The University Of Sheffield.

Investigating cortical homeostatic plasticity in the context of touch

Degree: MSc Cognitive & Computational Neuroscience

Department: Department of Psychology, The University of Sheffield, Sheffield, United Kingdom

Registration number: 190218319

Supervisor(s): Dr Hannes Saal & Laura Edmonson

Date of submission: 08/2020

1 Abstract

The cortices of humans and mammals display topographic maps of the body, with each area of the cortex being dedicated to responding to stimuli to a specific area of the body. The sizes of the cortical area dedicated to each body part is largely dependent on the density of receptors. Although the topographic organisation is known, the mechanisms that underpin their plastic nature are debated. Research has been dominated by Hebbian theories of synaptic plasticity, however, homeostatic plasticity has recently become a contending figure, playing an important role in maintaining cortical activity and regulating synaptic plasticity. The current study presents a computational model of homeostatic plasticity that adjusts the firing rate thresholds of cortical units to maintain activity at a desired level. The thresholds generated by the model differed following the presentation of tactile responses to precision grasps compared to power grasps. After applying these thresholds to tactile responses to a tapping paradigm, the cortical maps generated using a winner takes all approach differed. Removing input from digit two led the cortical maps to reduce the area dedicated to this finger, while increasing the similarity of this response to other fingers. These results provide the first proof of concept that homeostatic plasticity, in the form of threshold adjustments, may contribute to changes in cortical maps. Future studies should build on these findings by including homeostatic mechanisms alongside traditional Hebbian plasticity, to investigate the relative contributions to changes in cortical maps.

Contents

1 Abstract

2 Abbreviations

3 Introduction **1**

3.1 Touch . . . 1

3.2 Cortical representation of the body . . . 2

3.3 Cortical plasticity . . . 3

3.3.1 Mechanisms of plasticity . . . 5

3.4 Computational modelling of cortical maps . . . 7

3.5 The current study . . . 8

4 Methods **10**

4.1 Homeostatic model . . . 10

4.1.1 Map setup . . . 10

4.1.2 Model . . . 10

4.1.3 Model investigation inputs . . . 12

4.2 Experimental simulations . . . 12

4.2.1 Map setup . . . 13

4.2.2 Simulation 1: standard input . . . 13

4.2.3 Simulation 2: numbing of D2 . . . 14

4.2.4 Simulation 2: removal of input from D2 . . . 14

4.3 Map analysis . . . 14

5 Results **16**

5.1 Effect of input statistics on homeostasis . . . 16

5.2 Experimental simulations . . . 18

5.2.1 Initial afferent weight training . . . 18

5.2.2 Simulation 1: Standard inputs 19
5.2.3 Simulation 2: Numbing digit two 21
5.2.4 Simulation 3: Removal of input from D2 23
5.3 Summary of results 24

6 Discussion **26**
6.1 Aims and findings 26
6.2 Homeostatic plasticity in different scenarios 26
6.3 Homeostatic plasticity versus Hebbian plasticity 28
6.4 Study limitations and future directions 30
6.5 Conclusion 32

7 Acknowledgements **33**

List of Figures

1 A) The densities of SA1 receptors across the hand. B) An example of stimulus probe placement on the fingertip of D1 (the thumb). C) The SA1 responses to the stimulus placed on the hand 12

2 A figure showing (A) Average afferent response for each finger and palm region used as input to the model. (B) The homeostatic threshold over time and (C) the smoothed average activation of each unit. The vertical black dotted lines indicate a change in the input from power grasps to precision grasps and back to power grasps. The horizontal red line in C indicates the target activation, μ 17

3 The afferent weights pattern trained using a Kohonen SOM algorithm 18

4 Spatial plots of the thresholds for each cortical unit after the presentation of unedited input relating to power grasps (A) and precision grasps (C). Plot B indicates the change in threshold from power to precision. 19

5 Winner takes all activation map following the digit tapping minus the (A) power threshold and (B) precision threshold. Plots C and D show the dissimilarity matrix of the responses of each finger pair, with this represented in two-dimensions in E and F. 20

6 Spatial plots of the thresholds for each cortical unit after the presentation of input with the numbing of D2 relating to power grasps (A) and precision grasps (C). Plot B indicates the change in threshold from power to precision. 21

7 Winner takes all activation map following the digit tapping minus the (A) power threshold and (B) precision threshold. Plots C and D show the dissimilarity matrix of the responses of each finger pair, with this represented in two-dimensions in E and F. 22

8 Spatial plots of the thresholds for each cortical unit after the presentation of input with no input from D2 relating to power grasps (A) and precision grasps (C). Plot B indicates the change in threshold from power to precision. 23

9 Winner takes all activation map following the digit tapping minus the (A) power threshold and (B) precision threshold. Plots C and D show the dissimilarity matrix of the responses of each finger pair, with this represented in two-dimensions in E and F. 25

2 Abbreviations

AMPA α-amino-3-hydroxy-5-methyl-4-isoxazolepropiniod acid

D1 Digit one, the thumb

D2 Digit two, the index finger

D3 Digit three, the middle finger

D4 Digit four, the ring finger

D5 Digit five, the little finger

GCAL Gain control, adaptive, laterally connected

LISSOM Laterally connected synergistically self-organising map

LTD Long term depression

LTP Long term potentiation

MDS Multi-dimensional scaling

MD Monocular deprivation

RSA Representational similarity analysis

SA1 Slowly adapting I

SOM Self-organising map

WTA Winner takes all

3 Introduction

Somatosensation refers to the recognition of bodily sensations (Dunn et al., 2013) and the processing of somatic stimuli (Ferr and Haggard, 2016). One major sub-modality within somatosensation is touch, which relies upon input from a variety of mechanoreceptors (Kaas, 2011). Whilst the majority of sensory research has focused on the visual system, comparatively little research has been dedicated to investigating touch (Hutmacher, 2019). Input from tactile mechanoreceptors combines with other somatosensory input to allow one to get a sense of limb movement, limb position and force (Jones, 1994). The distribution of these receptors differs across the body (Corniani and Saal, 2020; Par et al., 2002). The cortical representation of the body in the sensory cortex was first mapped by Penfield and Boldrey (1937), yielding the sensory homunculus. This mapping showed that areas of the body with higher densities of mechanoreceptos possess a larger area of cortex. The general organisation of sensory cortices is known: that areas of the body with greater innervation densities have larger areas of the cortex dedicated to processing the information. However, this organisation is malleable through the process of cortical plasticity. The precise mechanism by which these maps change depending on changes in sensory input remains debated. Synaptic plasticity - the process by which the efficiency of the synapse between two neurons changes as a function of the timing of pre- and post-synaptic activity - has been the focus of research investigating these changes. Recently, homeostatic plasticity has been identified as a candidate with the potential to influence cortical maps (Li et al., 2014; Ranson et al., 2012). As homeostatic plasticity has not been investigated using a computational model, the current study first will fill this gap in the literature. First, a computational model a homeostatic mechanism that adjusts firing rate thresholds of cortical units to maintain activity at a desired level will be presented, before investigating how homeostasis influences the cortical representations of the hand.

3.1 Touch

Touch can be considered the most important sense (O'Shaughnessy, 1989), perhaps as deficits cannot be compensated for by other senses (Robles-De-La-Torre, 2006). One calls upon this sense in almost everything they do, from picking up a pen to stroking their pet. The fingertips of the hand are

especially important as they possess a greater density of receptors than in the palm (Johansson and Vallbo, 1979), allowing for improved sensory acuity (Johansson and Vallbo, 1983), as demonstrated by better sensitivity on two-point discrimination tasks (Gellis and Pool, 1977; Stevens and Choo, 1996).

The sense of touch relies upon four different mechanoreceptors, divided into classes depending on the feature of the stimulus that they respond to: rapidly adapting (I and II) and slowly adapting (I and II) fibres. Each receptor type responds in a distinct way to cutaneous stimuli (Johnson, 2001), with contributions from all converging to allow for effective tactile processing (Saal and Bensmaia, 2014). The density of these four receptors varies depending on the location in the hand at which they reside (Johansson and Vallbo, 1979).

Brodmann area 3b (Brodmann, 1909), often termed 'S1-proper' (Kaas, 2011), contains neurons that respond to tactile information (Iwamura et al., 1993). The information from cutaneous mechanoreceptors reaches 3b after being relayed via the ventral posterior lateral thalamus. The following section will detail the organisation of the neurons in area 3b before exploring mechanisms by which this organisation changes.

3.2 Cortical representation of the body

Within the cortex, there are cortical maps, which display the organisation of neuronal populations within an area of the brain (Bednar and Wilson, 2016). Neurons within a specific area of the cortical map respond to sensory input to a specific area of the body. This topography has been identified in primary visual cortex, in the form of retinotopic maps (Tootell et al., 1998; Fox et al., 1987) and in the primary somatosensory and motor cortices in the form of somatotopic maps (Penfield and Boldrey, 1937; Okada et al., 1984; Schweizer et al., 1984; Rao et al., 1995).

When comparing the relative densities of sensory receptors in the skin to the size of the cortex dedicated to processing its inputs, there is a clear relationship: areas with greater densities of mechanoreceptors in the somatosensory cortex and photoreceptors in the visual cortex have a larger area of the cortex devoted to processing the inputs from that area (Catania, 2011). The prime example of this is in the visual

cortex with the over-representation of the fovea, where there is the greatest density of cones (Goodchild et al., 1996; Curcio et al., 1990), in comparison to the periphery of the retina (Azzopardi and Cowey, 1993; Cowey, 1964). When considering the body, the exact sizes of the different body parts depend on the exact area of the brain (Hlutk et al., 2001). In area 3b, there are distinct regions for each of the digits on the hand (Martuzzi et al., 2014; Merzenich et al., 1987), which is expected due to the importance of being able to identify upon which finger a stimulus is present. In the context of touch, areas of the body with high densities of sensory receptors possess greater cortical areas. There is a correlation between tactile hyper-acuity thresholds and cortical area size, with larger areas allowing for a lower threshold (Duncan and Boynton, 2007). This indicates that fingers with larger areas of the cortex dedicated to their processing allows for greater acuity to be achieved. These maps are therefore thought to provide an effective structure to facilitate the processing of sensory input (Kaas, 1997; Maldjian et al., 1999).

3.3 Cortical plasticity

Topographic maps in the cortex are stable over time (Kolasinski et al., 2016) , but they are by no means fixed and many changes can be brought into fruition through multiple experimental paradigms, such as the removal of sensory input from a region through anaesthesia, deafferentation and amputation, the changing of input statistics through digital syndactyly (e.g gluing two fingers together) and implanting of new tissue (Merzenich and Jenkins, 1993). This flexibility of cortical maps is referred to as cortical plasticity. Plasticity can occur on multiple levels, from local influences on individual synapses to more global influences on firing thresholds.

The critical period is a phase during which an organism is influenced to a greater extent from sensory stimuli (Sengpiel, 2007). It is this period that the formation of cortical maps is highly dependent on, and plasticity is enhanced. In the case of the touch in humans, this period is between six and ten months post birth (Fabrizi et al., 2011; Kida and Shinohara, 2013). The period can also be shifted by rearing animals in different environments (Mower, 1991; Chang and Merzenich, 2003). The critical period is not the only time when plasticity is present, in fact plasticity is also present both before and after the critical period (Levelt and Hübener, 2012). Research into cortical plasticity typically uses sensory

deprivation. For example, monocular deprivation (MD) in humans has identified a short-term alteration in responses in primary visual cortex to stimulation of both eyes (Jamal and Dilks, 2020). This research also identifies that MD leads to the invasion of the cortical area dedicated to the deprived eye by the non-deprived eye. This shows that altering input statistics to the brain via sensory deprivation can elicit changes in cortical maps. However altering the luminance to each eyes did not affect ocular dominance maps (Jaffer et al., 2012). Therefore mechanisms of plasticity are likely to be different depending on which scale is being considered with different mechanisms being present in different layers of the cortex (Crozier et al., 2007).

In somatosensory cortex, acute changes in the somatotopic maps resulting from amputation can occur within a single 24-hour period (Borsook et al., 1998). Following upper limb amputation, it has been observed that areas in the cortex that respond to stimuli from elsewhere on the body, for example the face, begin to enlarge and intrude on the areas that previously responded to the now amputated hand (Yang et al., 1994). Additionally, following anaesthesia of the thumb, the distance between the representations of the thumb and neighbouring digits decreased (Waberski et al., 2003). Not only are changes observed within hemispheres, but the cortical hemisphere deprived of input following amputation can be employed to assist in processing of sensory input from the intact arm and hand (Makin et al., 2013). These studies all show that the deprivation of sensory input to the somatosensory cortex leads to a change in the cortical representations of the body and that such changes can occur quickly.

Studies have also investigated the effects of increased stimulation of the hand on the somatotopic organisation of the cortex. Results have shown that areas that are stimulated more begin to possess a larger area of the cortex (Jenkins et al., 1990), further showing that cortical plasticity is highly dependent on the input received. Furthermore, the increase in stimulation of the fingertip not only improves two-point discrimination ability of the finger, but this improvement also occurs on the face (Muret et al., 2016), which is the neighbouring area in the cortex. This improvement at across the cortical border also seems to only happen as a result of an increase in inputs, and the opposite does not occur when there is a decrease in input. This relationship is present following stimulation to the hand alone, not the forearm, indicating a relationship between the hand and face regions in the cortex (Muret and Dinse, 2018), with

plasticity occurs across neighbouring cortical regions, ot neighbouring body parts.

To summarise the research on plasticity discussed above, the findings demonstrates that changes occur following multiple interventions. However, it is not clear exactly what mechanisms contribute to the changes, although there is an indication that changes occur as a result of an increase in input more so than a decrease in input.

3.3.1 Mechanisms of plasticity

There are many different mechanisms thought to play a role in this dynamic feature of the cortex, but up until now, research has focused on synaptic plasticity involving Hebbian learning (Hebb, 1949). Hebb's postulate for learning states that "when an axon of cell A excite[s] cell B and repeatedly or persistently takes part in firing it A's efficiency, as one of the cells firing B, is increased" (Hebb, 1949) More specifically, long term potentiation (LTP) and long term depression (LTD), via spike timing dependent plasticity, have been accepted as the way that synaptic efficiency is increased and decreased respectively. The notion that "cells that fire together wire together" has been the primary driver of theories and models of cortical plasticity since. However, there are other forms of plasticity which have been discovered that may contribute to changes in cortical maps in sensory cortices.

When considering synaptic plasticity, there are multiple different avenues to consider (Klintsova and Greenough, 1999). It has been proposed that synaptic plasticity occurs in at least six forms (Lisman, 2017), with mechanisms occurring on either, or both, the pre- and post-synaptic neurons, as well as the formation of new synapses or removal of existing synapses, and there may even be contributions from 'silent' synapses (Rumpel et al., 1998). This synaptic growth is promoted by substances known as neurotrophins, which contribute to altering and maintaining connections in the mature central nervous system (Lindsay, 1994). When neurotrophins are added into a system, LTP is inducible much earlier (Figurov et al., 1996), indicating that this substance plays a vital role in the strengthening of synaptic connections, and therefore plays a role in synaptic plasticity. Neurotrophins have also been proposed to increase in the number of AMPA receptors on cortical neurons (Narisawa-Saito et al., 1999), which in turn are implicated as having a key role in synaptic plasticity over other forms of learning (Zamanillo

et al., 1999). This short description of the involvement of multiple different aspects of neuronal biology indicates the complexity of synaptic plasticity.

The mechanisms described above have been used as explanations for cortical plasticity. When a finger is stimulated continuously, the afferent neurons responding to the stimulus continues to fire, causing neurons downstream that are connected to these neurons to also fire. As these neurons are firing regularly, with the post-synaptic neuron firing shortly after the pre-synaptic neuron, the efficiency, or strength, of the synapse connecting these neurons increases. This increase occurs due to the growth of excitatory receptors, such as AMPA receptors. Furthermore, the neuron responding to the continuous stimulation will form synapses with other neurons. As a result of this, the number of neurons that respond in the cortex increases, and the strength of the response is also larger. After a series of sessions, the region in the cortex, and therefore the area in the cortical map, responding to input from the over-stimulated finger is then larger, and thus cortical plasticity has been induced via Hebbian long-term potentiation.

Not only is Hebbian synaptic plasticity complex, but there are some limitations associated with this. Hebbian plasticity relies upon a positive feedback loop (Zenke and Gerstner, 2017), which itself implies that changes can only occur when input is present as without input, there can be no positive feedback. This feedback strengthens synapses where there is co-activation of the pre- and post-synaptic neuron. Without a regulatory mechanism, this positive feedback will continue, strengthening synapses continuously. However, within the brain, this cannot occur and there must be a limit to the strength of the synapse. There is evidence that LTP cannot be evoked in synapses containing large dendritic spines (Matsuzaki et al., 2004) indicating there is point where synaptic strength is saturated. However, if too many synapses reached this point of saturation, then the network would become unstable as the positive feedback loop leads to an endless cycle of synapse strengthening, with cortical activity being continuously high. Therefore there must be another mechanism that prevents this from happening so that cortical activity remains stable, even through the strengthening of some synaptic weights.

Homeostatic plasticity is one of the newer mechanisms thought to influence cortical plasticity.

Although variants of this form of plasticity have been around for a long time, with the first paper on synaptic scaling being published in the 1990s (Turrigiano et al., 1998), research has recently begun to indicate its importance in cortical networks. Homeostatic mechanisms, which are much simpler that their synaptic counterparts, work alongside Hebbian alterations of synaptic weights to facilitate cortical plasticity (Turrigiano and Nelson, 2000). Homeostatic mechanisms are involved in maintaining a desired level of cortical activity (Turrigiano and Nelson, 2000), with alterations being made based on the input to the network (Hou and Man, 2012). These mechanisms can therefore be seen as regulating the activity and subsequent plasticity in the cortex. Multiple homeostatic mechanisms are present in the cortex and each one is responsible for the regulation of cortical circuits via different mechanisms (Wu et al., 2019).The adjustments of firing rate thresholds is essential for firing rates to recover to baseline levels following sensory deprivation whereas synaptic scaling is required for correlations in activity to recover (Wu et al., 2019). In order for homeostatic mechanisms to influence plasticity, attenuation of Hebbian mechanisms must occur due to the slower timescale along which homeostatic mechanisms exert their effects in comparison to synaptic adjustments. As a result of this, the current study will not include Hebbian adjustments to synaptic weights, but will focus solely on the alterations of cortical unit thresholds.

The thresholds of cortical neurons play a key role in the activity of neurons in response to stimuli, and this activity is key for the development and plasticity of cortical maps. By altering of these thresholds via a homeostatic mechanism, different cortical activation patterns may be identified in response to stimuli. For example, if the thresholds for neurons responding to the index finger are high, then the activation of these neurons following the presentation of a stimulus on this finger will be low. Conversely, if the thresholds for these units are low, then the activation of these neurons to the same stimulus will be higher. These changes in activation could therefore have knock-on effects on the cortical maps generated in response to stimuli, which is what this study will investigate.

3.4 Computational modelling of cortical maps

Such cortical representations and characteristic architectures have been the target of models investigating cortical map formation. These have been recreated using computational algorithms, such as the Kohonen self-organising map (Kohonen, 1982; Kohonen and Honkela, 2007), LISSOM (Sirosh and Miikkulainen, 1994a) and GCAL (Stevens et al., 2013). These algorithms all follow one accepted hypothesis for the formation of the topographic organisation in the cortex: they form as a result of self-organisation of neurons. Self-organisation refers to a process by which the global arrangement of a system arises from lower-level interactions in the system, without reference to the global pattern (Camazine et al., 2003). This hypothesis is driven by the notion mentioned earlier: that ”cells that fire together wire together”. Following this rule, neurons that respond to similar input develop strong synapses with each other and group together. The grouping of these neurons represents the groups of neurons seen in cortical maps in the brain. The majority of research creating and implementing models that follow Hebb's postulate in a self-organising manner has been carried out in the context of vision and have successfully been able to recreate some aspects of the characteristic architecture in the primary visual cortex revealed during experimental studies (Goodhill, 2007), such as ocular dominance columns and orientation preference pinwheels (Erwin et al., 1995; Obermayer et al., 1990; Miikkulainen et al., 2005; Sirosh and Miikkulainen, 1994a), as well as the discontinuities seen in the somatosensory cortex (Stafford and Wilson, 2007) and whisker orientation preference maps in the rodent whisker barrel cortex (Wilson et al., 2010). . The fundamental operation of each of the following models can be explained in terms of dimensionality reduction, that is taking high-dimensional data and finding the principle components that explain the majority of the variance in the inputs (Ritter et al., 1992).

The element of plasticity that these models focus on in the development of cortical maps is synaptic plasticity in the form of Hebbian learning. While this has been used successfully to recreate maps, it is not known whether a much simpler mechanism, such as the homeostasis presented in the current study, is able to explain the changes without the aid of local Hebbian alterations.

3.5 The current study

The current study will present a computational model of homeostasis. The model implemented focused on the altering of neuronal thresholds and thus overall activation of cortical units. Following the presentation of this mechanism, the model will be used to investigate whether homeostatic mechanisms influence cortical maps of the hand in the context of touch. Inputs to the model will be of tactile responses generated using Touchsim (Saal et al., 2017), a computational model of mechanoreceptor responses to stimuli on the glabrous skin of the hand.

Input sets relating to different categories of FEIX grasps (Feix et al., 2015) will be used to investigate how the threshold of each cortical unit changes. To examine whether homeostatic mechanisms are able to explain changes to the representation of the hand in the cortex, cortical maps will be generated. The settled homeostatic threshold will be applied to the unit activation prior to map generation. Further investigations will look to mirror experimental studies that have identified changes to cortical maps following the removal of sensory input from a finger (Merzenich and Jenkins, 1993). Following this change in responses, the current study will investigate how the threshold values and cortical maps change based on sensory deprivation of a finger.

It is hypothesised that:

1. **Training the homeostatic model on different inputs will yield different firing rate thresholds.** In order to maintain a desired level of cortical activity, thresholds must be adjusted individually. When there are high input levels to some units, the threshold will increase to bring cortical activity down to the desired level. Conversely, where there are low input levels, the threshold will decrease to all activity to reach the desired level.

2. **Applying different thresholds to activation values will lead to different cortical maps.** Different threshold values will alter activity in different ways. A high threshold will reduce activation levels dramatically, while a low threshold will have a smaller influence on activation. As a result, cortical maps will change based upon the thresholds applied.

3. **Following sensory deprivation, the area of the map responding to the deprived finger will shrink.**

   This is in line with previous research identifying a shrinking in cortical area following the reduction of input from a finger via deafferentation and amputation (Merzenich and Jenkins, 1993; Yang et al., 1994).

4 Methods

The current study consisted of two sections. First, the current study presents a homeostatic model designed to maintain the activity of each cortical unit to a target level. Second, three experimental simulations are run using this model investigating how the homeostatic model may influence cortical maps.

4.1 Homeostatic model

4.1.1 Map setup

The cortical sheet consisted of 900 units, arranged in a 30 x 30 square. Each input unit is connected to every cortical unit via feed-forward afferent weights, with there being no lateral connections between cortical sheet units. Prior to the training of the homeostatic model, during which threshold values for each cortical unit in the map are generated based on the inputs provided, the cortical units were initialised so that each section of the cortical sheet responded favourably to input from a single region of the hand. The weights in each section of the map were strongly biased to the same extent, so that each unit responded in the same manner. Following this, these afferent weights were kept static throughout the training of the homeostatic model.

4.1.2 Model

The model implemented in the current study focused solely on the implementation of a homeostatic mechanism responsible for adjusting neuronal firing rate thresholds. The model included only the input and a cortical sheet. Only feed-forward afferent connections were included in the model, with lateral connections omitted. Afferent weights are specified prior to running simulations and do not change throughout the training of the model. By not including Hebbian learning, the current study is able to focus solely on the contributions to cortical map changes based on homeostatic mechanisms. The activation,

η, of each unit is calculated as a dot product of the inputs, s, and afferent weights, w:

$$\eta_i = w_i s_i \tag{1}$$

The threshold from the previous time step is then taken away from the incoming activation value for each unit:

$$\eta_i = \eta_i - \theta(t-1) \tag{2}$$

where $\theta(0)$ is the initialised threshold value for all cortical units, set at 0.05 for the simulations in this study. The mechanism is summarised by the following equations, which ensure that the average activation converges to a target activation, μ. The core of the homeostatic model is a two-step mechanism. First, a smoothed 'average activation' for each unit, $\bar{\eta_i}$, is calculated:

$$\bar{\eta_i} = (1-\beta)\eta_i + (\beta\bar{\eta_i}(t-1)) \tag{3}$$

where $\bar{\eta}(0) = \mu = 0.05$ for all simulations in the current study and β is a smoothing parameter. The current study used a value of $\beta = .991$. In step two, the threshold for each unit, θ_i, is then calculated using the smoothed average activation value:

$$\theta_i(t) = \theta_i(t-1) + (\lambda\bar{\eta_i}(t) - \mu) \tag{4}$$

where λ is the homeostatic learning rate, with $\lambda = .001$ for the current study. The second half of this equation calculates the error between the smoothed average activation and the target activation so

the threshold is adjusted accordingly. The final activation value of each unit was then calculated.

$$\eta_i = \eta_i - \theta_i(t) \tag{5}$$

4.1.3 Model investigation inputs

To test that the homeostatic mechanism was functioning correctly, two sets of inputs were generated, corresponding to tactile responses, simulated using Touchsim (Saal et al., 2017) to different classes of FEIX grasps (Feix et al., 2015). These inputs were calculated based on which areas of the hand are in contact with the item being grasped. The first set of inputs were simulated tactile responses from the hand to a series of power grasps, where all four fingers and the thumb are used to grip something firmly, such as when gripping a tennis racket. The second set of inputs were simulated responses to a series of precision grasps, where few fingers are involved in holding an object lightly such as holding a pen when writing. The power grasp responses were presented prior to the responses to the precision grasps, before presenting the response to the power grasps once again. Each block consisted of 5000 iterations to allow the homeostasis to settle at a threshold value that maintains the activation of each unit at the desired activation.

4.2 Experimental simulations

The following experimental simulations focused on responses from one class of afferent: slowly adapting I. The densities of this receptor across the hand can be seen in Figure 1.

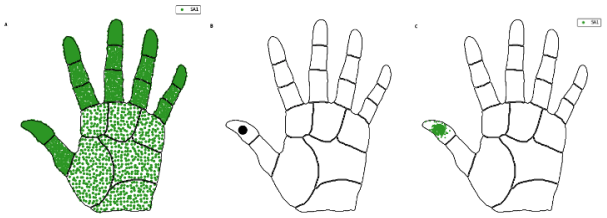

Figure 1. A) The densities of SA1 receptors across the hand. B) An example of stimulus probe placement on the fingertip of D1 (the thumb). C) The SA1 responses to the stimulus placed on the hand

Three different paradigms were simulated, each containing two separate conditions: unedited input, numbing of digit two and removing all input from digit two. All three paradigms involved simulating afferent responses to the a circular stimulus placed on each of the five finger tips sequentially to emulate tapping Figure 1, which is often carried out in fMRI experiments. The radius of the probe used in these simulations was 8mm, and the probe indentation into the skin was 5mm. The stimuli location used on each finger was the same for each of the following three simulations. The responses to these stimuli Figure 1 were then used to calculate cortical maps based on the activation of each cortical unit using a 'winner takes all' approach.

4.2.1 Map setup

In order to generate the initial afferent weights organised in a somatotopic manner, reflecting the cortical organisation of the primary somatosensory cortex, that would generate the weight matrix to be used in the homeostatic model and tapping paradigms, a Kohonen SOM algorithm was implemented. Weights were initially random, but following training the weights become more biased to input from a specific finger. Following the presentation of a stimulus to the cortical units, a 'winning unit' is calculated based on the strongest response to the stimulus. A Hebbian rule is then used to update the weights, thought to mirror cortical map development (Liang et al., 2008), with neighbouring units also receiving a strengthening in the weight. This neighbourhood update allows for units responding the similar inputs to be grouped together in the map, biasing the responses of the map to input from a certain finger. This map was trained using tactile responses to both power and precision grasps. Following this, these afferent weights were not further adjusted and the same weight arrangement was used for all of the following simulations.

4.2.2 Simulation 1: standard input

In this simulation, the homeostatic model was trained using unedited firing rate input to power and precision grasps and was allowed to settle after each stimulus set to generate two threshold values, one for each grasp type. Responses to the stimulus placed on each fingertip also remained unchanged prior

to the application of the two thresholds. To compare the effect of homeostasis on the maps generated, each threshold was subtracted from the responses to the stimuli. Activation maps were then generation using these new values.

4.2.3 Simulation 2: numbing of D2

To replicate studies investigating the effect of anaesthesia on cortical representations, the current study lowered the responses of digit two, the index finger, to stimuli by 90 percent. This mirrors the effect of anaesthesia, which blocks receptors and thus blocking sensory input from subsequently reaching the cortex, whilst some crude sensations are felt, such as pressure. This lowering of input was applied to both the homeostatic model, so that threshold values could be calculated accordingly, and the responses to the stimulus applied to each fingertip. These new threshold values were subsequently applied to the responses to the fingertip stimuli prior to the calculation of the activation map.

4.2.4 Simulation 2: removal of input from D2

Previous studies have often investigated how deafferentation or amputation can influence the cortical representation of the body. To simulate this, responses from digit two were completely removed in both the homeostatic model and in the responses to stimuli placed on the finger tip. As in the previous simulations detailed above, the homeostatic thresholds were applied to the fingertip responses prior to the calculation of the winner takes all activation map.

4.3 Map analysis

While it is possible to visually identify differences between the cortical maps generated in the current study, representational similarity analysis (RSA) (Kriegeskorte et al., 2008) was carried out on all of the maps generated. RSA yields a dissimilarity matrix is calculated based on how dissimilar the responses are from each pair of fingers. Within the dissimilarity matrix, high values indicate that responses from the two fingers being analysed are unique in that they are spatially distant. This therefore provides a measure of spatial similarity that allows for one to identify how alike evoked fMRI responses

to stimuli are. Multi-dimensional scaling (MDS) is then implemented to visualise the distance between responses from each finger on a two-dimensional plane, where high dissimilarity values are displayed as two points being further apart from each other, with similar responses being represented by two points being close together. Using MDS, it is clearer to see the differences in the maps elicited by the alterations of the input patterns used.

5 Results

5.1 Effect of input statistics on homeostasis

To ensure that the homeostatic mechanism was able to change the thresholds of the cortical units to maintain activity at the target level, datasets generated to two different grasp types were presented. The input data reflecting afferent responses to power and precision grasps differ and therefore provide an opportunity to ensure that the mechanism could change the threshold to maintain activity to a target following a change in the input statistics.

Figure 2 shows how the average responses of each finger to the different grasp types changes depending on the grasp type. It is clear to see that the responses from digits one (thumb) and two (index finger) increase when transitioning from power grasps to precision grasps. Conversely, the inputs from the palm are stronger for power grasps than precision grasps. This in turn has a clear influence on the homeostatic mechanism.

When the input statistics increase, such as with for digit one and two in the transition from power to precision grasps, there is a clear spike in the smoothed average activation for each unit responding to that finger. This in turn causes the threshold to increase to compensate for this increase in threshold value. The threshold increases to a point where the activation of the cortical unit reaches the target activation, μ. The opposite can be seen when considering the palm, where there is a decrease in the input statistics in the transition from power to precision grasps. Following this transition, the smoothed average activation for the respective cortical units drops. This drop in activation elicits an increase in the threshold for units responding to the palm. A lower threshold allows for the activation of these units to increase back to the target activation.

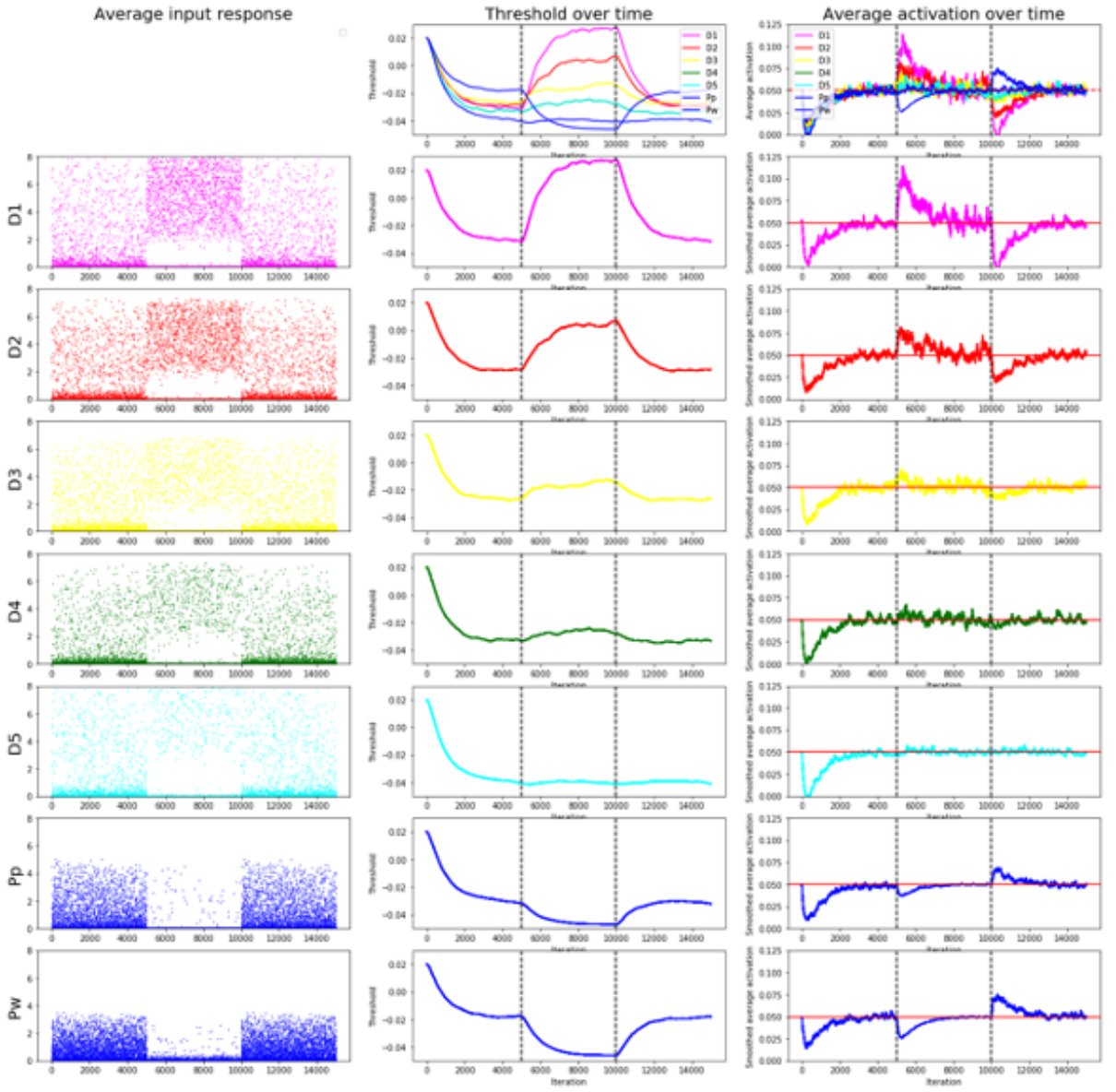

Figure 2. A figure showing (A) average afferent response for each finger and palm region used as input to the model. (B) The homeostatic threshold over time and (C) the smoothed average activation of each unit. The vertical black dotted lines indicate a change in the input from power grasps to precision grasps and back to power grasps. The horizontal red line in C indicates the target activation, μ

5.2 Experimental simulations

5.2.1 Initial afferent weight training

Using inputs relating to afferent responses to both power and precision grasps, the Kohonen SOM yielded the following afferent weights that would be used for the remaining simulations (Figure 3). This figure shows that there are large clusters of units responding to input from the palm, digit one and digit two, with small clusters responding to the remaining digits, similar to what is seen in cortex.

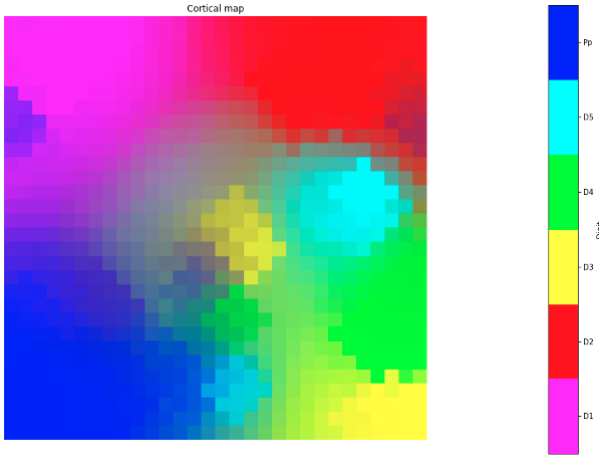

Figure 3. The afferent weights pattern trained using a Kohonen SOM algorithm

Following each simulation, three different plot types are presented. The first is an activation map, calculated using a 'winner takes all approach' following the application of the homeostatic thresholds. After the presentation of the stimulus on each fingertip sequentially, a response matrix is generated for each finger. These matrices are then combined, with the finger with the largest activation of each unit being the 'winner'. This winner takes all matrix is then plotted, with a different colour being used for each finger. The second plot is a dissimilarity matrix, calculated using representational similarity analysis (RSA). These plots are similar to correlation matrices. The darker the shade of blue in these plots, the more dissimilar the response between two fingers are, with lighter shades indicating low dissimilarity. Multi-dimensional scaling (MDS) plots transform the RSA dissimilarity matrices into two dimensions to better visualise the response similarities. In these plots, the further apart two points are, the more

dissimilar their responses, with similar responses being represented by points located close to each other

5.2.2 Simulation 1: Standard inputs

Thresholds: The homeostatic mechanism was trained using unedited inputs, yielding the following threshold patterns (Figure 4). It can be seen that there is a large increase in the thresholds for the units that respond to digit one (in the top left hand corner of the map). Conversely, there is a clear decrease in threshold for units that respond to the palm (in the bottom left corner of the map), supporting the previous investigation that revealed that the threshold changes based on input statistics.

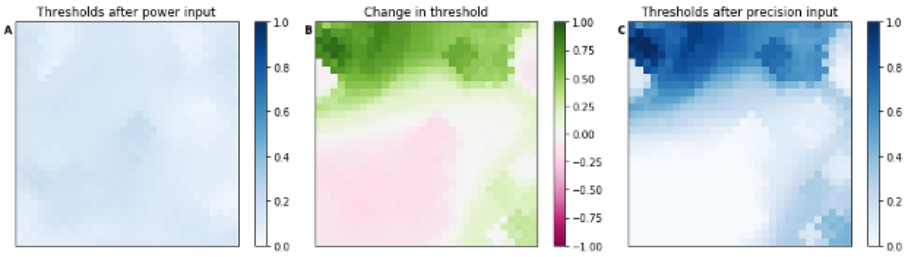

Figure 4. Spatial plots of the thresholds for each cortical unit after the presentation of unedited input relating to power grasps (A) and precision grasps (C). Plot B indicates the change in threshold from power to precision.

Tapping: Following the placement of a stimulus the each finger, each of the two thresholds (power and precision) were subtracted from the initial activation values. The WTA map following the subtraction of the power and precision thresholds can be seen in Figure 5. Clear differences can be seen by looking at these maps alone: There is a larger area dedicated to D1 following the subtraction of the power thresholds compared the precision thresholds. This change is concurrent with the differences in threshold values for units responding to D1 that are lower following training on the power grasps than the precision grasps. When comparing the power and precision conditions, the areas dedicated to digits one and two shrink, whereas the areas of the map reflecting digits four a five increase. This occurs due to there being a higher threshold for digits one and two in the precision condition than the power condition, with the opposite being the case for digits four and five. This difference provides the first indication that threshold changes determined using a homeostatic mechanism may alter cortical organisation.

Inspection of the dissimilarity matrix (Figure 5) reveals that, following the subtraction of the power thresholds, the response from digit one and digit two are dissimilar to the others. This dissimilarity is reduced when comparing the responses from each finger following the subtraction of the precision thresholds from the initial responses to tapping. This effect can be seen when viewing this matrix is two dimensions using the MDS plots (Figure 5). The distance from digit one and two to the remaining fingers is greatly reduced in the precision condition compared to power condition. This result occurs as the settled homeostatic threshold for these two fingers is significantly higher following training on precision grasps, which in turn lowers the responses from these fingers to a level that is more in line with the other digits.

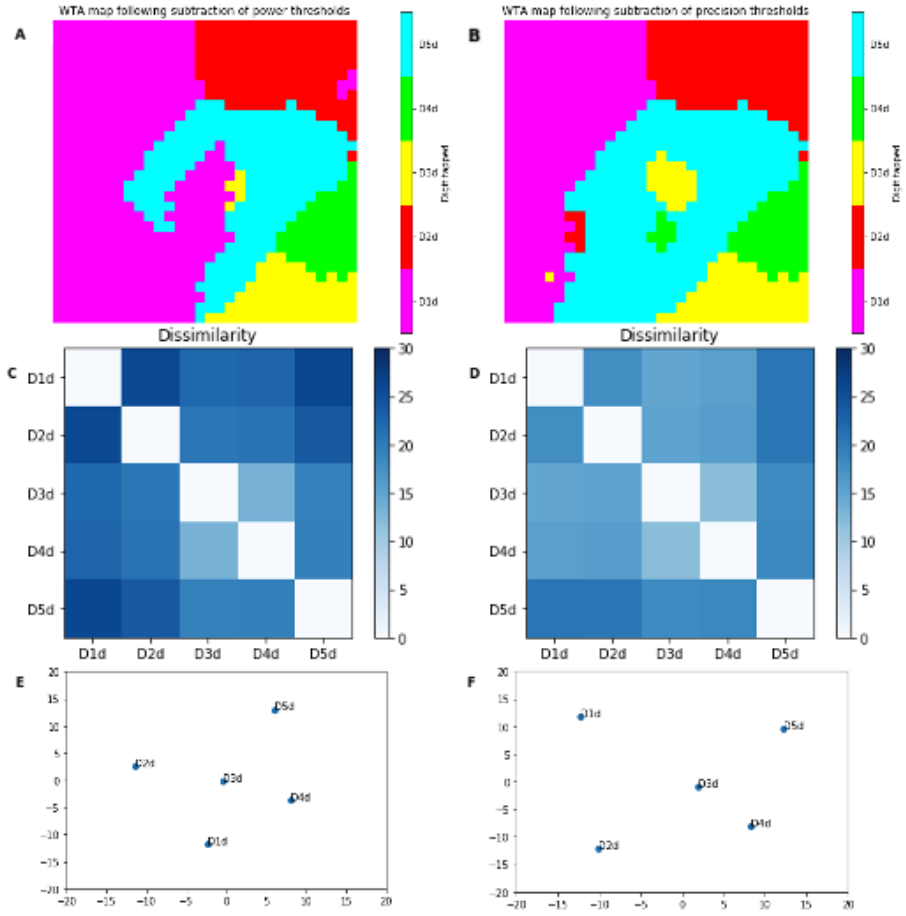

Figure 5. Winner takes all activation map following the digit tapping minus the (A) power threshold and (B) precision threshold. Plots C and D show the dissimilarity matrix of the responses of each finger pair, with this represented in two-dimensions in E and F.

5.2.3 Simulation 2: Numbing digit two

Thresholds: Following the numbing of digit two by reducing the inputs by 90 percent, the threshold for units responding to this finger were consistently lower across the power and precision conditions. The threshold for these units exhibited almost no change between the two conditions (Figure 6).

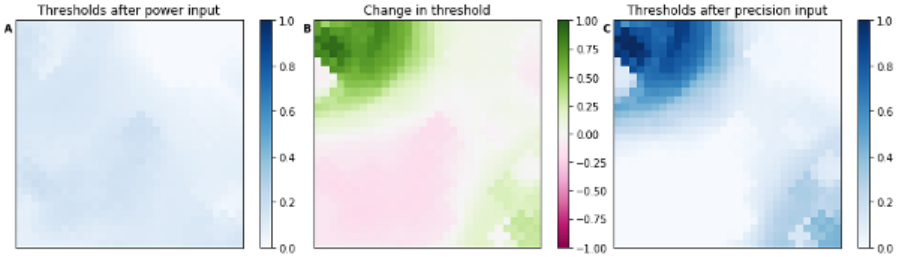

Figure 6. Spatial plots of the thresholds for each cortical unit after the presentation of input with the numbing of D2 relating to power grasps (A) and precision grasps (C). Plot B indicates the change in threshold from power to precision.

Tapping: Reducing the input to the homeostatic model, and the responses to the digit tapping, by 90 percent of the original had some interesting effects on the activation maps generated shown in Figure 7. Comparing between the two conditions in this simulation, it is clear to see that D1 possesses the largest area of the map following the subtraction of the power thresholds. However, following the subtraction of the precision thresholds, the area dedicated to D1 shrinks as the threshold is higher for units responding to this finger. Some units previously responding to digit one change to respond to digit three in the bottom left of the map. This occurs due to the threshold for digit two being a lot lower than digit one. This further indicates that homeostatic adjustments of thresholds for cortical units has an influence over the activation maps generated.

Another observation can be made when comparing these maps to the maps generated in simulation one; the maps generating using inputs involving the numbing of D2, following the subtraction of the settled precision thresholds, have more units responding the digit three. This indicates that the adjustments of thresholds for one finger may have knock-on effects on the representations of other digits. Changes in the map may therefore be explained by the altered threshold produced via homeostatic mechanisms resulting from the change in input statistics for one finger.

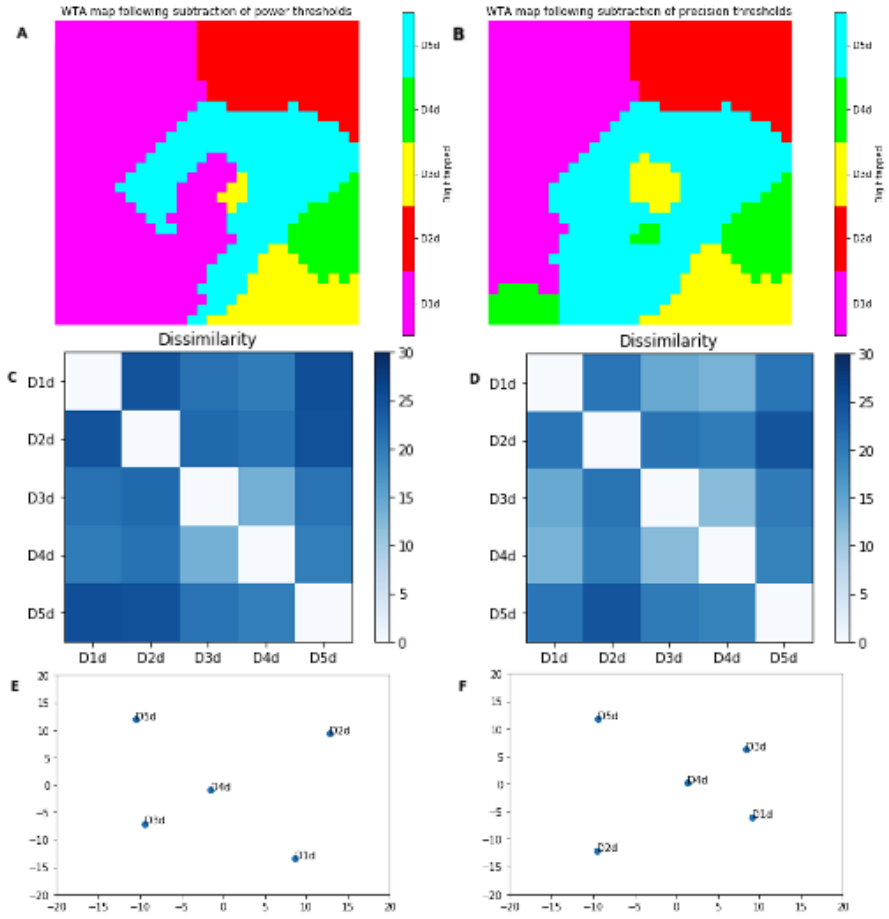

Figure 7. Winner takes all activation map following the digit tapping minus the (A) power threshold and (B) precision threshold. Plots C and D show the dissimilarity matrix of the responses of each finger pair, with this represented in two-dimensions in E and F.

There are also clear differences in the dissimilarity matrices between the power and precision conditions. In the power condition, the RSA matrix reveals that digit one remains dissimilar to the other fingers, as with the standard inputs. This can also be seen when looking at the MDS plots, where it is clear that each digit is spaced out more for this edited input compared to the unedited input. When considering the precision thresholds, digit two, although numbed, possesses the most dissimilar response, with the other responses being equally dissimilar, perhaps due to the lower threshold for the finger. This is as the threshold subtracted from the tapping response is also lower. Digit one's response is also more similar to the other fingers compared to when unedited inputs were used, shown by both the RSA dissimilarity

matrix and the MDS plot. These findings also indicate that the lower thresholds of digit two due to the reduction in input may have an influence on the response from other fingers.

5.2.4 Simulation 3: Removal of input from D2

Thresholds: As in the numbing simulation, the complete removal of input from digit two led to the threshold for units responding to this finger being consistently lower across the power and precision conditions with those units responding the digit two exhibiting no change between the conditions (Figure 8).

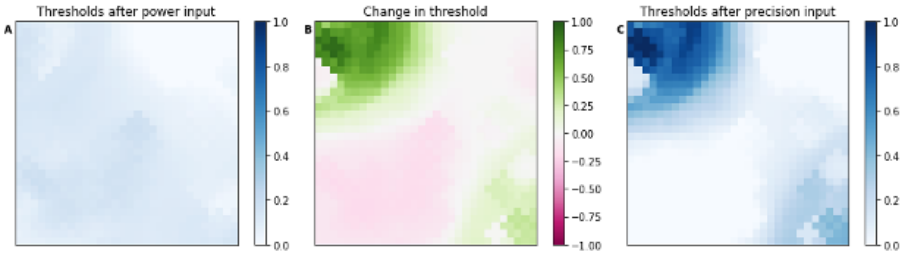

Figure 8. Spatial plots of the thresholds for each cortical unit after the presentation of input with no input from D2 relating to power grasps (A) and precision grasps (C). Plot B indicates the change in threshold from power to precision.

Tapping: When looking at the activation maps, it is clear to see that D2 is barely represented in both maps (Figure 9). Following the subtraction of the power thresholds, D1 possesses the largest area, and in in the precision threshold condition, there is a larger representation of all other digits than in previous simulations. When comparing these maps to the previous maps generated in the two prior simulations detailed above, the space that previously represented D2 is predominantly representing D1, with D3 and D4 also now responding in that region of the map. This finding indicates that homeostatic threshold adjustments, resulting from changes in the input statistics, contribute to changes in map responses. Removing input from a finger leads to drastic changes in the representation of that finger, as well as the neighbouring fingers.

Inspection of the RSA dissimilarity matrices (Figure 9) shows that the response of D1 is more dissimilar relative to other digits. Inspection of the MDS plot reinforces this, showing that D1 is more

distant from the other fingers. The other four fingers are more evenly spaced, with a lower dissimilarity values, indicating their responses are equally similar to each other. This indicates that the homeostatic mechanism influences not on the digit that no longer responds, but also influences the responses of the other fingers. The RSA dissimilarity matrix and MDS plots indicate that, following the subtraction of the precision thresholds from the initial response to the stimulus placed on each finger, each finger exhibits equally dissimilar responses compared to the unchanged inputs and the inputs involving numbed responses from digit two. Throughout all of the simulations, the dissimilarity values for the responses of D4 and D5 remain almost constant, indicating that changes in the input of one finger may influence the representations of neighbouring fingers, while having little effect on digits further apart.

5.3 Summary of results

In summary, the threshold for cortical units increases and decreases depending on input to that unit. For example, units that respond to digit one possess a higher threshold following training on precision grasps, where the input is high, compared to power grasps. Conversely, when the input from the palm decreases following the transition from precision to power grasps, the threshold also decreases. This threshold in turn influences the activation map generated following finger tapping. When the power thresholds are applied, D1 possesses a much larger region of the map than when precision thresholds apply, due to the difference in threshold. When precision thresholds are applied, the area of the map dedicated to D4 and D5 increases relative to when the power threshold is applied. Both of these findings demonstrate the effect of firing rate thresholds on the cortical organisation.

Furthermore, following the changes in input statistics to one finger, the map changes in a way where neighbouring fingers possess a larger response, even when the input statistics for these neighbouring fingers are the same. The response similarity, as measured using representational similarity analysis, also changes; when the input statistics for digit two are set to zero, the response similarity of digit two in comparison to digits three, four and five increases, while the response similarity to digit one decreases. These findings demonstrate that homeostatic plasticity, in the form of threshold adjustments of cortical units, leads to map changes in response to finger tapping in a variety of situations, including the removal

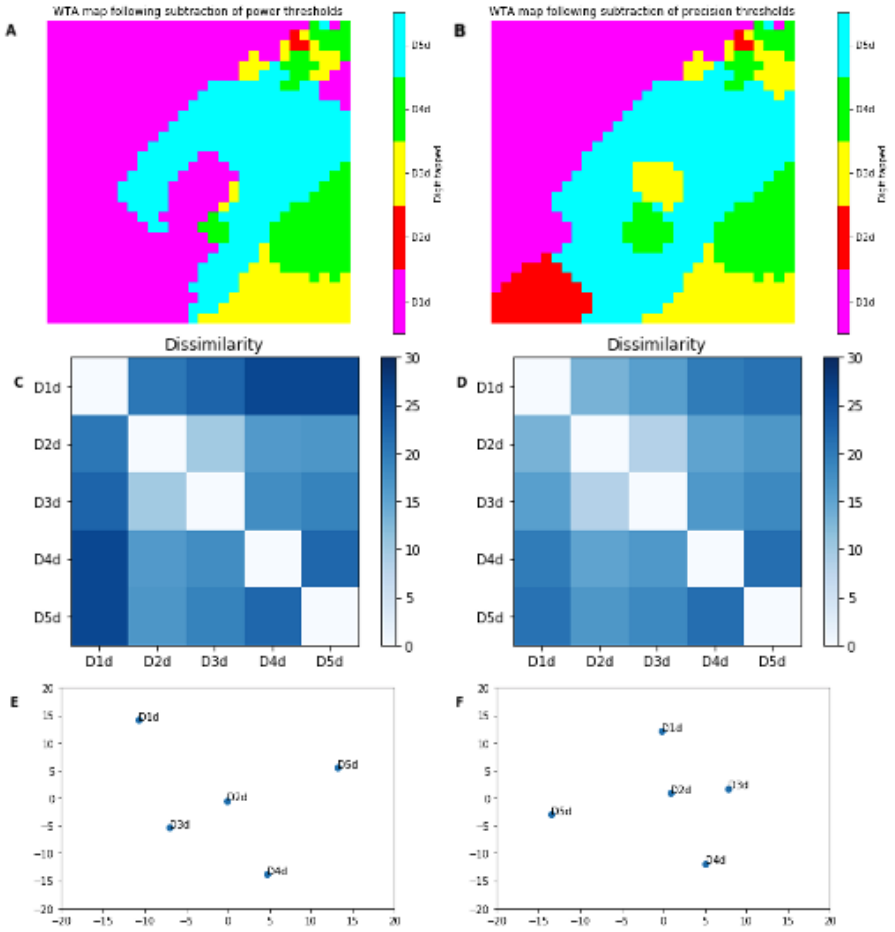

Figure 9. Winner takes all activation map following the digit tapping minus the (A) power threshold and (B) precision threshold. Plots C and D show the dissimilarity matrix of the responses of each finger pair, with this represented in two-dimensions in E and F.

of input from a finger, such as deafferentation. Moreover, changes are not restricted to the finger where the input statistics are changed, but changes also occur in the representations other digits.

6 Discussion

6.1 Aims and findings

The current study aimed to present a homeostatic model that alters the firing rate threshold of cortical units, to maintain activation to the target level, before implementing the model in the context of touch to investigate the role of homeostasis in the generation of cortical maps. Three different scenarios were simulated: unchanged input, the numbing of digit two and the removal of input from digit two. Tactile responses to different grasp types were used to train the model. The settled threshold values were then applied to a tapping paradigm to generate cortical maps.

Homeostatic adjustments of firing rate thresholds of units in the cortical sheet increased and decreased in correspondence with increases and decreases in input to the unit. The application of settled thresholds following power grasp input led to different cortical maps compared to the application of thresholds following precision grasp input. The response similarities, as calculated using representational similarity analysis, also changed depending on the thresholds applied. These findings indicate that homeostatic adjustments of thresholds may contribute to some aspects of cortical map plasticity.

6.2 Homeostatic plasticity in different scenarios

The cortical unit thresholds generated by the homeostatic model differed between the two different input statistics. A large contributor to this is the specific input statistics of each finger. Following the presentation of input relating to precision grasps, the thresholds generated for units responding to the thumb and index finger, which are both used heavily in this grasp type, were a lot higher than those for units responding to the palm, which does not play a big role in these grasps. However, when the model was presented with inputs relating to power grasps, the opposite pattern occurred: units responding to the thumb and index finger possessed a lower threshold compared to the palm, which is used more in power grasps. This finding supports hypothesis one, which posited that different input statistics would lead to different firing rate thresholds and indicates that hand use is a key factor in this homeostatic mechanism. This finding also suggests that mammals with different grasping portfolios, such as marmosets, who can

only execute power grasps, and macaques, who can execute both power and precision grasps (Pouydebat et al., 2009), will possess different cortical firing rate thresholds. Moreover, the same idea can be applied to humans, where not everyone will possess the same threshold values, with different jobs requiring different hand use (Bullock et al., 2013). The differences in hand use will lead to differences in the input statistics to the homeostatic model, leading to each participant possessing unique threshold values. The next step in the study was to investigate the potential consequences of these different threshold values.

To investigate how the differences in homeostatic thresholds would influence cortical maps, simulation one applied thresholds generated following training on inputs reflecting tactile responses to power and precision grasps. This simulation applied the thresholds to the firing rates of tactile receptors in response to a tapping paradigm. The maps generated differed greatly, providing evidence supporting hypothesis two which stated that the application of different cortical firing rate thresholds would lead to different cortical maps. When the power thresholds were applied, digit one possessed a much larger area of the map than following the application of the precision thresholds. This occurred as the threshold for units responding to digits one and two are much higher in the precision condition than the power condition. Similarly, the number of units responding to digits three, four and five increased following the application of the power thresholds. As a result, were both marmosets and macaques to receive the same stimuli to the hand, the maps generated will be different due to the different threshold values. When applying this logic to experimental studies, it is therefore important to consider the impact of differences in hand use, as outlined above, on the threshold values of cortical neurons as these differences may impact the cortical maps identified. While difference in hand use has already been identified as a factor influencing cortical organisation (Lissek et al., 2011), this is the first study to provide an indication that hand use can influence cortical organisation via a homeostatic mechanism. When implementing tapping paradigms, such as the one used in the current study, in experimental research, homeostatic mechanisms should be considered when explaining the mechanisms underlying the changes in cortical maps.

In other areas of the cortex, evidence of different cortical organisations resulting from hand use can be seen. For example, in area 3a, which is responsible for processing proprioception, fingers that are used more often possess distinct representations (Huffman and Krubitzer, 2001; Krubitzer et al., 2004).

In monkeys that are able to execute precision grasps, there is a distinct area for both the thumb and index finger (Krubitzer et al., 2004), and in the striped possum, there is a distinct area for digit four (Huffman et al., 1999) which is used independently to extract insects from deep within trees (Strahan, 1983). The similarities between the cortical organisation of humans and non-human primates allow for the findings to be applied to the human cortex (Sutherling et al., 1992), where one would expect the thumb and index finger to possess distinct representations in area 3a due to their independent movement and use. Experimental studies should therefore consider hand use when investigating the cortical representation of the hand in multiple sample populations as the current study indicates that homeostatic adjustments of cortical firing rate thresholds may be involved in the differences in cortical maps seen between species with different hand use statistics.

Previous studies have changed the input statistics to sensory cortices through many paradigms, often using sensory deprivation (Merzenich and Jenkins, 1993). Simulations two and three were designed to replicate these studies. Following deafferentation, Merzenich and Jenkins (1993) demonstrated that the area of the cortex previously dedicated to processing information from the now deafferented finger has been invaded by neighbouring regions. This finding was replicated in the current study in simulation three where the input from the index finger was completely removed. The removal of input from digit two led to the map generated following finger tapping containing much less of an area dedicated to digit two and thus supporting hypothesis three, which suggested that the removal of input from one digit would lead to the map containing a smaller area dedicated to that finger. This intervention also led to the number of units responding to neighbouring digits increasing. This finding is in line with previous experimental research, and indicates that homeostatic mechanisms may contribute to the reorganisation of the cortical representation of the hand.

6.3 Homeostatic plasticity versus Hebbian plasticity

The results from the three simulations carried out in this study demonstrate that changes to cortical maps can arise without cortical activity increasing or decreasing, and without synaptic weights strengthening beyond a pre-specified point. Whilst evidence is present that suggests homeostatic mechanisms

play a role in cortical plasticity alongside Hebbian learning (Zenke and Gerstner, 2017), the current study is the first to provide proof of concept that homeostatic mechanisms alone may be able to elicit changes in cortical maps.

Hebbian synaptic plasticity has been widely accepted as the main factor influencing cortical circuitry, occurring in at least six forms (Lisman, 2017), with there being a large and continuously growing body of literature investigating its role in the brain. When considering synaptic plasticity, one must consider carefully the timing of both pre- and post-synaptic activity (Stent, 1973), among other things (Klintsova and Greenough, 1999). Although there has been a multitude of studies suggesting that synaptic plasticity can explain changes in cortical reorganisation following changes in the input statistics (Godde et al., 1996; Yazdan-Shahmorad et al., 2018), there are debates regarding the exact mechanism by which it occurs and whether it alone can explain observed changes in the cortex, with evidence growing suggesting the collaboration of Hebbian mechanisms with other mechanisms (Lechner and Byrne, 1998; Turrigiano and Nelson, 2000; Vitureira and Goda, 2013; Zenke and Gerstner, 2017). The current study provides evidence indicating that Hebbian mechanisms are not required to explain some changes in cortical maps. Moreover, compared to Hebbian learning, the homeostatic mechanism outlined in the current study is extremely simple and is able to maintain cortical activity to a desired level. Therefore, the results pave the way to a new interpretation of what causes the changes in cortical maps observed following sensory deprivation, or increased sensory activity, seen in experimental research.

Not only can homeostatic mechanisms go some way in explaining changes in cortical maps following changes in input statistics, but the mechanism modelled in this study overcomes some well-known weaknesses of Hebbian learning. Were Hebbian mechanisms allowed to run free, synaptic weights would strengthen infinitely, leading the network into a recurring positive feedback loop and thus becoming unstable. This does not happen in the cortex, but instead there seems to be a sliding scale of thresholds to ensure that weights run between a minimum and maximum value, as described in the Bienenstock-Cooper-Munro theory (Bienenstock et al., 1982). The current study implements a version of this idea to ensure that cortical activation is maintained at a set level without increasing infinitely. Furthermore, as Hebbian synaptic plasticity, it can be suggested that input must be present for plasticity to take place.

This is not the case with the homeostatic model presented in this study, which adjusts thresholds based on the amount of, or lack of, input data, thus overcoming another problem with Hebbian synaptic plasticity. The activity within the model was able to rebound following a decrease in the input statistics, supporting previous studies that found that homeostatic mechanisms are essential in the rebounding of firing rates back to baseline after inputs were reduced due to LTD, following the attenuation of the Hebbian mechanism (Wu et al., 2019) and research concluding that changes in cortical maps can occur without changes in network connectivity (Hegner et al., 2006).

The varying timescales of Hebbian and homeostatic plasticity (fast and slow respectively) (Zenke et al., 2017) is also important. As homeostatic plasticity occurs over a lengthier time frame than Hebbian plasticity, it is unlikely that the effects will be seen in typical fMRI studies, during which multiple scanning sessions are carried out within hours. Instead, homeostatic plasticity likely mediates changes occurring over days, while Hebbian learning drives the rapid changes seen in most studies. One key role homeostatic mechanisms have in regulating Hebbian weight changes is by ensuring that weights do not continue to strengthen infinitely, but instead work to ensure that there is saturation after a certain point.

6.4 Study limitations and future directions

Although the current study was able to replicate findings of previous literature, the results following the removal of digit two may have an alternative explanation. As cortical maps and cortical plasticity are highly dependent on sensory input (Kilgard et al., 2002), altering these inputs will have an effect. It can be expected that if there is no input from a finger, due to deafferentation, then there will be no representation in the brain

Previous research has identified structural changes at both inhibitory and excitatory synapses following sensory deprivation (Keck et al., 2011), which in turn elicit changes in the organisation of cortical maps (Merzenich and Kaas, 1982). In the context of touch, if there is no tactile input from a finger, then there would not need to be any area of the cortex dedicated to processing this finger. Moreover, there is still information reaching the cortex from the remaining fingers, and their relative importance increases

as there are fewer fingers in total. Because of this, you would expect a larger area dedicated to the remaining fingers and a smaller, or no, area for the deafferented finger in the cortex. Considering both the current study's methodology and findings from previous research, the changes observed in simulations two and three are expected, and are likely to occur as a change of the input statistics, rather than as a result of the homeostatic model presented here.

It is important to note that the adjustment of cortical neuron firing rate thresholds is not the only kind of homeostatic mechanism present in the cortex, with different mechanisms playing different roles (Wu et al., 2019). Some other mechanisms identified in the cortex include synaptic scaling, inhibitory feedback and plasticity of intrinsic membrane properties (Fox and Stryker, 2017). Synaptic scaling has been the focus of homeostatic research, with this mechanism operating globally upon excitatory post-synaptic weights (Turrigiano, 2008). As the name 'synaptic scaling' suggests, this form of homeostasis up- or down-regulates synaptic weights depending on activity, through the use of an error signal, so as to prevent the network becoming unstable. Synaptic scaling can also occur at inhibitory synapses (Kilman et al., 2002), with mechanisms being tuned to match the specific requirements of the neuron and circuit (Maffei et al., 2004). With increasing evidence indicating that synaptic scaling at both excitatory and inhibitory occurs following sensory deprivation (Desai et al., 2002; Lambo and Turrigiano, 2013; Maffei et al., 2004), future studies should incorporate multiple mechanisms into computational models of cortical plasticity. By including multiple mechanisms, researchers would be able to turn mechanisms on and off to investigate their individual contribution to cortical plasticity.

While previous models of cortical development, such as LISSOM (Sirosh and Miikkulainen, 1994a) and GCAL (Stevens et al., 2013) included lateral connections, the current study did not. This was in order to isolate the possible effects of homeostatic plasticity on the cortical maps. However, lateral excitatory and inhibitory connections provide important contributions to the activation of cortical neurons in many sensory areas (Asher et al., 2015; Pantev et al., 2004; Sirosh, 1995; Liang et al., 2017) and their weights are dynamic, with weak lateral connections dying off over time (Sirosh and Miikkulainen, 1994b). Inhibitory lateral connections also aid homeostatic mechanisms by reducing cortical activity levels through their contribution to the calculation of the activity of a neuron. Inhibition-dominant models

have also demonstrated that, in the absence of synaptic plasticity, the dynamic properties of inhibitory connections are able to account for some aspects of cortical plasticity, including the enlargement of receptive fields following sensory deprivation through cortical lesions or deafferentation (Xing and Gerstein, 1996). Therefore, future models investigating cortical plasticity in the absence of Hebbian synaptic learning should include lateral connections as these, in combination with homeostatic mechanisms, such as the one implemented in the current study, may be able to account for more cortical changes following changes in the sensory input statistics.

6.5 Conclusion

The current study presented a computational model of a homeostatic mechanism that adjusts cortical firing rate thresholds to maintain cortical activity at a desired level in the context of touch. As sensory input from a finger increases, such as for the thumb and index finger in precision grasps, cortical units responding to this finger possess higher thresholds. By not including Hebbian learning and lateral connections, the current study isolated the effects of this mechanism on cortical maps. Changes in cortical maps were observed when different thresholds, trained using the homeostatic model, were applied to tactile responses in a finger tapping paradigm. Furthermore, changing the input statistics through the numbing or removal of input from digit two led to clear changes in the cortical maps generated. Not only did the maps contain less of an area responding to the finger with reduced input due to numbing or deafferentation, but the responses of neighbouring fingers were increased, indicating that homeostatic mechanisms have global influences rather than local effects focused on the finger on which deafferentation was conducted.

While this model demonstrates that changes in cortical maps following sensory deprivation can occur via simpler mechanisms than Hebbian learning, the time frame by which homeostatic mechanisms work suggests that this explanation can only be applied to changes over the course of days. Future studies should include lateral connections, which are a key part of cortical architecture, and other homeostatic mechanisms such as synaptic scaling to investigate their relative contributions to cortical plasticity in the form of cortical maps in the absence of Hebbian synaptic learning.

7 Acknowledgements

I would like to thank the entirety of the Active Touch Laboratory at The University of Sheffield, with particular thanks to Dr Hannes Saal and Laura Edmonson for their support throughout this project. Their guidance has enabled me to both conduct the thesis that I have, whilst teaching me key skills that will be used going into my PhD. I would also like to thank my parents for reading through my many drafts prior to submission, and my mentor, Helen Hodgson, for helping me when my workload piled up. I'd like to thank Dr Stuart Wilson and the Department of Psychology for putting on such a great masters course, especially during the COVID-19 pandemic.

References

Asher, D. E., Oros, N., and Krichmar, J. L. (2015). The importance of lateral connections in the parietal cortex for generating motor plans. *PloS one*, 8(10):e0134669.

Azzopardi, P. and Cowey, A. (1993). Preferential representation of the fovea in the primary visual cortex. *Nature*, 361:719–721.

Bednar, J. A. and Wilson, S. P. (2016). Cortical maps. *The Neuroscientist*, 22:604–617.

Bienenstock, E. L., Cooper, L. N., and Munro, P. W. (1982). Theory for the development of neuron selectivity: orientation specificity and binocular interaction in visual cortex. *Journal of Neuroscience*, 1(2):32–48.

Borsook, D., Becerra, L., Fishman, S., Edwards, A., Jennings, C. L., Stojanovic, M., Papinicolas, L., Ramachandran, V. S., Gonzalez, R. G., and Breiter, H. (1998). Acute plasticity in the human somatosensory cortex following amputation. *Neuroreport*, 9(6):1013–1017.

Brodmann, K. (1909). *Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues.* Barth.

Bullock, I. M., Zheng, J. Z., De La Rosa, S., Guertler, C., and Dollar, A. M. (2013). Grasp frequency and usage in daily household and machine shop tasks. *IEEE transactions on haptics*, 3(6):296–308.

Camazine, S., Deneubourg, J. L., Franks, N. R., Sneyd, J., Bonabeau, E., and Theraula, G. (2003). *Self-organization in biological systems*, volume 7. Princeton university press.

Catania, K. C. (2011). The sense of touch in the star-nosed mole: from mechanoreceptors to the brain. *Transactions of the Royal Society B: Biological Sciences*, 366:3016–3025.

Chang, E. F. and Merzenich, M. M. (2003). Environmental noise retards auditory cortical development. *science*, 300(5618):498–502.

Corniani, G. and Saal, H. P. (2020). Tactile innervation densities across the whole body. *bioRxiv*.

690 Cowey, A. (1964). Projection of the retina on to striate and prestriate cortex in the squirrel monkey, saimiri sciureus. *Journal of Neurophysiology*, 87(21):366–393.

Crozier, R. A., Wang, Y., Liu, C. H., and Bear, M. F. (2007). Deprivation-induced synaptic depression by distinct mechanisms in different layers of mouse visual cortex. *Proceedings of the National Academy of Sciences*, 4(104):1383–1388.

695 Curcio, C. A., Sloan, K. R., Kalina, R. E., and Hendrickson, A. E. (1990). Human photoreceptor topography. *Journal of comparative neurology*, 292(4):497–523.

Desai, N. S., Cudmore, R. H., Nelson, S. B., and Turrigiano, G. G. (2002). Critical periods for experience-dependent synaptic scaling in visual cortex. *Nature neuroscience*, 8(5):783–789.

Duncan, R. O. and Boynton, G. M. (2007). Tactile hyperacuity thresholds correlate with finger maps in
700 primary somatosensory cortex (s1). *Cerebral Cortex*, 17(12):2878–2891.

Dunn, W., Griffith, J. W., M. T., M., Tanquary, J., Sabata, D., Victorson, D., ..., and Gershon, C. R. (2013). Somatosensation assessment using the nih toolbox. *Neurology*, pages S41–S44.

Erwin, E., Obermayer, K., and Schulten, K. (1995). Models of orientation and ocular dominance columns in the visual cortex: A critical comparison. *Neural Computation*, 7(3):425–468.

705 Fabrizi, L., Slater, R., Worley, A., Meek, J., Boyd, S., Olhede, S., and Fitzgerald, M. (2011). A shift in sensory processing that enables the developing human brain to discriminate touch from pain. *Current Biology*, 18(21):1552–1558.

Feix, T., Romero, J., Schmiedmayer, H. B., Dollar, A. M., and Kragic, D. (2015). The grasp taxonomy of human grasp types. *IEEE Transactions on Human-Machine Systems*, 46(1):66–77.

710 Ferr, E. R. and Haggard, P. (2016). The vestibular body: vestibular contributions to bodily representations. *Cognitive neuropsychology*, 33:67–81.

Figurov, A., Pozzo-Miller, L. D., Olafsson, P., Wang, T., and Lu, B. (1996). Regulation of synap-

tic responses to high-frequency stimulation and ltp by neurotrophins in the hippocampus. *Nature*, 6584(381):706–709.

Fox, K. and Stryker, M. (2017). Integrating hebbian and homeostatic plasticity: introduction.

Fox, P. T., Miezin, F. M., Allman, J. M., Van Essen, D. C., and Raichle, M. E. (1987). Retinotopic organization of human visual cortex mapped with positron-emission tomography. *Journal of Neuroscience*, 7(3):913–922.

Gellis, M. and Pool, R. (1977). Two-point discrimination distances in the normal hand and forearm: application to various methods of fingertip reconstruction. *Plastic and Reconstructive Surgery*, 59:57–63.

Godde, B., Spengler, F., and Dinse, H. R. (1996). Associative pairing of tactile stimulation induces somatosensory cortical reorganization in rats and humans. *Neuroreport*, 1(8):281–285.

Goodchild, A. K., Ghosh, K. K., and Martin, P. R. (1996). Comparison of photoreceptor spatial density and ganglion cell morphology in the retina of human, macaque monkey, cat, and the marmoset callithrix jacchus. *Journal of Comparative Neurology*, 366(1):55–75.

Goodhill, G. J. (2007). Contributions of theoretical modeling to the understanding of neural map development. *Neuron*, 56:301–311.

Hebb, D. O. (1949). *The organization of behaviour: a neuropsychological theory*. J. Wiley.

Hegner, Y. L., Wiech, K., Preissl, H., and Braun, C. (2006). Do cortical maps depend on the timing of sensory input? experimental evidence and computational model. *Biological cybernetics*, 2(94):110–117.

Hlutk, P., Solodkin, A., Gullapalli, R. P., Noll, D. C., and Small, S. L. (2001). Somatotopy in human primary motor and somatosensory hand representations revisited. *Cerebral Cortex*, 11(4):312–321.

Hou, Q. and Man, H. Y. (2012). Input-specific homeostatic regulation of ampa receptor accumulation at central synapses. *Communicative integrative biology*, 6(5):553–556.

Huffman, K. J. and Krubitzer, L. (2001). Area 3a: topographic organization and cortical connections in marmoset monkeys. *Cerebral Cortex*, 11(9):849–867.

Huffman, K. J., Nelson, J., Clarey, J., and Krubitzer, L. (1999). Organization of somatosensory cortex in three species of marsupials, dasyurus hallucatus, dactylopsila trivirgata, and monodelphis domestica: neural correlates of morphological specializations. *Journal of Comparative Neurology*, 403(1):5–32.

Hutmacher, F. (2019). Why is there so much more research on vision than any other sensory modality. *Frontiers in psychology*, 10:2246–2257.

Iwamura, Y., Tanaka, M., Sakamoto, M., and Hikosaka, O. (1993). Rostrocaudal gradients in the neuronal receptive field complexity in the finger region of the alert monkey's postcentral gyrus. *Experimental Brain Research*, 92(3):360–368.

Jaffer, S., Vorobyov, V., and Sengpiel, F. (2012). Effects of different forms of monocular deprivation on primary visual cortex maps. *Visual neuroscience*, 29(4-5):247–253.

Jamal, Y. and Dilks, D. (2020). Rapid topographic reorganization in adult human primary visual cortex (v1) during noninvasive and reversible deprivation. *Proceedings of the National Academy of Sciences*, 20(117):11059–11067.

Jenkins, W. M., Merzenich, M. M., Ochs, M. T., Allard, T., and Guic-Robles, E. (1990). Functional reorganization of primary somatosensory cortex in adult owl monkeys after behaviorally controlled tactile stimulation. *Journal of neurophysiology*.

Johansson, R. S. and Vallbo, . B. (1979). Tactile sensibility in the human hand: relative and absolute densities of four types of mechanoreceptive units in glabrous skin. *The journal of physiology*, 286:283–300.

Johansson, R. S. and Vallbo, . B. (1983). Tactile sensory coding in the glaborous skin of the human hand. *Trends in neuroscience*, 6:27–32.

Johnson, K. O. (2001). The roles and functions of cutaneous mechanoreceptors. *Current opinions in neurobiology*, 11:484–487.

Jones, L. A. (1994). Peripheral mechanisms of touch and proprioception. *Canadian journal of physiology and pharmacology*, 72(5):484–487.

Kaas, J. H. (1997). Topographic maps are fundamental to sensory processing. *Brain research bulletin*, 44(2):107–112.

Kaas, J. H. (2011). *Human nervous system*, chapter Somatosensory system. Academic Press, 3rd edition edition.

Keck, T., Scheuss, V., Jacobsen, R. I., Wierenga, C. J., Eysel, U. T., Bonhoeffer, T., and Hbener, M. (2011). Loss of sensory input causes rapid structural changes of inhibitory neurons in adult mouse visual cortex. *Neuron*, 5(71):869–882.

Kida, T. and Shinohara, K. (2013). Gentle touch activates the prefrontal cortex in infancy: an nirs study. *Neuroscience letters*, (541):63–66.

Kilgard, M. P., Pandya, P. K., Engineer, N. D., and Moucha, R. (2002). Cortical network reorganization guided by sensory input features. *Biological cybernetics*, 5-6(87):333–343.

Kilman, V., Van Rossum, M. C., and Turrigiano, G. G. (2002). Activity deprivation reduces miniature ipsc amplitude by decreasing the number of postsynaptic gabaa receptors clustered at neocortical synapses. *Journal of Neuroscience*, 4(22):1328–1337.

Klintsova, A. Y. and Greenough, W. T. (1999). Synaptic plasticity in cortical systems. *Current opinion in neurobiology*, 2(9):203–208.

Kohonen, T. (1982). Self-organized formation of topologically correct feature maps. *Biological cybernetics*, 43(1):59–69.

Kohonen, T. and Honkela, T. (2007). Kohonen network. *Scholarpedia*, 2(1):1568.

Kolasinski, J., Makin, T. R., Jbabdi, S., Clare, S., Stagg, C. J., and Johansen-Berg, H. (2016). In-

vestigating the stability of fine-grain digit somatotopy in individual human participants. *Journal of Neuroscience*, 36(4):1113–1127.

Kriegeskorte, N., Mur, M., and Bandettini, P. A. (2008). Representational similarity analysis-connecting the branches of systems neuroscience. *Frontiers in systems neuroscience*, 2:4.

Krubitzer, L., Huffman, K. J., Disbrow, E., and Recanzone, G. (2004). Organization of area 3a in macaque monkeys: contributions to the cortical phenotype. *Journal of Comparative Neurology*, 471(1):97–111.

Lambo, M. E. and Turrigiano, G. G. (2013). Synaptic and intrinsic homeostatic mechanisms cooperate to increase l2/3 pyramidal neuron excitability during a late phase of critical period plasticity. *Journal of Neuroscience*, 20(33):8810–8819.

Lechner, H. A. and Byrne, J. H. (1998). New perspectives on classical conditioning: a synthesis of hebbian and non-hebbian mechanisms. *Neuron*, 3(20):355–358.

Levelt, C. N. and Hübener, M. (2012). Critical-period plasticity in the visual cortex. *Annual review of neuroscience*, 35:309–330.

Li, L., Gainey, M. A., Goldbeck, J. E., and Feldman, D. E. (2014). Rapid homeostasis by disinhibition during whisker map plasticity. *Proceedings of the National Academy of Sciences*, 4(111):1616–1621.

Liang, H., Gong, X., Chen, M., Yan, Y., Li, W., and Gilbert, C. D. (2017). Interactions between feedback and lateral connections in the primary visual cortex. *Proceedings of the National Academy of Sciences*, 32(114):8637–8642.

Liang, M., Shen, J., and Wang, G. (2008). Identification of illicit drugs by using som neural networks. *Journal of Physics D: Applied Physics*, 41(13):135306.

Lindsay, R. M. (1994). *Progress in brain research*, volume 103, chapter Neurotrophins and receptors, pages 3–14. Elsevier.

Lisman, J. (2017). Glutamatergic synapses are structurally and biochemically complex because of mul-

tiple plasticity processes: long-term potentiation, long-term depression, short-term potentiation and scaling. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 1715(372):20160260.

Lissek, S., W. C. S. P. P. B. K. T. M. C., Peters, S. A., Nicolas, V., Tegenthoff, M., and Dinse, H. R. (2011). Immobilization impairs tactile perception and shrinks somatosensory cortical maps. *Current Biology*, 10(19):837–842.

Maffei, A., Nelson, S. B., and Turrigiano, G. G. (2004). Selective reconfiguration of layer 4 visual cortical circuitry by visual deprivation. *Nature neuroscience*, 12(7):1353–1359.

Makin, T. R., Cramer, A. O., Scholz, J., Hahamy, A., Slater, D. H., Tracey, I., and Johansen-Berg, H. (2013). Deprivation-related and use-dependent plasticity go hand in hand. *Elife*, 2:e01273.

Maldjian, J. A., Gottschalk, A., Patel, R. S., Detre, J. A., and Alsop, D. C. (1999). The sensory somatotopic map of the human hand demonstrated at 4 tesla. *Neuroimage*, 10(1):55–62.

Martuzzi, R., van der Zwaag, W., Farthouat, J., Gruetter, R., and Blanke, O. (2014). Human finger somatotopy in areas 3b, 1, and 2: a 7t fmri study using a natural stimulus. *Human brain mapping*, 35(1):213–226.

Matsuzaki, M., Honkura, N., Ellis-Davies, G. C., and Kasai, H. (2004). Structural basis of long-term potentiation in single dendritic spines. *Nature*, 6993(429):761–766.

Merzenich, M. M. and Jenkins, W. M. (1993). Reorganization of cortical representations of the hand following alterations of skin inputs induced by nerve injury, skin island transfers, and experience. *Journal of hand therapy*, 6(2):89–104.

Merzenich, M. M. and Kaas, J. H. (1982). Reorganization of mammalian somatosensory cortex following peripheral nerve injury. *Trends in Neurosciences*, (5):434–436.

Merzenich, M. M., Nelson, R. J., Kaas, J. H., Stryker, M. P., Jenkins, W. M., Zook, J. M., Cynader, M. S., and Schoppmann, A. (1987). Variability in hand surface representations in areas 3b and 1 in adult owl and squirrel monkeys. *Journal of Comparative Neurology*, 258(2):281–296.

Miikkulainen, R., Bednar, J. A., Choe, Y., and Sirosh, J. (2005). *Computational maps in the visual cortex*. Springer Science and Business Media.

Mower, G. D. (1991). The effect of dark rearing on the time course of the critical period in cat visual cortex. *Developmental Brain Research*, 58(2):151–158.

Muret, D., Daligault, S., Dinse, H. R., Delpuech, C., Mattout, J., Reilly, K. T., and Farnè, A. (2016). Neuromagnetic correlates of adaptive plasticity across the hand-face border in human primary somatosensory cortex. *Journal of Neurophysiology*, 115(4):2095–2104.

Muret, D. and Dinse, H. R. (2018). Tactile learning transfer from the hand to the face but not to the forearm implies a special hand-face relationship. *Scientific Reports*, 1(8):1–8.

Narisawa-Saito, M., Carnahan, J., Araki, K., Yamaguchi, T., and Nawa, H. (1999). Brain-derived neurotrophic factor regulates the expression of ampa receptor proteins in neocortical neurons. *Neuroscience*, 4(88):1009–1014.

Obermayer, K., Ritter, H., and Schulten, K. (1990). A principle for the formation of the spatial structure of cortical feature maps. *Proceedings of the National Academy Of Sciences*, 87(21):8345–8349.

Okada, Y. C., Tanenbaum, R., Williamson, S. J., and Kaufman, L. (1984). Somatotopic organization of the human somatosensory cortex revealed by neuromagnetic measurements. *Experimental Brain Research*, 56(2):197–205.

O'Shaughnessy, B. (1989). The sense of touch. *Australasian journal of philosophy*, 67:37–58.

Pantev, C., Okamoto, H., Ross, B., Stoll, W., CiurliaGuy, E., Kakigi, R., and Kubo, T. (2004). Lateral inhibition and habituation of the human auditory cortex. *European Journal of Neuroscience*, 8(19):2337–2344.

Par, M., Smith, A. M., and Rice, F. L. (2002). Distribution and terminal arborizations of cutaneous mechanoreceptors in the glaborous finger pads of the monkey. *Journal of Comparative Neurobiology*, 445:437–359.

Penfield, W. and Boldrey, E. (1937). Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. *Brain*, 60:389–443.

Pouydebat, E., Gorce, P., Coppens, Y., and Bels, V. (2009). Biomechanical study of grasping according to the volume of the object: human versus non-human primates. *Journal of biomechanics*, 42(3):266–
860 272.

Ranson, A., Cheetham, C. E., Fox, K., and Sengpiel, F. (2012). Homeostatic plasticity mechanisms are required for juvenile, but not adult, ocular dominance plasticity. *Proceedings of the National Academy of Sciences*, 4(109):1311–1316.

Rao, S. M., Binder, J. R., Hammeke, T., Bandettini, P. A., Bobholz, J. A., Frost, J. A., Myklebust, B. M.,
865 Jacobson, R. D., and Hyde, J. S. (1995). Somatotopic mapping of the human primary motor cortex with functional magnetic resonance imaging. *Neurology*, 45(5):919–924.

Ritter, H., Martinetz, T., Schulten, K., Barsky, D., Tesch, M., and Kates, R. (1992). *Neural computation and self-organizing maps: an introduction*. Reading, MA: Addison-Wesley.

Robles-De-La-Torre, G. (2006). The importance of the sense of touch in virtual and real environments.
870 *IEEE Multimedia*, 13(3):24–30.

Rumpel, S., Hatt, H., and Gottmann, K. (1998). Silent synapses in the developing rat visual cortex: evidence for postsynaptic expression of synaptic plasticity. *Journal of Neuroscience*, 21(18):8863–8874.

Saal, H. P. and Bensmaia, S. J. (2014). Touch is a team effort: interplay of submodalities in cutaneous
875 sensibility. *Trends in neuroscience*, 37:689–697.

Saal, H. P., Delhaye, B. P., Rayhaun, B. C., and Bensmaia, S. J. (2017). Simulating tactile signals from the whole hand with millisecond precision. *Proceedings of the national academy of sciences*, 114:E5693–5702.

Schweizer, R., Voit, D., and Frahm, J. (1984). Finger representations in human primary somatosensory cortex as revealed by high-resolution functional mri of tactile stimulation. *Neuroimage*, 42(1):28–35.

Sengpiel, F. (2007). The critical period. *Current Biology*, 17(17):R742–R743.

Sirosh, J., . M. R. (1995). *The Neurobiology of Computation*, chapter Modeling cortical plasticity based on adapting lateral interaction, pages 305–310. Springer, Boston, MA.

Sirosh, J. and Miikkulainen, R. (1994a). Cooperative self-organization of afferent and lateral connections in cortical maps. *Biological Cybernetics*, 71(1):65–78.

Sirosh, J. and Miikkulainen, R. (1994b). Cooperative self-organization of afferent and lateral connections in cortical maps. *Biological Cybernetics*, 1(71):65–78.

Stafford, T. and Wilson, S. P. (2007). Self-organisation can generate the discontinuities in the somatosensory map. *Neurocomputing*, 70(10-12):1932–1937.

Stent, G. S. (1973). A physiological mechanism for hebb's postulate of learning. *Proceedings of the National Academy of Sciences*, 70(4):997–1001.

Stevens, J. C. and Choo, K. K. (1996). Spatial acuity of the body surface over the life span. *Somatosensory and motor research*, 13:153–166.

Stevens, J. L. R., Law, J. S., Antolk, J., and Bednar, J. A. (2013). Mechanisms for stable, robust, and adaptive development of orientation maps in the primary visual cortex. *Journal of Neuroscience*, 33(30):15747–15766.

Strahan, R. (1983). *The complete book of Australian mammals*.

Sutherling, W. W., Levesque, M. F., and Baumgartner, C. (1992). Cortical sensory representation of the human hand: size of finger regions and nonoverlapping digit somatotopy. *Neurology*, 42(5):1020–1028.

Tootell, R. B., Hadjikhani, N. K., Vanduffel, W., Liu, A. K., Mendola, J. D., Sereno, M. I., and Dale,

A. M. (1998). Functional analysis of primary visual cortex (v1) in humans. *Proceedings of the National Academy of Sciences*, 95(3):811–817.

Turrigiano, G. G. (2008). The self-tuning neuron: synaptic scaling of excitatory synapses. *Cell*, 3(135):422–435.

Turrigiano, G. G., Leslie, K. R., Desai, N. S., Rutherford, L. C., and Nelson, S. B. (1998). Activity-dependent scaling of quantal amplitude in neocortical neurons. *Nature*, 6670(391):892–896.

Turrigiano, G. G. and Nelson, S. B. (2000). Hebb and homeostasis in neuronal plasticity. *Current opinion in neurobiology*, 3(10):358–364.

Vitureira, N. and Goda, Y. (2013). The interplay between hebbian and homeostatic synaptic plasticity. *Journal of Cell Biology*, 2(203):175–186.

Waberski, T., Gobbele, R., Kawohl, W., Cordes, C., and Buchner, H. (2003). Immediate cortical reorganization after local anesthetic block of the thumb: source localization of somatosensory evoked potentials in human subjects. *Neuroscience letters*, 347(3):151–154.

Wilson, S. P., Law, J. S., Mitchinson, B., Prescott, T. J., and Bednar, J. A. (2010). Modeling the emergence of whisker direction maps in rat barrel cortex. *PLoS one*, 5(1):e8778.

Wu, Y., Hengen, K. B., Turrigiano, G. G., and Gjorgjieva, J. (2019). Homeostatic mechanisms regulate distinct aspects of cortical circuit dynamics. *bioRxiv*, page 790410.

Xing, J. and Gerstein, G. L. (1996). Networks with lateral connectivity. i. dynamic properties mediated by the balance of intrinsic excitation and inhibition. *Journal of neurophysiology*, 1(75):184–199.

Yang, T. T., Gallen, C., Ramachandran, V., Cobb, S., Schwartz, B., and Bloom, F. (1994). Noninvasive detection of cerebral plasticity in adult human somatosensory cortex. *Neuroreport: An International Journal for the Rapid Communication of Research in Neuroscience*.

Yazdan-Shahmorad, A., Silversmith, D. B., Kharazia, V., and Sabes, P. N. (2018). Targeted cortical reorganization using optogenetics in non-human primates. *Elife*, (7):e31034.

Zamanillo, D., Sprengel, R., Hvalby, ., Jensen, V., Burnashev, N., Rosoc, A., Kaiser, K. M., Kster, H. J., Borchardt, T., Worley, P., and Lbke, J. (1999). Importance of ampa receptors for hippocampal synaptic plasticity but not for spatial learning. *Science*, 5421(284):1805–1811.

Zenke, F. and Gerstner, W. (2017). Hebbian plasticity requires compensatory processes on multiple timescales. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 1715(372):20160259.

Zenke, F., Gerstner, W., and Ganguli, S. (2017). The temporal paradox of hebbian learning and homeostatic plasticity. *Current opinion in neurobiology*.