Case Study: Visualization of Mechanical Properties and Deformations of Living Cells

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Abstract: This case study shows how mechanical properties (like elasticity or attenuation) of living biological cells can be visually revealed by applying three-dimensional and animated visualization techniques. The benefits of these techniques over visualization methodologies used so far are discussed and experiences with end users from the application domain of cell biology are reported. In addition, this case study describes how visualization techniques can support the pre-processing of the underlying data that was collected using ultrasound microscopy. The case study provides an example how invisible mechanical properties of objects can be made visible in the context of a specific application domain. And the case study provides some experience how end user acceptance can be achieved by using visualization techniques not only for presenting the resulting data but also for the data pre-processing step.

1. Introduction

How do cells move? How do they physically react on certain biochemical substances? In how far do cells change their mechanical properties over time? Although fundamental and of high importance for biologists, these questions are still unanswered today. Ultrasound microscopy is a key technology for these kind of questions since it allows the observation of living cells and the collection of physical data (like elasticity, attenuation or thickness) opposed to conventional microscopy. From a visualization point of view, depicting data collected with an ultrasound microscope is a challenging task: in contrast to an optical microscope the data cannot be readily interpreted by a human observer; and mechanical properties that can not directly be seen have to be visually revealed.

In this case study we will present for the first time three-dimensional and animated techniques for visualizing ultrasound microscopy data. We show how their usage can improve the interpretation of data about living cells compared with visualization techniques used today. In addition, this use case is an example that visualization techniques need not only be designed for showing the results but also for pre-processing the raw data. Visualization techniques help to speed-up the data filtering process and enhance the quality of the results. A carefully designed, seamless visualization used for data pre-processing as well as interpretation of the results has proven to be a key for end-user acceptance of visualization techniques in this use case.

This paper is organized as follows. First, we provide some background on ultrasound microscopy and the state-of-the-art of visualization techniques used. Then, we describe our new technique for data pre-processing including an according visualization as well as our 3D reconstruction of the cell. Next, we describe our visualization of the mechanical properties of the cell (like attenuation or elasticity of certain regions of the cell) using 3D animation. Finally, we report on the feedback we got from our users from the cell biology domain before we summarize the case study and give a brief outlook on future work.

2. Application Background

The research of the kinematic properties of biological cells deals with the study of the supramolecular organisation of the cell cytoplasm and the cytoskeleton. Among the aspects of the supramolecular organisation of the cytoplasm is cell mechanics, the structural basis of cell locomotion. These mechanical properties of cells are studied using ultrasound microscopy. Such an ultrasound microscope, the so called scanning acoustic microscope (SAM) or its successor the phase sensitive scanning acoustic microscope (PSAM) scans the respective target sequentially, point by point, not in parallel like conventional light microscopy. Figure 1A shows the amplitude and phase image of a cell [GRIL96]. The microscope registers the signal delay for each ultrasound impulse. The used frequencies range form 0.9 to 1.3 GHz. The mechanical properties like thickness, elasticity and sound attenuation can not be obtained directly but are computed from these data [KUN00].

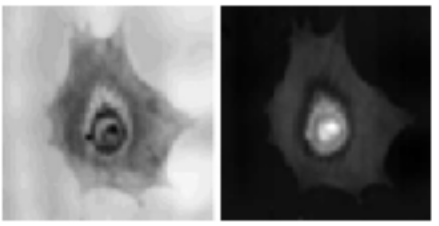
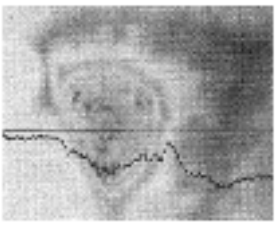
A  B 

Fig. 1: (A) Amplitude and phase image of an XTH2 cell [SCH97].
(B) Amplitude Image of an XTH2-cell. The graph shows the gray values of the line above [KUN00].

The purpose of the research is to obtain a model about cell movement. Preliminary results show a correlation between elasticity of cell areas and subsequent movement in a particular direction, i.e. some cells get **soft** in the direction they will move. It is yet to be discovered how these changes in elasticity and attenuation are effected [KANN90, BER98].

There are two main problems in the current approach to ultrasound microscopy for living cells: The first is that the quality of the computations vary with the frequency in which the cell is scanned. It is necessary to accumulate the results of different scans at different frequencies into one image in order to increase the computation quality. However, time is a limitation factor in the procedure. Since a single cell is sampled sequentially it takes up to 20 seconds to record a single image. In order to obtain the desired quality, it is necessary to record several images. This may take several minutes in which the cell should change as little as possible. Thus, fast moving cells can only be investigated at a lower quality. Up to now, the relevant mechanical properties were not computed or visualized for the whole cell. Most of the computations were done for one-dimensional cuts through the cells as depicted in figure 1B, thus avoiding to reconstruct the cell surface.

3. Visualization Techniques

Currently used visualization of cell properties lacks the possibility to track the movement adequately, especially the three-dimensional character of the cell movement. We addressed three main tasks in this work to overcome these limitations. The first was to find a new, fast method to derive the relevant cell properties in an adequate quality with as few images as possible. Thus, this enables the investigation of fast moving cells. The second task is closely related to the first one and deals with an efficient surface reconstruction for the whole cell in order to reconstruct a three-dimensional model of the cell. The third task was to find a new and intuitive visualization for the mechanical properties **elasticity** and **attenuation** (the property **thickness** can be trivially visualized with a 3D representation of the cell). In this section we will focus on the boundary representation of the cell and the visualization of the properties **elasticity** and **attenuation**. Details on the algorithm and computations necessary to derive the mechanical properties can be found in [BER95b].

How is the described PSAM data to be visualized in order to support biologist preparing their experimental data? What parameters and properties should be made visible in our visualization process? On the one hand, we have to create single images out of the PSAM data to get an effective and expressive visualization of a cell. On the other hand, we will focus on the question how an animation can be used to visualize single mechanical attributes as well as to represent time-based movements and deformations of cells.

To create single images we have selected a three-dimensional model in order to represent the cell and its spatial dimension. The paradigms of scene-in-hand and eyeball-in-hand are used for a flexible and fast user-interaction. Colors are used to visualize mechanical properties on top of the cell's reconstructed surface, e.g. to emphasize dependencies between thickness and elasticity or thickness and attenuation. This is possible, since the cell-inside is assumed as homogeneous and since the scanning is done vertically from a top view.

But how can mechanical attributes of cell at a single point in time be visualized using 3D animation? The idea is to take advantage of the user's prior knowledge about physical phenomena. Elasticity and attenuation themselves are not visible qualities, but their effects are well-known. The attenuation, the temporal and spatial decrease of a vibration, is shown here by the decrease of the amplitude of falling balls, whereby the cell is represented as a two-dimensional elastical surface. In our simulation the balls fall from their initial height and they bounce until the movement of all balls is stopped through the elasticity of the cell and the balls' loss of energy. The characteristic movement of one ball represents the value of cell elasticity for the position, where the ball falls. The amount of lost energy of a ball depends directly on the corresponding cell elasticity. The duration of a ball's movement as well as the magnitude of its amplitude are visible characteristics based on the elasticity and attenuation of a cell. A ball stops more quickly if the attenuation is high and vice versa. To control the length of the animation we multiply the original cell elasticity with an adjustable factor.

Animation is used to show time-based deformations and movements of a cell. In order to guarantee a smooth animation all images are rendered off-line as single images based on user defined camera and object parameters like camera position and orientation. The combination of all single images to a movie allows a representation of cell deformations and movements.

4. Results and Evaluation

In this section we show how the concept described above was realized. The pre-processing and preparation of the PSAM data as well as the rendering was done with the Visualization Toolkit VTK [VTK]. Starting with the raw data, which consists of images of amplitudes and phases for each recording frequency, the first step is to subtract correction images to eliminate recording errors. The second and most important step is to define the interference fringes. It takes a lot of experience to identify the order of an interference fringe due to ambiguity. To support the user in this task several tools are offered, e.g. a filling tool to mark the area of an interference fringe. After the definition of all interference fringes and their orders the further calculation is done automatically.

The visualization of a data set can be customized by choosing several parameters (like mapping of mechanical properties to color, selection of color palette or scaling factors). Figure 2 shows a three-dimensional visualization with its elasticity represented as color. In order to enhance the visualization several adjustments are possible. For example, if the user seeks to emphasize the thickness he may scale up the height of the 3D model. Different kinds of legends are added to display all chosen parameters like the selected scale or color palette (see bottom of Figure 2). Examples of the visualization results can be found in Figure 3, where snapshots of a cell deformation is shown, and in Figure 4, where an animated visualization of cell elasticity is shown.

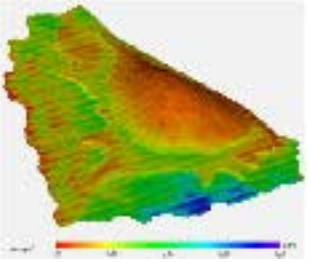


Fig. 2: 3D-Visualization of the elasticity of an XTH2 cell

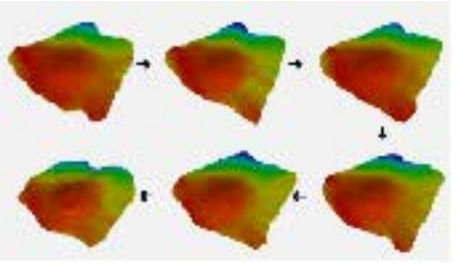


Fig. 3: Snapshot of a deformation animation.

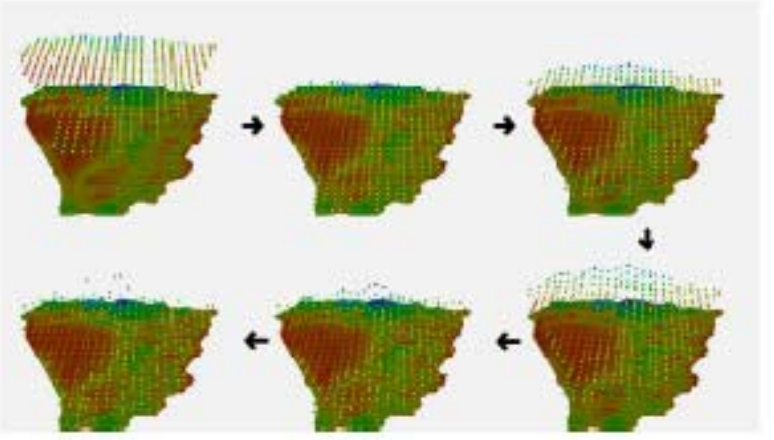


Fig. 4: Snapshots of an animated 3D visualization of cell elasticity.

Our concept and realization was developed within a cooperation with biologists of the University of Frankfurt [BER95b]. We used the qualitative feedback from this team of PSAM experts to evaluate our visualization system. In addition, we conducted observational studies. The 3D aspects of our visualization technique proved to be valuable for the end users. The animated visualization of elasticity and attenuation was assessed to be intuitive, however, it was criticized that no quantitative information could be perceived. Thus, the application focus of this kind of visualization was on presenting of experimental data to non-experts. The end-users pointed out that the major advantage is the direct integration of the visualization system in their workflow of experiment evaluation from a first data scanning up to preparation for publications.

5. Summary and Future Work

In this paper, we present for the first time how height, elasticity and attenuation of living cells can be visualized. In addition, we have shown how 3D animation can be used to represent single mechanical properties. First, we had to introduce new visualization techniques to the domain expert users, in our case biologists who research the movement of cells. We used a mixture of techniques some of which are well known in the scientific visualization community (but not in the users' domain), like 3D surface reconstruction

and mapping of properties to color. Some concepts are new like the usage of animation to visualize material properties like elasticity that are not as readily visible as thickness. Second, we had to address the time constrained environment which is posed by the application domain. We therefore had to develop a new approach for the fast reconstruction of crucial material properties of living cells from phase sensitive scanning acoustic microscope images. The challenge was to facilitate the reconstruction by activating the users' expert knowledge using visual tools. The visualization techniques and the visualization system used for this task had to be integrated with the visualization system designed for the first task. As future work, we identified two main areas. The first area focuses on extending the 3D animation techniques of cell deformations, e.g. to animate differences between two images in order to emphasize which parts of a cell are moving faster. For instance, an animated field of motion gradients could be employed. The second area focuses on the incorporation of quantitative information in our animated visualization techniques (as it was requested by the end users).

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