A mathematical model of receptive field reorganization following stroke

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***Abstract*— Insufficient blood transport to neurons in the brain due to blocked or ruptured blood vessels (stroke) can lead to damage or death of cells, causing functional impairment. Intact neurons surrounding a stroke-like lesion have been shown to adapt to the damage by expanding their sensory receptive fields in the direction towards the lesion, thereby restoring information processing capacity within the cortex. We developed model of the effect of focal ischaemia on the performance of a neuronal population code, in order to study physiological parameters that could be influenced to enhance recovery from stroke. Our findings show that recovery of the accuracy of the population code is optimal by a specific amount of receptive field plasticity. This plasticity may be influenced by changing the level of γ-aminobutyric acid (GABA-ergic) inhibition in the areas surrounding the damaged tissue.**

I. Introduction

Excitatory neurons in the sensory areas (visual, auditory, and somatosensory) of the brain respond only to stimuli in restricted regions of the sensory field, referred as their receptive fields. Studies on stroke recovery associate restoration of function with reorganization in the brain [1], [2], [3]. The reorganization of neural activity that follows after stroke is very important in producing functional recovery. Moreover, it has been observed that reorganization after stroke can lead to an enlargement of the receptive fields (RFs) in the region surrounding the lesion [4-12].

Several observations have shown that following stroke, the levels of γ-aminobutyric acid (GABAergic) inhibition in neighboring brain areas drop and others have shown that a reduction of GABAergic inhibition may favor cortical plasticity ([13], [14], [15], [16] [17]). From these findings its has been hypothesised that the brain supports recovery from lesion by decreasing GABAergic inhibition and thereby facilitating plasticity and reorganization of the cortical representation in surrounding areas. The expansion of the receptive fields can then be explained by the dis-inhibition caused by reduction in GABA. Changes in levels of GABA only affect the inhibitory parts of receptive fields but leave the excitatory parts unaffected. This disrupted balance between excitation and inhibition causes the receptive field to expand, where dis-inhibition is apparent, asymmetrically from its original position towards the lesion.

A remarkable feature of sensory cortices in the brain is that the sensory world can be mapped topographically onto the cortical surface. This means that neighboring points in the sensory field evoke activity in neighboring regions of the cortex. Since receptive fields overlap, each point is monitored by a population of neighboring cells, rather than a single cell, and when a point is stimulated the population of neurons whose receptive fields include that particular site are excited. In this work, we present a computational model of a topographically mapped population code which includes a focal lesion as well as a process for receptive field enlargement (plasticity). The model simulates the recovery processes in the brain, and allows us to investigate mechanisms which increase the ability of the cortex to restore lost brain functions. Changes in the degree of plasticity of the receptive fields of the neurons, which could potentially be influenced to enhance information transfer through the cortex post stroke, were incorporated into the model. This allowed the exploration of effects resulting from changes in the concentration of this parameter on the level of functional restoration. Neurons close to the damaged region expand their receptive field more than those neurons further away in the cortex.

We use Fisher Information in order to calculate how much information a neural response carries about the stimuli. We estimate the Fisher Information carried by the topographic map before and after the stroke. We find that by tuning the receptive field plasticity to a certain value, the information transfer through the cortex after stroke can be optimized.

II. Methods

For simplicity we use a simple Gaussian receptive field which does not take into account any dependency in the orientation of the object. A centre-surround receptive field can be represented by a two-dimensional spatial Gaussian function. Our model is based on the assumption that a population of neurons with Gaussian receptive fields can be mapped topographically onto a two dimensional lattice. The model could therefore be taken to represent neurons which exhibit centre surrounding receptive field such as retinal ganglions cells adapting to a retinal lesion. However, this will also be used to describe the recovery process of the envelopes of cortical receptive fields. That is, functional recovery due to the reorganization of neuronal activity that takes place in the cortex after a stroke-like lesion will be investigated. The modeling will be based on the finding that intact neurons surrounding the lesion partially restore cortical function by taking up some of the role of the damaged neurons [13], [14].

The prototypical cortex model

Simple cells in the primary visual cortex are selective not only to for the size of the object but also for their orientation. However, for sake of simplicity we choose to use a simple Gaussian model which it does not include orientation dependency. The core of the model is an uncorrelated population of n neurons, each defined by a two dimensional centre-surround Gaussian receptive field, $G(x,y)_n$, with x and y representing the spatial coordinates of the stimulus, and x_0, y_0 the centre of the receptive field for a given neuron. In order to name explicitly the excitatory and inhibitory part, we can write this equation as

$$G(x,y)_n = \pm(f^0_{ex}(x,y)_n + f^0_{in}(x,y)_n) \tag{1}$$

where $f^0_{ex}(x,y)_n$ and $f^0_{in}(x,y)_n$ are defined as,

$$f^0_{ex}(x,y)_n = \frac{1}{2\pi\sigma^2_{cen}} \exp\left(-\frac{(x-x_0)^2+(y-y_0)^2}{2\sigma^2_{cen}}\right) \tag{2}$$

and

$$f^0_{in}(x,y)_n = -\frac{B}{2\pi\sigma^2_{sur}} \exp\left(-\frac{(x-x_0)^2+(y-y_0)^2}{2\sigma^2_{sur}}\right) \tag{3}$$

The standard deviation σ_{cen} determines the width of the central part of the curve and σ^2_{sur} determines the width of the annular surrounding region. The value of B determines the balance between excitatory and inhibitory regions.

Each receptive field is constructed by adding positive and negative Gaussian functions together. The positive function represents the excitatory part of the receptive field, i.e. where positive stimulus, s, elicits an increase in firing rate. The negative function represents the inhibitory part, where a positive stimulus causes decreasing firing rate. The excitatory part for each neuron n is termed $f_{ex}(x,y)_n$ and the inhibitory part for each neuron n is termed $f_{in}(x,y)_n$.

The superscript f^0 stresses the fact that these are the definitions for the receptive field of neuron n pre lesion.

Neuronal responses are complex and variable thus describing the relationship between stimulus and response is a difficult task. A simple neuronal model can estimate firing rates as instantaneous functions of the corresponding applied stimulus by assuming that contributions from different locations within the visual field sum linearly. That is, the spatial input stimulus, $s(x,y)$, is weighted linearly by the receptive field of each neuron, $G(x,y)_n$. The linear response of each neuron n to the input stimulus is thus generated by:

$$r_{linear}(x,y)_n = \sum_{x=1}^{size_x} \sum_{y=1}^{size_y} G(x,y)_n \cdot s(x,y) \tag{4}$$

$size_x$ and $size_y$ determine the height and width of the spatially mapped visual field respectively. By adding to the model a threshold-gain function, T, which is appropriately bounded from above and below the firing rate will be never be negative or unrealistically large.

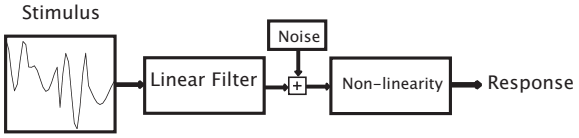

Fig. 1. Block diagram of the generation of non-linear neuronal responses. The stimulus s is weighted by the linear filter, G, and noise is added to the system to incorporate response variability from trial to trial even if the same stimulus is applied.

White noise, w_n, is added to the system to incorporate the fact that a neuron does not always respond in the same way to a repeatedly applied stimulus. Thus, the actual response of each neuron n to a spatial stimulus s in the model is:

$$r_{nonlinear}(x,y)_n = T(r_{linear}(x,y)_n + w_n) \tag{5}$$

For the simulations that will be shown, the transfer function T was

$$T(r_{linear} + w_n) = g[r_{linear} + w_n - r_0]_+ \tag{6}$$

whereas the analytical results which we will present have currently been obtained for the simple case

$$T(r_{linear} + w_n) = r_{linear} + w_n. \tag{7}$$

In the above, r_0 is the threshold value that the sum $(r_{linear} + w_n)$ must reach before firing starts. Above threshold level, the firing rate is a linear function of r_{linear} and g is the gain.

The cortical lesion model

The model described above generates a neuronal population response to input stimuli. It does not include any kind of plasticity or adaptation of neurons in the population. The cortical lesion model includes the prototypical response model but also incorporates the ability of neurons to adapt to a stroke-like lesion according to the literature.

A lesion is induced in the model by destroying a specific number of neurons in the population and zero-ing out their receptive fields. The damaged neurons are thus unable to respond to any incoming stimuli and do not contribute to the information transferred about the applied stimuli by the population across the cortex. The size of the lesion determines the number of damaged neurons and can be tuned to explore the effects of various sizes on the cortex. The site of a lesion within the cortex can also be specified.

The intact neurons situated around the damage adapt by changing the shape of their receptive fields and thereby take up some of the functional roles of the damaged neurons. This ability is represented in the model by the plasticity parameter γ. The levels of GABA-ergic inhibition drop in neighbouring cortical areas following a stroke-like lesion. The amount of GABA decrease is dependent on the size of the lesion, $L_j - L_i$, and influences the value of γ directly; a large damage causes a great drop in GABA levels which in turn leads to a large increase in the value of γ.

Since GABA is an inhibitory neurotransmitter, changes in its levels affect the inhibitory parts of the receptive fields but

leave excitation unaffected. The reduction of GABA causes dis-inhibition of adapting receptive fields in the direction of the lesion. The amount of dis-inhibition apparent in neuron n is controlled by the receptive field plasticity parameter γ and the distance d_n between the damage and the neuron in question. The dis-inhibited inhibitory part, $f_{in}(x,y)_n$, of a receptive field facing in the direction of the lesion can be described in terms of the original inhibitory function, $f^0_{in}(x,y)_n$, plasticity and distance by:

$$f_{in}(x,y)_n = f^0_{in}(x,y)_n \cdot F(\gamma, d_n) \tag{8}$$

where $F(\gamma, d_n)$ is defined as

$$F(\gamma, d_n) = 1 - exp\left(\frac{-d}{\gamma}\right) \tag{9}$$

Eq. (9) fulfills the requirement that the dis-inhibition should increase with increasing values of γ and decrease with increasing values of d_n but the equation is purely hypothetical and this relationship remains to be fitted to experimental data.

The total receptive field structure is given by the summation of the Gaussian excitatory and inhibitory functions. Since the excitatory part, f^0_{ex} is left unaffected during the recovery process, the new total receptive field G is expanded from its original position towards the lesion and has the form:

$$G(x,y)_n = f^0_{ex}(x,y)_n + f^0_{in}(x,y)_n \cdot \left[1 - exp\left(\frac{-d}{\gamma}\right)\right] \tag{10}$$

According to eq. 8 - 10, neurons close to the damage experience greater dis-inhibition and therefore greater expansion of their receptive fields than neurons further away in the cortex.

Analytical approach

In the following, we denote the cortical spontaneous neuronal activity r, and making use of the Central Limit Theorem, assume that r is normally distributed about f_n.

$$P(r_n \mid xy) = \frac{1}{\sqrt{2\sigma_n^2}} \exp\{-\frac{[r - f_n(x,y)]^2}{2\sigma_n}\} \tag{11}$$

where $f_n(x,y)$ is a 2-D well shape tuning function. Fisher information ([18],[19],[20]) can be calculated as

$$I = -\int_0^R dr P(r \mid xy) \frac{\partial^2}{\partial x \partial y} log_2 P(r \mid xy) \tag{12}$$

As we described, the receptive field is made up of an excitatory and inhibitory part $f = f_{in} + f_{ex}$, which may also account modifications in the receptive field when a localized damage take place. This is, considering that a finite number of cells have been removed the inhibitory part changes after the lesion as states in eq (9):

$$fin = f^0_{in}(x,y)_n(1 - exp(-d(n)/(\gamma(n)))) \tag{13}$$

were $d(n)$ is the minimal distance from a given cell to the damage and $\gamma(n)$ is defined as the plasticity after the lesion removes the neuron of cartesian coordinates x_i, y_j .

$$d(n) = \sqrt{(x_n - x_i)^2 + (y_n - y_j)^2} \tag{14}$$

Notice that x_i and y_j correspond to the position (i,j) of the sites which have been removed. After some algebra, and by assuming $R \to \infty$ this leads to

$$I = I_{ex} + I_{in} + I_{in-ex} \tag{15}$$

where I_{ex} and I_{in} are the excitatory and inhibitory contributions respectively. But, I_{in-ex} correspond to a mixed contribution made up of excitatory and inhibitory elements.

The excitatory term can be written as

$$I_{ex} = \sum_n ((\frac{f^{ex}_0(x,y)}{\sigma_n})^2 \frac{(x_n - y_{0n})(y_n - y_{0n})}{(\sigma_{ex})^2} \tag{16}$$

the pure inhibitory term,

$$\begin{aligned} I_{in} = \sum_n (\frac{f^{in}_0(x,y)}{\sigma_n})^2 \\ \{\frac{(x_n - x_{0n}) + (y_n - y_{0n})}{(\sigma_{in})^4}(1 - exp(-\frac{d(n)}{\gamma})^2 \\ ((x_n - x_{0n})(y_n - y_i) + (y_n - y_{0n})(x_n - x_i)) \\ + \frac{(x_n - x_i)(y_n - y_i)}{d(n)^2\gamma^2} exp(-\frac{2d(n)}{\gamma})\} \end{aligned} \tag{17}$$

and the mixed term,

$$\begin{aligned} I_{in-ex} = \sum_n (\frac{f^{in}_0(x,y) f^{ex}_0(x,y)}{\sigma_n^2}) \\ \{\frac{2(x_n - y_{0n})(y_n - y_{0n})(1 - exp(\frac{-d(n)}{\gamma}))}{(\sigma_{ex})^2} \\ - \frac{(y_n - y_j)(x_n - x_{0n}) exp(\frac{-d(n)}{\gamma})}{(\sigma_{ex})^2 d(n)\gamma} \\ + \frac{(x_n - x_i)(y_n - y_{0n}) exp(\frac{-d(n)}{\gamma})}{(\sigma_{ex})^2 d(n)\gamma}\} \end{aligned} \tag{18}$$

This allows us to represent the Fisher topographic information as function of the plasticity γ, with respect to the distance to the lesion $d(n)$ and the size of the lesion which is implicitly included in the number of removed sites (x_i, y_j) .

III. Results

A. Enlargement of receptive field

We initially present simulation results which show the effect of the post-lesion plasticity on the receptive fields, before following with analytical results which have been numerically solved for precisely the same situation as that simulated.

The results in this section all stem from the same population, the number of neurons is 225 and it spans 16 degrees of the visual field in both the x- and the y directions. Once a lesion has been induced, GABA levels in the cortex drop, the plasticity parameter γ is increased and dis-inhibition takes place in the intact surrounding neurons, in the direction of the damage. The drop in the GABA levels, and therefore the increase in plasticity, is dependent on the size of the lesion and on γ.

Figure 2 shows a contour plot of a receptive field of a single neuron in the neural population. The peak of the receptive field, $(x_0, y_0)_n$ is dependent of the position of the neuron

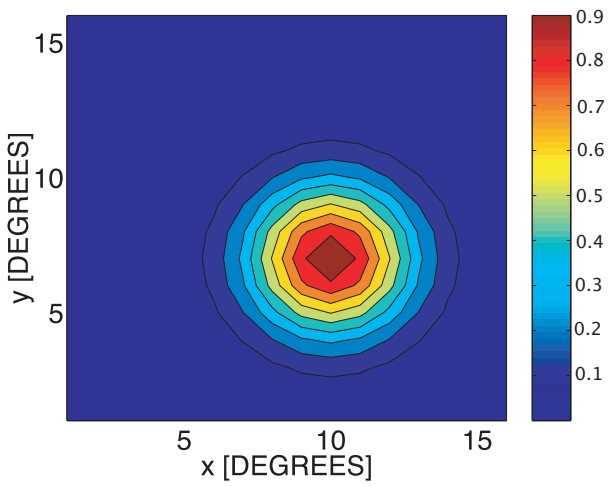

Fig. 2. A contour plot of the mapped receptive field of a single neuron, in the population before the a stroke lesion is induced The x- and y- corrdinates represent degrees of visual field

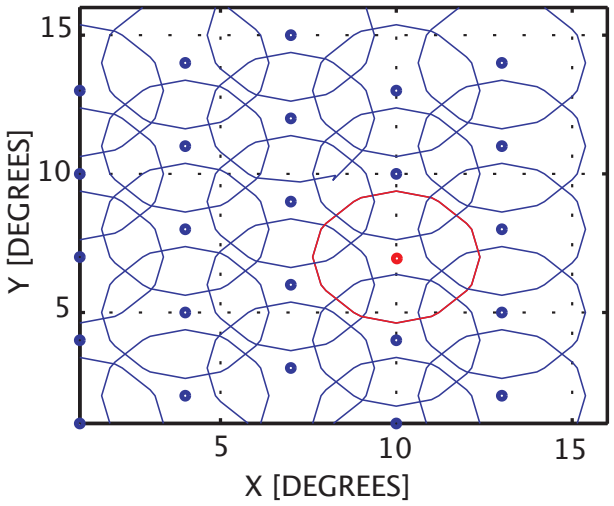

Fig. 3. Topographic map of receptive fields in a population of 225 neurons, but for simplicity the figure is restricted to every ninth neurons. Each exhibited neuron is represented by the peak point of its receptive field, and a curve indicating the half width of the field. The receptive field of the neuron showed in Figure 2 is shown with a red curve

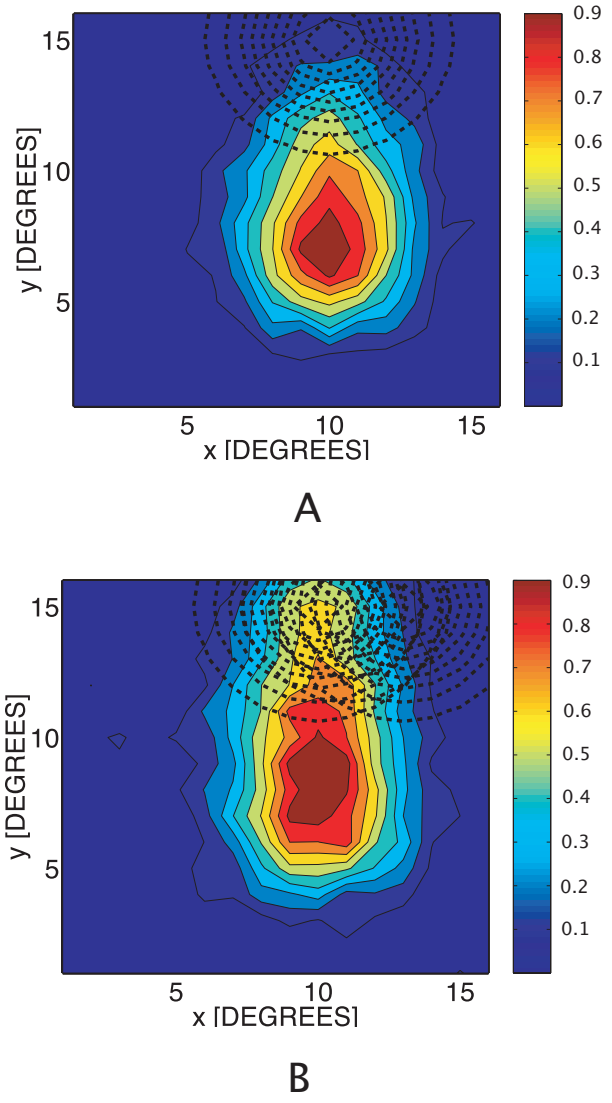

Fig. 4. Receptive field adaptation following stroke-like lesion of different sizes, obtained by computer simulation. The damage is represented with black dotted lines. The intact neuron responds to the lesion by expanding its receptive field towards the damaged area.

within the cortex because its receptive field are mapped across it. In each trial, a white noise is applied to the population and the response of each neuron is recorded and used to calculate the points of the receptive field.

The amount of overlap in the receptive field is important in terms of information transfer. Figure 3 shows how receptive fields of neurons in a population of neurons are topographically mapped across the cortex. Only a few of the neurons present in the population are shown in order to make the figure more understandable. Each receptive field is represented by its peak point, $(x_0, y_0)_n$ and a curve indicating the half width of the field. The amount of overlap of receptive fields is determined by the number of neurons in the population, the size of the visual field being represented and the width of the receptive fields σ.

Figure 4 shows how the size of a damage influences the enlargement of receptive field. The damage in Figure 4 B covers a larger area of neurons than the damage in Figure 4 A and therefore influences a greater drop in inhibition. The plasticity levels are increased, dependent on the drop in GABA and for these simulations, $\gamma = 0.02$ refers to the plasticity level in the cortex following a small lesion shown in Figure 4 A and $\gamma = 0.1$ is the plasticity value induced by the larger lesion shown in Figure 4B.

The distance between neurons and the damage is a significant parameter. Neurons that lie closer to the lesion in Figure 4 exhibit even larger changes in their receptive fields due to damages of the same sizes as presented in the figure. On the other hand, neurons lying further away from the lesion experience less enlargement in their receptive field. Figure 5 shows the relationship between the expansion of receptive fields and the distance of neurons to the lesion. The expansion of each receptive field is represented as the deviation, in

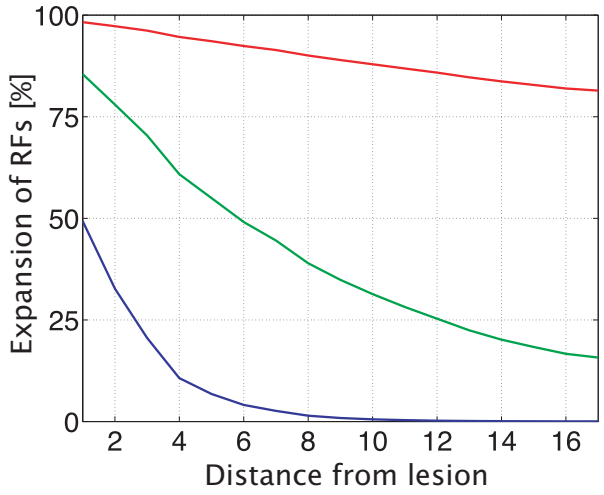

Fig. 5. Expansion in the receptive field versus the distance between the damage and the neurons is shown for different values of plasticity γ, which are dependent on the size of the damage. The blue line refers to $\gamma = 0.02$, green line to $\gamma = 0.1$ and the red line to $\gamma = 0.81$. Expansion is defined as the change in percentage between the base wiidth of the receptive field pre- and post lesion.

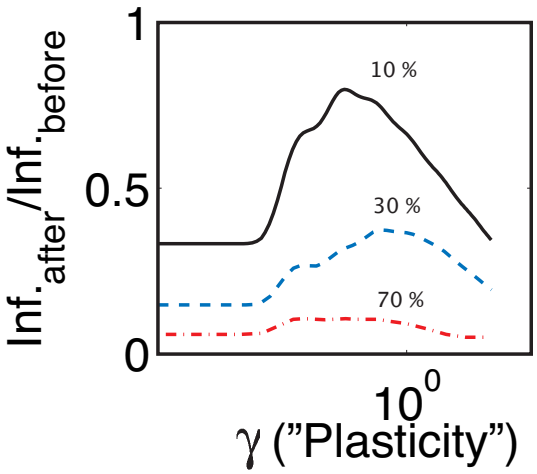

Fig. 6. Analytical results for Fisher Information as a function of the degree of plasticity γ. The black line indicates coding accuracy when the damage covers 10 % of the neurons in the population, the blue line refers to 30 % damage and the red line refers to 70 % damage. The population includes 225 neurons with original receptive field spread $\sigma = 2$. The curves are normalised to the Fisher information prior to the stroke. The left asymptote corresponds to the performance after stroke, but prior to functional recovery.

percentage, from the original base width, pre-lesion. The distance d_n from the damage is presented in arbitrary model units and is defined to be the shortest distance between neuron n and each cell within the damaged area.

The two lowest plasticity values presented in Figure 5 are the values induced by the two damages shown in Figure 4 A and B respectively. The value of $\gamma = 0.02$ only affects neurons closer to the damage than $d = 10$. It is evident that $\gamma = 0.81$ causes substantial enlargement in all neurons in the population, even the ones at the greatest, d. However, if the population were larger than the one presented here, the effects would decrease further away from the damage in the same manner and with the same relationship as for plasticity valuues $\gamma = 0.02$ and $\gamma = 0.1$.

B. Fisher Topographic information

Equations (17), (18) and (19) were implemented in order to explore the effects of different values of γ on the Fisher Information I. Figure 6 shows that the information transfer post stroke is dependent on the plasticity, γ. Following a stroke-like damage, the information transfer drops from its original value because neurons within the damaged area do not convey information about the applied stimuli. When the plasticity level is raised, the neurons surrounding the damage start to expand their receptive fields in order to take up lost functions, and the information transfer increases. However, when γ is raised even further and the expansion increases, overlap of the receptive fields becomes too much and information is lost again. This is due to the fact that infinitely large receptive field do not provide any information about applied stimuli because every stimulus pattern is weighted in the same way and no discrimination is accomplished. Large overlapping receptive fields are therefore not specific enough to give information about the input. There is therefore a certain value, γ^0 which optimises the performance of the cortex. Figure 6 shows the Fisher Information for three different sizes of damages. Bigger lesion led to more information loss and less recovery with increasing γ.

Note that although we have presented results here using the analytical formulae derived, we have obtained very similar results using a purely numerical implementation of the Fisher information calculation. The analytical formulation has particular advantages, in that it allows the effects to be broken down into excitatory, inhibitory, and interaction terms. The purely computational approach of course may be applied to a wider range of models.

IV. Conclusion

The current model describes how intact neurons surrounding a stroke-like cortical lesion adapt to the damage and to the resulting functional impairment. The neurons experience a dis-inhibition in their receptive fields and therefore their total receptive field expands in the direction of the lesion. The amount of enlargement apparent in each neuron is determined by two factors: the distance of the neuron in question from the damge and the size of the damage. Neurons close to to the damage expand their receptive field more than neurons further away. Our findings suggest that by tuning the receptive field plasticity levels to certain value, the information transfer through the cortex post stroke can be optimized. This may be of interest both for understanding the effects of potential therapeutic interventions in stroke, as well as for developing engineering principles for incorporating brain-like redundancy into machines.

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