 2001) that follow rules of object perception (e.g., figure-ground separation). In our model, the processed objects are frequency-modulated (FM) sweeps and the primary task is a delayed-match-to-sample (DMS) task. The model simulates a cortical pathway from the primary auditory cortex to the frontal cortex. The model was validated using fMRI experiments that employed similar stimuli and tasks as in the simulations.

In this paper, we will describe the model first and then the critical assumptions that were made in constructing the model. These assumptions are supported by experimental evidence and had important consequences, for instance in the prediction of the existence of a type of neuron. The model predictions led to new experiments and the latter in turn, led to new simulations.

2. Auditory Object Processing Model (AOM)

The large-scale, neurobiologically-realistic model of cortical auditory processing we developed is shown in Figure 1a. The model processes FM sweeps during performance of a delayed-match-to-sample task. The first two stages of the model, Ai (primary auditory cortex) and Aii (secondary auditory cortex), perform feature detection: FM-sweep selective neuronal subpopulations in Ai and Aii respond to the presence of upward and downward sweeps in the input signal. The units of Aii have a longer spectro-temporal window of integration than the Ai units; therefore they are selective to longer-duration FM-sweeps. In addition to these types of units, Aii has a third type of units – the ‘contour-selective’ units. These units respond to changes in sweep direction that occur in relatively brief periods of time. The ST (superior temporal sulcus/gyral area) region receives inputs from all three subpopulations of Aii and integrates the features into an abstract distributed representation, or a ‘percept’. The percept is then forwarded onto the short-term working memory system of the PFC (prefrontal cortex).

There are four types of units in the PFC: cue-sensitive (C) units that respond to the presence of an input; two types of delay units, D1 and D2, that maintain a stable representation of the percept of the first stimulus and facilitate its comparison with that of the second stimulus; and response units (R) which are active to a greater extent when the second stimulus is a match than when it is not a match. The delay unit D1 is active during the delay period between the presentations of the stimuli whereas delay unit D2 is active during both the delay and during stimulus presentation. The input to the model is via the medial geniculate nucleus (MGN), each unit of which represents a neuronal population selective for a particular range of frequencies. The activity of these units over time can be represented by a “neural spectrogram”.

The basic unit underlying all the regions of the model, shown in Figure 1b, consists of excitatory and inhibitory elements, with the excitatory element contributing more to the overall activation of the basic unit due to its larger synaptic weights. Each basic unit can be thought of as representing a simplified cortical column with the excitatory element corresponding to the pyramidal neuronal population, and the inhibitory element corresponding to the population of inhibitory interneurons. Such a unit is commonly used in modeling studies and was first introduced by Wilson and Cowan (1972). Each module of the network is composed of 81 basic units. The activities of the excitatory and inhibitory elements of each basic unit are governed by a sigmoidal activation rule, whose parameters represent different aspects of cortical dynamics:

$$\frac{dE_i(t)}{dt} = \Delta \left(\frac{1}{1 + e^{-K_E [w_{EE}E_i(t) + w_{IE}I_i(t) + in_{iE}(t) - \tau_E + N(t)]}} \right) - \delta E_i(t) \quad (1)$$

$$\frac{dI_i(t)}{dt} = \Delta \left(\frac{1}{1 + e^{-K_I [w_{EI}E_i(t) + in_{iI}(t) - \tau_I + N(t)]}} \right) - \delta I_i(t) \quad (2)$$

where $E_i(t)$ and $I_i(t)$ represent the electrical activities of the i th excitatory and inhibitory elements at time t respectively. K_E and K_I are the gains, or steepnesses, of the sigmoid functions for excitatory and inhibitory units, respectively, τ_E and τ_I are the input thresholds of excitatory and inhibitory units, Δ is the rate of change, δ is the decay rate, and $N(t)$ is a term that contributes low-level, random, spontaneous activity to each neural element at all times. w_{EE} , w_{IE} and w_{EI} are the weights within a unit: excitatory to excitatory (value = 0.6), inhibitory-to-excitatory (value = -0.15), and excitatory-to-inhibitory (value = 0.15), respectively. $in_{iE}(t)$ and $in_{iI}(t)$ are the total inputs coming from other areas into the excitatory and inhibitory units at time t :

$$in_{iE}(t) = \sum_j w_{ji}^E E_j(t) + \sum_j w_{ji}^I I_j(t) \quad (3)$$

$$in_{iI}(t) = \sum_k w_{ki}^E E_k(t) + \sum_k w_{ki}^I I_k(t) \quad (4)$$

where w_{ji}^E and w_{ji}^I are weights coming from excitatory/inhibitory unit j in another area into the i th excitatory unit and w_{ki}^E and w_{ki}^I are weights coming from excitatory/inhibitory unit k into the i th inhibitory unit, respectively. The electrical activities of the basic units range between 0 and 1 (with a threshold of 0.6 to indicate if a unit is active), and can be said to reflect something akin to the percentage of active units within a local population. The parameters of each module's basic units were chosen by both analytical and empirical means such that the desired neural dynamics were achieved within the various regions. For details see Husain et al. (2004).

We validated the model using an fMRI experiment employing stimuli and tasks identical to those used in our simulations. The stimuli were tonal contours (composed of FM sweeps interspersed with brief tones) and tones. In the experiment, 12 subjects (7 men, 5 women) discriminated between pairs of the stimuli in a series of task blocks interspersed with rest blocks. The tonal contours and tones were discriminated in different fMRI scanning runs. The fMRI data were processed and analyzed using statistical parametric mapping (SPM) software (SPM99, Wellcome Dept. of Cognitive Neurology, London, <http://www.fil.ion.ucl.ac.uk/spm>). A fixed-effects regression analysis was performed across all subjects to determine which voxels were significantly activated in the task compared to rest. To compare simulated and experimental data, we evaluated percentage signal change in the fMRI BOLD (blood-oxygen-level-dependent) signal between the tonal contours and tone conditions in the different regions involved in the DMS task. We first chose regions of interest in the functional images corresponding to the modules in the model. The hemodynamic fMRI data were simulated by integrating the absolute value of the synaptic activities over the time course of the study within the different regions for each task. We assumed that increases in either excitatory or inhibitory synaptic activity, or both, are manifest as increased BOLD activity (see Jueptner and Weiller, 1995; Logothetis et al., 2001). The percentage signal change (PSC) in the BOLD signal was first calculated with respect to the baseline control task for both the tonal contours task block and the tones task block and subsequently for the tonal contour task versus tones task. As shown in Figure 2, the PSC data from both the experiment and the simulations showed a similar trend of increasing BOLD values for Aii, ST and PFC regions (we report experimental data from only the right hemisphere which showed a better match between experiment and the model; for a more complete picture see Husain et al. (2004). The match in Ai between experimental and simulated PSC was poor and the reasons are outlined in Husain et al. (2004), with a primary reason being that the human auditory cortex responds to many different features of the sounds whereas the modeled primary auditory cortex responds only to direction of the sweeps. Efforts are underway to improve this module by incorporating greater functionality. Our results thus demonstrated that the model is capable of exhibiting the salient features of both electrophysiological neuronal activities and fMRI values that are in agreement with empirically observed data.

3. Assumptions

One objective of modeling is to reduce data complexity by focusing on a few dimensions or variables that can explain a significant fraction of the data. This inherent data reduction is a result of the assumptions made in constructing the model. Understanding the assumptions is important in gaining greater insights into both the model and phenomenon being studied. To illustrate this point, we consider the assumptions made in constructing the Auditory Object Processing Model (AOM).

3.1 Visual-Auditory processing analog

A principal hypothesis of our work is that after initial sensory processing in the cortex, the brain regions areas involved in visual and auditory object processing function in a similar manner (but along different dimensions of an object's features).

Evidence—The auditory-visual correspondence hypothesis has both experimental and theoretical support (Kubovy and Van Valkenburg, 2001; Rauschecker, 1999; Schreiner et al., 2000; Shamma, 2001; Sur et al., 1988). There are FM-sweep-selective neurons in the core and belt areas (Bieser, 1998; Rauschecker, 1999), just as there are orientation-selective neurons in visual areas such as V1, V2 and V4 (Desimone and Ungerleider, 1989).

Consequences—A consequence of this assumption was that it allowed us to make an analogy between short-term memory processing of visual and auditory objects in the PFC. The PFC module in the visual model was constructed based on the experimental work of Funahashi et al. (1990). Although, the working memory circuit of the auditory system currently is not as well defined as the visual one, we hypothesized that based on published experimental data (Bodner et al., 1996; Gifford et al., 2005; Kikuchi-Yorioka and Sawaguchi, 2000; Romanski and Goldman-Rakic, 2002) the two are sufficiently alike for us to model them in the same manner.

Another consequence of this assumption was that it allowed us to make an analogy between increasing spatial receptive fields in the visual model and increasing spectro-temporal receptive fields in the auditory model. Whereas there is long-established experimental evidence for the increasing visual receptive fields in the cortex (e.g., Desimone et al., 1984), the evidence for increasing cortical spectro-temporal receptive fields is sparser (e.g. Harrison et al., 2000).

3.2 Direction selectivity as key feature

Another assumption made in constructing the AOM was to use the direction selectivity of FM sweeps as the primary feature of the auditory objects being processed. Although, sounds have other features such as intensity, bandwidth, timbre, etc., FM sweeps (and their attendant feature of direction selectivity) are important features of communication sounds across species and using them allows us to explore these sounds better.

Evidence—FM sweeps are ubiquitous in communication sounds and can be likened to line segments of visual objects. In mammalian studies (monkey, ferret, cat, rat), the neurons of primary auditory cortex respond to the direction of FM sweeps (Bieser, 1998; Mendelson and Cynader, 1985; Metherate et al., 2005; Rauschecker, 1997; Rauschecker, 1998; Shamma et al., 1993). Direction selectivity in most cases is modulated by lateral inhibition (Chang et al., 2005; Ohl et al., 2001; Shamma et al., 1993; Zhang et al., 2003). Recently, in an MEG study of humans (Pantev et al., 2004) the authors found evidence for different levels of lateral inhibition and habituation in primary and non-primary auditory cortices, supporting the idea of hierarchical processing in the human auditory cortex.

Consequences—An important consequence of making this assumption was the prediction of a type of neurons or neuronal ensemble that responds to changes in sweep direction. We presumed such neurons to be analogous to complex feature selective neurons in the visual processing pathway responding to corners (change in line orientation). We needed this type of neuronal unit in the model in order to bind together sweep segments with different directions occurring in close temporal proximity. At the time of including this type of neuronal unit in the model, we had no direct evidence of their existence. However, some recent preliminary evidence suggests that such neurons may exist in the rostral superior temporal gyrus in the Macaque monkey (Kikuchi et al., unpublished data).

3.3 Using data from non-primate animals

Another assumption made was that data from multiple species would be used to construct the model. In other words, although our goal is to simulate human cortical auditory processing, there are few, if any, human electrophysiological studies of auditory processing. Therefore, we based the model's physiological behavior on non-human primate data where possible, but also appropriate non-primate mammalian data.

Evidence—A prime motivation for combining data from multiple species was the relative lack of neuroanatomical and neurophysiological data on auditory processing (compared to visual processing) in the non-human primate cortex. For instance, our previous model (Tagamets and Horwitz, 1998) was informed almost entirely by visual processing studies in

monkeys. In contrast, we employed data about FM sweep processing from experimental studies that used monkeys, ferrets and cats (more details in Section 3.2). However, we chose not to include data regarding specialized auditory processing such as echolocation in bats.

Consequences—Although, the model was developed to match non-human neurophysiological and neuroanatomical data, it was also constructed to generate simulated behavior that could be matched against human behavior, and simulated fMRI BOLD activity that could be matched against human fMRI BOLD activity. Thus, human experimental data (from neuroimaging studies) and animal electrophysiological data can be reconciled in the model. As detailed earlier, we conducted an fMRI study using the same stimuli and experimental parameters as in the modeling study. The experimental and simulated fMRI data showed a reasonable match.

4. Testing robustness on a novel problem (perceptual grouping)

We tested the robustness of the model using a perceptual grouping phenomenon known as the auditory continuity illusion (Husain et al., 2005). The auditory continuity illusion (sometimes called ‘temporal induction’, ‘spectral restoration’ or ‘phonemic restoration’) occurs when a sound is perceived to continue through interrupting noise, even though the sound is not physically present in the noise. The illusion makes communication sounds intelligible in a noisy environment, as for instance when a cough obscures some part of speech. It further serves the ecological purpose of auditory scene analysis (Bregman, 1990) by grouping events or features as belonging to the same object or by separating different sources of sounds. For a review of human behavioral studies of the auditory continuity illusion studies see Chapter 6 of Warren (1999). Additionally, there have been animal behavioral studies (Petkov et al., 2003a; Sugita, 1997) of the illusion and electrophysiological studies in humans (Micheyl et al., 2003) and animals (Petkov et al., 2003b; Sugita, 1997).

Using the AOM, we tested the continuity illusion with simulated stimuli and matched the model’s behavioral results with those from human and animal psychophysical studies. Note that the model was not changed in any way from its original formulation (Husain et al., 2004), including the notion of what constitutes a “match”. A match for two identical stimuli in the DMS task was taken to be 5 or more active response units in the PFC module. In order to test the continuity illusion in the model, we simulated stimuli with silence and noise-filled gaps of increasing duration. A match with a continuous first stimulus was interpreted as indicating that the model “perceived” the second stimulus as continuous. Using this criterion we found that the model exhibited a perceived continuity for stimuli with small gaps but not for large gaps; however, the same large gaps, when filled with noise, were also perceived as continuous. This finding is in agreement with reported behavior in humans (Dannenbring, 1976; Pollack, 1977).

We will briefly examine the simulated and experimental behavioral data for one such study (Ciocca and Bregman, 1987). In the Ciocca and Bregman study, the authors used noise-inserted gapped sweeps with different post-noise sweeps (varying in onset frequency) as shown in Figure 3a. Thus a stimulus can be divided into three periods, a pre-noise sweep, noise, and a post-noise sweep. They asked listeners to rate the continuity of different post-noise sweeps, while maintaining a constant pre-noise sweep. We simulated similar stimuli, with matching stimulus d gapped noise duration. In keeping with the Ciocca and Bregman experiment, the starting frequencies of the post-noise sweeps were chosen by adding $1/2$, 0 , $-1/2$, -1 , $-3/2$, and -3 times the reference interval (the difference between the final frequency of the pre-noise glide and the starting frequency of the trajectory post-noise glide) to the final frequency of the pre-noise sweep. In the experiment, listeners rated the continuity of different stimuli through noise on a scale from 1 to 9, with 1 being the most continuous and 9 being the least continuous.

We adapted this paradigm to our DMS task: The first of the pair of the trial was a continuous sweep; the second was the noise-interrupted sweep. For the simulations, we assigned 1 to the highest response (for a response of 10 units active, in order to get a rating of 1 we subtracted it from 11; thus the ratings were obtained by subtracting the number of active units from 11). The matching response of the model for the two stimuli indicated the continuity of the second stimulus; the greater the match, the greater the “continuity.” The results of the simulations, along with a redrawing of the behavioral results of Ciocca and Bregman (Figure 8), are shown in Figure 3B. Both the model and human observers responded similarly: post-noise stimuli with a starting frequency at or near the point in frequency space in direct line trajectory from the end of the pre-noise sweep was judged to have the best continuity.

The result of our simulation study showed not only that the AOM was robust but also that the AOM could be used to illuminate the neurobiological mechanisms underlying the auditory continuity illusion. The robustness of the AOM was demonstrated by the fact that its behavior in processing stimuli that were different from those used in its original construction agreed with the experimental behavioral data.

In the AOM, the illusion occurs in an emergent manner due to the pattern of connectivity (divergent or increased fan-out) in the first three stages of the model. We show this in Figure 4, which depicts activities for three trials from three modules: MGN, Ai up-selective and ST regions. Because we are using only up-sweeps to illustrate how the continuity illusion occurs, the activities of the Ai down-selective units are not shown. Time is shown along the *x*-axis and neuronal units (frequency) are shown along the *y*-axis. The first sweep of all three trials is a continuous upward sweep and is registered as such by the Ai up-sweep selective units and the ST units. In Figure 4a, the second up-sweep of the trial has a small gap in it. This is registered as a small gap by the Ai up-sweep selective units but is registered as a complete sweep at ST. When the gap in the sweep is larger as in Figure 4b, the gap is registered both at Ai and ST leading to the perception of discontinuous sweep. If noise is inserted into the large gap as in Figure 4c, the gap is reduced at Ai and a complete sweep is registered at ST.

The reduction in gap at Ai (and further at Aii) coupled with the increasing spectro-temporal windows of integration from Ai to ST (including Aii) produces the perception of a continuous sweep. The anatomic connectivity from Ai to ST results in increasing spectro-temporal windows of integration that allows for small silent gaps in sweeps or noise-filled larger gaps to be perceived at the ST stage as continuous. In the AOM, the illusion is achieved without any top-down cues in the form of attentional changes, or template- or rule-matching, thus suggesting the sufficiency of bottom-up cues in the continuity illusion.

The predictions of the model are that the changes in fMRI-BOLD activity in the auditory cortices, especially in the ST region, will reflect the illusory continuity of noise-filled sounds as it will normal continuous sounds compared to discontinuous sounds. We are in the process of conducting fMRI studies using stimuli similar to the ones used in the modeling studies to test these predictions.

5. Other experimental-modeling studies

There have been other combined experimental-modeling studies with a tight coherence between experimental and simulation paradigms. The different types of models have been reviewed at length in (Horwitz and Husain, In press). For instance, Newman et al. (2003) used fMRI and modeling in order to understand high-level perceptual problem solving as in the Tower of London problem. Brown and Braver (2005) used a combination of fMRI and computational modeling in an effort to understand the function of the anterior cingulate cortex in cognitive control of tasks. Deco et al. (2004) employed an attractor model to simulate fMRI data characteristic of prefrontal cortex during both visual spatial (“where”) and object (“what”)

processing and showed how spatial versus object-processing may be implemented in the prefrontal cortex. These studies while illustrative of the combined experimental-modeling approach, differ from ours primarily in the type of model used, which in turns dictates the coherence with the experiments. In brief, in the AOM the higher-level cognitive functions are an emergent property of the bottom-up neuroanatomically-based construction and physiology. The simulated fMRI is a consequence of the electrical activities of the neuronal units which are similar to those reported in physiological studies. Thus there is agreement at two levels, qualitative at the level of electrical activities and quantitative at the level of fMRI-BOLD. In the work of Newman et al., Brown and Braver, and others, the qualitative agreement is at the level of the simulated fMRI activities.

6. Conclusions

In this article, we showed how a neuromodeling-neuroimaging framework can accelerate investigations of brain function, specifically that of auditory object processing. Our large-scale neurobiologically-realistic auditory object processing model was constructed based on available neurophysiological and neuroanatomical data. The model simulated BOLD activity that was quantitatively matched against experimental BOLD data obtained using similar stimuli and tasks. We then used this validated model to understand the neural basis of the auditory continuity illusion without changing any model parameters. We found that the mechanism underlying the illusion in the model was the divergence of the feedforward connections along the initial auditory processing pathway in the temporal cortex. Our results not only attested to the robustness of the model, but further, predicted a primary role of the anatomical connectivity for the auditory processing areas in mediating the continuity illusion.

In the future, we plan to add additional modules to the model, primarily to deal with other phenomena, such as categorization of sounds. Categorization is important in studying speech and language (Lakoff, 1987; Liberman, 1996; Lotto, 2000). In order to categorize the incoming stimulus, the proposed model has to correctly classify stimulus as belonging to a particular category and subsequently use that category label in working memory processing. We have conducted fMRI (Husain et al., 2006a; Husain et al., 2006b) and magnetoencephalographic (Luo et al., 2005) studies to investigate the categorization of simple speech and non-speech sounds. The proposed categorization model will be tested using these experimental data. The modeling results in turn will be used to design more focused fMRI studies investigating categorization of complex, higher-order auditory stimuli.

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Figure 1.

(a) Network diagram of the Auditory Object-processing Model (AOM). (b) Basic unit. Each individual module in the network is composed of 81 basic units, each of which is composed of an excitatory and an inhibitory element.

Figure 2.

Shown are the percentage signal change in each experimental region of interest (white) from the right hemisphere and each region of the model (stripes) for the tonal contour task compared to tones (both compared to rest).

Figure 3.

(a) Schematic of the different post-noise glides used in the simulations reported in Husain et al. (2005) and in Experiment 3 of Ciocca and Bregman (1987). (b) Continuity ratings for the modeling and experimental studies. The results from the modeling study are redrawn, shown by dashed lines, solid triangles for the upward glides and solid squares for the downward glides. The solid lines are a replotting of the results depicted in Figure 8 of Ciocca and Bregman, with the asterisks representing steep slopes and open circles shallow slopes of glides.

Figure 4.

Electrical activities of neuronal units in MGN, Ai up-selective and ST modules for three delayed-match-to-sample trials. The y-axis represents the neuronal unit number (indicative of frequency dimension for MGN and Ai; in the figure showing a subset of units numbered 36 to 52) and the x-axis represents time (0 to 200 timesteps). In (a), single upward sweeps are depicted; the second sweep has a small gap. In (b), the second upward sweeps has a larger gap. In (c), noise is inserted in the gap of the second upward sweep. Refer to the text for details about the trials shown. Due to space restrictions we do not show activities of Aii units, for a complete version see Figure 6 of Husain et al. (2005).