Title:
Progressive Extraction of Neural Models from High-resolution 3D Images of Brain

Authors:
Giulia Clementi, Clementi@dia.uniroma3.it, Università Roma Tre
Danilo Salvati, Salvati@dia.uniroma3.it, Università Roma Tre
Giorgio Scorzelli, Scorzelli@ sci.utah.edu, University of Utah
Alberto Paoluzzi, Paoluzzi@dia.uniroma3.it, Università Roma Tre
Valerio Pascucci, Pascucci@sci.utah.edu, University of Utah

Introduction:
In the last few years, the fast progresses of scanning technologies have produced a great increment of resolution of 2D/3D images, measured by the number of distinct pixels in each dimension that can be displayed on a display device. This growth of resolution is about one order of magnitude (10 times) in each single spatial dimension, and therefore of second order in the number of pixels in 2D and of order three for the number of 3D voxels. Hence, the sectional image of a neuronal or vessel structure in the brain, depicted in the past --- at maximum resolution --- by few pixels in its average section, say less than 10x10, is currently reproduced by the newest imaging technologies as measuring more than ten times that number.

In the past years, aiming to accurately describe a curved shape, we needed to consider the voxels as the elements of a discrete intensity field, and to compute a triangulated equi-surface of the field, in order to get some adequately approximated boundary representation of the studied structures. The well-known "marching cubes" algorithm was the typical computational method used for this purpose [2], together with its several variants.

Conversely, in this research we aim to experiment a novel decompositive approach [3] to the computation of boundaries of biological structures to be extracted from extreme-resolution three-dimensional images. The new method is based on the topological extraction of boundaries of "chains" of image elements, as performed by boundary and coboundary maps between the linear spaces generated by the cell decomposition of the image, possibly followed by a non-iterative Laplacian smoothing of the extracted surface, in order to smooth-out the resulting model.

This method benefits by several advantages with respect to current marching cubes algorithms, and in particular provides a *topologically exact* model representation, at any available resolution of the data: the extracted geometric model always enjoys a *closed boundary* surface, allowing for an exact separation of the interior from the exterior of the structures, independently on the geometrical or topological complexity of the boundary. Also, it is extracted through a *single algebraic operation* of product between the compressed binary matrix of the operator, and the coordinate (binary) representation of the chain, *spanning any subset* of the voxels (or pixels) of the image.

The results of the proposed method with respect to those provided by current marching-cubes implementations are clearly demonstrated by the images shown in the following pages, coming (for now) from very preliminary experiments. In few months we will be able to make a full demonstration of the novel method introduced here.

<u>Aims and Methods:</u>
The aim of this research is the adaptation of the LAR extraction of *topologically exact* geometric models of biological structures (see [3]) to *hierarchical multi-resolution* computational environments for *real-time interaction* with big geometric and imaging data of extreme-resolution, like the ones provided by PIDX/ViSUS systems [4,5]. A very general procedure of this kind is shortly described in the following of this section. The representation scheme introduced by LAR, the Linear Algebraic Representation of topological structures is discussed in Reference [1].

The main idea
In few words, we preprocess the data at maximum resolution, so extracting the best possible geometric model providing topological correctness, and transporting the model at inferior resolutions, while guaranteeing the invariance of topology between models of less weight.

Our preprocessing algorithm can therefore be split into (a) the extraction of geometric models at maximum resolution level, say at level m; (b) the model transport and *compression*, with invariant topology, between levels k and k-1, with $0 \le k$-1, $k \le m$.

Let assume that n^3 is the number of *voxels* provided at the *maximum resolution* level of the image data, corresponding to the 3D images ($n^3 = 8k \times 8k \times k = 64k^3$, with $k = 1024$) produced by electronic microscopes of extreme resolution available nowadays.
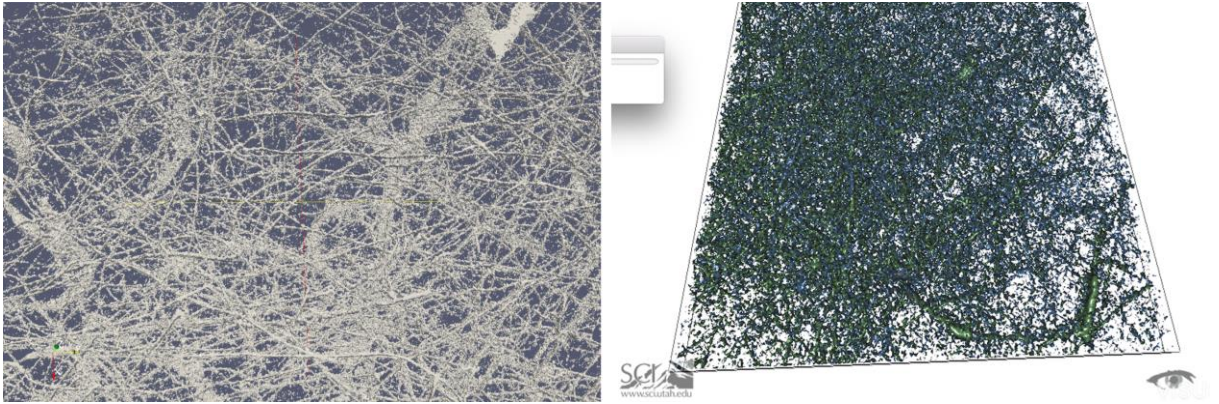

Fig. 1: The same portion of 3D data (micro-vessels between neurons) with LAR-based model extraction and with Marching-Cube extraction, using the same threshold value 8.
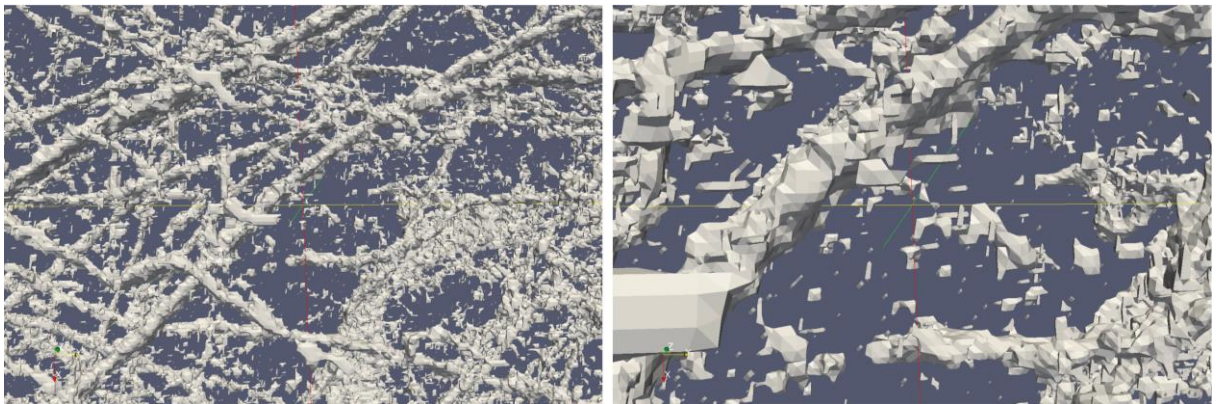

Fig. 2: Two close-up of the same model. Notice the topological correctness: every connected component (even noise) is closed (without boundary).

In the ViSUS progressive multi-resolution environment [5] the number of voxels, indexed out-of-core by fractal curves, is divided by a factor 8 (i.e. 2^3) at each resolution level.

Model extraction at maximum resolution
The whole 3D image, as generated by the electron microscopy, is first subdivided into a grid of $64k^3$ *bricks* of data. The closed and not necessarily connected boundary surface of the interesting image segments is extracted in parallel from 128^3 chunks of data, using the *divide-et-impera* LAR-based method described in Reference [2]. For this purpose, the matrix of the *boundary operator* between linear *chain spaces* ∂_3: $C_3 \rightarrow C_2$ is computed, once and for all, and used to multiply, in parallel, the (binary) coordinate representations of the interesting chains (image segments) in each brick.

The result is a collection of quasi-connected quad *surfaces*, in the sense of algebraic topology, that we call *pipework* in the following. Every pair of adjacent *pipework* is then glued on the common side of their bricks, by just removing the quads lying on the side.

Multi-resolution model transport and compression
The multi-resolution real-time imaging environment ViSUS requires that data to stream towards the system GUI are referred to new compressed bricks at *k-1* resolution level, resulting from the unification and compression of 2^3 bricks at resolution level *k.*
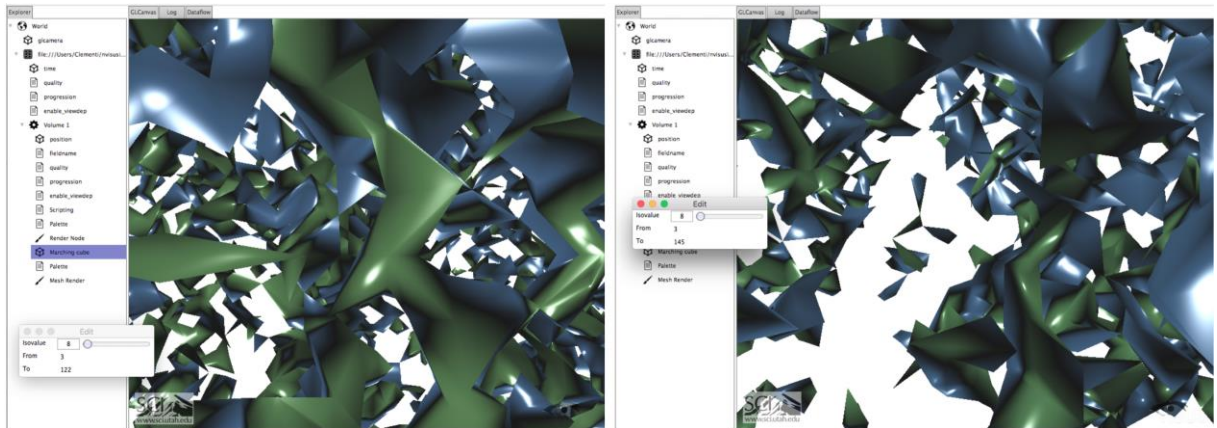

Fig. 3: Some close-up of standard marching-cube extraction at the same threshold level. Notice the topological errors: most of surfaces are open (look at the two colors—blue and green—for interior and exterior surface faces). Great part of reconstructed data at this very low threshold level is just plain garbage, whereas the extraction at higher thresholds, i.e. of greater structures, is pretty good.

Therefore, in the hypothesis of an image space $8k \times 8k \times k$, the gluing of no more than 4 pipework will take place, allocated inside a single new brick of size k^3. In the case of an image space of size $(8k)^3$ the brick gluing will conversely apply to 2^3 bricks.

Let us consider the 4 bricks case, for the sake of discussion simplicity.

Two operations are performed independently: (a) pipework translation and uniform scaling, in order to refer back the model coordinates to the image normalized space $[0,1024]^3$; and (b) pipework simplification, in order to keep under control the quantity of geometric data that must be posted to the GPUs to maintain the refresh rate in accord with real-time visualization requirements.

The isometric step is pretty pointless, and just transforms the model coordinates from integer to double, while maintaining invariant the aspect ratio of the geometric model. The compression step is more algorithmically interesting, since it is a very simple application of algebraic topology methods (SpMV and SpMSpM multiplications, and binary vector differences) and reduces by a factor 0.5 the number of boundary cells (remember they are quadrilaterals) in each pipework, while maintaining invariant their Euler characteristic.

The compression step operates on each pipework as follows. A matrix of ∂_2 operator on each pipework space is built. This one is now dependent on the 2- and 1-cells of the pipework itself, considered as a two-dimensional topological space. An iterated application of $(\partial_2 \text{ o } \partial_2^T)$ and $(\partial_2^T \text{ o } \partial_2)$ operators, intermixed with progressive accumulation of traversed 1- and 2-cells, will *cover* every pipework with a sort of *intrinsic coordinate curves*, made by 1-cycles and in a later step used to alternatively maintain or remove the 1-cycles, depending on their either even or odd "coordinate" value, respectively. The coboundary 2-chains of the removed "coordinate" 1-cycles are replaced by a half number of 2-cells with same boundary. This compression stage will halve, in average, the size of every pipework, and in general, the quantity of data streamed to the user at every lower multi-resolution level, without changing the Euler characteristic and hence the topological genus of the compressed pipework components.

Conclusions:
In this research we are experimenting with a novel extraction of geometric models of biological structures, from huge 3D imaging data provided by recent electron microscopy at extreme resolution, using fast algebraic methods.

This approach, that currently just started, is already producing very interesting results, primarily because it may take into account the exact topology of data at maximum resolution, and transport it without topological errors to inferior resolutions, providing the neurobiologist with real-time accurate interaction with intricate biological structures.

The purpose of this kind of research is to provide the neurobiologist a tool for long-distance connectome reconstruction, i.e. for the building of a comprehensive map of neural connections in the brain, based on the tracing and reconstruction of their cellular connections. Our first experiments show that LAR methods seem to work much better than consolidated types of algorithms, aka marching-cubes, in analyzing extreme-resolution images.

We hope that greater evidence of the merits of this approach can be given in the next few months.

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