

# Chapter 2

## Sensory Fusion

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**Abstract** Multisensory integration is known to occur in many regions of the brain, and involves several aspects of our daily life; however, the underlying neural mechanisms are still insufficiently understood. This chapter presents two mathematical models of multisensory integration, inspired by real neurophysiological systems. The first considers the integration of visual and auditory stimuli, as it occurs in the superior colliculus (a subcortical region involved in orienting eyes and head toward external events). The second model considers the integration of tactile stimuli and visual stimuli close to the body to form the perception of the peripersonal space (the space immediately around our body, within which we can interact with the external world). Although devoted to two specific problems, the mechanisms delineated in the models (lateral inhibition and excitation, nonlinear neuron characteristics, recurrent connections, and competition) may govern more generally the fusion of senses in the brain. The models, besides improving our comprehension of brain function, may drive future neurophysiological experiments and provide valuable ideas to build artificial systems devoted to sensory fusion.

### 2.1 Introduction

A fundamental problem in cognitive neuroscience is how we perceive and represent the external world starting from information produced by our senses. Traditional research on this topic generally adopted a “sense by sense” approach, i.e., attention was focused on the single sensory modalities to study how information is coded in each sensory channel and subsequently processed and transmitted. The motivation of this approach was to reveal the characteristics of single senses (vision, hearing, touch, etc.) to point out their specific neural substrates and correlate this information with perception. Indeed, it has been assumed for many decades that information

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from individual senses is initially coded and processed in segregate brain areas (such as the visual cortex in the occipital lobes, the auditory cortex in the temporal lobes, and the somatosensory cortex in the parietal lobes) and that only later in the processing pathways, this distributed information may be merged together. This traditional view posits that a large part of the brain can be reduced into a collection of unisensory modules that can be studied in isolation.

However, recent research challenges this traditional view, clearly demonstrating that our senses are designed to work in concert, and not as separate modules. Indeed, almost any experience in daily life consists of a multisensory stream of data that provide concurrent and complementary information about the same external event or object: the multiple sensory information must be simultaneously considered by the brain and globally processed to reach a unique coherent percept. Moreover, compelling evidence now exists that information represented by each of the primary sensory systems (visual, auditory, somatosensory, and olfactory) is highly susceptible to influences from other senses. This signifies that the theory of multisensory integration must move beyond the notion of a purely sum of individual contributions and must consider a more complex cooperation among the senses.

This sophisticated integration of multiple sensory cues provides animals and humans with enormous behavior and response flexibility. Indeed, the fundamental aim of the brain with respect to the external world is to reach a clear recognition of objects and events (especially of those essential for surviving) and to drive the suitable behavior and physical reactions. Decision on objects and events in the environment requires that information from all the senses is simultaneously exploited to maximize the probability of a correct detection and minimize the probability of errors. To reach this objective, sensory signals that originate from congruent spatial positions and in temporal proximity – hence that likely derive from the same event – must be linked together, whereas sensory signals that do not exhibit temporal and/or spatial coherence must be separated. Moreover, conflict situations must be resolved favoring one or another possibility (either sense merging or sense separation).

Multisensory processing is known to occur in many cortical and subcortical regions of the brain, and involves a lot of different aspects of our daily life and overt behavior: among the others, the rapid head and eye movements directed toward external visual and auditory cues; the merging of smell and taste during eating; the integration of tactile and visual information close to the body, to create the perception of a peripersonal space; and the merging of auditory, visual, and other senses to recognize objects (for instance, the shape of a cow and its moo). The importance of all these aspects for survival is evident.

Unfortunately, despite the enormous role that multisensory integration plays in our daily life, the neural mechanisms that subserve this property are still insufficiently understood. It is worth noting that neural circuits for multisensory integration must not merely sum the information coming from different sensory modalities, but must perform complex, nonlinear computation to emphasize stimuli coming from coherent spatial and temporal characteristics, neglect incongruent stimuli, and solve conflicts. As it is illustrated throughout this chapter, this requires the presence of complex excitatory and inhibitory mechanisms and a sophisticated topological representation of the external space.

The aim of this chapter is to present two recent mathematical models of multisensory integration, inspired by real neurophysiological systems. The first model considers the integration of visual and auditory stimuli, as it occurs in a subcortical region of the midbrain, named the superior colliculus, which is implicated in driving overt responses (such as eye movements) toward external events. The second model treats the problem of how visual stimuli close to the body (for instance, stimuli on and close to the hands) and tactile stimuli in the same body parts are integrated to form the perception of a peripersonal space (i.e., the space immediately around our body surface, from which objects can hit us and where we can manipulate objects).

As just stated above, the two models are devoted to two different and specific problems; they have been formalized separately, and of course, their development is founded on different data in the literature. The visual–auditory model is mainly based on electrophysiological recordings in superior colliculus neurons, and, to a less extent, behavioral data concerning interplay between vision and audition; the visual–tactile model has been conceptualized on the basis of single-cell recordings in multisensory regions of the associative cortex (frontal–parietal cortex) and on the basis of neuroimaging and behavioral data on both healthy subjects and brain damage patients. The so obtained models obviously differ for some aspects (as they are conceived for different aims); however, they share some important features concerning the architecture, the synaptic mechanisms, and the individual characteristics of the single neurons: in both models, these features are fundamental to reproduce and explain *in vivo* data. First of all, both models include upstream areas of unimodal neurons, which project feedforward convergence to a downstream area; hence, neurons in the downstream area are multisensory, responding to stimuli in more than one modality. The patterns of the feedforward synapses are fundamental to establish the shape and position of the multiple receptive fields of the multimodal neurons. Moreover, in both models, neurons in the same area are connected via lateral synapses characterized by short-range excitation and long-range inhibition; this lateral connectivity implements a *topological organization* of the single areas, realizes an efficient competitive mechanism among neurons in the same area, and influences the shape of the neurons' receptive fields. Again, both models include feedback synapses from the higher level multimodal area down to the lower level unimodal areas; accordingly, a stimulus in one modality may influence the activity of neurons coding for a different modality. This mechanism explains how the subjective experience in one modality may be dramatically affected by stimulation in another modality, even creating illusory perception. Finally, neurons in both models are characterized by a nonlinear sigmoidal input–output relationship (with a lower threshold and an upper saturation). Such nonlinearity is fundamental to reproduce a general principle of multisensory integration, named *inverse effectiveness*, according to which cross-modal enhancement is highly effective when the information provided by the unisensory channels is weak.

The important fact is that in both models these mechanisms are essential to replicate experimental data, although the two models refer to different stimuli combinations (visual and auditory on the one hand, visual and tactile on the other

hand) and to different regions of multisensory integration in the brain (the superior colliculus, a subcortical structure, and the parieto–frontal associative cortex). Hence, we can postulate that the mechanisms exploited in these two models may have a larger validity, can be probably found in many other multisensory regions of the brain, and explain integration among other different modalities. In fact, as pointed out by some authors (Dalton et al. 2000), the same principles governing the fusion of some senses (for instance, integrating visual and auditory information) apply to other combinations of senses, and multisensory integration probably shares some common principles.

As we describe in detail in subsequent sections, the developed models not only enhance coherent cross-modal stimuli but also allow depression of incoherent stimuli; in certain conditions, they afford conflict resolution among stimuli and account for phenomena such as ventriloquism or phantom perception. They may be subject to learning and plasticity, thus allowing a modification of our multisensory perception driven by previous experience; finally, they may be under attention mechanisms, which modify our multisensory perception on the basis of exogenous or endogenous expectation. Finally, they may be used to simulate clinical deficits, by simply adjusting some model parameters. Of course, some of these aspects have been considered more extensively in one model than in the other and vice versa, in relation to the specific aim of each model and to data available in the literature. A crucial point is that both models allow behavioral and psychophysical results (e.g., ventriloquism in one case, extinction in the other case) to be interpreted in terms of the individual neuron properties and of the reciprocal interconnections among neurons; hence, they may give an important contribution to bridge the gap between behavioral and neuronal responses.

As a last point, we wish to stress that the present models, although inspired by neurophysiology, and especially aimed at improving our understanding of brain function, may furnish valuable ideas to build artificial systems devoted to sensory fusion. Some of the basic mechanisms presented below (mutual excitation, mutual inhibition, enhancement vs. depression, spatial arrangement of the inputs, and non-linear sensitivity to the strength of the stimuli) have a general role in perception and can represent paradigms for any advanced multisensory processing system.

## 2.2 Audio–Visual Integration

### 2.2.1 *Audio–Visual Integration in the Superior Colliculus: Neurophysiological and Behavioral Evidence (Overview and Model Justification)*

Let us consider the problem of integration of visual and auditory stimuli to drive overt behavior. The concepts described below refer to a particular midbrain area, the superior colliculus (SC), that has been deeply studied in the context of multisensory integration; however, they may have a more general validity and are suitable

to illustrate how a biologically inspired neural network can realize multisensory integration to improve the response to external stimuli.

The role of the SC is to initiate and control overt movements in response to important stimuli from the external world, for instance, to control the shift of gaze or to orient various sensory organs to a correct direction (Stein and Meredith 1993). Various brain regions involved in auditory, somatosensory, and visual processing send inputs to the SC (Edwards et al. 1979; Huerta and Harting 1984; Stein and Meredith 1993).

The behavior of the SC neurons exhibits quite trivial characteristics in response to a single spatially localized unisensory stimulus (either auditory or visual or somatosensory) (Perrault et al. 2005). If the stimulus amplitude is too small, it is neglected and the neuron does not respond at all. If the stimulus overcomes a given threshold, it activates a response: the higher the stimulus the higher the response up to an upper saturation. This kind of behavior can be reproduced fairly well using a dynamical block (for instance, a low-pass filter), which mimics the temporal aspects of the response, followed by a sigmoidal relationship. Moreover, different neurons in the SC have different receptive fields (RFs), i.e., they respond to stimuli coming from different positions in space. These RFs are topographically organized, so that proximal neurons in the SC have RFs with proximal centers in the environment. Of course, only those neurons whose receptive field overlaps the stimulus will respond, by driving the behavior.

However, different problems complicate the previous scenario. First, while some neurons in the SC are unisensory, and they respond only to stimuli of a single modality [visual: 21% of neurons, auditory: 15% of neurons, somatosensory: 6% of neurons (Kadunce et al. 1997)], more than half are multisensory, i.e., they respond to stimuli of different sensory modalities [visual–auditory: 35%, visual–auditory–somatosensory: 8% (Kadunce et al. 1997)]; however, different percentage values are reported in Wallace et al. (1998): visual: 23%, auditory: 13%, somatosensory: 10%, audio–visual: 25%, trimodal: 9%]. Multisensory neurons, in general, have receptive fields for different modalities in spatial register; this means not only that a visual–auditory neuron will have two RFs (one for the auditory and one for the visual modality) but also that these RFs have a large superimposed region (Meredith and Stein 1996).

The presence of multisensory neurons, whose RFs are in spatial register, can explain a phenomenon named “multisensory enhancement”: when two cross-modal stimuli (for instance, one visual and one auditory) come from proximal positions of space and in close temporal proximity, the response of the SC neuron is generally greater than each of the individual unisensory responses. This enhancement may be subadditive, additive, or superadditive depending on whether the cross-modal response is smaller, equal, or greater than the sum of the individual unisensory responses (Kadunce et al. 2001; Perrault et al. 2005). Furthermore, the response of a multisensory SC neuron follows a rule named “inverse effectiveness”: the enhancement produced by two spatially aligned cross-modal stimuli is inversely related to the effectiveness of the individual unimodal stimuli (Perrault et al. 2005). Consequently, the weaker the unisensory stimuli, the greater the enhancement they

produce when occurring together in spatial proximity. The practical effect of these rules on behavior is easily understandable: two-weak targets, which do not produce an appreciable response if applied alone, can induce a vigorous response when occurring together but from the same spatial source.

The complexity of the SC response, however, is much greater than that emerging from a single nonlinearity, i.e., from the behavior of a single neuron. Several other aspects related with the interactions among neurons should be considered.

First, if two within-modal stimuli (i.e., two stimuli of the same modality, for instance, both auditory or both visual) or two cross-modal stimuli (i.e., stimuli of different modalities, one auditory and the other visual) originate from disparate positions in space, the final response of the SC is reduced or eliminated compared with the response to an individual stimulus alone (“within modal and cross-modal suppression”) (Kadunce et al. 1997). This behavior implicates the presence of some competitive interactions among neurons, whose RFs are located at different spatial positions.

Another important property of SC neurons, however, is that within-modal suppression is stronger and more robust than cross-modal suppression. Kadunce et al. (1997) demonstrated that, in the cat, power within-modal suppression can be present even in the absence of cross-modal suppression. However, the converse is not true, i.e., cross-modal suppression always occurs together with within-modal suppression. This result suggests the presence of at least two different mechanisms: the first, which may affect both cross-modal and within-modal suppression, can be ascribed to a competition among multimodal neurons in the SC; the second, which affects unimodal suppression only, probably reflects interactions occurring at the level of the single input channels (i.e., a competition in unimodal areas targeting to the SC).

Finally, a further mechanism should be mentioned, related to the well-known phenomenon of ventriloquism: in certain cases, in the presence of two stimuli with disparate spatial positions, a stronger stimulus may capture the position of the other one (Bermant and Welch 1976; Woods and Recanzone 2004). This occurs in case of a conflict between the position of two stimuli, and the system solves the conflict assuming a single position for both. Worth noting is that, in general, the visual stimulus predominates over the position of the auditory stimulus. We are not aware whether a ventriloquism effect actually occurs in the SC, but inclusion of this possibility makes our study of multisensory integration much more general and suitable for a variety of further applications.

A further related aspect is that perception of a unimodal stimulus (for instance, a poor auditory or visual target) can be improved, not only at the SC level (multimodal), but also at the level of unimodal areas, by a second stimulus of the other modality given at the same spatial position (Bolognini et al. 2005).

Despite the large amount of results published in the literature and qualitative explanations currently available, we were not aware of a comprehensive theoretical model able to summarize these data. Previous important models were especially focused on information theory, but were not inspired by neurobiological mechanisms. In particular, Anastasio et al. (2000), Anastasio and Patton (2003),

Patton et al. (2002), Patton and Anastasio (2003) developed some models in which neurons implement the Bayes rule to compute the probability that a target is present in their receptive field. With these models, they were able to account for the existence of both multimodal and unimodal neurons and for the existence of cross-modal enhancement as well as within-modal suppression (Anastasio and Patton 2003; Patton and Anastasio 2003). A similar approach was used by Colonius and Diederich (2004) who developed a Bayes' ratio model of multisensory enhancement.

In earlier years, we presented a model (Magosso et al. 2008; Ursino et al. 2009) that is inspired by biological mechanisms and can explain most of the results delineated above; moreover, by changing some model parameters (especially those related with the synaptic strength), the model can account for the presence of neurons with different characteristics, as experimentally observed.

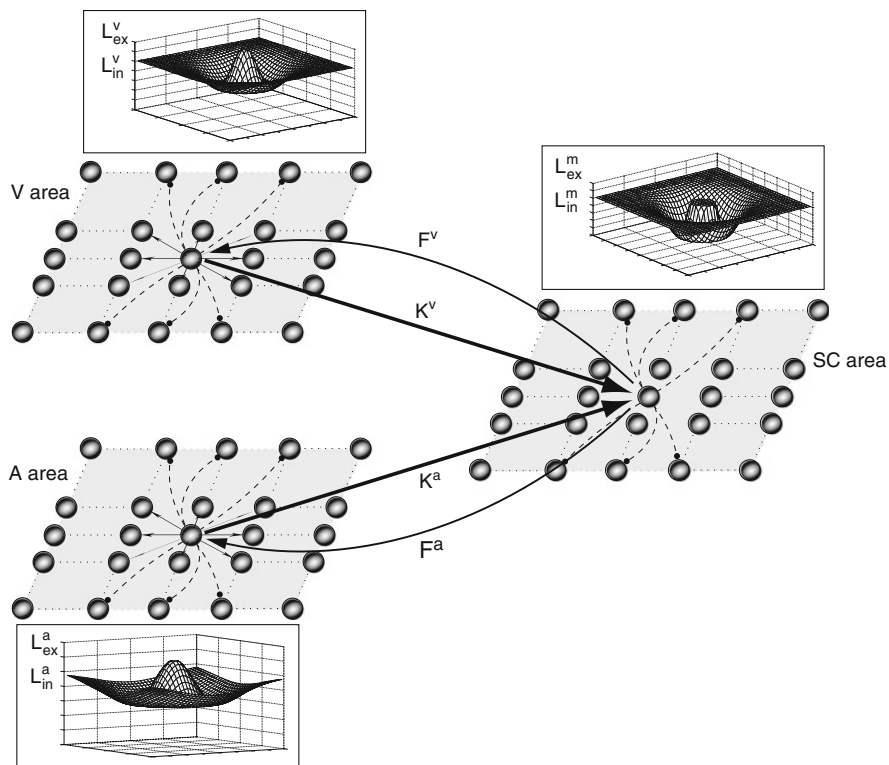
In the following, the main aspects of the model are first presented and justified. Then, some simulation exempla are given and commented on the basis of the mechanisms incorporated in the model.

### 2.2.2 Model Components

A qualitative sketch of the model is given in Fig. 2.1. Fundamental aspects are explained below, while all equations, mathematical details, and parameter numerical values can be found in previous publications of the authors (Magosso et al. 2008; Ursino et al. 2009).

- Each neuron is described through a sigmoidal relationship (with lower threshold and upper saturation) and a first-order dynamic (with a given time constant). Neurons normally are in a silent state (or exhibit just a mild basal activity) and can be activated if stimulated by a sufficiently strong input. In vivo the sigmoidal nonlinearity can be ascribed to the typical characteristics of neurons, which need a sufficient input current to generate spikes and which saturate: this behavior may be further accentuated by nonlinearities in the receptor responses at the synapse levels (for instance, the response of NMDA receptors).
- The model is composed of three areas (Fig. 2.1). Elements of each area are organized in  $N \times M$  dimension matrices, so that the structure keeps a spatial and geometrical similarity with the external world: neurons of each area respond only to stimuli coming from a limited zone of the space. Furthermore, the two upstream areas are unimodal, and respond to auditory and visual stimuli, respectively. A third downstream area represents neurons in the SC responsible for multisensory integration. These three areas have a topological organization, i.e., proximal neurons respond to stimuli in proximal position of space.
- Each element of the unisensory areas has its own receptive field (RF) that can be partially superimposed on that of the other elements of the same area. The elements of the same unisensory area interact via lateral synapses, which can be both excitatory and inhibitory. These synapses are arranged according to a Mexican hat disposition (i.e., a circular excitatory region surrounded by a larger inhibitory annulus).





**Fig. 2.1** Schematic diagram describing the general structure of the network. Each *gray circle* represents a neuron. Neurons are organized into three distinct areas of  $40 \times 40$  elements. Each neuron of these areas (*V* visual, *A* auditory, *SC* multimodal in the superior colliculus) is connected with other elements in the same area via lateral excitatory and inhibitory intra-area synapses (arrows  $L_{ex}$  and  $L_{in}$  within the area). Neurons of the unimodal areas send feedforward excitatory interarea synapses to multimodal neurons in the superior colliculus area located at the same position (arrows  $K$ ). Multimodal neurons, in turn, send excitatory feedback interarea connections to neurons of the unisensory areas (arrows  $F$ )

- The elements of the multisensory area in the superior colliculus receive inputs from the two neurons in the upstream areas (visual and auditory) whose RFs are located in the same spatial position. Moreover, elements in the SC are connected by lateral synapses, which also have a Mexican hat disposition.
- The multimodal neurons in the SC send a feedback excitatory input to the unimodal neurons whose RFs are located in the same spatial position; in this way, detection of a multimodal stimulus may help reinforcement of the unisensory stimuli in the upstream areas.



### 2.2.3 Results

In the following lines, we separately consider how the different aspects of the model may contribute to explain the results of multisensory integration delineated before.

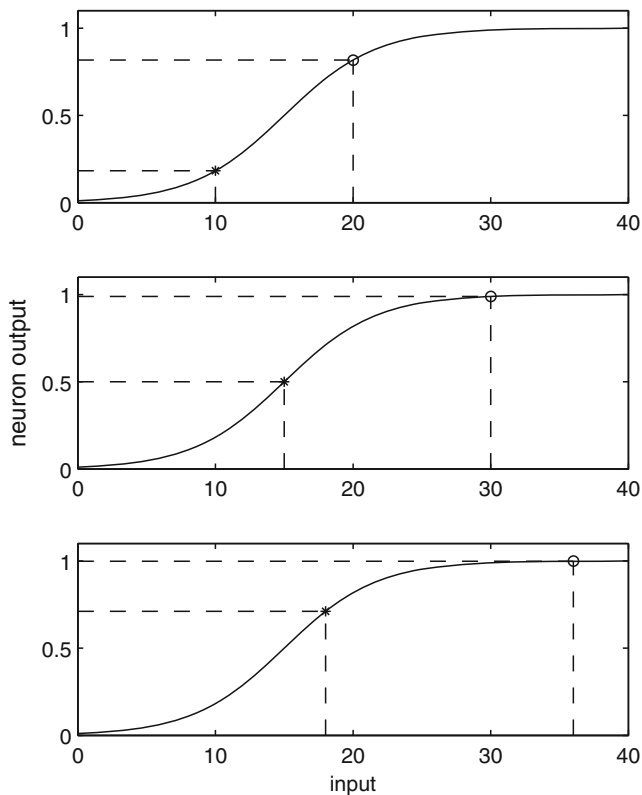
#### 2.2.3.1 Enhancement and Inverse Effectiveness

Let us first consider the problem of multisensory enhancement and the inverse effectiveness rule. To simulate this phenomenon, we imagine two cross-modal stimuli (one auditory and one visual) located at approximately the same position in space. Each of these two stimuli causes an activation bubble in the respective unisensory area, as a consequence of superimposed RFs and lateral connections among neurons; hence, some contiguous neurons are simultaneously active. Since multimodal neurons in the third area have the visual and auditory RFs in spatial register, a group of contiguous multimodal neurons receive excitation from both the visual and auditory neurons, which are active together. Finally, this input is converted into a multimodal output, which can drive overt behavior, via the monotonic sigmoidal relationship. It is worth noting that enhancement will occur only if the two cross-modal stimuli fall within the receptive field of the same multimodal neuron, i.e., they must be in close spatial register. But how can we explain the inverse effectiveness? This property simply depends on the presence of the sigmoidal characteristic, which describes neuron output, as illustrated in Fig. 2.2.

If the two cross-modal stimuli have a small intensity, each of them produces just a negligible response in the multimodal neurons when acting alone, since the neuron working point is located close to the lower threshold of the sigmoidal relationship. In this condition, a second cross-modal stimulus moves the working point of the multimodal neuron to the linear region of the sigmoid, thus causing a disproportionate increase in the final response. Hence, we may observe this quasi-paradoxical result: two stimuli, which produce no response when acting separately, may cause a strong response if they act together, provided they occur in close spatial and temporal proximity. This property is named superadditivity and is illustrated via a quantitative exemplum in Fig. 2.2 upper panel.

If the two unimodal stimuli have sufficient amplitude, so that each of them can set the working point of the multimodal neuron to the linear region, their simultaneous occurrence may cause a quasi-linear behavior, named simple additivity: this signifies that the cross-modal response is close to the sum of the individual responses (Fig. 2.2, middle panel).

Finally, in case of strong stimuli, the simultaneous occurrence of both may lead the multimodal neuron to its saturation region: as a consequence, the multimodal response is much smaller than the sum of the individual responses (subadditivity, see Fig. 2.2, bottom panel).

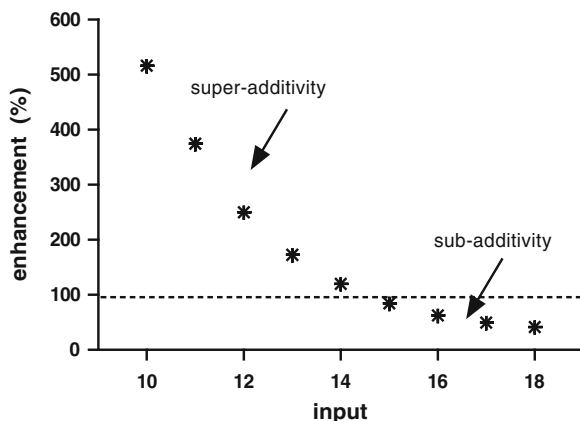


**Fig. 2.2** Explanation of the inverse effectiveness. The figure represents the sigmoidal characteristic of a multimodal neuron. *Upper panel*: a small input (value = 10) is applied to the neuron, causing just a mild activity (*asterisk*). A second equal cross-modal stimulus moves the working point into the linear region (*open circle*). Enhancement is about 400%. *Middle panel*: a moderate input (value = 15) is applied to the neuron, leading the working point exactly at the mid of the linear region (*asterisk*). A second equal cross-modal stimulus moves the working point close to saturation (*open circle*). Enhancement is about 100%. *Bottom panel*: a stronger input (value = 18) is applied to the neuron, leading the working point proximal to saturation (*asterisk*). A second equal cross-modal stimulus moves the working point inside the saturation region (*open circle*). Enhancement is less than 50%

A summary of the results is presented in Fig. 2.3. Here, enhancement is computed through the so-called “interactive index”; this is a measure of the response increase induced by two cross-modal stimuli compared to a single stimulus, and is defined as follows:

$$\text{Interactive Index} = \left[ \frac{\text{Mr} - \text{Ur}_{\max}}{\text{Ur}_{\max}} \right] \times 100, \quad (2.1)$$

where Mr (multisensory response) is the response evoked by the combined-modality stimulus and  $\text{Ur}_{\max}$  (unisensory response) is the response evoked by the most effective unisensory stimulus. In these results, enhancement is presented as a function



**Fig. 2.3** Multisensory enhancement computed with the model in steady state conditions, in response to two superimposed cross-modal stimuli of the same intensity, placed at the center of the RF. The intensity of the stimuli is plotted in the  $x$ -axis. Hundred percent represents the threshold between subadditivity and superadditivity. Enhancement decreases with stimulus strength, according to the inverse effectiveness principle explained in Fig. 2.2

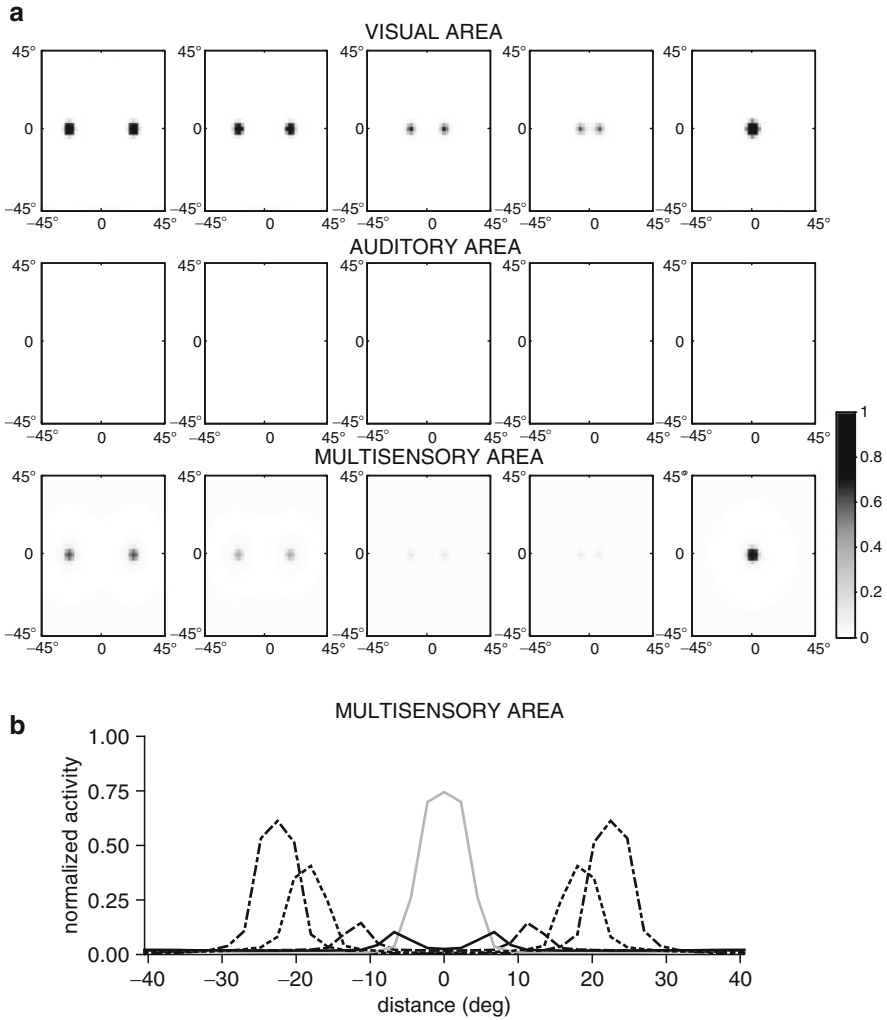
of the input intensity, assuming two cross-modal stimuli (one auditory and one visual) with identical strength (i.e., which can produce the same SC output when applied individually) and located at the same spatial position. In case of weak stimuli, enhancement can reach 500% or more (i.e., the cross-modal response is fivefold greater than the unisensory response). In case of strong stimuli, enhancement becomes close to zero. It is worth noting that, in these simulations, 100% is the threshold between subadditivity and superadditivity.

In conclusion, the previous results can be explained by the following characteristics of our model (1) the presence of two unimodal areas, with unimodal RFs; (2) the presence of a downstream multimodal area, whose neurons have auditory and visual RFs in spatial register; and (3) the presence of a sigmoidal relationship for neurons.

However, further aspects must be incorporated to explain suppression.

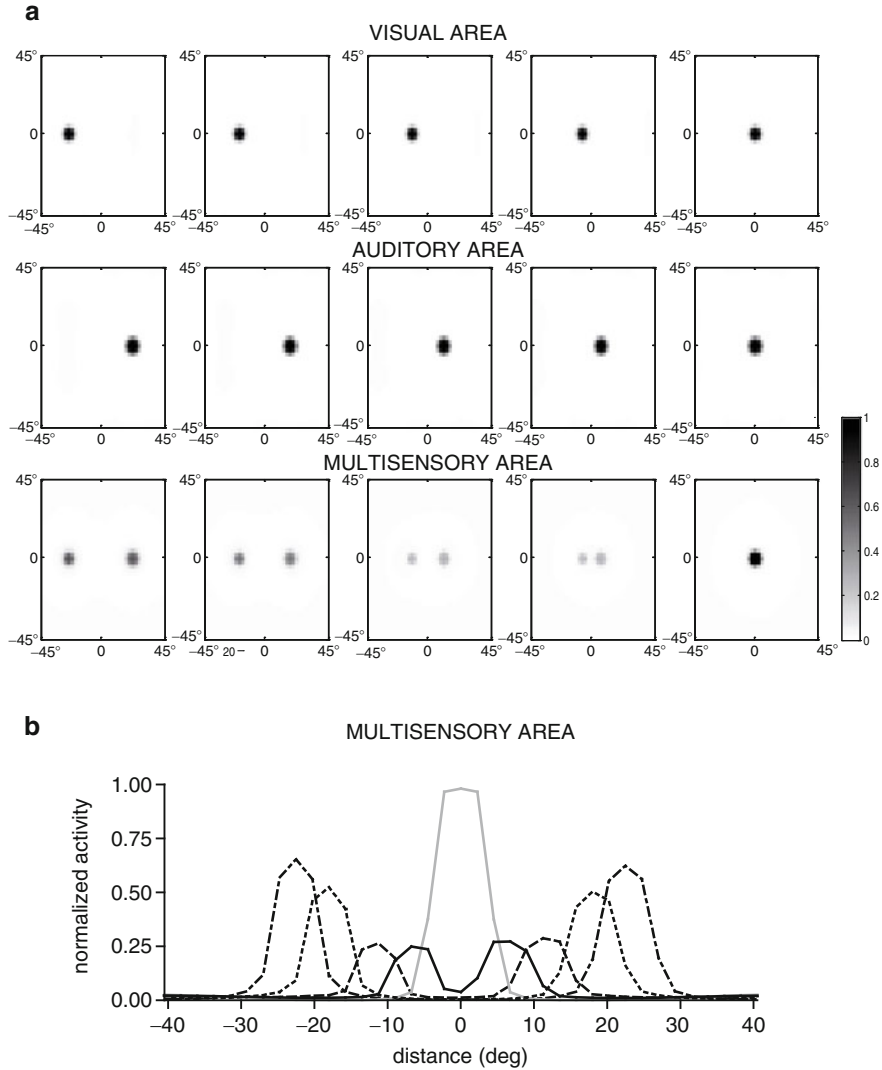
### 2.2.3.2 Cross-Modal Suppression

For the model to explain cross-modal suppression, we need the presence of lateral synapses among multimodal neurons. To this end, as anticipated above, we included lateral synapses in the SC with a Mexican hat disposition: proximal neurons in the multimodal area send reciprocal excitatory connections, but send and receive inhibitory connections to/from more distal neurons. Hence, each neuron in the multimodal area is surrounded by a small excitatory region and a wider inhibitory annulus. Indeed, the presence of this inhibitory suppressive region can explain both cross-modal and within-modal suppression. Two exempla are provided, the first



**Fig. 2.4** Model response to two simultaneous visual stimuli placed at five different positions in space. **(a)** Each column depicts the activity in the three areas of the model (visual, auditory and multisensory) in steady state conditions, after application of two stimuli with decreasing spatial distance. A strong within modality suppression in the multisensory area is evident in the third and fourth columns. **(b)** Profile showing the response of neurons in the multisensory area whose RF is centered at the vertical coordinate  $0^\circ$  (i.e., positioned at the middle of the vertical field) during the five simulations depicted in **(a)**. Within modality suppression is evident (greater than 80%). Within modality enhancement of two superimposed stimuli is mild

(Fig. 2.4) with reference to two within-modal stimuli located at different positions in space, the second (Fig. 2.5) with reference to two cross-modal stimuli. The simulations have been repeated by varying the distance between the two stimuli, and examining its effect on the response of the multimodal neurons. Results show that a



**Fig. 2.5** Model response to two simultaneous cross-modal stimuli placed at five different positions in space. The meaning of panel (a) and panel (b) is the same as in Fig. 2.4. Cross modality suppression is evident (greater than 60%). Cross-modal enhancement of two superimposed stimuli is also evident (about +50%)

second stimulus of a different modality located within the receptive field causes significant cross-modal enhancement (Fig. 2.5), whereas in the case of a within-modal stimuli, the enhancement is mild (i.e., a second stimulus of the same modality located inside the RF does not evoke a significantly greater response, Fig. 2.4). If the second stimulus is moved away from the RF, one can observe significant

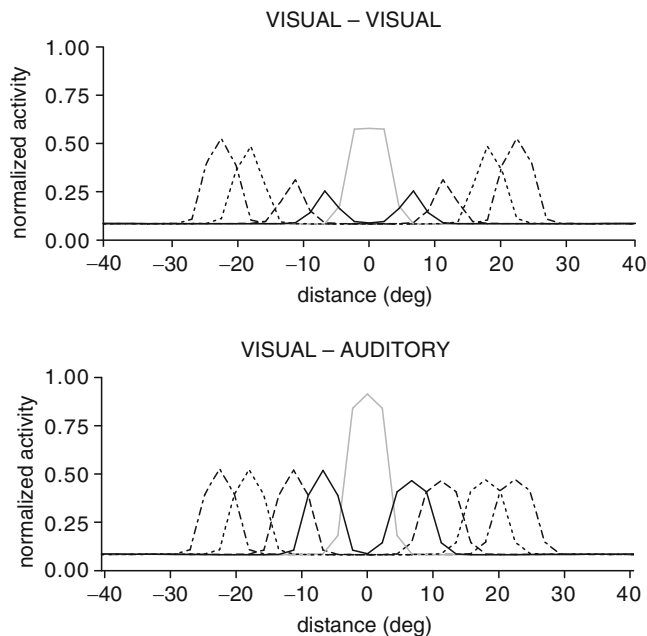
within-modal suppression (up to 80%, Fig. 2.4) and significant cross-modal suppression (about 60%, Fig. 2.5). The suppressive regions are quite large (25–30°) in accordance with physiological data (Kadunce et al. 1997).

### 2.2.3.3 Within-Modal Suppression Without Cross-Modal Suppression

According to the previous simulations, a single mechanism (i.e., lateral inhibition within the multimodal area) can explain both within-modal and cross-modal suppression. However, results in the literature summarized in the introduction (Kadunce et al. 1997), suggest the presence of a further mechanism responsible for within-modal suppression. In fact, while cross-modal suppression is always accompanied by within-modal suppression, the reverse is not true. Furthermore, within-modal suppression is generally stronger than cross-modal suppression, as already evident comparing simulation results in Figs. 2.4 and 2.5. According to these results, in our model, within-modal suppression is affected not only by the presence of lateral inhibition within the multimodal area (that is the mechanism responsible for suppression in Fig. 2.5) but also by a second similar mechanism operating at the level of the unimodal areas. In fact, in our model also unimodal neurons receive and send lateral synapses arranged as a Mexican hat. If the suppressive annulus in the unimodal area is weak compared to that in the multimodal area, within-modal and cross-modal suppression will have approximately the same strength. Conversely, if we assume the existence of strong inhibitory synapses in one unimodal area, but poor inhibitory synapses in the multimodal area, we obtain strong within-modal suppression without cross-modal suppression. In this case, within-modal suppression is determined by inhibitory competition within the unimodal area, whereas two cross-modal stimuli do not compete in the multimodal area due to the absence of significant reciprocal inhibition. An example of the latter behavior, which has been experimentally observed in some SC neurons (Kadunce et al. 1997), is illustrated in Fig. 2.6.

### 2.2.3.4 Cross-Modal Facilitation and Ventriloquism Phenomenon

As shown above, the presence of lateral inhibitory mechanisms can explain suppression between spatially disparate stimuli and the model developed until now can account for a variety of phenomena observed in the intact superior colliculus. However, at least another important phenomenon deserves attention when discussing audio–visual integration: auditory and visual stimuli interact not only at the level of the multimodal areas (like the SC) but also at the level of the unimodal areas. By way of example in patients with unimodal visual impairments, the visual perception is improved when acoustic stimuli are given in close temporal and spatial proximity to visual stimuli (Bolognini et al. 2005). In other words, the presence of an auditory cue may improve visual perception of a poorly perceived visual cue. Another example is provided by ventriloquism tricks, in which a visual stimulus “captures”

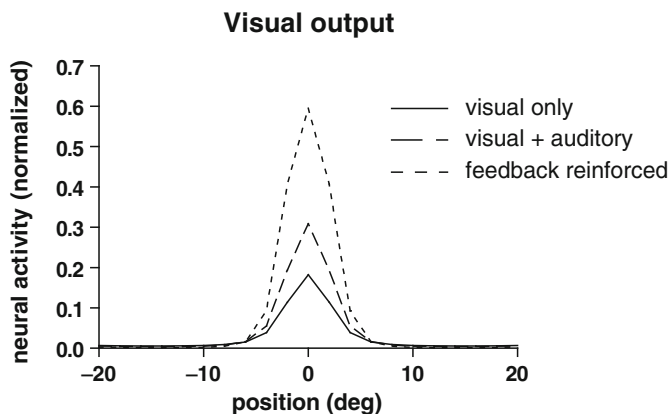


**Fig. 2.6** Response of multisensory neurons with RF centered at the vertical coordinate  $0^\circ$  (i.e., positioned at the middle of the vertical field) during the five simulations depicted in Fig. 2.4 (visual–visual, *upper panel*), and in Fig. 2.5 (visual–auditory, *lower panel*). Results differ from those in Figs. 2.4 and 2.5, since the strength of lateral synapses in the multisensory area has been set at zero

or biases the perceived location of a spatially discordant auditory sound (Bermant and Welch 1976). Inclusion of such phenomena within a model for audio–visual integration requires that the two unimodal areas communicate, so that activity in one area may affect activity in the other. This might occur in two alternative ways: either postulating the existence of direct connections among the unimodal areas, or assuming the presence of a feedback from the multimodal neurons to the unimodal areas. In both cases, an input stimulus in one unimodal area would affect the other unimodal area. Actually, there is now some preliminary neurophysiological evidence showing that brain areas traditionally assumed as unimodal can be affected by input coming from different modalities (Ghazanfar and Schroeder 2006; Schroeder and Foxe 2005).

In the present model, we assumed the existence of a feedback link from the multimodal neuron in the SC to the neurons (visual and auditory) in the unimodal areas at the same spatial position (Fig. 2.1). In this way, activity in a unimodal area can be affected by a cross-modal stimulus via a top-down strategy (i.e., from a higher hierarchical level, represented by the multisensory area in our model). If feedback synapses are weak, this effect is almost negligible and the model replicates all simulations shown above. Conversely, if the feedback synapse gain is increased, one can observe significant interaction between the two unimodal areas.



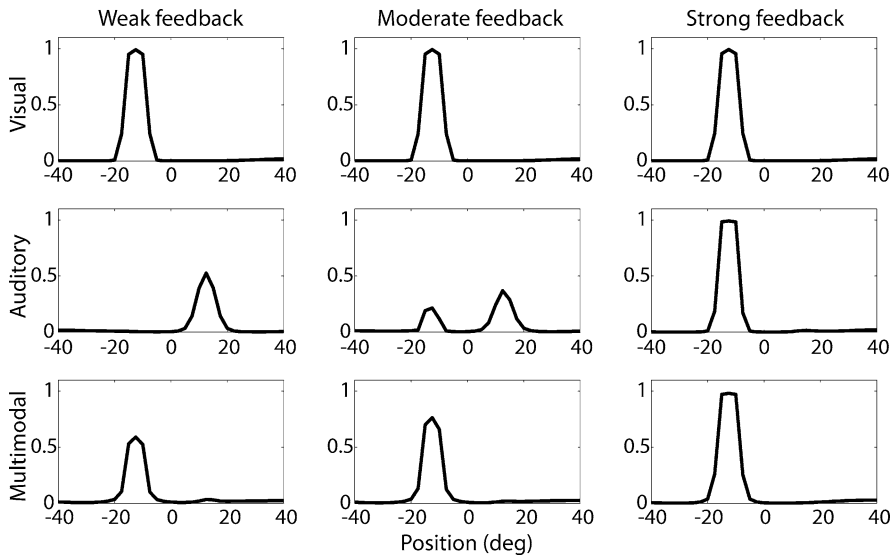


**Fig. 2.7** Response of neurons in the visual unisensory area, whose RF is centered at the vertical coordinate  $0^\circ$  (i.e., positioned at the middle of the vertical field), in the steady-state condition following a poor visual stimulus, applied at the horizontal coordinate  $0^\circ$

An example, in which an auditory stimulus may help perception of a visual stimulus (cross-modal facilitation) is shown in Fig. 2.7. In this case, to simulate a patient with poor visual perception, a visual stimulus with low-amplitude was applied to the visual area. The stimulus produces just a moderate visual activity (about 10–15% of the maximal activity), which, due to intrinsic neural noise, may not be perceived in real conditions. However, let us assume that an acoustic stimulus is provided to the patient at the same spatial point. Since the acoustic area is not impaired, we assumed that this stimulus is strong enough to cause strong activation in the unisensory acoustic area (almost 100% at the corresponding position) and is able to activate the multimodal neuron. The latter, in turn, causes an increased activity in the visual area (up to 30–35%) thanks to the presence of feedback synapses from the multimodal to the unimodal areas. Hence, a visual stimulus, which is just poorly perceived, may be perceived much better, thanks to the simultaneous acoustic help. It is worth noting that, in this case, the acoustic stimulus not only evokes a response in the multimodal area, which is quite obvious, but can also help the formation of some activity in the visual area, i.e., it actively concurs to the formation of a visual target.

Let us now assume that the situation depicted above occurs frequently (the visual stimulus is continuously paired with an acoustic stimulus) and that the feedback synapses improve. In this condition, an acoustic stimulus can evoke a stronger activity (up to 60%) in the visual unimodal area (Fig. 2.7). This situation may have important potential consequences in therapeutic rehabilitation procedures.

As a last example, let us consider the case of ventriloquism. To simulate this phenomenon, we imagined the presence of a strong visual stimulus occurring together with a weaker auditory stimulus at different (but not too far) positions (Fig. 2.8). When the model are given basal parameter values (in particular, weak feedback synapses), both stimuli cause activation in the respective unimodal area (hence, the



**Fig. 2.8** Response of neurons, whose RF is centered at the vertical coordinate  $0^\circ$  (i.e., positioned at the middle of the vertical field), in the visual (*upper line*), auditory (*middle line*) and multimodal (*bottom line*) areas, in response to two cross-modal stimuli at different horizontal positions. The visual stimulus is stronger and applied at position  $-15^\circ$ . The auditory stimulus is weaker and applied at position  $+15^\circ$ . The *left column* refers to the case of normal feedback synapses from the multimodal to the unisensory areas (basal synapse strength = 1). Results in the *middle column* were obtained by increasing the feedback synapse strength from the multimodal to the auditory area (synapse strength = 15) while feedback synapse to the visual area was unchanged. It is remarkable the appearance of a second “phantom” activity in the auditory area. The *right column* describes the case in which the feedback synapse strength from the multimodal to the auditory area was further increased (synapse strength = 20). The original auditory activity is suppressed and the visual stimulus captures the auditory one

subject is perceiving both a visual and an auditory stimulus, at different positions) (Fig. 2.8, left column). However, only the stronger visual stimulus can excite the multimodal neurons thus producing overt behavior. In fact, activity of multimodal neurons induced by the auditory stimulus is almost entirely suppressed in the SC as a consequence of lateral competition. Let us now consider that, to solve a conflict between the auditory and visual stimuli, some mechanisms (maybe attentive) increase the feedback from the multimodal area to the auditory unimodal area. Increasing this feedback, one can first observe the occurrence of two activities at different locations in the auditory area (Fig. 2.8, middle column): the subject perceives the original activity and a second “phantom” activity at the same position as the visual input. If feedback is increased further, the original auditory activity is suppressed by competition in the unimodal area, and only the second “phantom” auditory activity keeps on (Fig. 2.8, right column). This signifies that the visual stimulus captures the auditory one at its position, suppressing the original auditory input.

## 2.2.4 *Successes, Limitations and Future Challenges*

The present model is based on the idea that multimodal neurons in the superior colliculus receive their inputs from two upstream unimodal areas, one devoted to a topological organization of visual stimuli and another devoted to a topological organization of auditory stimuli. For the sake of simplicity, in this model, somatosensory stimuli are neglected, i.e., we consider only the problem of audio–visual integration. Moreover, the exact location of these areas is not established in our model, i.e., we did not look for a definite anatomical counterpart.

Several mechanisms have been included in this simple basal circuit, each with a specific significance and a possible role in affecting final responses:

1. Nonlinearities in the activation function of single neurons (i.e., a lower threshold and upper saturation, expressed with a sigmoidal relationship). These nonlinearities are essential to understand some important properties of multisensory integration, such as the inverse effectiveness, and the possibility of superadditive, additive, or subadditive integration.
2. Lateral (mainly inhibitory) synapses among multisensory neurons. These synapses are necessary to obtain a significant cross-modal suppression between spatially separated auditory and visual stimuli, as documented in recent experiments.
3. Lateral synapses (excitatory and inhibitory) among neurons in the same unimodal area. They have been modeled with a classical “Mexican hat” disposition, i.e., a close facilitatory area surrounded by an inhibitory annulus. These synapses play a fundamental role in producing the receptive field of multimodal neurons and in producing an “activation bubble” (i.e., a group of contiguous neurons simultaneously active) in response to punctual stimuli. Moreover, they contribute to the within-modal suppression documented in many experiments (Kadunce et al. 1997, 2001) even in the absence of cross-modal suppression (Kadunce et al. 2001).
4. Feedforward connections from unimodal to multimodal neurons. The strength of these synapses affects the sensitivity of multimodal neurons and the maximum response they can attain to a single stimulus of a given modality.
5. Excitatory backward connections from multimodal neurons to unimodal neurons at the same spatial position. Inclusion of these connections considers the possibility that the response by a multimodal neuron reinforces the response at an earlier unimodal area and allows a reciprocal influence between unisensory areas.

By incorporating the previous mechanisms, the model can make several predictions, which can be compared with experimental data. In the following, the main simulation results are critically commented:

1. Inverse effectiveness – As it is evident in Fig. 2.3, the capacity of multisensory neurons to integrate cross-modal stimuli depends on the intensity of unisensory inputs. As in Perrault et al. (2005), enhancement is affected by the intensity of the unisensory inputs, and it exhibits a significant decrease if stimulus intensity is progressively raised.

2. Cross-modal vs. within-modal integration – According to the literature (Stein and Meredith 1993), in our model, a combination of two cross-modal stimuli within the RF results in significant enhancement of the SC response, but the same effect is not visible when the two stimuli are presented as a within-modal pair. A second within-modal stimulus applied within the RF causes just a mild enhancement (Fig. 2.4).
3. Spatial relationship between two (within-modal or cross-modal) stimuli – In agreement with experimental data (Kadunce et al. 1997, 2001), our model shows that, as the spatial distance between two stimuli increases, multisensory integration in SC layer shifts from enhancement to suppression. In the present model, with the basal parameter values used in Figs. 2.4 and 2.5, the suppressive effect is evident both using within-modal and cross-modal stimuli.
4. Differences between within-modal and cross-modal suppression – By increasing the strength of lateral inhibition in the unimodal areas and decreasing the strength of lateral inhibition in cross-modal areas, the model can explain the occurrence of within-modal suppression even in the absence of cross-modal suppression, a result that has been reported in the literature. Furthermore, if different lateral inhibitory synapses are used for the two unisensory areas (for instance, weak inhibition in the visual area and strong inhibition in the auditory), model can explain the occurrence of within-modal suppression in one modality only.
5. By introducing feedback synapses, the model can explain phenomena like ventriloquism, or the improvement in perception of one unisensory stimulus occurring in the presence of a cue from the other modality. However, to this end, we need to suppose that feedback synapses are stronger than normal. It is worth noting that ventriloquism was simulated assuming a huge increase in feedback synapses directed toward the auditory unisensory area only. In this way, the visual stimulus created a phantom activity in its position, which suppresses the other activity. Conversely, improvement in perception can occur even with moderate feedback synapses, and appears as a more normal behavior (i.e., one which does not require excessive parameter changes from basal).

The latter aspect opens the problem of synaptic plasticity in the model, an issue that may have the greatest importance both in clinical-therapeutic problems (for instance, for the rehabilitation of patients with neurological deficits) and for achieving a deeper understanding of adaptation to complex situations. One possibility, which should be tested in future works, is that some synapses are subjected to rapid change, in a short-time basis, to adapt model behavior to the particular conditions. Another possibility is that some model parameters are under the influence of top-down attentional mechanisms, which may work by modulating the threshold of some neurons (thus making them more or less prompt to respond to input stimuli) or may affect synaptic transmission via a gating mechanism. All these aspects may represent future applications of the model.

A further future possible application of the model concerns the study of multisensory maturation in early life. Indeed, multisensory enhancement is not present in SC at birth and develops gradually with sensory experience (Stein 2005). To study this aspect, however, a more sophisticated model is necessary, which comprehends

more inputs to the SC. In fact, several recent neurophysiological works show that the SC neurons receive at least four distinct unimodal paths (two visual and two auditory), which have a different functional role in multisensory integration: descending paths from cortico-collicular regions (especially the anterior ectosylvian sulcus and the rostral lateral suprasylvian area) are responsible for multisensory integration; ascending paths coming from a variety of other subcortical sources do not produce multisensory integration (Jiang et al. 2001; Jiang and Stein 2003; Wallace et al. 1993). The present model considers only two unimodal descending inputs, i.e., those responsible for multisensory integration. It is probable that, at birth, only the ascending subcortical inputs are functionally active, whereas the descending paths mature subsequently with sensory experience. Of course, formulation of a more complex model (with four inputs related through nonlinear multiplicative relationships and with a learning rule for the descending paths) might be the subject of future refinements and extensions.

Finally, we wish to stress that the present model circuitry, inspired by neurophysiological considerations, may not only contribute to our understanding of the neural system, but also drive the project of artificial systems for sensory fusion. In fact, most of the mechanisms adopted here can have a general validity: nonlinearity to regulate the degree of integration among different stimuli and favor enhancement in the presence of poor stimulation; the presence of lateral competition to suppress less-relevant information; the presence of feedback plastic mechanisms to realize more sophisticated top-down control strategies. Moreover, all these mechanisms are working in parallel and in an integrated fashion to achieve a highly distributed and efficient system, as that emerged after millions of years of animal and human evolution.

## 2.3 Visual–Tactile Integration

### 2.3.1 *Visual–Tactile Representation of Peripersonal Space: Neurophysiological and Behavioral Evidence (Overview and Model Justification)*

The crucial factor that distinguishes the space immediately surrounding our body [peripersonal space (Rizzolatti et al. 1997)] from the more distant space (extrapersonal space) is our potential ability to interact with objects located within it. Objects within peripersonal space may be reached, grasped, and manipulated; potentially harmful objects (requiring avoidance and defensive movements) are those closest to, and moving rapidly toward, our body. Hence, it makes functional sense that the brain represents peripersonal space differently from the more distant space. In particular, objects near to or in contact with the body may be perceived via a sensory system (the touch), which is not involved at all by objects located in the extrapersonal space.

In the last two decades, neurophysiological research on monkeys has yielded a large body of evidence supporting the notion that peripersonal space is represented in a multisensory fashion, by integrating visual and tactile stimuli. Multimodal neurons have been found in several brain structures (putamen, parietal, premotor areas) (Bremmer et al. 2001; Duhamel et al. 1998; Fogassi et al. 1996; Graziano et al. 1997; Rizzolatti et al. 1998), which respond both to touches delivered on a specific body part (e.g., the hand or the face) and to visual stimuli presented close to the same body part, where the tactile receptive field (RF) is located. The visual RF of these neurons has a limited extension in depth, being typically restricted to the space immediately surrounding the body part: the neuronal response to visual stimuli decreases as the distance between stimuli and the cutaneous RF increases (Duhamel et al. 1998; Fogassi et al. 1996; Graziano et al. 1994).

The main evidence for the existence of a multisensory system in humans, functionally similar to that in monkeys, comes from neuropsychological studies conducted on right brain-damaged (RBD) patients with extinction (di Pellegrino et al. 1997; Làdavas et al. 1998, 2000; Làdavas 2002). Extinction patients fail to detect a contralesional stimulus only under conditions of bilateral (ipsilateral and contralateral) simultaneous stimulation. Extinction phenomenon has been attributed to an unbalance competition between concurrent representations: the unilateral brain damage gives rise to a weaker representation of the contralateral side, which is disadvantaged in terms of competitive weights (Mattingley et al. 1997). Extinction can occur when the concurrent stimuli are in the same modality (unimodal extinction) or in different modalities (cross-modal extinction). In cross-modal extinction, presentation of a visual stimulus in the ipsilesional (right) visual field can extinguish a simultaneous tactile stimulus on the contralesional (left) hand. Crucially, tactile extinction on the contralesional hand is modulated by the spatial arrangement of the simultaneous visual stimulus with respect to the body (Làdavas and Farnè 2004; Làdavas et al. 1998, 2000). Tactile extinction is more severe when the visual stimulus is presented near ( $\sim 5$  cm) the ipsilesional hand, than when it is presented away ( $\sim 35$  cm) from the ipsilesional hand; moreover, a visual stimulus presented near the contralesional hand improves the detection of the tactile stimulus applied to the same hand. Such findings can be explained by referring to the activity of bimodal neurons, similar to those observed in monkeys, which have tactile receptive fields on the hand and corresponding visual receptive field in the space immediately adjacent to the tactile field; the activation of such bimodal neurons would activate the perceptual representation of the corresponding hand (di Pellegrino et al. 1997).

Recent functional neuroimaging studies, indeed, have identified multimodal structures in the human brain responding selectively to tactile and visual information on a single body part (the hand or head), suggesting that such areas may represent the human equivalent of macaque's areas for peripersonal space representation (Bremmer et al. 2001; Makin et al. 2007; Sereno and Huang 2006).

Peripersonal space representation both in humans and monkeys has basically a motor function (Bremmer et al. 2001; Cooke and Graziano 2004; Rizzolatti et al. 1998); spatial locations of multisensory stimuli are encoded in relationship to body parts to generate appropriate motor responses (goal-directed, defensive,

or avoidance movements) (Graziano and Cooke 2006; Làdavas and Farnè 2004; Legrand et al. 2007; Rizzolatti et al. 1998). Normally, such action space is delimited by the physical length of our effectors (mainly the arms). However, we can use many different tools to extend our physical body structure, and consequently our action space. While using a tool, the tactile information felt at the hand can be related to visual information from distant objects. There are several evidences that the use of a tool, linking tactile events with far visual events, induces a plastic modification of peripersonal space, with a recoding of the far space as near space.

Resizing of peri-hand space representation following tool use was first reported in monkeys by Iriki et al. (1996). They observed that, after the animal had repeatedly used a tool to retrieve distant food, the visual RF of intraparietal bimodal neurons was elongated to include the entire length of the tool, whereas originally it was limited to the space around the hand. The emergence of novel projections from visual-related areas to bimodal intraparietal regions (Hihara et al. 2006; Ishibashi et al. 2002) has been suggested as a possible neural mechanism underlying such phenomenon. Evidence for a similar tool incorporation into peri-hand space representation has been reported in humans at behavioral level. In extinction patients, a visual stimulus located at the end of a right hand-held tool induced more severe left tactile extinction immediately after the tool use than before (Farnè and Làdavas 2000; Maravita et al. 2001), suggesting an extension of the integrative peri-hand space.

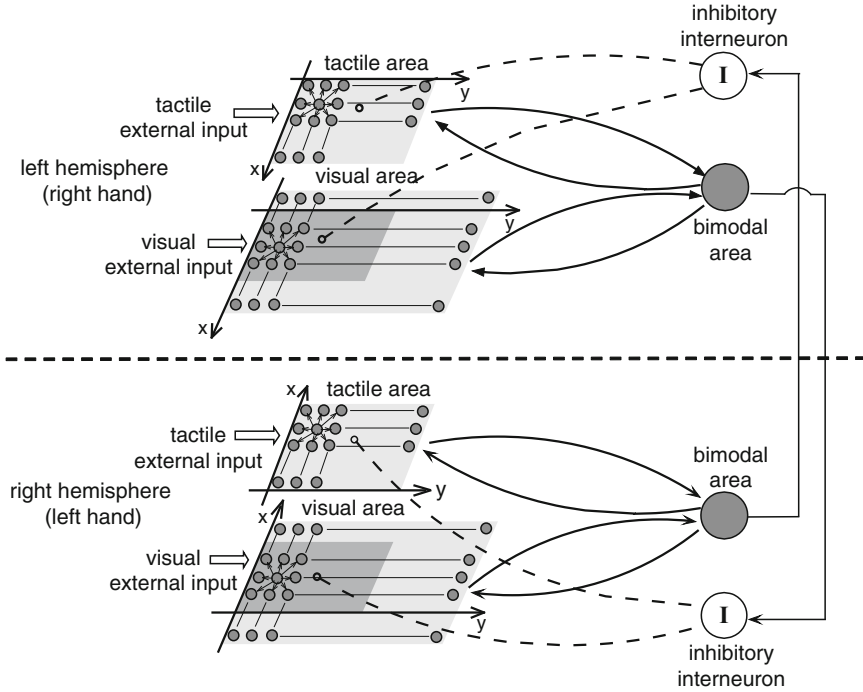
In summary, a massive amount of data contributed to describe functional and dynamical properties of peripersonal space representation. Recently, we have exploited computational modeling via artificial neural networks to shed light on the neural mechanisms and circuits underlying such properties (Maggioso et al. 2010a, b). In particular, with our models, we aspire to address the following questions: What is the organization of the neural network subserving peripersonal space representation? How does it relate with the multimodal neurons identified by electrophysiological studies? How do multimodal and modality-specific areas communicate reciprocally? Which are the alterations in the neural circuitry that may explain extinction in brain-damaged patients? Which are the neural correlates of peripersonal space plasticity following tool use? How can behavioral results be related with responses of individual neurons?

Although some computational models have been proposed in the past to investigate some properties of multimodal neurons in the parietal cortex (Avillac et al. 2005; Denève et al. 2001; Pouget and Sejnowski 1997; Salinas and Abbott 1995), none of them has tackled the above questions explicitly.

### ***2.3.2 A Neural Network Model for Peri-Hand Space Representation: Simulation of a Healthy Subject and a RBD Patient (Model Components and Results 1)***

The model consists of two subnetworks, reciprocally interconnected; each subnetwork refers to the contralateral hand of a hypothetical subject (Fig. 2.9).





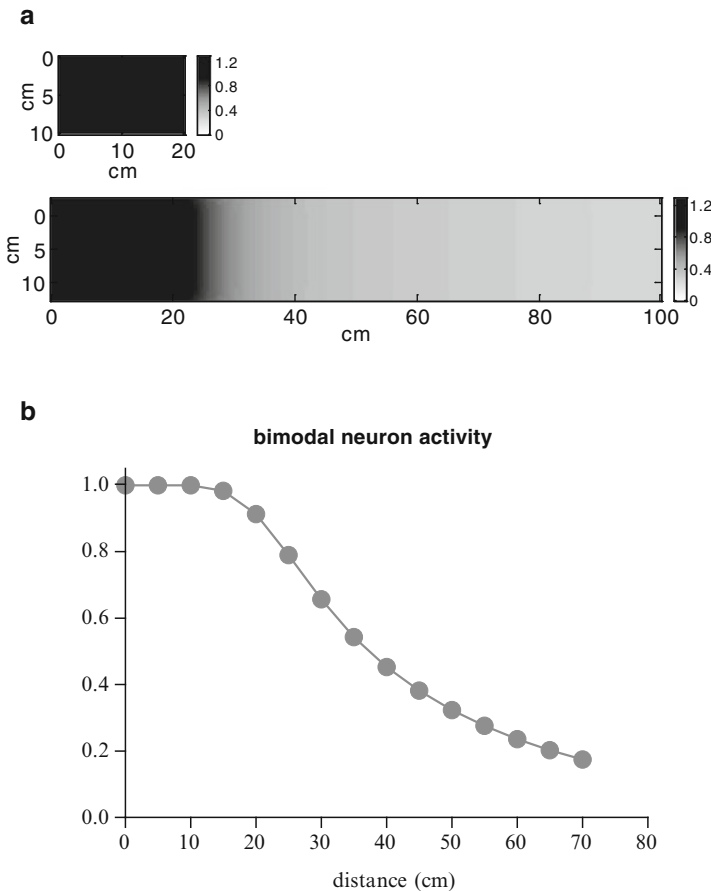
**Fig. 2.9** Layout of the neural network. The model includes two subnetworks, one per hemisphere, each corresponding to the contralateral hand and surrounding space. The *gray circles* represent excitatory neurons; the *continuous arrows* linking neurons or areas of neurons denote excitatory connections, the *dashed lines* denote inhibitory connections. *I* indicate inhibitory interneurons

The single subnetwork embodies three areas of neurons. The two upstream areas are bidimensional matrices of unimodal neurons: neurons in one area respond to tactile stimuli on the contralateral hand (*tactile area*); neurons in the other area respond to visual stimulation on the same hand and around it (*visual area*). Each neuron has its own receptive field (RF), described by means of a Gaussian function. In both areas, the RFs are in hand-centered coordinates and are arranged at a distance of 0.5 cm, so that proximal neurons within each area respond to stimuli coming from proximal positions of the hand and space. RFs of proximal neurons are partially superimposed. The tactile area maps a surface of  $10 \times 20$  cm, roughly representing the surface of the hand. The visual area covers a space of  $15 \times 100$  cm, representing the visual space *on* the hand and *around* it (extending by 2.5 cm on each side and 80 cm ahead). Moreover, the units within each unimodal area interact via *lateral synapses* with a “Mexican hat” arrangement (i.e., with short-range excitation and long-range inhibition).

The unimodal neurons send *feedforward synapses* to a third downstream multimodal area devoted to visual–tactile representation of peri-hand space. The multimodal area might represent multisensory regions in the premotor or parietal cortex,

which receive feedforward projections from sensory-specific areas (Duhamel et al. 1998; Graziano et al. 1997; Rizzolatti et al. 1981). For the sake of simplicity, we considered a single visual–tactile neuron, covering the entire peri-hand space. Data in the literature (Graziano et al. 1997; Rizzolatti et al. 1981) indeed, stress the existence of multimodal neurons with a RF as large as the whole hand. The tactile feedforward synapses have a uniform distribution (their strength is independent of the position of single tactile neuron’s RF).

The strength of the visual feedforward synapses is constant on the hand and decreases exponentially as the distance between the neuron’s RF and the hand increases. Figure 2.10a shows the pattern arrangement of the feedforward synapses



**Fig. 2.10** (a) Pattern of the feedforward synapses from the tactile (*upper plot*) and visual (*lower plot*) area to the downstream bimodal area in the left hemisphere (for basal parameter values, i.e., healthy subject). The *x* (*vertical*) and *y* (*horizontal*) axes represent the coordinates of the RF center of the unimodal neurons; the *gray scale* indicates the strength of the synapse connection. (b) Response of the bimodal neuron in one hemisphere to a visual stimulus at different distances from the contralateral hand. Neuron response is normalized with respect to its maximum saturation activity (i.e., value one corresponds to the maximal neuron activation)

from the tactile and visual area. According to such synapses arrangement, the bimodal neuron has a tactile RF covering the entire hand, and a visual RF matching the tactile RF and extending some centimetres around it. Figure 2.10b displays the response of the bimodal neuron in one hemisphere to a visual stimulus located at different distances from the contralateral hand. Activity of the neuron is evaluated after the initial transient has exhausted and the network has reached a new steady state (the stimulus is maintained throughout the entire simulation). The visual-related activity of the bimodal neuron decreases as the distance between the visual stimulus and the hand increases, in agreement with neurophysiological data (Graziano et al. 1997; Rizzolatti et al. 1981). It is worth noticing that in the model, activation of the bimodal neuron in one hemisphere mimics the perceptual representation of the contralateral hand, triggered by a somatosensory stimulation or by a near visual stimulation.

The visual–tactile neuron within one hemisphere sends *feedback excitatory synapses* to the upstream unimodal areas in the same hemisphere, in agreement with recent neuroimaging data suggesting that higher level multimodal areas may send back-projections to modality-specific areas (Kennett et al. 2001; Macaluso et al. 2000; Taylor-Clarke et al. 2002). The feedback synapses have the same arrangement as the feedforward synapses, with different parameter values.

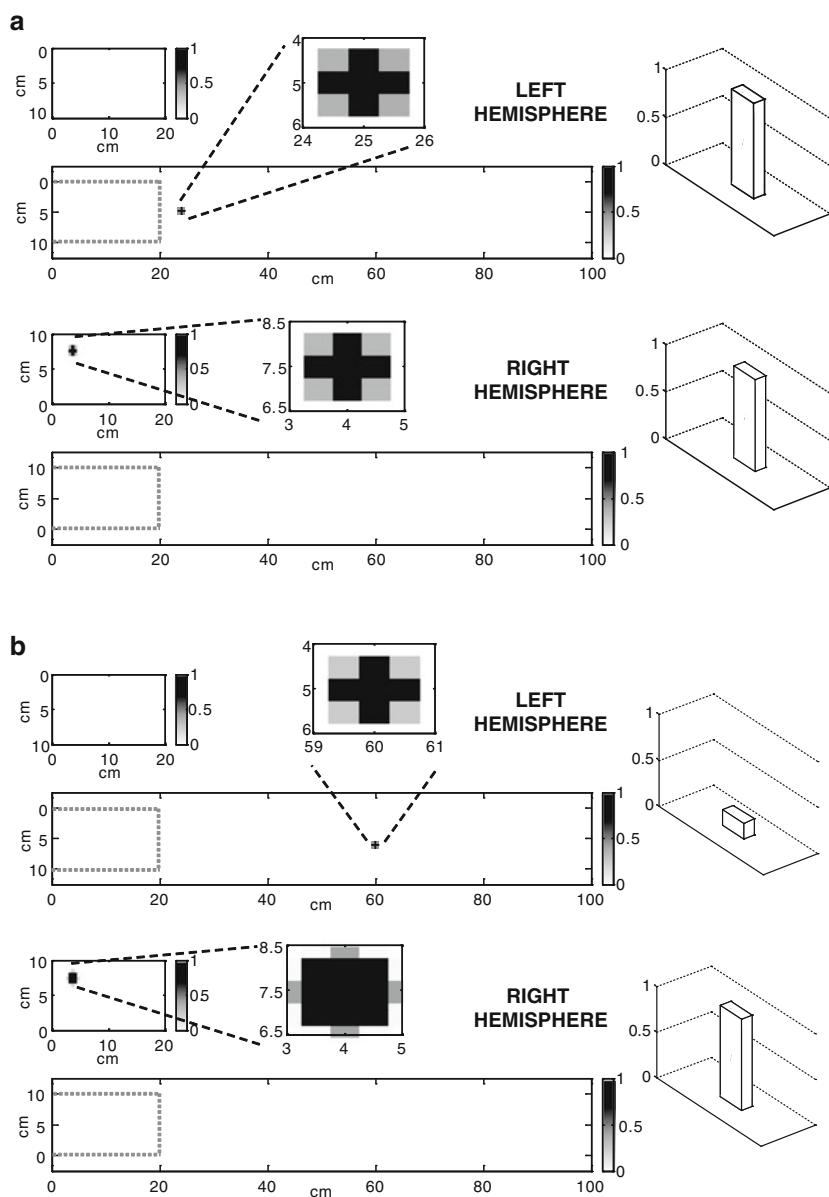
The two hemispheres interact via a competitive mechanism realized by means of inhibitory interneurons. The inhibitory interneuron in one hemisphere receives information from the bimodal neuron in the other hemisphere via a synapse, characterized by a pure delay to account for the interhemispheric transit time. Then, the interneuron sends inhibitory synapses locally to the unimodal visual and tactile neurons. The inhibitory synapses from the interneuron to the tactile and visual areas have the same spatial arrangement as the feedforward and feedback synapses, with a different set of parameters.

The input–output relationship of each neuron (both unimodal, bimodal and inhibitory) includes a first-order dynamics and a static sigmoidal relationship with a lower threshold and an upper saturation. Each neuron is normally in a silent state and can be activated if stimulated by a sufficiently high excitatory input.

Basal values for all model parameters were assigned on the basis of neurophysiological and behavioral literature to reproduce a healthy subject. In particular, in basal conditions, the two hemispheres are characterized by the same parameter values.

### 2.3.2.1 Simulation of the Healthy Subject

Figure 2.11 shows network activity in response to bilateral cross-modal stimulations in the healthy subject (basal parameter values). Each panel (a and b) shows the activity in the unimodal areas (represented by a gray plot) and in the bimodal area (represented by a 3D bar), in the left and right hemispheres. Network activity is displayed in the steady-state conditions reached by the network following the stimuli application. In panel a, a tactile stimulus is applied on the left hand [stimulus position:  $x(\text{vertical}) = 7.5 \text{ cm}$ ;  $y(\text{horizontal}) = 4 \text{ cm}$ ] and a simultaneous visual



**Fig. 2.11** Network activity in response to two different bilateral cross-modal stimulations in the healthy subject. Each panel shows the activity in the unimodal areas (represented by a *gray plot*, where the  $x$  and  $y$  axes represent the coordinates of the neuron's RF center, and the *gray scale* denotes the activation level of the neurons), and in the bimodal area (represented by a 3D bar), in the left and right hemispheres. The inserted plots are magnified images of the activated group of unimodal neurons. The *dotted gray line* in the visual areas borders the visual space *on* the hand. (a) Network response to a tactile stimulus applied on the left hand, and to a visual stimulus applied *near* the right hand (5 cm distance). (b) Network response to a tactile stimulus applied on the left hand, and to a visual stimulus applied *far* from the right hand

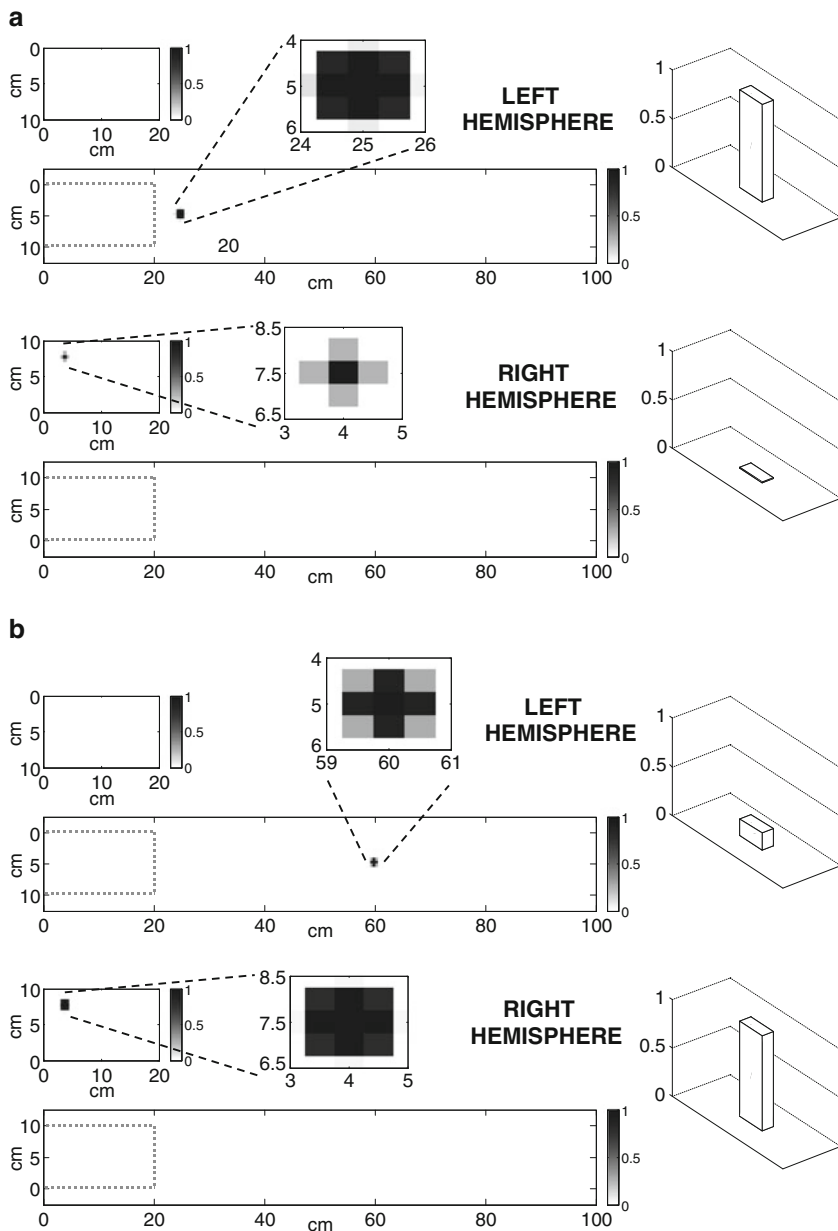
stimulus is applied *near* the right hand (stimulus position:  $x = 5$  cm;  $y = 25$  cm, at a distance of 5 cm from the hand). Each stimulus produces a significant activation in the respective unimodal area, that is, an activation bubble emerges in each area. The formation of an activation bubble is due to the partial superimposition of the RFs of adjacent neurons and to the lateral excitation that produces reciprocal reinforcement of neighboring neurons activity. Unimodal activity, in turn triggers – via feedforward synapses – the corresponding bimodal neuron; it is worth noticing that activation of the bimodal neuron further reinforces the activity in the unimodal area owing to the feedback excitatory projection on and near the hand. Moreover, the simultaneous activation of the two bimodal neurons leads to a competition between the two hemispheres. In this case (healthy subject), the competition is unbiased and the final outcome is the coexistence of activations in both hemispheres; in particular, in each hemisphere the bimodal neuron is in the *on* state. This model result agrees with *in vivo* data showing that in healthy subjects, the representations of both hands coexist in case of a simultaneous right- and left-hand stimulation (Hillis et al. 2006).

In Fig. 2.11b, the left tactile stimulus is applied in the same position ( $x = 7.5$  cm;  $y = 4$  cm), whereas the right visual stimulus is applied *far* from the hand (stimulus position:  $x = 5$  cm;  $y = 60$  cm, i.e., at a distance of 40 cm from the hand). The two stimuli have the same intensity. The left tactile stimulus triggers the right hemisphere bimodal neuron to its maximum saturation. The far visual stimulus still activates a group of neuron in the unimodal visual area; however, because of its distance from the hand, it produces only a slight activity of the corresponding bimodal neuron. At that position, indeed, feedforward synapses are weaker (see Fig. 2.10a). Accordingly, the far visual stimulus does not trigger the right-hand representation, and only the left hand representation is activated, boosted by the somatosensory stimulus.

### 2.3.2.2 Simulation of the RBD Patient with Left Tactile Extinction

In order to simulate an RBD patient suffering from left tactile extinction, we decreased the strength of all excitatory synapses (both lateral and feedforward) originating from the tactile unimodal neurons in the right hemisphere. The hypothesized reduction in synaptic strength has to be interpreted not as a real synaptic depression, but, rather, as the effect of a reduction in the number of effective excitatory units that contribute to activity in that region. Of course, the smaller the number of effective excitatory cells, the smaller the overall excitatory input emerging from that area. Under these conditions, we replicated the same bilateral stimulations as in Fig. 2.11; results are reported in Fig. 2.12a, b.

In Fig. 2.12a, the left tactile stimulus (stimulus position:  $x = 7.5$  cm;  $y = 4$  cm) is applied simultaneously with a right visual stimulus *near* the right hand (stimulus position:  $x = 5$  cm;  $y = 25$  cm, i.e., at a distance of 5 cm from the hand). The two stimuli have the same intensity. The *near* right-hand visual stimulus activates the bimodal neuron in the left hemisphere, competing with the simultaneous left tactile stimulus. In this case, the competition is unbalanced, since right hemisphere



**Fig. 2.12** Network activity in response to two different bilateral cross-modal stimulations in the RBD patient. The figure has the same meaning as Fig. 2.11. **(a)** Network response to a tactile stimulus applied on the left hand, and to a visual stimulus applied *near* the right hand (5 cm distance). The activity of the bimodal neuron in the right hemisphere is extinguished by the concurrent activation in the opposite hemisphere. **(b)** Network response to a tactile stimulus applied on the left hand, and to a visual stimulus applied *far* from the right hand (40 cm distance). The far visual stimulus does not extinguish the activation of the right hemisphere bimodal neuron

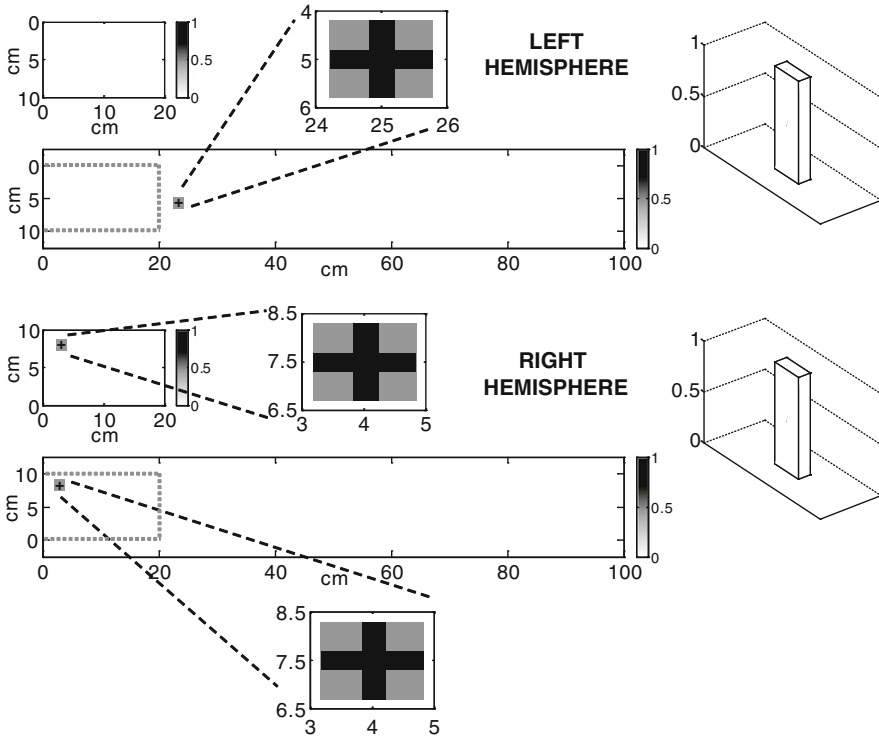
activation is weakened by the lesion. In particular, the reduction of lateral excitation in the right tactile area diminishes the intensity and extension of the activation bubble in response to a tactile stimulus; the reduction of feedforward synapses from the right tactile area impairs the ability for tactile unimodal neurons to trigger the bimodal neuron. Thus, the right visual stimulus has a higher competitive strength than the left tactile stimulus. The final outcome is a strong reduction of the activity in the right hemisphere tactile area and a consequent deactivation of the bimodal neuron; i.e., the left hand representation is extinguished and only the right-hand representation survives. In Fig. 2.12b, the tactile stimulus at the same position is associated with a visual stimulus *far* from the right hand (stimulus position:  $x = 5$  cm;  $y = 60$  cm, i.e., at a distance of 40 cm from the hand). The two stimuli have the same intensity. The right visual stimulus, being far from the hand, exerts only a weak competition with the left tactile stimulus; then, the latter is able to activate the corresponding bimodal neuron, triggering the left hand representation. Simulation results displayed in Fig. 2.12 show that the model can reproduce the near–far modulation of left tactile extinction as reported in vivo (Làdavas and Farnè 2004; Làdavas et al. 1998, 2000). It is worth noticing that extinction of the left touch can be obtained also by applying a tactile stimulus on the right hand, in agreement with experimental data (unpublished simulations) (di Pellegrino et al. 1997; Làdavas et al. 1998, 2000).

Furthermore, behavioral studies in extinction patients indicate that under conditions of bilateral stimulation, the detection of the left tactile stimulus is ameliorated by a simultaneous left visual stimulus (Làdavas et al. 1998, 2000) (cross-modal facilitation). This situation is simulated in Fig. 2.13, where a visual stimulus is applied near the right hand (position:  $x = 5$  cm;  $y = 25$  cm, i.e., 5 cm distance from the hand) and a double stimulation (tactile and visual) is delivered to the left hand (stimuli position:  $x = 7.5$  cm,  $y = 4$  cm). All stimuli have the same intensity. In this case, the left visual stimulus sustains the activation of the bimodal neuron (despite the competition with the concurrent right-hand visual stimulus); the bimodal neuron, in turn, reinforces the activity in the tactile area via the feedback projections. Consequently, the activation in the right hemisphere tactile area ameliorates significantly (compare Fig. 2.13 with Fig. 2.12a); this might correspond to an improved detection of the left tactile stimulus.

### 2.3.3 *Modeling Peri-Hand Space Resizing: Simulation of Tool-Use Training (Model Components and Results 2)*

The model can be exploited to investigate the neural mechanisms underlying plasticity of the peri-hand space representation consequent to tool use. In particular, we hypothesized a neurobiological mechanism for synapses plasticity, and assessed whether this mechanism can account for dynamic changes in peri-hand space representation after tool use.

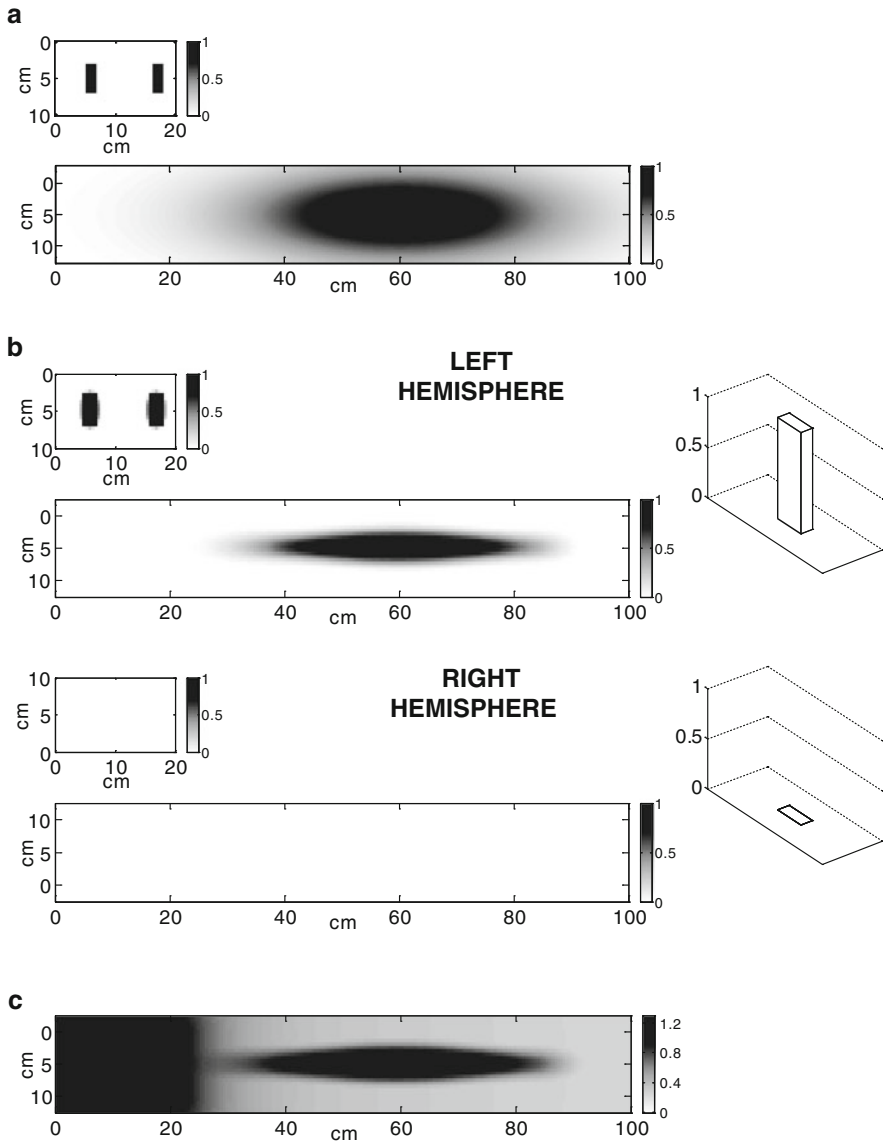




**Fig. 2.13** Cross-modal facilitation in the RBD patient. Response to a bilateral stimulation: the left tactile stimulus is paired with a simultaneous visual stimulus on the left hand, and a visual stimulus is applied *near* the right hand. Bimodal neuron in the right hemisphere is not extinguished (thanks to the visual stimulus), and reinforces the activity in the right tactile area via back projections (compare with Fig. 2.12a)

To this aim, a training experiment has been simulated in which the hypothetical subject utilizes a tool with the right hand to interact with the far space. We assumed that the tip of the tool lies in position 5, 60 cm in the  $x$ ,  $y$  plane (i.e., at a distance of 40 cm from the hand along the parasagittal plane). The use of the tool by the right hand has been mimicked by applying both a tactile and a visual input to the left hemisphere (Fig. 2.14a).

The tactile input represents the portion of the hand stimulated while holding the tool. The visual input represents the region of the visual space functionally relevant for the tool use, selected, for instance, by top-down attentive mechanisms. Here, we adopted an elongated visual input, centered on the tip of the tool, and spread both before and behind it: such input might simulate the case of using a rake to retrieve objects from the far space toward the body, a task adopted in several *in vivo* studies (Bonifazi et al. 2007; Farnè et al. 2005, 2007; Iriki et al. 1996). Indeed, retrieving objects may require attention to cover a wide portion of the visual space, including the area where the distant objects are located and the region of space between the



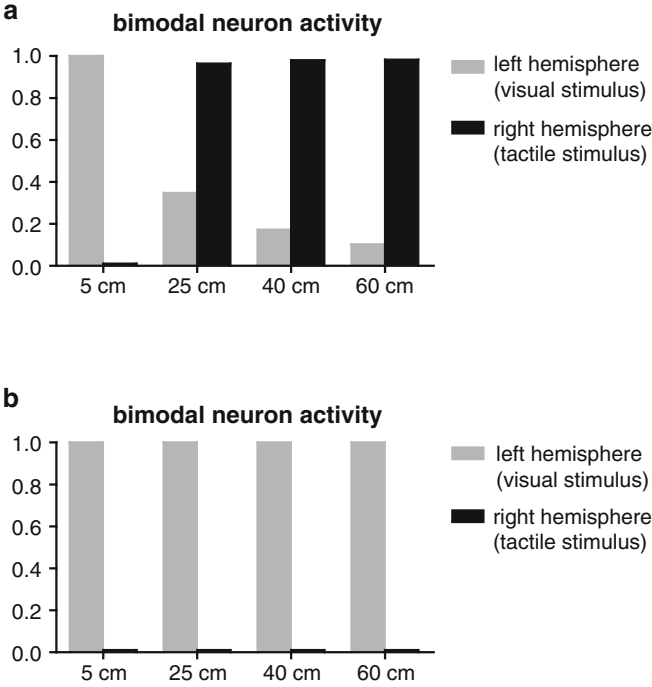
**Fig. 2.14** Tool-use training. (a) Tactile and visual inputs used to simulate tool-use training with the model. These inputs were applied to the left hemisphere since we simulated the use of the tool with the right hand. (b) Network response to the previous inputs. Only the left hemisphere is active since no stimulation was applied to the right hemisphere. (c) Feedforward synapses from the visual area to the bimodal neuron in the left hemisphere after training, computed via the application of a Hebbian rule during stimulation of the network by the tool-related inputs (compare with Fig. 2.10a)

tip of the tool and the hand, along which the objects are dragged toward the subject body. The application of the previous inputs to the network produces the activation of the corresponding regions in the unimodal areas within the left hemisphere, as well as the activation of the bimodal neuron (Fig. 2.14b).

We assumed that during the application of these inputs, the feedforward synapses linking unimodal neurons to the bimodal neuron in the left hemisphere modify via a classical Hebbian learning rule with an upper saturation: i.e., synapses are reinforced in presence of the simultaneous activation of the presynaptic and postsynaptic neurons, until a maximal value is reached. Moreover, we assumed that synapses *on* the hand are already at their maximum value even before tool use. This assumption is reasonable since these synapses are frequently and repeatedly involved in the daily perception of the peri-hand space. Therefore, synapses from the tactile neurons and from the visual neurons coding the space on the hand do not modify; conversely, visual synapses reinforce significantly along the extended visual input highlighted during the training. Figure 2.14c shows the pattern of the visual feedforward synapses after the Hebbian learning.

All equations and parameters concerning model training and plasticity can be found in our previous paper (Magosso et al. 2010a).

To evaluate the effect of the tool-use training on the integrative visual–tactile peri-hand area, bilateral visual–tactile stimulations have been simulated in the RBD patient, with the right visual stimulus at different distances from the right hand, before and after the training. For each position, the tactile and visual stimuli have the same intensity. Results of these simulations are reported in Fig. 2.15, which merely shows the activation of the bimodal neurons in the two hemispheres as a function of the right visual stimulus location. Before the training, the bimodal neuron in the left hemisphere responds only to near visual stimuli. Consequently, left tactile extinction occurs only in case of a visual stimulus in proximity to the right hand (5 cm distance); more distant visual stimuli on the right side do not compete, or compete only slightly, with the left hand representation, which, therefore, survives (Fig. 2.15a; near–far modulation of left tactile extinction). Conversely, after the training, cross-modal extinction is no longer modulated by the distance of the right visual stimulus; the right visual stimulus located in any of the four positions activates the bimodal neuron in the left hemisphere, and left hand representation is extinguished in all four cases (Fig. 2.15b). Hence, the model predicts an extension of the visual–tactile integrative area to include the elongated visual space highlighted during tool training. These model predictions are in agreement with *in vivo* results. Iriki and colleagues, in their work on monkeys (Iriki et al. 1996), documented an elongation of visual RFs of bimodal neurons along the tool. Studies on extinction patients report that, after 5 min of tool use, left tactile extinction produced by visual stimuli located at the distal edge of the tool, and midway between the hand and tip, was as severe as that obtained by a visual stimulation near the ipsilesional hand (Bonifazi et al. 2007; Farnè et al. 2007). Moreover, in another study (Farnè et al. 2005), extinction was also caused by a visual stimulus placed several centimetres beyond the tip of the tool, suggesting that the elongated peri-hand area is not coincident with the tool length, but includes also space located beyond the tip (as



**Fig. 2.15** Effects of tool-use training on visual–tactile interaction. The histogram shows the activity of the bimodal neurons in response to bilateral cross-modal stimulation (left touch and right visual stimulus) in the RBD patient as a function of the distance of the visual stimulus from the right hand. **(a)** Before training conditions. Left tactile extinction occurs only in case of a near visual stimulus. **(b)** After training conditions. Left tactile extinction occurs also for visual stimuli far from the right hand, at several positions along the tool axis

in our simulations). It is worth noticing that in all the mentioned in vivo studies, participants were required to use a rake to reach distant items, located out of the hand-reaching space, and to bring them back to the near space.

**2.3.4 Successes, Limitations and Future Challenges**

We proposed a simple network architecture for visual–tactile integration and peri-hand space representation, consisting of two unimodal areas and one bimodal area in each hemisphere connected via feedback and feedforward synapses, and including a competitive mechanism between the two hemispheres via inhibitory interneurons. The model does not aspire to have a definite neurophysiological and neuroanatomical counterpart, but rather to identify a plausible structure of the network and the functional links between its different parts, able to account for psychophysical and

behavioral results. In particular, one of the main over-simplification in the present model is that the spatial arrangement of visual and tactile receptive fields of the unimodal neurons has been set a priori on and around the hand; that is, we avoid considering explicitly the problem of coordinate transformations between different reference frames (e.g., from eye- to hand-centered coordinates). We assumed that the computational analysis performing coordinate transformation of the visual stimuli from retinotopic to hand-centered reference frames has been carried out by other areas in upstream, not represented, levels of the neural network, using postural information (e.g., eye, head, and hand positions). The problem of coordinate transformations has been widely investigated in other studies by means of neural network models (Avillac et al. 2005; Denève et al. 2001; Pouget et al. 2002).

The model is able to reproduce a variety of results concerning peripersonal space representation and its plastic modifications; in the following, we will highlight how the model may help interpretation of *in vivo* data, and, on the basis of the generated predictions, can suggest new experiments to validate the involved hypotheses.

An important point is that the model may be of value to gain insights into the neural mechanisms underlying extinction in unilateral brain-damaged patients. Consistent reproduction of *in vivo* data in these patients has been obtained by assuming a reduction of the excitatory synapses (both lateral and feedforward) emerging from the tactile neurons in the right hemisphere. Such reduction in synaptic strength wishes to represent the effect of a reduction in the number of effective excitatory units, which contribute to activity in the right tactile region. With this modification, a left tactile stimulus is able to activate the corresponding bimodal neuron (thus boosting the representation of the left hand), in absence of a simultaneous competition with the right-hand representation (Fig. 2.12b). This model outcome reflects neuroimaging data in extinction patients showing that right parietal and frontal regions (corresponding to the downstream bimodal area in the model) are activated when the left tactile stimulus is perceived (Sarri et al. 2006). Conversely, when a competition with the right-hand representation occurs (Fig. 2.12a), a weak activity still survives in the right tactile area, but it is insufficient to excite the bimodal neuron. This might corresponds to the lack of activation of the right parietal–frontal cortex, despite activation of sensory cortex, reported by fMRI studies in case of extinguished left touches (Sarri et al. 2006). Hence, the model identifies potential functional alterations in the neural circuitry able to explain extinction and relating cortical phenomena; in particular, the model suggests that several mechanisms (reduction of the overall excitation emerging from the right tactile area and the presence of a competition between two simultaneous spatial representations) are concurrently involved in such pathological sign.

The scenario provided by the model is also able to reproduce the phenomenon of cross-modal visual–tactile facilitation in the pathological subject (see Fig. 2.13), thanks to the back-projection from the bimodal area to the unimodal areas. Several recent studies have evidenced the adaptive advantage of multisensory integration in producing response enhancement when the information from one modality is weak (Calvert et al. 2004; Kennett et al. 2001; Press et al. 2004; Tipper et al. 1998),

and have suggested the exploitation of brain multisensory capabilities to recovery sensory or spatial deficits after damage (see [Ladavas 2008](#) for a review). In perspective, the model could provide important contribution in this field, by shedding light on the neural correlates of rehabilitation procedures and suggesting new strategies of rehabilitation. For example, according to the model, systematic visuo-tactile stimulation of the pathological side in extinction patients may promote a Hebbian reinforcement of the feedback and feedforward synapses in the damage hemisphere that could be effective to reequilibrate – in a long-lasting way – the competition between the two hemispheres.

A neurobiologically plausible hypothesis has been generated by the model, concerning the resizing of visual–tactile integrative area following tool use. The model assumes that the modification of peri-hand space arises from a Hebbian growing of visual synapses converging into the multimodal area, which extends the visual RF of the peripersonal bimodal neurons. Crucially, in the model, the change in visual RF strictly depends upon the visual input used during the learning phase (see [Fig. 2.14](#)); the latter might be selected – during the use of the tool – by top-down, probably attentive, mechanisms that identify the region of the visual space of interest for the task. Two important predictions descend from the previous model hypotheses that may be validated experimentally:

1. The hypothesis that peripersonal space modification depends on reinforcement of visual synapses converging into the bimodal area has the following implication: once the effect of tool use has been achieved via the training, the recoding of a far visual stimulus as a near one should be independent of the presence of the tool (at least for a certain period immediately after the training). Thus, after tool use, an extension of the visuo-tactile peri-hand area should be observed even in absence of any physical connection between the patient's hand and the far visual stimulus. At best of our knowledge, no *in vivo* study in the literature has evaluated visual–tactile interaction after tool use in conditions of tool absence. Hence, *ad hoc* behavioral experiments may be conceived to confirm (or refute) model prediction, thus supporting (or rejecting) the validity of the hypothesized mechanism of plasticity. We obtained a preliminary validation of model hypothesis and prediction in our recent work ([Maggosso et al. 2010a](#)) via a behavioral experiment on one RBD patient with extinction: the same extension of peri-hand space was measured after tool use both when the patient held the tool with her right hand, and when the tool was removed from the patient's hand.
2. The model predicts that different tool use-mediated tasks (e.g., retrieving objects, pressing buttons with the tip, sorting objects in the far space, etc.), requiring direction of movements and attention toward different regions of the visual space, may produce different resizing of the peri-hand visual–tactile space (e.g., the formation of a novel integrative peri-hand area at the tip of the tool rather than an elongation along the tool axis). These model predictions might be tested *in vivo*, for example, by exposing the participants to different kinds of tool-mediated tasks.

In conclusions, the present model of visual–tactile interaction exemplarily illustrates the importance of integrating experimental research with theoretical and computational studies. On the one hand, empirical results are fundamental to build the mathematical model, identifying model components and parameters. On the other hand, the model is fundamental to synthesize the data into a coherent theoretical framework, helping interpretation of behavioral results in terms of neuron responses and interconnections; moreover and of great importance, simulations results can generate new predictions and inspire new related experiments, which may further support, in a feedback fashion, the validity of the model.

## 2.4 Conclusions

In conclusion of this chapter, we wish to underline some basic ideas and fundamental mechanisms that emerge from the previous two models: knowledge of these aspects may drive the implementation of future neurocomputational models for multisensory integration in the brain, and perhaps the design of innovative devices for sensory fusion.

The reader can certainly recognize that the two models presented above, although devoted to different problems and simulating different brain regions (the superior colliculus in the first model, a parietal cortex association area in the second), share some common mechanisms. They are:

1. *A topological organization of the input space.* A topological organization (i.e., similar stimuli are coded by proximal neurons) can be encountered everywhere in the cortex and allows the implementation of a very efficient competitive mechanism directly in the single areas. This has several advantages: (a) *robustness*: a stimulus is coded by a group of mutually excited units, not by a single cell; (b) *similarity*: similar stimuli are coded by proximal units and, due to the superimposition of their receptive fields, a same unit responds to various similar stimuli; (c) *suppression*: an incongruent stimulus can be depressed or even eliminated by a proximal stronger stimulus.
2. *A nonlinear (sigmoid-like) input–output response.* This kind of response offers several major advantages, both in case of within-modal and cross-modal stimulation. (a) *thresholding*: all stimuli below a given threshold are neglected, in accordance with a parsimony requirement; (b) *saturation*: strongest stimuli do not produce an excessive (and often deleterious) response; (c) *inverse effectiveness*: the benefit of multisensory integration is higher in case of lower stimuli, i.e., in conditions where the individual stimuli carry uncertain information and may produce an inaccurate response, hence the need for sensory integration is higher.
3. *A feedback from multisensory to unisensory areas.* Our models assume that the multisensory representation sends a feedback to the primary sensory areas



(see also [Driver and Spence 2000](#)). In view of this feedback, the unisensory areas can be affected by the other sensory modality, i.e., the unisensory representation can change as a consequence of a change in the other unisensory representation, with the occurrence of interesting cross-talk effects. This is an essential aspect to implement a reciprocal influence between the two unisensory representations (for instance, to mimic ventriloquism). It is worth noting that our models suggest that the strength of this feedback mechanism should be reinforced in situations of conflict (to favor the prevalence of the stronger stimulus), but reduced in normal conditions (to avoid illusory experience). This consideration opens the problem of how the system can be actively controlled by external inputs. Such a problem, in turn, may deal with the role of attention in neurocognitive science, and with the existence of higher hierarchical centers, which can plan and implement more sophisticated high-level strategies.

4. *Parameter changes.* Several parameters in the model can be modified to simulate individual variability and/or pathological conditions. This aspect opens the possibility to build a family of models, which share the same theoretical structure and make use of the same mechanisms, but exhibit different behavior in response to the same stimuli. While the potentialities of this approach are evident for what concerns the study of neuroclinical problems and the simulation of procedures for neurorehabilitation, they may also be exploited to build flexible artificial systems.
5. *Synaptic plasticity.* Certainly the most intriguing aspects of neurocomputational models consist in the possibility to learn from the external environment and to adapt behavior on the basis of previous experience. The model of visuo-tactile integration presented above is an excellent example of these possibilities, in that it can mimic how the peripersonal space representation may be plastic and modified by practice. Presently, we are working on an extension of the audio-visual integration model in the superior colliculus, assuming that multisensory enhancement is not an innate property of the system, but one which develops from experience in a multisensory environment [this hypothesis agrees with physiological experiments, see ([Stein 2005](#))]. The reader can find preliminary results on this extended model in [Cuppini et al. \(2008\)](#). We claim that inclusion of synaptic plasticity may open enormous possibilities to any multisensory system, providing it with the capability to track the statistical changes in its environment, and to adapt its behavior to maximize specific goals.

Although we are aware that inclusion of all these aspects in real devices is still at a pioneering stage, we hope that at least some of these ideas may inspire new artificial systems devoted to sensory fusion in a not-too-distant future. Regardless of practical applications, however, neurocomputational models are invaluable to improve our comprehension of how the brain works, and to summarize the plethora of existing data on sensory merging into a coherent theoretical structure. The latter may be a repository of our knowledge and may drive future neurophysiologic experimentation, as well as may inspire new ideas for future research.

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