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ART: Automatic reconstruction of tubular structures: from single neuron to whole brain – a multiscale approach to integrated brain function

M Sibila(1,2,3), A Hess(4), K Obermayer(1,2)
1) Berlin University of Technology, Faculty IV, Electrical Engeneering and Computer Science, Neural Information Processing Group, Germany; 2) Bernstein Centre for Computational Neuroscience Berlin, Germany; 3) Humboldt University Berlin, Institute for Theoretical Biology, Systems Immunology Group, Germany; 4) Friedrich-Alexander University Erlangen Nuremberg, Institute for Experimental and Clinical Pharmacology and Toxicology, Pharmacological Imaging and Image Processing Group, Germany

Our ongoing research aims at a combined experimental and theoretical breakthrough in the registration and interpretation of spatially extended and at the same time spatially highly resolved data of brain activity. This will be achieved by a combination of different brain imaging methods - electrophysiological recording (Ephys), optical recording of intrinsic signals (ORIS), recording of neuronal activity using voltage sensitive dyes (VSD) and functional magnetic resonance imaging (fMRI) on rodent brains - exploiting the complementary advantages of each method.
We plan to develop methods for automatic generation of anatomical reference systems for rodent brains as we have already established for histological and autoradiographic data (see Fig. 1 left). The multicontrast (T1,T2, PD etc.) MR data will be preprocessed to reduce artifacts, automatically segmented (see Fig. 1 right) and geometrically reconstructed as closed surfaces (see Fig. 1 left). Besides many technical issues not addressed here, the main problem in analyzing multimodal image data is the registration of the individual measurements. Since the brain vasculature is visible using all applied techniques (MR, ORIS, VSD and Ephys) we will register all data using the geometrically reconstructed vascularization pattern. Data from different animals will by geometrically transformed (warped), based on the surface description of the identified structures, to correct for interindividual variations. This will allow matching of data from several individuals onto a generic reference. A dynamic reference system and moreover algorithms to generate it would increase the interpretability of data gained from e.g. transgenic animal models in medical diagnostics and pharmacological testing, thus boosting their usefulness for human research.

We present here methods for automatically reconstruction of tubular structures (Schmitt et. al 2004, Gaudnek et. al 2005), which are already successfully applied to reconstruct individually stained neurons (Evers et. al 2004) and brain vascularization of rats, imaged by magnetic resonance angiography (MRA) and computer tomography (CT). Whereas the neuron reconstruction method needs some user interaction, namely a rough initialization of the branch points, we succeded to develop a fully automatic reconstruction method of vascularization patterns. For the neuron reconstruction we used generalized cylinders, whose radii and axes are fitted to the data minimizing an energy functional, regularized by a smoothness constraint. To achieve the required accuracy (under 0.1 microns) we additionally implemented a segmentation method on top of this, based on geodesic active contours, which allow for arbitrary shapes. For the reconstruction of blood vessels, we automatically segment the data first, derive a midline skeleton and fit gereralized cylinders to the image data. Since the topology of the brain vasculature is much simpler than that of a complex motoneuron, no further user interaction is needed.

• Evers JF, Schmitt S, Sibila M, Duch C. Progress in functional neuroanatomy: precise automatic geometric reconstruction of neuronal morphology from confocal image stacks. J Neurophysiol. 2004 Nov 10

• Gaudnek M., Hess A., Obermayer K., Budinsky L., Brune K., and Sibila M. Geometric reconstruction of the rat vascular system imaged by mra. IEEE ICIP, 1278-1281, 2005

• Mohr, J., Hess, A., Scholz, M. and Obermayer, K. A method for the automatic segmentation and functional evaluation of autoradiographic image stacks." *J Neurosci Methods* 134:45-58, 2004

• Pielot, R., Scholz, M., Obermayer, K., Gundelfinger, E. D. and Hess, A. A new method of point-based warping to reduce inter-individual variations in brain imaging." *Neuroimage 19*, 1716-1729, 2003

• Schmitt S., Evers JF., Duch C., Scholz M., and Obermayer K., New methods for the computer-assisted 3D reconstruction of neurons from confocal image stacks, NeuroImage, 23:1283-1298, 2004.

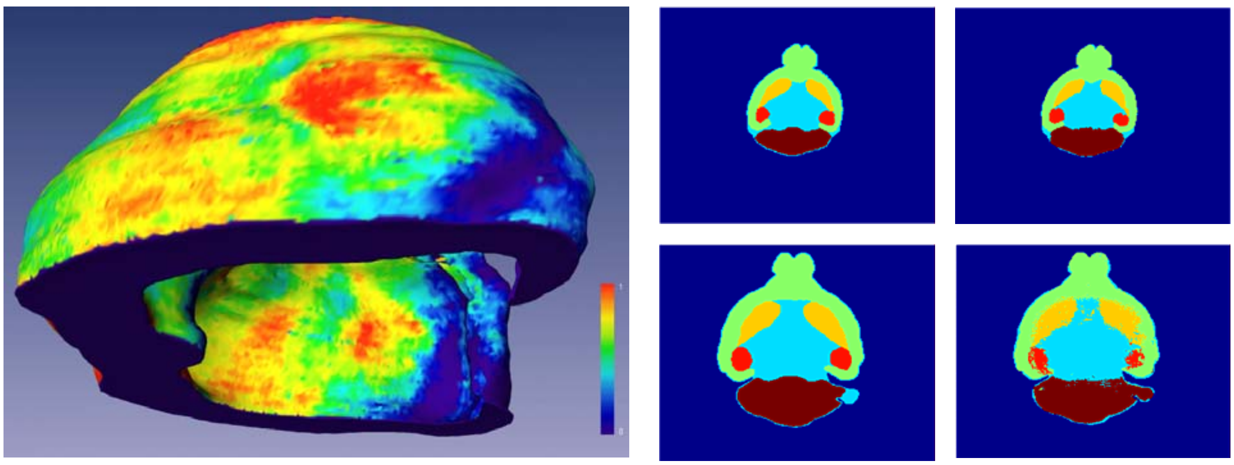

Fig 1: [left]: Projection of functional data from 2FDG autoradiographs onto automatically reconstructed cortical surface (Mohr et al. 2004). [right]: Automatic 2D segmentation of brain structures of mouse (top) and rat (bottom). The dataset consisted of T2 weighted MR scans (MSME, first 8 echoes) from 10 animals each. Results (right) are shown for training of an SVM on the other 9 sets and compared to manual segmentation of brain structures (left). Less than 10% voxels were classified wrong based on 10-fold crossvalidation.

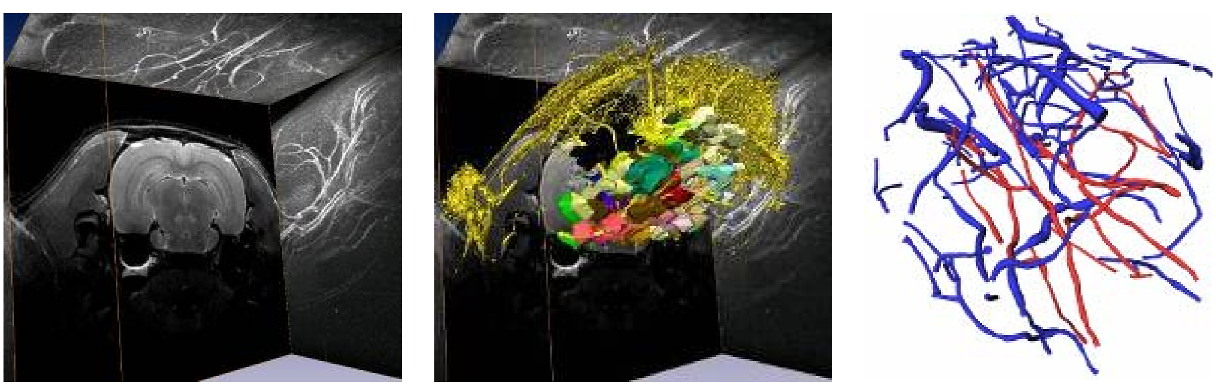

Fig 2: [left]: Maximum intensity projection of Time-of-flight MR Angiogram of the rat brain registered with an T2 weighted high resolution anatomical scan. [middle]: The additionally displayed colored areas code for different significantly activated brain structures after a painful stimulus. [right]: Automatically reconstructed and registered vascularization pattern

of rat brain from four MR angiograms (3 orthogonal Time-of-flight scans and one axial scan with contrast agent). (Gaudnek et al. 2005).

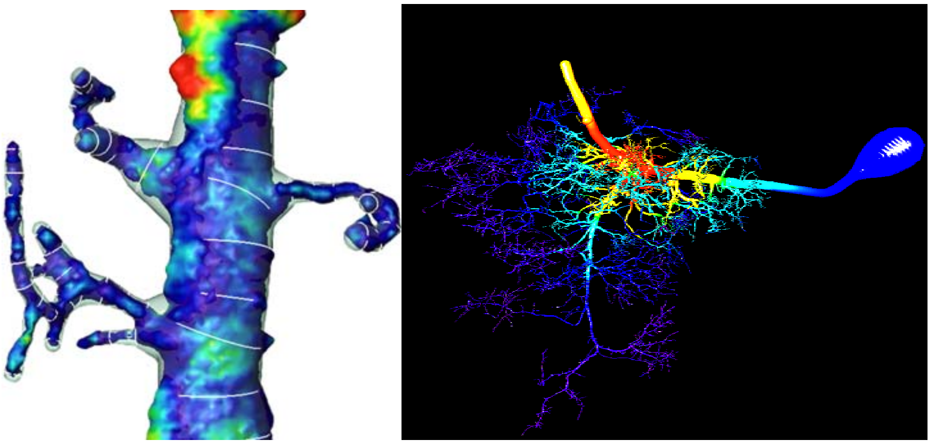

Fig. 3. [left]: Reconstruction of a neuron, showing the fitted generalized cylinders as transparent surface and white circles, the refinement using geodesic active contours and the distance of both color coded. (Schmitt et. al 2004, Evers et. al 2004) [right]: Simulation of electric potential after a spike in a multicompartment model automatically generated from our reconstruction method. This work was carried out in a collaboration with Prof. Duch, Dr. Evers and Dipl.-Ing. Schönknecht