

## QUANTITATIVE IMAGE ANALYSIS FOR STRUCTURAL GENOMICS

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The use of fluorescence microscopy in combination with DNA specific probes to produce three-(or four-) dimensional data has grown into a mature state in the last decade. The improvements in imaging microscopy methods (hard- and software) and specific labeling methods (wetware) enables us to get a better understanding of the genome structure. These improvements have led to the research of structural genomics; that allows to bridge the gap with functional genomics and correlates these two. The organization of the interphase nucleus has been studied since the late 19<sup>th</sup> century. It is now well accepted that the position of chromosomes in the nucleus plays an important role in gene regulation.

A recent point of interest is the study of telomeres, the ends of DNA-strands. The telomeres prevent the ends of DNA sticking together and also prevent DNA degradation during DNA syntheses. By studying the three-dimensional organization of the telomeres in interface nuclei, we found the telomeres (the telomeric territory) to be re-organized during the cell cycle[1]. While in G0/G1 and S phase the telomeres are in a volume that is sphere-like, in G2 they move into a volume which is more disk-like (the telomeric disk). We also observed that this organization in G2 is lost in cancerous cases. Furthermore, it looks like the telomeres tend to clump together, forming aggregates, in these cancerous cases.

The data acquisition (the recording of images) is usually based on digital imaging, producing enormous sets of data to be analyzed. Therefore the need for quantitative image analysis methods and algorithms in this field of cancer research has also grown. These algorithms have to consider the whole procedure that is being used to acquire the data, including optical properties of the microscope, nature of the probes and acquisition parameters.

We are in the process of developing tools for the quantitative analysis of the three-dimensional structure of the genome in the nucleus. This includes: loading and display of 3D images, automatic segmentation of regions of interest (e.g. nuclei, telomeres, chromosomes) and 3D image analysis algorithms (e.g. calculation of the distribution parameter,  $\rho_T$ , describing the flatness of the disk in which the telomeres are distributed[2]).

The analysis method, the algorithms and part of the results on normal and cancerous cells will be presented.

[1] Chuang, T.C.Y., et al., *The three-dimensional organization of telomeres in the nucleus of mammalian cells*. BMC Biology, 2004. **2**(12).

[2] Vermolen, B.J., et al., *Characterizing the Three-Dimensional Organization of Telomeres*. Cytometry, 2005. **in print**.