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Imaging and Modelling of a Degenerative Disease of Retina

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***Abstract* - Dynamical systems like neural networks based on lateral inhibition have a large field of applications in image processing, robotics and morphogenesis modelling. In this paper, we deal with a double approach, image processing and neural networks modelling both based on lateral inhibition in Markov random field to understand a degenerative disease, the retinitis pigmentosa.**

Keywords: neural networks, lateral inhibition, retinitis pigmentosa, image processing, Markov random fields.

I. INTRODUCTION

In the vertebrate retina, cones are hyperpolarized when illuminated by light, but also receive a depolarizing input when receptors some distance away are illuminated. This antagonistic center-surround response is mediated by amacrine horizontal cells (Fig. 1 and Fig. 3), through a sign-reversing synapse to cones called *feed-back synapse* and a global mechanism, *lateral inhibition* [1], involved in edge enhancement and image contrasting [6,35], realizing concretely the Mach (boundary brightness overshoot) and Marr (Laplacian zero-crossing edge enhancement) effects.

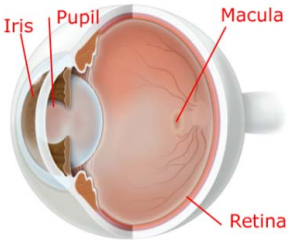

Fig. 1 - The retina inside the eye structure

Multiple contrast illusions (Fig. 2) are based on the lateral inhibition principle. Here, we will study how functions of rods and cones are differentially affected during the retinal degeneration of the *retinitis pigmentosa* and how this pathologic process can be modelled.

II. PHYSIOLOGICAL AND PATHOLOGICAL RETINA

In physiological retina, lateral inhibition causes illusions like the perception of artefactual stripes or spots. The lateral inhibition causes a reinforcement (or a decline) of brightness in a pixel if its neighbours are black (resp. white). This illusion is easy to simulate by computer and is illustrated in Fig. 2.

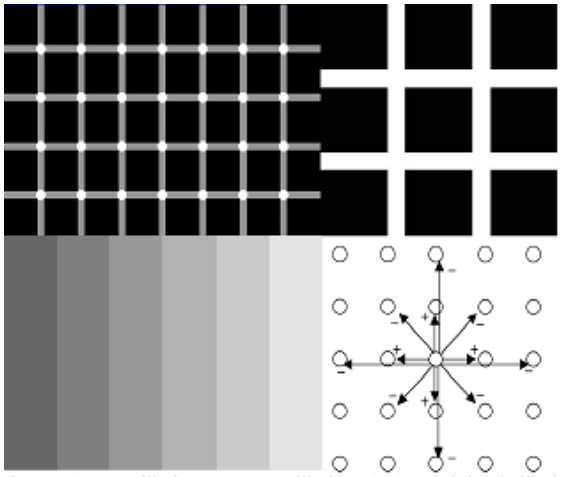

Fig. 2 - Contrast illusions: Hermann illusions (top); Mach bands illusion (bottom-left) and lateral inhibition with activation at short range (nearest neighbours neurons) and lateral inhibition at medium range (bottom-right)

In Fig. 2, the Hermann illusion is provoked by the local organization of inhibition and activation between retinal cells (bottom-right) and shows bright points at the intersection of grey stripes (top-left) and grey squares at the intersection of white stripes (top-right). On the bottom-left, Mach band illusion gives an enhancement of the vertical lines separating the different grey zones.

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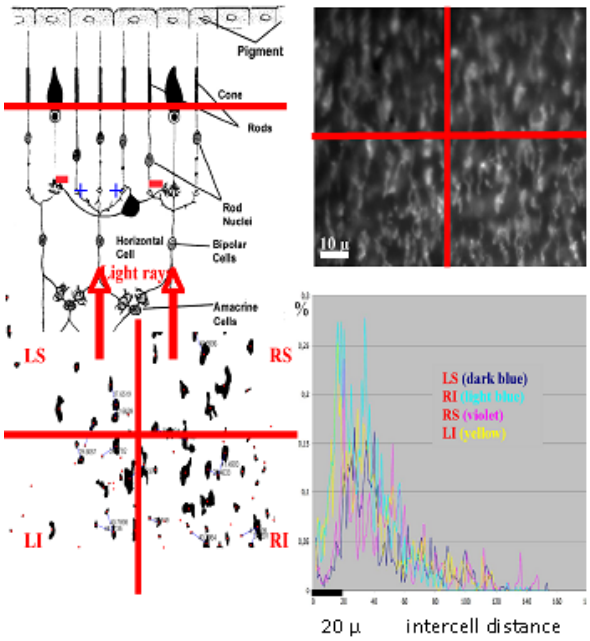

Fig. 3 - Physiological and pathological retina. Top-left: Lateral inhibition due to horizontal-cell synapses. Top-right: Confocal microscopy slice of mouse retina having retinitis pigmentosa [34]. Bottom-left: Segmentation of cones and rods showing an important cell deficit in the Left Superior quadrant (LS). Bottom-right: Histogram of the intercept distances showing a significant increase of the inter-cell distance in the LS quadrant (dark blue).

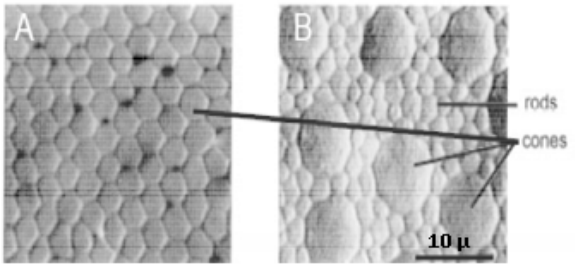

Fig. 4 - Local organisation of cones and rods in macula (A) and retinal periphery (B) [38]

The pathologies of the retina provoke a progressive death of the rods (like in retinitis pigmentosa in Fig. 3), which leads to cones apoptosis, due to non-secretion (by rods) of growth factor favouring the cones survival, causing the disappearance of the lateral inhibition, hence of the contrasting ability. Fig. 3 (Top-right and Bottom-left) shows a confocal slice of a sick retina where we can observe an important loss of both rods and cones in the left superior quadrant (LS). An analysis of the cells interdistance in the three other quadrants shows that the mean interdistance between cones in the peripheral retina (about 15μ) is better conserved than the interdistance between rods (about 3μ), proving the primary rod degeneracy.

III. Nearest Neighbour Models

A formal deterministic neural network R of size n is defined by its state variables $\{x_i(t)\}_{i=1\dots n}$, where $x_i(t)$ denotes the state of the neuron i at time t (equal to '1' if the neuron fires at this time and '0' otherwise). Then the discrete iterative system ruling the change of states in the network is given by the following equations:

$$x_i(t+1) = 1; \text{ if } H_i(t) = u_0 + \sum_{j,k \in V(i)} w_{ij}x_j(t) + v_{ijk}x_j(t)x_k(t) > \theta,$$
$$= 0; \text{ otherwise}$$

where $V(i)$ is a neighbourhood of i; $H_i(t)$ plays the role of the somatic electric potential; u_0 denotes an external field; w_{ij} designates the synaptic weight resuming the interactions of the neuron j on the neuron i; v_{ijk} is a non-linear effect coefficient (due to the presence of a triplet of neighbouring neurons firing together); and θ is a firing threshold (Fig. 5). The updating of the neuronal states can be operated [11]:

- either sequentially, after having chosen a certain order for the neurons,
- or block-sequentially, by parallel updating of each sub-network of partition R and then activating these sub-networks sequentially,
- or in a massively parallel way.

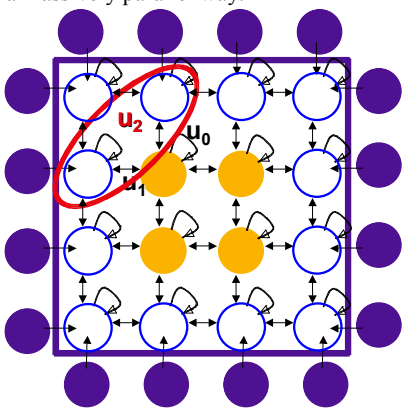

Fig. 5 - Translation invariant isotropic $4x4$ neural network with boundary neurons (violet), external field u_0, synaptic weight $u_1 = w_{ij}$, and non-linear effect coefficient $u_2 = v_{ijk}$

The updating rule can be randomized as follows:

$$P\left(x_i(t+1) = 1 \middle| x_j, j \in V(i)\right) = \frac{e^{H_i(t)/T}}{1 + e^{H_i(t)/T}}$$

We can easily show that this rule is the same as the deterministic rule above, when $T = 0$. The presence of a cone growth factor secreted by neighbouring rods will be taken into account by putting a '1' in a square of $100\mu^2$, containing at least one cone (Fig. 6), and a '0' if there is no cone. The deterministic or stochastic dynamics of such neural networks and their robustness has been extensively studied in [2-5] and [7-22].

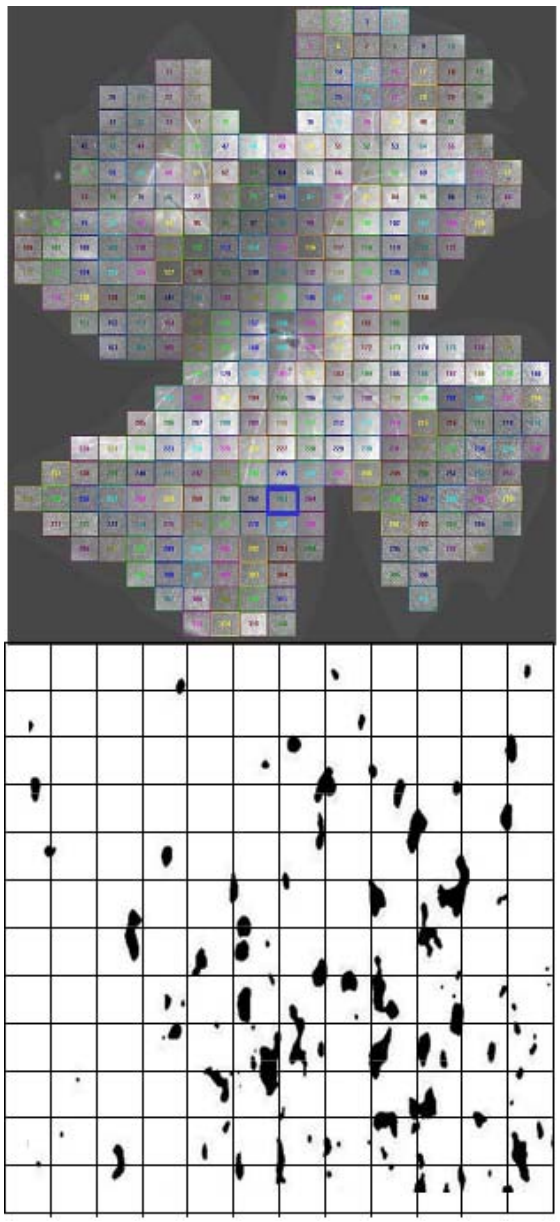

Fig. 6 - Top: Confocal slices of the retina: blue square indicates the slice of Fig. 3 (Top right). Bottom: Segmentation of the rods and cones of this slice

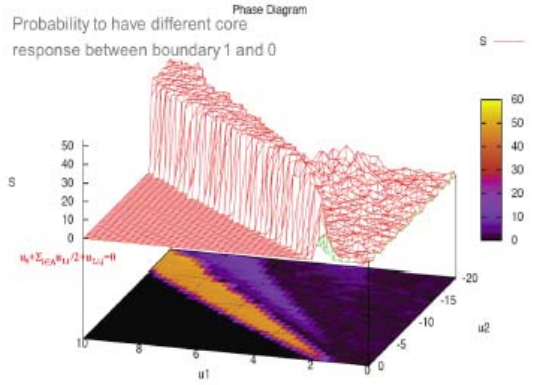

Fig. 7 - Dependence of the core states on the boundary states '1' and '0'

The occurrence of the values '1' in a grid made of squares, each of $100\mu^2$, will be supposed to be ruled by a nearest neighbour Markov random field [24-32] and [36,37], which corresponds exactly to the fixed configuration of the random neural networks defined above. There exists a classical unbiased maximum likelihood inference procedure for estimating all the coefficients (u_0, u_1, u_2) of the neural network (in the hypothesis of a translation invariant isotropic field with temperature '1'), since the corresponding statistical structure is exponential [18].

In the example of Fig. 6, the estimates are significantly different between the quadrants LS and RI, showing the presence of a pathologic process. If we assume the network states determined by this nearest neighbour modelling, we have to check if there is an influence of the boundary neurons (in violet in Fig. 5). It is possible to systematically study this influence by searching phase transition parametric conditions, i.e. values of the coefficients u_0, u_1, u_2 for which the states on the core depend on the states on the boundary. In the parametric circumstances where:

$$u_0 + 2u_1 + u_2 = 0, \text{ (cf. Fig. 8 where } u_0 = -3),$$

we observe a phase transition with the dependency of the core on the boundary, which proves that we have to be very careful in fixing the states on the frontiers of the retina [16,17].

IV. Spatial Renewal Binary Processes

There exist different alternatives to the nearest neighbour random neural networks, like the *reaction-diffusion process*, in which one can identify the diffusion coefficient and also the lateral inhibition parameters of the reaction part. There is also a way to escape the spatial Markovian character of the previous model, by supposing that the occurrence of the state '1' at time $t+1$ in the neuron i, given by $x_i(t+1) = 1$, is depending on the states on the first sphere (for the Manhattan distance L_1) centered at i, where we can meet a neuron in state '1'.

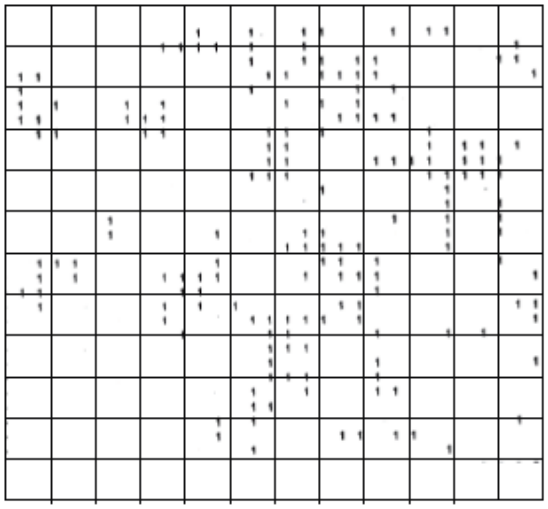

Fig. 8 - Simulated configuration of the states of a 2-dimensional renewal spatial binary random field [23]

A spatial random process verifying such a condition is called a *renewal spatial random field* [20,23] (analogous to the renewal temporal processes observed, for example, while tossing a coin) and we can estimate its parameters in the same way as for the spatial Markov random fields, that is by considering the associated statistical exponential structure in which estimates are of the maximum likelihood, unbiased and almost surely convergent.

We can see, in Fig. 8, a simulation of such a renewal spatial random field, showing configurations sparser than those observed for a spatial Markovian field, correlating more to the data in Fig. 6. A test of data adequacy can be performed over the spatial Markovian and renewal fields and we can retain the structure which best-fits the data, where the first model favours rod-cone interactions and the second model favours long-range interactions between cones.

V. CONTRAST ENHANCEMENT

Another way to detect an abnormality in the rod and cone distribution is to use the observed configuration as an artificial retina in order to contrast an input image. The latter can be made of pixels of different grey levels as in Fig. 9 (top-left). A normal retina treating the image must enhance homogeneous zones, by exploiting the fact that a square of pixels (or a peak) having the same medium (respectively high) grey level is reinforced (respectively undermined) by the presence (respectively absence) of a local activation and its boundaries are contrasted because of the absence of external inhibition (Fig. 10). If the distribution of the weights follows the scheme given in Fig. 2 (bottom-right) and if the neurons are dispatched in the four quadrants as in Fig. 3 (bottom left), then the contrasting is realised only in RI quadrant as in Fig. 9 and Fig. 10.

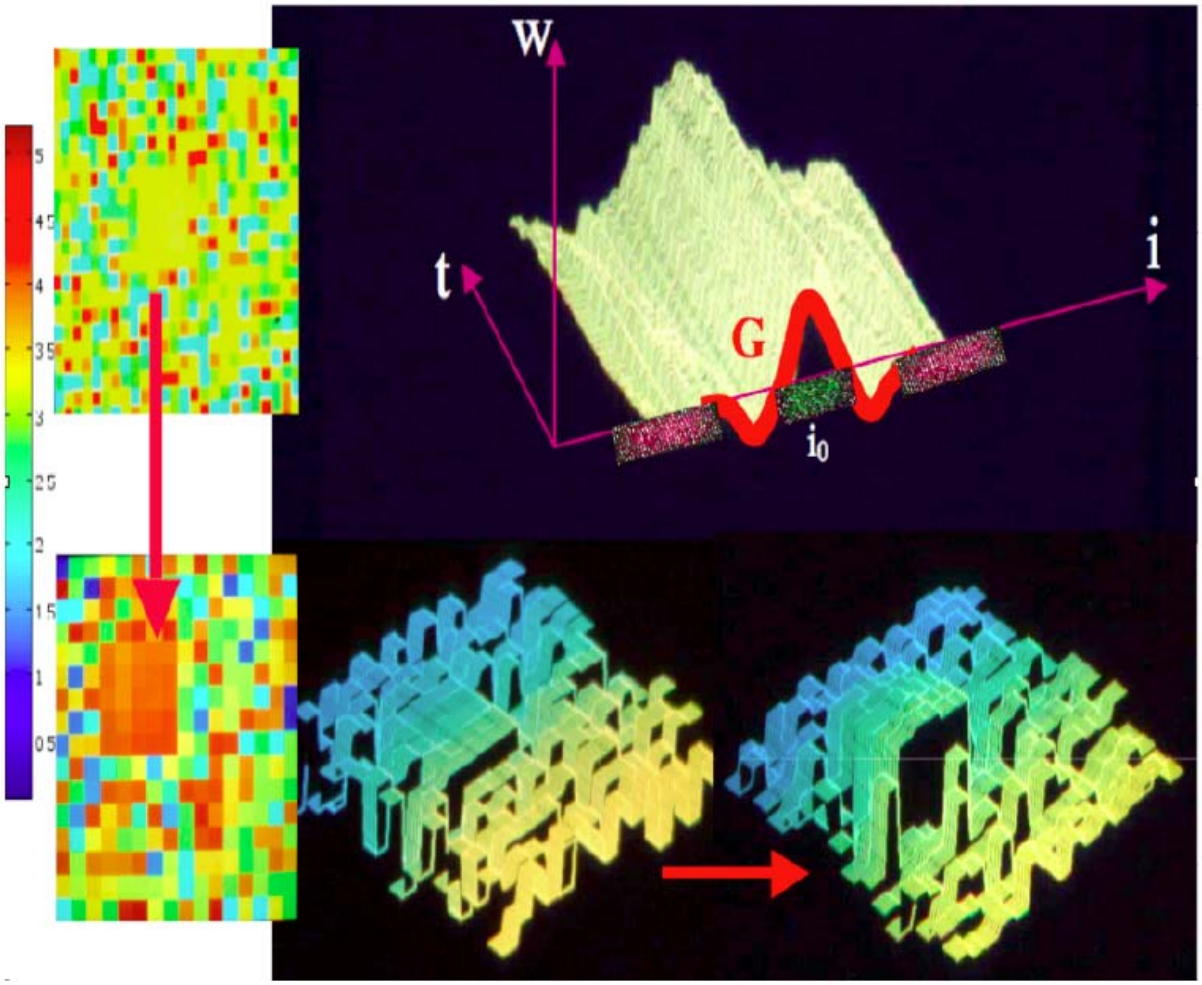

Fig. 9 - Contrast enhancement. Bottom-left: Lateral inhibition causes the local contrast enhancement of the yellow square (with medium level in false colors) into a contrasted bright orange square. Top-right: Evolution in time of the DOG function representing an *activation* near the central neuron, i_0 (green links) and an *inhibition* (red links) farther away. Bottom: Same processing in grey level with initial image in the middle and contrasted on the right.

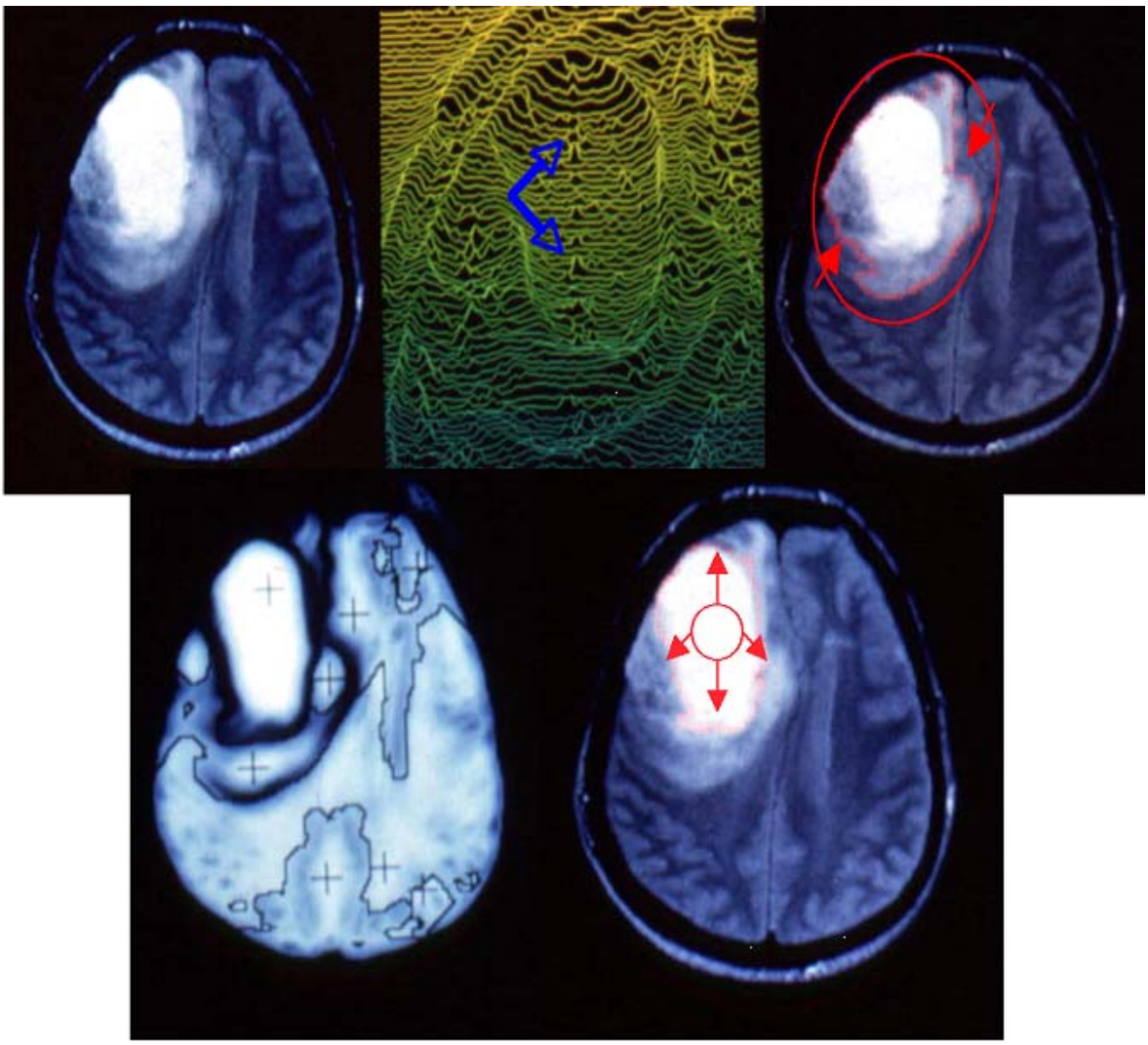

Fig. 10 - Contrasting and contouring medical images. Top-left: initial NMR image of a brain tumour. Top-middle: contrast enhancement with apparition of a central activity (blue arrows). Top-right: boundary of the compressed tissue (external snake-spline). Bottom-left: tumour segmentation. Bottom-right: tumour boundary (internal snake spline)

VI. CONCLUSION

We have shown in this paper that a retinal pathology, as in retinitis *pigmentosa*, could be studied by identifying from observed data, either a Markovian or a renewal spatial random field, leading to the hypothesis of local rod-cone interactions or of a long-range cone-cone interactions. In the first case, the interactions fading due to disappearing of rods depicts existence of an action by rods, like secretion of a specific cone growth factor, which is in agreement with the genetic studies. The conservation of the contrasting retinal function can be tested for the still healthy zones by using, as input, a reference image having inside a homogeneous zone to enhance. This is being extensively used in image processing applications as in Fig. 10. The absence of contrasting power could constitue a good test of loss of this major functionality related to the integrity of the lateral inhibition rod-cone architecture.

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