

APOPTOTIC NUCLEAR VOLUME DECREASE: ANALYSIS OF CONFOCAL IMAGES AND MATHEMATICAL MODEL

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Motivation and aim: Apoptosis, a programmed cell death, is a safe mechanism for destroying damaged or useless cells without inflammation. The understanding of the apoptosis mechanism will help to diagnose and treat such diseases as: cancer, leukemia, lymphoma, immunodeficiency, infectious and virus disease. Unfortunately, there is no model, describing this process.

The first stage of the apoptosis is determined by the enzyme, PI3K, which enters into the nucleus and phosphorylates the histone proteins(H2) [1]. This results in chromatin condensation and the formation of the apoptotic ring. So, the aim is to develop molecular kinetic model based on this literature fact and the experimental data and to obtain several parameters relevant for medical and biological applications.

Methods and algorithms: We used the scanning laser confocal microscope to obtain stack of nuclear slices of tumor liver cells, called HepG2. We used two methods to measure a nuclear volume. First one uses the Sobel method for computing the gradient of intensity along the vector (from inside the nucleus to outside). If the value of a gradient changes rapidly, this pixel is assigned to a boundary surface. Everything inside this boundary is a nucleus; its volume is computed by summing enclosed areas in each layer. Overall, this approach determines the volume of star-shaped hull of the nucleus. Second method, software Imaris, is based on 3D interpolation, thus measuring only the volume occupied by the chromatin. Kinetic model is based on known five reactions between PI3K and related molecules and the osmotic balance.

Results: The developed model was used to fit the experimental data of nuclear volume decrease during the apoptosis. Several relevant model parameters were obtained with good accuracy, in particular the lag phase time, volume fraction of the chromatin in the nucleus, and the speed of the apoptosis.

Conclusion: The proposed model explains the formation and evolution of the apoptotic ring in the nucleus. The developed approach allows one to determine the dynamic characteristics of early apoptosis by experimental data. The total depletion of the nuclear volume agrees with the literature data.

References:

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