The Application of GHMRF to 3-D Synthetic Proliferation

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ABSTRACT

This paper presents a novel tissue proliferation model of extraneuronal filaceous material consisting of accumulation of the amyloid beta-proteins. Proposed model is constructed using a 3-D Gaussian Hidden Markov Random Field obtained from fluorescent microscopy measurements.

Keywords: neurodegenerative diseases, variant of Creutzfeldt-Jakob disease, Alzheimer disease, Bovine Spongiform Encephalopathy, 3-D Gaussian Hidden Markov Random Field, artificial proliferation, Iterated Conditional Modes

1 INTRODUCTION

The neurodegenerative diseases, such as Alzheimer, BSE (Bovine Spongiform Encephalopathy), CJD (Creutzfeldt-Jakob Disease) and vCJD (variant of Creutzfeldt-Jakob) [4], are disorders of a great socio-agricultural significance as seen in many WHO testimonials. These diseases are characterised by an accumulation of the extraneuronal filaceous material consisting of amyloid beta-proteins [1][5][6][7]. The structurally modified protein izoform (prion) is reduplicated into surrounding proteins (S. B. Prusiner). The spatial characteristic form of the disordered protein plaque is observed as the so-called florid plaque in the vCJD.

The study presented in this paper is an integral part of the scientific research program concerning the investigation into the cerebral amyloidoses pathology by ultrastructural and image analysis techniques [8][9][10][11]. It is foreseen that the results will make it possible to recognize the plaque's nature and the disease's evolution progress. The previous study has been focused on the 3-D florid plaque reconstruction using some serial sections of the human hipocamp sliced by a microtome and observed using a TME (Transmission Electron Microscope). The overall description of the 3-D object reconstruction using the photographed specimen slices has been presented in papers [8][9][10].

In this article, the 3-D acquired data (512×512×13 voxels) from a fluorescent microscope has been used to build a statistical model of plaque construction using GHMRF (Gaussian Hidden Markov Random Field), see Figure 1. The model permits reconstructions of the hypothetical tissue proliferation in space and time.

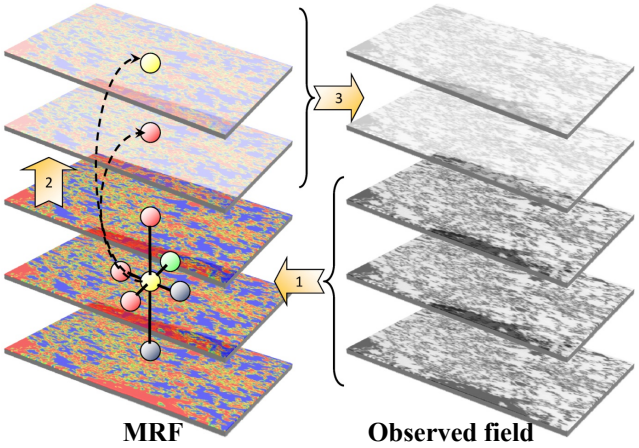

Figure 1 Application of a GHMRF model to 3-D tissue representation of protein plaques. The picture has been presented in [11].

2 THE PLAQUE MODEL

The plaque model in a vCJD has been prepared using a GHMRF in the 3-D space, where the cliques are constructed in a 6-neighbourhood system (see Figure 1). Internal relations are described by a hidden Markov Random Field (MRF) in a finite 6-state space with a Gibbs probability distribution. An observed random finite field is defined in the 256 states finite domain and generated by the MRF by the emission probability function.

The values of the hidden random field of the analyzed tissue (Figure 2a) are estimated using Iterated Conditional Modes (ICM) [1] and expectation-maximization (EM) algorithm [2]. The estimated MRF has been presented in Figure 2b. The accumulation of the extraneuronal filaceous material is not a reversible process; therefore, the MRF state flow can be represented by a unidirectional graph, where states 0÷2 and 3÷5 are associated with the regular tissue and plaque, respectively.

The obtained information about the probability of appearance of a given state for the given neighborhood states ($p_{1x2},\ldots$) can be used for generation of a plaque hypothetical shape beyond the fluorescent microscope penetration depth (Figure 3).

Most of the information about the protein izoform reduplication can be obtained from the input image and simple MRF analysis:

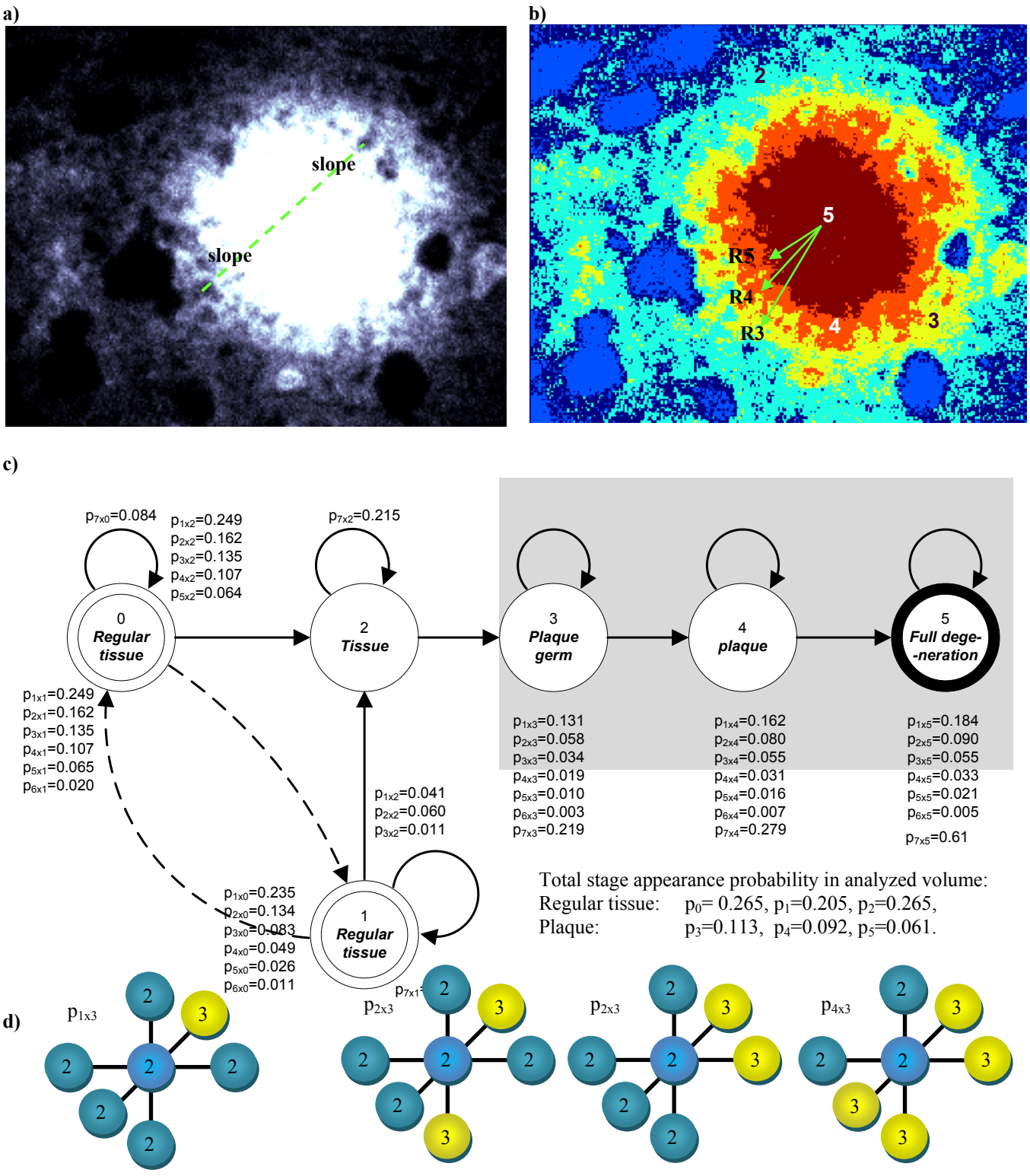

Figure 2 a) The image of a vCJD tissue prepared PrP obtained from a fluorescent microscope. b) GHMRF model of the vCJD tissue obtained using ICM and EM algorithms for the estimation of a 3-D GHMRF (0,1- regular tissue, 2-5 tissue containing PrP markers). c) The tissue degeneration graph deduced using estimated GHMRF. d) Several examples of the appearance boundary probability $p_{i\times j}$, where ***i*** is the number of neighboring elements in the ***j****-state*.

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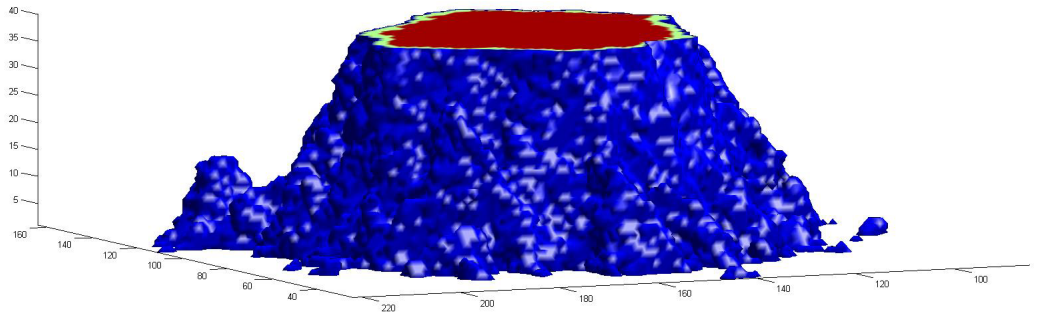

Figure 3 Hypothetical shape of a plaque generated using estimated MRF and the state appearance probability.

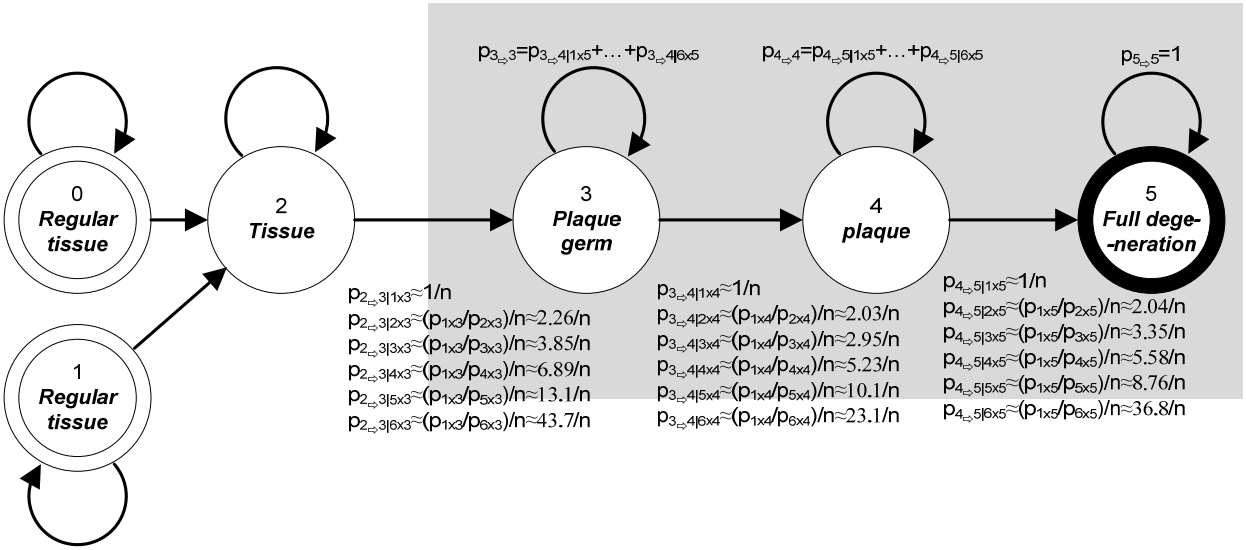

Figure 4 Proposed model of the tissue proliferation. The state transition probability is defined for given neighborhoods state.

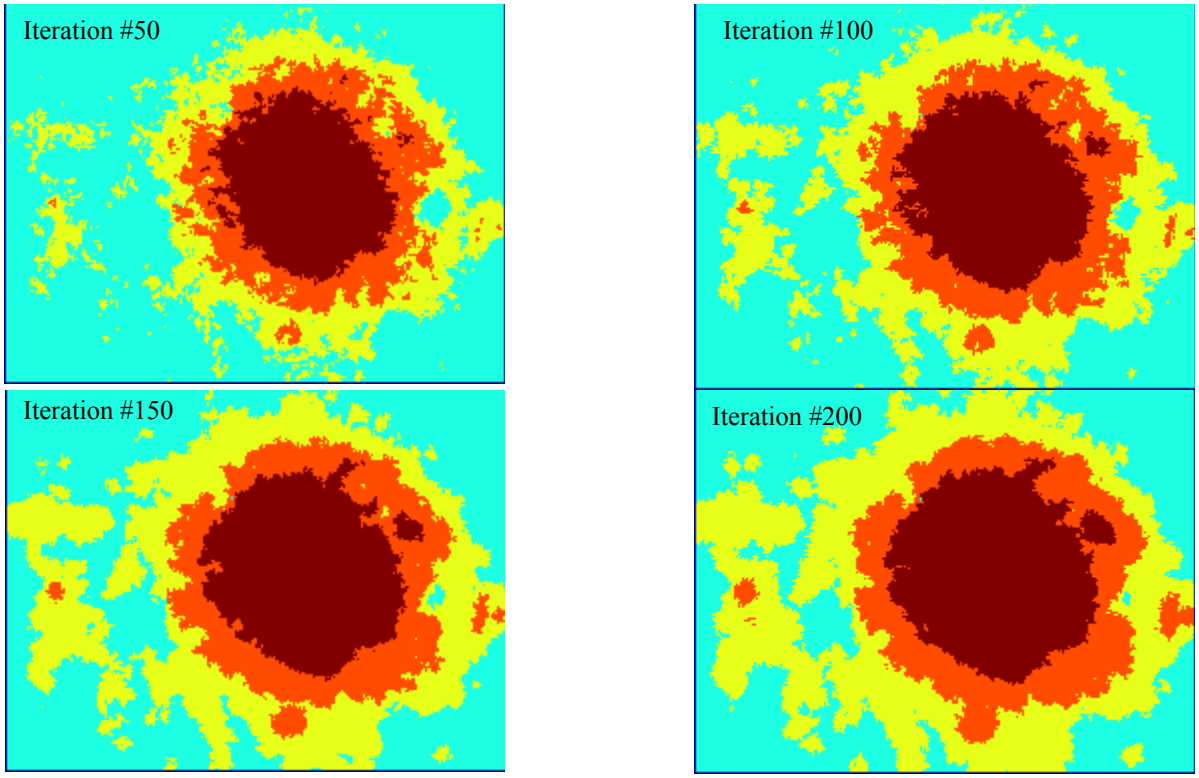

Figure 5 Examples of the proliferation of an amyloid plaque from Figure 2b using model in Figure 4 for n=100.

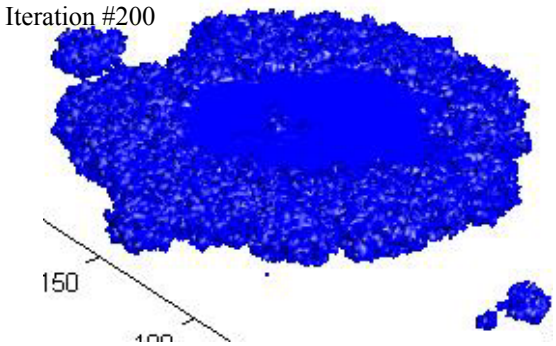

Figure 6 The 3-D visualization of plaque.

1) The appearance probability of given state for given neighborhood states ($p_{2\Rightarrow 3|1x3}/p_{2\Rightarrow 3|2x3},\ldots$) can be used for the estimation of the final transition probability $p_{A\Rightarrow B|mxC}$, where A⇨B describes transition from the stage A to B, m×C describe the number of neighborhoods in the C state. It can be observed that in the majority of cases the final probability is proportional to the number of neighborhood elements with higher accumulated extraneuronal filaceous material.
2) Only probabilities $p_{mxC}>0.001$ are included in Figure 2c; therefore, it can be observed that most of the transitions can be omitted because of their low probability.
3) The ratios of the probabilities ($p_{2\Rightarrow 3|1x3}/p_{3\Rightarrow 4|1x3}$, $p_{3\Rightarrow 4|1x4}/p_{4\Rightarrow 5|1x5}$) can be estimated from the slope of the emitted random field and the ratio of the equivalent lengths of the radii R3, R4, R5 (Figure 2b). It will be assumed that $p_{2\Rightarrow 3|1x3}\approx p_{3\Rightarrow 4|1x3}\approx p_{4\Rightarrow 5|1x5}$.
4) The proliferation speed cannot be estimated directly; therefore, an additional parameter *n* is introduced to describe this phenomenon.

3 SUMMARY

The proliferation model based of the accumulation of the extraneuronal filaceous material obtained from empirical data has been presented (Figure 4). The main advantage of proposed approach is a possibility of conducting a hypothetical proliferation analysis of the neurodegenerative diseases (Figure 5,Figure 6).

Future research should also take into consideration experimental analysis of the proliferation in stages 0 and 1 as well as more accurate modeling of the plaque germ formation and experimental estimation of the proliferation speed.

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REFERENCES

[1] Julian Besag: "On the Statistical Analysis of Dirty Pictures" Journal of the Royal Statistical Society. Series B (Methodological), Vol. 48, No. 3. (1986), pp. 259-302

[2] A. P. Dempster, N. M. Laird, and D. B. Bubin. "Maximum likelihood from incomplete data via EM algorithm". *J. of Royal Statist. Soc.*, series B, 39(1):1-38, 1977

[3] L. C. Serpella, M. Sundea, C. C. F. Blakea. "The molecular basis of amyloidosis". CMLS, *Cell. mol. life sci.* 53 (1997), Birkhauser Verlag, pp. 871–887

[4] A. Grams, P. Liberski, T. Sobów, M. Napieralska, M. Zubert, A. Napieralski: „The morphometric analysis and recognition an amyloid plaque in microscope images by computer image processing". *Folia Neuropathologica*, Vol.39(4) 2000,pp.183-187

[5] N. Streichenberger, et al. "The first case of new variant Creutzfeldt-Jakob disease in France: clinical data and neuropathological findings". *Acta Neuropathol* (2000) 99, pp. 704–708

[6] P. P. Liberski, Don C. Guiroy, E. S. Williams, A. Walis, H. Budka. "Deposition patterns of disease-associated prion protein in captive mule deer brains with chronic wasting disease". *Acta Neuropathol* (2001) 102, pp. 496–500

[7] M. Zubert, M. Napieralska, A. Napieralski, P. Liberski, A. Grams.: "The Amyloid Plaque Model and its Application to Neurodegenerative Disease Diagnosis". *11-th International Conference MIXDES 2004*, Szczecin, Poland 24-26 June 2004, pp.595-598

[8] A. Grams, P. Liberski, T. Sobów, M. Napieralska, M. Zubert, A. Napieralski.: „The morphometric analysis and recognition an amyloid plaque in microscope images by computer image processing.". *Folia Neuropathologica*, Vol. 39 (4) 2000, pp. 183-187

[9] Zubert M., Napieralska M., Napieralski A., Sikorska B., Liberski P. P., Grams R.: "Three-Dimensional Reconstruction of the Florid Plaque in variant Creutzfeldt-Jakob Diseases". *NSTI NanoTech 2006 (NSTI BioNano 2006)*, Vol. 2, pp. 473-476, Boston, May 7-11 2006, ISBN 0-9767985-7-3.

[10] M. Zubert, M. Napieralska, A. Napieralski, B. Sikorska, P.P. Liberski, and R. Grams. "The Image Registration of TME Biomedical Images in variant Creutzfeldt-Jakob Diseases". *IEEE Symposium on Computational Intelligence in Bioinformatics and Computational Biology - 2006 IEEE CIBCB*, Toronto, Sep 2006, pp. 443-450

[11] M. Zubert, "The application of numerical methods and computational geometry to solving interdisciplinary scientific problems". *Scientific Bulletine of the Technical University Lodz, No. 1031, Scientific Thesis No. 373*, pp. 255, Lodz 2008 r. -