MODELING OF GLAUCOMA INDUCED CHANGES IN THE RETINA AND NEURAL NET ASSISTED DIAGNOSIS

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Abstract. A system for modeling and early detection of Glaucoma induced chances in the human retina is described. The system includes a modeling tool for design of semi-realistic retinal pictures, that may either be used for educational purposes or (as here) as a laboratory for controlled signal processing experiments. The detection system includes preprocessing algorithms for elimination of intensity variations and other artefacts. The final segmentation step is based on a cellular neural network.

INTRODUCTION

Vision is the most important of the human senses. The human eye can be considered a spherical structure with a radius of about $12mm$. The inside is filled up by a transparent substance *corpus vitreum*. The *retina* covers the inside surface and holds the optically sensitive nerve ends. Furthermore the retina holds nerve fibers collecting the optical signals. These fibers leave the eye through the optical disc (the so-called blind spot). If the internal pressure of the eye increases or if the blood supply to the optic disc or retina is decreased nerve fibers can degenerate and defects in the visual field appear. Since the human visual system can partly compensate for the lack of visual field, the increased pressure may go undetected beyond the limit where the induced changes are reversible. The pathological changes are collectively called *Primary Open Angled Glaucoma* (POAG). Early diagnosis is essential for preserving good visual function. If untreated POAG will lead to blindness within five to ten years. The diagnosis is quite common, in Denmark involving about 2% of the population, mostly elderly [10]. About 5% of the diagnosed eventually end up blind.

In this project the objective is to develop tools for early diagnosis of POAG based on so-called *fundus* pictures, i.e., images of the retina taken though the pupilla with a dedicated camera system. First, a model has been developed for modeling of the changes in the retina induced by Glaucoma. This model may be used for training of physicians, and as in this study, a laboratory for controlled experiments with pattern recognition devices. Secondly, we have developed a preprocessing scheme and cellular neural networks for detection of the nerve fiber pattern as seen in fundus pictures, for more details see [10, 7].

An image analysis study of Glaucoma detection was carried out by Yamazaki et al. [11]. In this investigation diagnosis is based on a analysis of a single intensity profile approximately orthogonal to the line connecting the optical disc and the fixation point. In our experiment this scheme has shown not to be robust to the variations in image quality of standard fundus pictures.

MODELING OF FUNDUS PICTURES AND GLAUCOMA

In order to create a workbench for comparison of various computer algorithms for enhancement and diagnosis, we have created a simple parametric model of fundus pictures. The model is based on analysis of original fundus pictures c.f. figure 1. The prominent features of the scene are *blood vessels* here seen as dark structures emanating from the periphery of the optical disc. The black spot is *Macula* (the fixation point), where the optical sensor density is maximal. Close visual inspection reveals that the nerve fibers form a multi-layered quite noisy line-pattern texture. For a discussion of textures see e.g. [6]. A close-up is shown in the right panel of figure 1. Glaucoma induced nerve fiber loss takes two different forms: a uniform reduction of fiber density or a characteristic regional (wedge) disappearance of fibers. An example of the latter is seen in figure 2.

ARTIFICIAL FUNDUS PICTURES

The image model consist of two modules that add features to a matrix with predefined optical disc and fixation point locations: *Blood vessel design* is a mouse based drawing module in which a semi-realistic design can be created with varying vessel diameter and vessel edge smooting. The *nerve fiber generator* draws line patterns of parametric second order curves. The parameters can be defined separately in 36 sectors surrounding the optical disc. The orientation of these sectors is defined by the optical disc and the fixation point. Noise is added with controlable signal to noise ratio to provide a realistic local appearence of the texture.

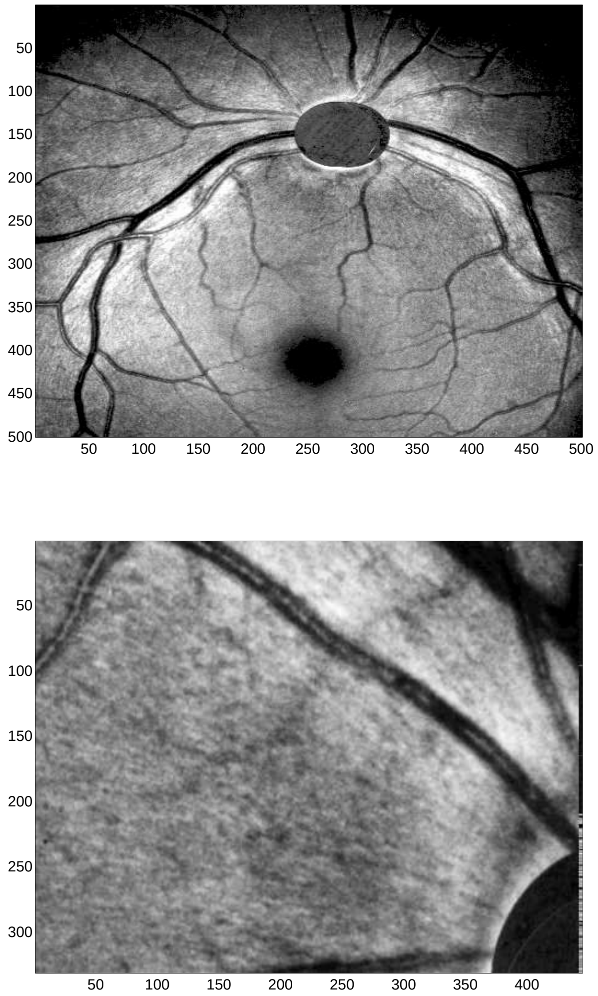


Figure 1: A socalled *fundus* picture showing the retina. Note the blood vessels emanating from the blind spot and *Macula*, the fixation point, where optical sensitivity is maximal. In the lower panel we show a close-up with the characteristic texture due to nerve fibers.

To emulate the multi-layered structure found in real fundus pictures several families of curves can be added. The curve parameters are slightly modified from one family to the next. In the images generated for the present study we have used four such layers. Two layers were added before addition of the blood vessel system and two layers added after, reflecting the layering in the real photograph.

PREPROCESSING

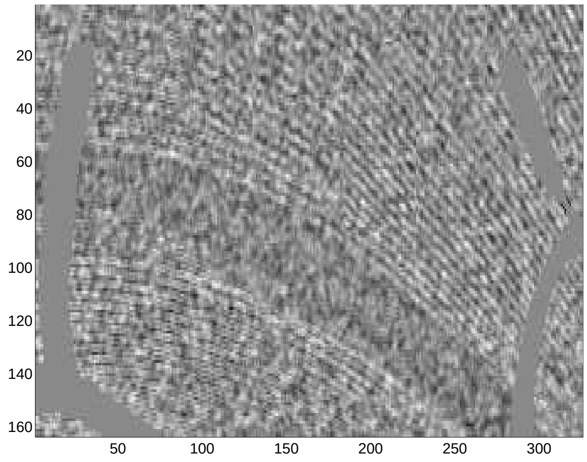
The first steps in the preprocessing of a fundus picture concern elimination of illumination artifacts and of the blood vessel system. These steps involve band-pass filtering and simple thresholding to segment the (dark) blood vessels. The location of the blood vessel system is kept in a separate mask.

TEXTURE PREPROCESSING

Texture detection algorithms are legio. Many such algorithms are based on a two-level design in which a basic filter detect local features followed by a merging algorithm that forms a global segmentation in regions of textures see e.g. [6] for a recent example. We follow a similar approach here. Our preprocessor consist of simple adaptive, quadratic, local discriminant trained by example. The segmentation step is carried out by a cellular neural network based on mean field annealing.

QUADRATIC DISCRIMINANT

The preprocessor classifies individual pixels based on the statistics of its neighborhood (a square window of MxM pixels). A simple maximum likelihood discriminator was found sufficient. The two populations of MxM windows (nerve fiber texture presence/absence) are modeled as two Gaussian distributions with individual means and covariance structures. The mean and covariances are estimated from a sub-image of $350x350$ pixels generated by the Glaucoma model. Since the line textures show the characteristic directions of flow c.f. figure 2 individual populations are trained for eight regions determined by the location of the optical disc and the fixation point. To illustrate the performance of the quadratic discriminant we show in the left panel of figure 2 a synthetic image with a characteristic regional defect (note also that the blood vessels have been eliminated leaving areas of uniform grey value). In the right panel of figure 2 we show the output (difference in log likelihoods) provided by the discriminant (window size $M = 13$). To segment the noisy result of the preprocessor into regions that quantifies the presence of nerve fiber a global segmentation algorithm is needed.



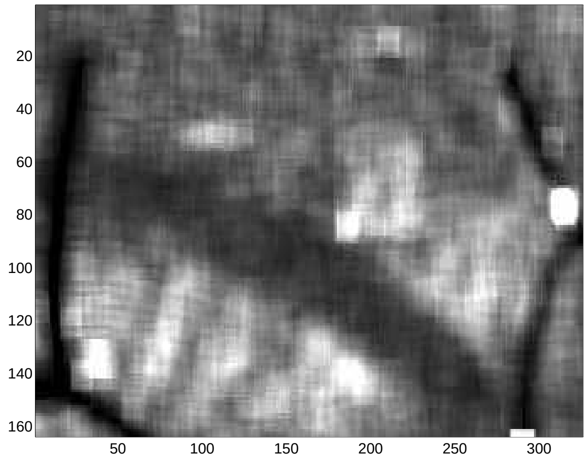


Figure 2: Upper panel: Synthetic fundus picture with a characteristic wedge regional absence of nerve fibers. Lower panel: Output of likelihood based discriminant.

CELLULAR NETWORK DESIGN

The cellular network concept was developed by Chua and Yang [2]. A cellular neural net is a locally connected network of simple processing units, typically operating as feed-back processes converging to a fixed point. The Bayesian or *Maximum Posterior* approach is a very successful device for signal processing (see [9] for a review), a particular attraction is that it leads to algorithms that map well onto cellular neural networks. The basic idea of the Bayes approach is to consider both the source (un-degraded) signal and the degradation as stochastic processes. Bayes' formula can then be used to construct the distribution of the reconstructed signal, conditioned on the observed degraded signal. Segmentation is an important step in many computer vision systems. Here we use the Bayes scheme to derive a simple cost-function that can be minimized by a cellular neural network. The resulting cost-function is identical to the one used by Carnevali *et al.* [1]. The target signal is a "smooth" binarization of a grey-scale image d_j, in terms of two-valued pixels $S_j \in \{-1, +1\}$. The prior distribution is designed to emphasize smoothness

$$P[S] \propto \exp\left(-\sum_{j=1}^{N}\sum_{j'=1}^{N} M(j,j')(S_j - S_{j'})^2\right) \qquad (1)$$

$M(j,j')$ defines the connectivity, hence the unit cell of the cellular network. Here we just connect the nearest neighbors with strenght w_{M}.

We furthermore assume the signal degradation to consist in addition of white Gaussian noise. This degradation process leads to the following conditional distribution:

$$P[d|S] \propto \exp\left(-\frac{1}{2\sigma^2}\sum_{j=1}^{N}(S_j - d_j)^2\right) \qquad (2)$$

We use Bayes' formula to obtain the posterior distribution: $P[S|d] \propto P[d|S] * P[S]$. Clearly the posterior distribution is of the Gibbs form[1], with a cost-function given by the negative logarithm of the posterior distribution: $-\log P[S|d]$. We also note that the state dependent part of the cost-function is linear in the parameters w_{M} and $w_{\mathrm{d}} \equiv 1/\sigma^2$. This makes it suitable for Boltzmann machine learning [3, 4]. In this communication, however, we apply the cellular network with fixed parameters.

The Mean Field annealing method for estimation of averages over Gibbs distributions is well documented in the litterature see e.g. Hertz *et al.* [5]. The cellular neural network minimizes the Mean Field *free energy* and can be implemented either in analog mode or in discrete time mode:

[1]A distribution of the form $P(x) = Z^{-1} exp(-E(x)/T)$, where $E(x)$ is a cost-function, bounded from below, and T is a parameter

$$\langle S_j^{t+1} \rangle = (1 - \frac{\Delta}{\tau})\langle S_j^t \rangle + \frac{\Delta}{\tau} \tanh \left(\beta^t \left(\sum_{j'=1}^{N} M(j,j')\langle S_{j'}^t \rangle + w_d d_j \right) \right) \qquad (3)$$

where the time-scale Δ/τ can be used to control the stability of the iteration process in digital implementation[8]. β^t quantifies the annealing schedule, in this work we use the simple schedule: $\beta^t = \beta^1 + (t/t_{max})(\beta^2 - \beta^1)$.

We illustrate the performance on the image produced by our synthetic fundus picture system. In particular we use the Mean Field scheme for segmentation of the output of the quadratic texture discriminant (figure 2). We set the parameters to $w_{\mathrm{M}} = 1.0$, $w_{\mathrm{d}} = 0.01$. The resulting segmentation after 20 iterations of the deterministic equation (3) is presented in figure 3.

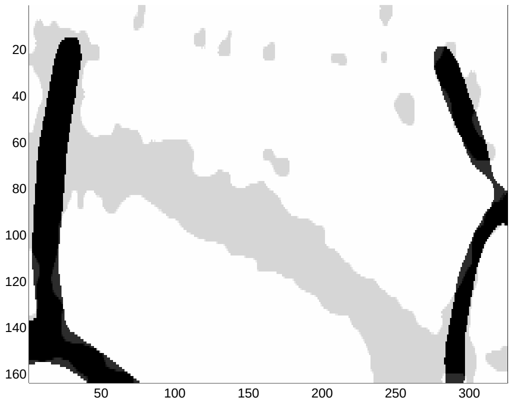


Figure 3: Output of the cellular segmentation network. The black areas represent the blood vessels that have been identified independently. Grey color signify areas of nerve fiber loss. The characteristic regional defect is assigned correctly. Close visual inspection of the synthetic input corresponding to the smaller grey spots indeed shows that the noise has degraded the texture significantly and it is unclear what the "true" classification should be.

Note that the segmentation network eliminates local noise. The resulting segmented image can be used either for rutine inspections to produce early warnings or for quantitation of the progress of the desease state and response to medication.

CONCLUSION

We have presented a modeling tool for design of synthetic fundus pictures. The system may be used either for educational purposes or as here for use as a laboratory for experiments with pattern recognition devices aimed at diagnosis of Glaucoma. We have designed and presented results of a simple and fast system for detection of nerve fibers in fundus pictures. Quantitative nerve fiber detection will be a key component in future automatic systems for rutine screening against Glaucoma. Current work concerns further test of the system and experiments on real fundus pictures.

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