SUPPLEMENTARY MATERIAL

Fractal analysis by box counting method

Fractal dimension (FD) represents irregularity or complexity of binary mask surface [18] and is calculated using the box counting algorithm [16]. In a box counting scan, a series of grids of increasing boxes are placed over an image, and the number of boxes required to cover the binary mask are counted. Mathematically, FD is obtained by the following equation:

$$FD = \lim_{\epsilon \to 0} \frac{log\left(N(\epsilon)\right)}{log\left(1/\epsilon\right)}, \tag{1}$$

where ϵ is a box size and $N(\epsilon)$ is the number of counted boxes. For empirical estimation of equation (1), FD is computed by dividing the gradient of logarithmic value of the inverse of box size ϵ to the gradient of logarithmic value of count $N(\epsilon)$ as:

$$FD_t = \frac{log\left(N(\epsilon_{t+1})\right) - log\left(N(\epsilon_{t-1})\right)}{log\left(\frac{1}{\epsilon_{t+1}}\right) - log\left(\frac{1}{\epsilon_{t-1}}\right)}, \tag{2}$$

where ϵ_1 is the smallest box size 1, ϵ_2 is the following larger box size 2, ϵ_3 is the following larger box size 4, ϵ_4 is the following larger box size 8, and so on. Since there is no previous box size ϵ_{t-1} for the smallest box size, ϵ_{t-1} is set as ϵ_1. For the largest box size, ϵ_{t+1} is set as ϵ_t. The rougher the surface of the 3D binary mask is, the higher the value of FD (slope in log-log plot) is obtained.

Lacunarity represents the amount of voids inside the 3D binary mask [17]. To measure the lacunarity, coefficient of variation (CV_ϵ) values are first computed for the counted boxes which include a part of 3D binary mask. CV_ϵ is computed by a ratio of standard deviation σ_ϵ to mean μ_ϵ of the pixel intensities inside the box with a size ϵ as:

$$CV_\epsilon = \frac{\sigma_\epsilon}{\mu_\epsilon}. \tag{3}$$

Then, the lacunarity λ_ϵ is computed by the mean of the squares of CV_ϵ values as:

$$\lambda_\epsilon = \frac{1}{N(\epsilon)} \sum_k (CV_\epsilon^k)^2, \tag{4}$$

where CV_ϵ^1, CV_ϵ^2,…, CV_ϵ^k are the CV_ϵ values computed from K counted boxes. If there are many hole or gaps in the 3D binary mask, collected CV_ϵ values are high and thus the high lacunarity is obtained with the equation (4) [19].