

Evaluation of the Spatial Arrangement of the Biologic Structure

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The first-order stereology methods are applied to estimate the volume, surface, length, and number of the biologic structures under normal and experimental conditions (1). Hitherto, the quantitative information concerning the three-dimensional (3D) arrangement of structural and ultra-structural particles has received less attention (1). The second-order stereology can also provide additional information about the spatial arrangement of the components, e.g. cells or organelles. The description of these spatial arrangements can reveal structural changes in different condition including healthy and pathologic conditions. There are different methods to explore the spatial arrangements of the particles. Estimation of covariance and pair correlation functions, i.e. $g(r)$, is one of these methods and is an appropriate method of explanation of the spatial arrangement to reconnoiter the 3D cellular and/or organelle arrangements. However, with the development of measurable methods for evaluating structures through the second-order stereology, it is possible to explain the various descriptors of spatial arrangement including covariance function, i.e. $C(r)$, and $g(r)$ (1). This technique has been applied in some research including estimation of spatial distribution of tissue components in benign and malignant prostate gland, salivary gland acinar cells, diabetic heart, and the cells of dorsal root ganglion (2-6). The technique has been also applied to analyze the spatial pattern by investigation of mathematical function in the subjects with psychologic disorder. In these studies, the $C(r)$ and $g(r)$ has delivered quantitative description of differences in 3D arrangements within and between parameters in the histologic tissue samples. In this approach, the covariance of a particle at a distance of "r" units into reference space can be defined using the "dipole" (1). Briefly, using the dipole, the $C(r)$ is obtained and the result is plotted. The plot explains how much two variables change together. The $g(r)$ is related to the probability of exploring the center of a particle (cells or

organelles) at a given distance from the center of another particle. For short distances, the covariance is related to how the particles are crowded or bunched together. When the layers of the particles show a more scattered pattern, the probability of finding two particles with a given separation - depends on the density. The $g(r)$, accounts for these influences by normalizing by the density; thus, at large values of distances, it drives to one; ie, uniform probability. In another word, the $g(r)$ explains the arrangement through normalizing by the density (1). The term cross-correlation function is used to express how different particles are clustered or dispersed together. For example the vessels and cardiomyocytes are clustered or dispersed together in the diabetic heart (4). Placing the second-order stereological methods in the toolbox of the quantitative research can be useful to light some of the dark edge of the biologic research.

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