Chapter 1

Introduction

1.1 Problem Formulation

The goal of this work is to develop, describe, and implement a complete set of methods and algorithms for the computer based generation and treatment of explicit geometric representations of anatomical structures from three dimensional image data. Specifically we will concentrate on neuronal structures in insect brains. The results however can be generalized to other applications as well.

The palette of scientific questions, that has to be dealt with in order to transform the full work-flow of conventional neuro-anatomy into a virtual laboratory, is broad. It is not possible to answer each of these questions independently. Instead, the requirements of subsequent steps must already be taken into account at earlier steps of the project. For example the requirements for a polygonal mesh generator are quite different depending on whether the result is to be used for pure graphical display, surface area measurement, or finite element grid generation. The solution to the overall practical requirements is a mosaic of many small tesserae, which must fit together. Therefore this work involves many different disciplines including graphical display, image segmentation, or geometry reconstruction. Rather than treating only one of these fields, the overall structure of the problem is the focus of this work.

The methods should in particular meet the following criteria:

Accuracy: With the development of the methods in this work we aim to contribute to a change of paradigm in image based diagnosis in medicine and biology towards a three-dimensional approach. It is therefore essential, that all visualization and model generation methods have a well defined and controlled accuracy in order to achieve meaningful and reliable results.

Performance: The methods should be reasonably fast. The data sets often have hundred mega bytes or more, therefore an efficient treatment is crucial for the usability. Achieving high performance requires the use of well-designed algorithms and data structures as well as the exploitation of modern (graphics) hardware, where possible.

Interactivity: We strive to provide tools for scientific research, which often involves trial-and-error processes until a routine procedure is developed. Second we have to deal with requirements that cannot always be fulfilled by fully automatic algorithms, due to the nature

of the data sets. Therefore, a visual control and the possibility of human intervention and correction in all steps is desirable. Beside a high performance, interactivity requires a good perceptual coupling (visualization) and a suitable mapping of the algorithms' parameters to *intuitively* understandable quantities.

Practicability: In this work it has been our goal to not only develop algorithms for the individual steps but to provide a complete solution for researchers in neuro-biology. Therefore, the integration of the algorithms into a common frame-work has been an important consideration in the design.

Sometimes theoretically plausible suggestions do not survive in practice, due to the additional side constraints there. Therefore a challenging application project from is taken as a workhorse to study the efficiency of the developed methods, as is described in the next section.

1.2   Motivation

Imaging techniques have played a key role in science for centuries. For a long time, imaging devices, like telescopes or conventional light-microscopes, have produced mainly two-dimensional images. With the increasing capacity of computers it has become possible to compute volumetric intensity distributions from a set of projections, as it is done in computer tomography (CT). Computers are also a prerequisite to accurately handle three dimensional data once acquired. This includes visualization and statistical analysis as we will see in this work.

In medicine, three dimensional image data sets from CT and MRI scanners have become standard in diagnostics in the last decade. Three dimensional ultrasound is developing. A similar development can be seen in biology, where confocal microscopes extend microscopic imaging to the third dimension. It is sure that the importance of three-dimensional imaging and image data processing will continue to increase.

It is interesting that especially in medicine the actual examination of the image data is still done mainly in a two-dimensional fashion on a per-slice basis. Currently, this changes in cases where a proper diagnosis requires a three-dimensional understanding of the structure, like in the investigation of vessel stenosis in the brain. There is good evidence that the situation will change in other fields as well with the availability of reliable and usable methods for three-dimensional visualization.

Beside the pure visual investigation and analysis of a data set the generation of anatomical models becomes more and more important. Such models can be used (and are a prerequisite) for quantitative analysis like the accurate measurement of volumes. Appropriate models are also the basis for numerical simulations used e.g. for treatment planning.

Another important aspect of the computer based treatment and visualization is the possibility to bring different data sets into a common reference frame. This makes it possible to fuse information from different recording modalities, different recording times, and to compare data from different individuals. In medicine as well as in biology the standardized collection of already acquired data sets in a common anatomical atlas (a reference) can be highly synergistic. For illustration we give an example that is of particular importance for this work: It is possible to stain and record individual neuron cells in the brain of a honey-bee. Not amazing the experimental procedure is

very difficult. Therefore, in most cases it is not possible to specifically target more than one neuron in one experiment. Actually in many cases it is not even sure that any neuron is properly hit at all. If for the understanding of the neuronal structure on a network level one is interested in finding the regions of interaction and the topology of the network by using the three dimensional recordings, hence it is necessary to bring data sets from different individuals into the same anatomical atlas.

In summary it is clear that the ability to properly handle three-dimensional image data sets, to create models of the structures contained in the data sets and to merge such data sets and models is of high and further increasing interest in the bio-medical sciences in general and in the context of the neuro-anatomy of (insect) brains in particular.

1.3   Overview

The primary focus of this work is the description and development of tools needed for the computer based analysis of three-dimensional image data from neuro-biology. This includes in particular the generation of geometric models and anatomical atlases. Most of the algorithms have also been tested and and used in other applications, especially in medicine.

Many different fields of research are involved, including visualization of different types of data, image processing and analysis, image segmentation, line extraction, geometry reconstruction, mesh processing, and registration. Many well recognized research groups work in each of these fields and algorithms and tools for a lot of sub-problems exist already. However, they are not integrated into a common environment and do not have compatible interfaces. We have tried to develop a *complete* visualization and geometry reconstruction pipeline, thereby identifiying and developing the missing algorithmic pieces and improving existing algorithms where necessary.

All the methods described in this thesis have been implemented within the Amira visualization system [40]. Amira is based on a system called HyperPlan originally developed by Detlev Stalling for hyperthermia treatment planning in cancer therapy. In 1996 the author of this thesis has joined into the Amira development team and took over major development tasks to create a *Virtual Neuroanatomy Laboratory* for the Verbundprojekt "Virtual Brain" funded by the German BMBF.

Today Amira is the software basis of all research projects in the department of Scientific Visualization in ZIB and it is utilized by a growing number of international research groups. They use the commercial version of the system developed by the ZIB spin-off *Indeed - Visual Concepts GmbH* and distributed by *TGS Inc.* Many of the research results presented in this work are part of the commercial version already or will be part of one of the next releases. This satisfies our goal to make our algorithms available as a solution for practical problems of scientists. At the same time the growing dissemination is a prove of the relevancy of our research.

1.4   Outline of the Thesis

The structure of this thesis follows the typical work-flow in our virtual neuroanatomy lab. After an introduction of the basic concepts and a discussion of the data acquisition techniques used, Chapter 3 discusses the relevant visualization techniques. Visualization algorithms are usually the first tool applied to an unknown data set and will accompany all subsequent steps. Chapter 4 is

dedicated to the important field of image segmentation, which decomposes an image into subsets with a semantic meaning. Algorithms for the extraction of very thin, line-like structures like dendritic trees of neuron cells, are presented in Chapter 5. From the resulting data sets of these two chapters, polygonal models can be created. Algorithms for the efficient generation of consistent and high-quality triangular models are given in 6. In Chapter 7 we discuss the problems involved with importing data sets from multiple individuals into a common anatomical atlas and discuss the related problems, namely registration and averaging. Finally, we show results from specific biological applications in Chapter 8 and close with concluding remarks in Chapter 9.

1.5 Specific Contributions

Key ideas described in this work have been presented at international conferences and in scientific journals over the last 5 years. This includes the specific rendering methods first published in [151] in a joint paper with Detlev Stalling and Hans-Christian Hege, awarded *Best Paper of Conference* at IEEE Vis'96. Parts of this work have also built the basis for the implementation of the enhanced transparency model presented in this work. The first ideas for the geometry reconstruction algorithms have been carried out together with Hans-Christian Hege, Martin Seebass, and Detlev Stalling [142]. The methods for establishing a correspondence between polygonal objects that we use in specific cases to solve the registration problem have been presented in [152]. New and unpublished results presented herein include the interpolation methods for image segmentation, the automatic and the interactive methods for line extraction, parts of the geometry reconstruction process, especially the algorithms for generation of consistent smooth surfaces and specific methods for registration. Applications of our methods to biological questions have been carried out and published in joint work with Karlheinz Rein and other members of Prof. Heisenberg's group [143, 144, 145] and with members of Prof. Menzel's group [94]. The contributions are detailed in the *Results* sections in each chapter.

All figures in this work have been created by the author using the described algorithms and software unless otherwise stated in the figure caption.