

# Optimal Whole Slide Image Segmentation Using Generalized Normal Distribution Optimization

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## Abstract

Whole slide image (WSI) segmentation is a crucial task aiding tumour and cancerous cell diagnosis. Generalized Normal Distribution Optimization (GNDO) algorithm is adopted for whole slide image segmentation based on thresholding in this paper. GNDO algorithm utilizes the generalized normal distribution's properties to determine the ideal thresholds for image segmentation. Through various metrics, the efficacy of GNDO in comparison to traditional Otsu thresholding methods is demonstrated. As demonstrated by the results, it can offer reliable and flexible solutions for different histopathology images.

**Keywords:** Generalized Normal Distribution; Image Thresholding; Optimization Algorithm; Whole Slide Image Processing; Histopathology Image Segmentation.

## 1. Introduction

The advent of artificial intelligence techniques has brought about a revolution in the field of pathology in the recent past. Digital pathology offers several advantages, such as easy archiving, remote diagnosis, and the application of image analysis to boost diagnostic efficiency [1]. Artificial Engineering techniques could lead to the development of new clinical instruments that are more objective, reproducible, and accurate than those currently employed in ordinary clinical settings if it is effectively applied to WSIs (Morrison, Harris-Birtill, and Caie 2021; Naylor et al. 2019; Wang et al. 2020). A key stage in image processing that is essential for segmentation and further analysis is image thresholding [2]. Owing to WSIs high resolution, regions of interest are segmented using the common image processing approach of thresholding. Thresholding is an easy and effective traditional image segmentation technique. Its methodology distinguishes between bright and dark areas using a histogram that allows pixels in a region to share their intensity (Madabhushi 2009). The choice of the best threshold, which is utilised to separate targeted

items from their application-dependent background, is the key to effective threshold segmentation (Houssein et al. 2023) [3]. A thresholding method based on between-class variance was developed by Japanese scientist Nobuyuki Otsu and is widely utilized in a number of applications (Otsu 1979) [4]. Otsu thresholding segments the image into double region based on grayscale data of the image [5]. Another effective strategy that many authors have used extensively in the research is the application of nature-inspired optimisation algorithms to the optimal threshold problem as an optimisation problem (Kanadath, Jothi, and Urolagin 2023) . (Zheng et al. 2022) proposes an Otsu multi-threshold segmentation of image built on an improved particle swarm optimization algorithm applied on images and verified for standard benchmark functions. Authors in (Bangare et al. 2015) provide information on the choice of the threshold value and outlines how Otsu's method is used to image segmentation. (N and S 2016) proposed a local adaptive thresholding technique that uses the local mean and standard deviation to threshold images, enhancing the image

segmentation quality [6]. The MRFO-OBL approach, which is based on opposition-based learning, proposes the Manta Ray Foraging Optimization (MRFO) (Houssein, Emam, and Ali 2021) algorithm to extract region of interest from CT images of COVID -19 patients thus improving classification. Multi-level thresholding segmentation using equilibrium optimizer algorithm for a set of CT images of COVID-19 by maximizing the fuzzy entropy is proposed in (Houssein et al. 2022). For cytology picture segmentation, authors in (Mohammadian-khoshnoud et al. 2022) suggested a hybrid methodology which combines fuzzy c-means and gray wolf optimization. A structure for CT and MR images for image segmentation is proposed in (Vaiyapuri and Alaskar 2020) which combines characteristics of wavelet quality and WOA. In order to segment images of CT COVID-19, the authors in (Q. Zhang et al. 2021) used stochastic fractal search technique in conjunction with a gaussian barebone salp swarm algorithm [7]. This paper proposes the adaptation of the Generalized Normal Distribution Optimization (GNDO) algorithm to address the challenges associated with conventional Otsu thresholding method for WSI segmentation. GNDO is a recently introduced optimization methodology which was adopted for parameter extraction difficulty of the single diode and double diode photovoltaic models (Y. Zhang, Jin, and Mirjalili 2020). GNDO is distinct in that it doesn't require any additional controlling parameters to be established before the algorithm is started; all that's needed are the required population size and terminal condition (Vega-Forero, Ramos-Castellanos, and Montoya 2023). Moreover, the position of an individual is updated by GNDO using an easy-to-use method that updates the generalized normal distribution formula. The innovative GNDO method seeks to improve the precision and versatility of picture thresholding by drawing inspiration from the characteristics of the generalized normal distribution (Rad et al. 2022). Following are the contributions made by this work: WSI thresholding model with a novel GNDO algorithm is proposed and validated for histopathology images. The competence of the

proposed model for effective segmentation is validated through various metrics such as Dice coefficient, Jaccard coefficient, Accuracy and Precision. The rest of this paper is ordered as follows. Section 2 describes the methodologies and workflow of the proposed study. Section 3 gives datasets used for this work and results attained. The paper is concluded in the final Section [8].

## 2. Proposed Work

### 2.1. Generalized Normal Distribution Optimization (GNDO) Algorithm

The GNDO algorithm is aimed to optimize image thresholds by exploiting the statistical properties of the generalized normal distribution. This section provides an overview of the algorithmic steps involved in GNDO. The definition of a normal distribution is as follows. Given a probability distribution with location parameter  $\mu$  and scaling parameter  $\delta$ , the probability density function of a random variable  $x$  may be written as:[9]

$$f(x) = \frac{1}{\sqrt{2\pi}\delta} \exp\left(-\frac{(x-\mu)^2}{2\delta^2}\right) \quad (1)$$

With a straightforward structure, GNDO uses both local and global exploration as its planned information exchange tactics.

#### 2.1.1. Local exploitation

The process of locating better solutions inside the search space that includes each individual's current place is referred to as local exploitation. An optimized generalized normal distribution model can be constructed by, based on the connection between the population's individual distribution and normal distribution: [10]

$$V_i^t = \mu_i + \delta_i \times \eta, \quad i=1,2,3,\dots,N \quad (2)$$

Where  $i^{\text{th}}$  individual's vector at time  $t$  is represented by  $V_i^t$ , generalized mean position of the  $i^{\text{th}}$  individual is  $\mu_i$ , generalized standard variance is  $\delta_i$  and penalty factor is  $\eta$ . Also,  $\mu_i$ ,  $\delta_i$  and  $\eta$  are expressed as:[11]

$$\mu_i = \frac{1}{3}(x_i^t + x_{\text{Best}}^t + M) \quad (3)$$

$$\delta_i = \sqrt{\frac{1}{3}[(x_i^t - \mu)^2 + (x_{\text{Best}}^t - \mu)^2 + (M - \mu)^2]} \quad (4)$$

$$\eta = \begin{cases} \sqrt{-\log(\lambda_1)} \times \cos(2\pi\lambda_2), & \text{if } a \leq b \\ \sqrt{-\log(\lambda_1)} \times \cos(2\pi\lambda_2 + \pi), & \text{otherwise} \end{cases} \quad (5)$$

Where  $a$ ,  $b$ ,  $\lambda_1$ , and  $\lambda_2$ , are arbitrary values between 0 and 1,  $x_{Best}^t$  is the present appropriate location and  $M$  is the mean location of the present population which is calculated as:[12]

$$M = \frac{\sum_{i=1}^N x_i^t}{N} \quad (6)$$

### 2.1.2. Global Exploration

Global exploration searches global space to find the optimal solution. It depends on three randomly chosen individuals, which is given as: [13]

$$V_i^t = x_i^t + \beta \times (|\lambda_3| \times v_1) + (1 - \beta) \times (|\lambda_4| \times v_2) \quad (7)$$

Where  $\lambda_3$  and  $\lambda_4$  are two arbitrary values subjected to standard normal distribution,  $\beta$  is adjust parameter, which is a random value between 0 and 1, and  $v_1$  and  $v_2$  are two trajectory vectors. Moreover,  $v_1$  and  $v_2$  are two trail vectors. Moreover  $v_1$  and  $v_2$  can be computed by: [14]

$$v_1 = \begin{cases} x_i^t - x_{p1}^t, & \text{if } f(x_i^t) < f(x_{p1}^t) \\ x_{p1}^t - x_i^t, & \text{otherwise} \end{cases} \quad (8)$$

$$v_2 = \begin{cases} x_{p2}^t - x_{p3}^t, & \text{if } f(x_{p2}^t) < f(x_{p3}^t) \\ x_{p3}^t - x_{p2}^t, & \text{otherwise} \end{cases} \quad (9)$$

Where  $p1$ ,  $p2$  and  $p3$  are three arbitrary integers chose between 1 to  $N$ , and also  $p1 \neq p2 \neq p3 \neq i$ . Figure 1 depicts the flowchart for GNDO algorithm.

### 2.2. Thresholding Model

Most often, between class variance method is used widely for image segmentation. Based on the pixel values, between class variance expresses how diverse the various segments are from one another. This work adapts maximizing between class variance as the objective function, expressed as below:

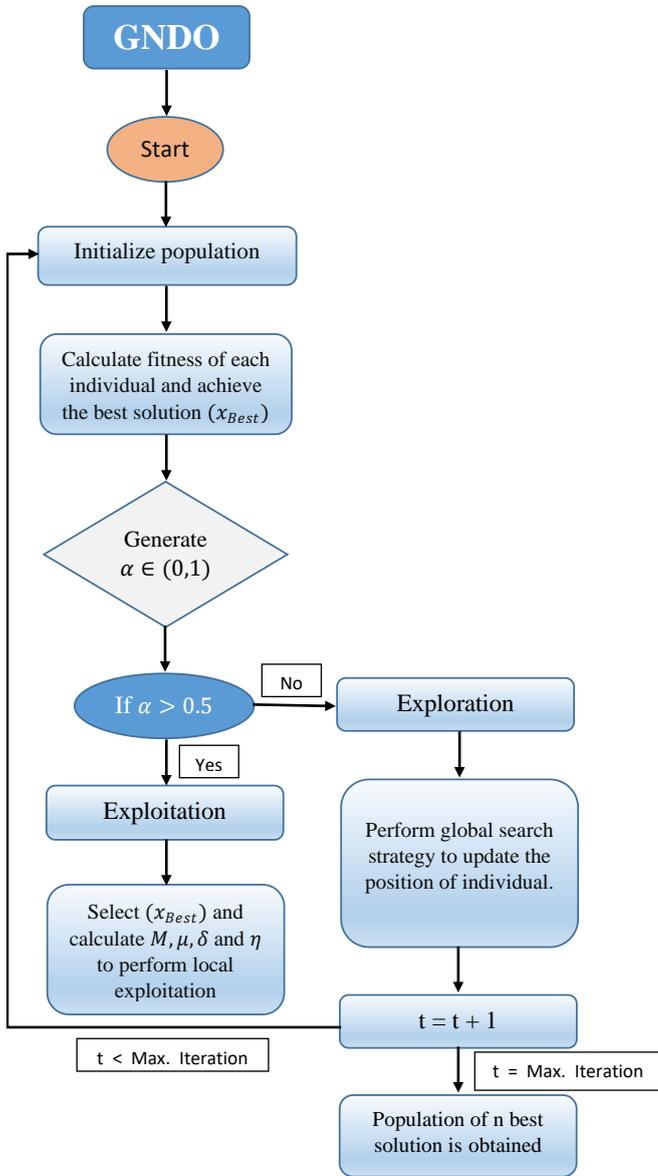
$$\text{Objective function} = \text{Max} (\sigma^2) \quad (10)$$

$$\text{where, } \sigma^2(t) = P_F(t) * P_B(t) * (\mu_F(t) - \mu_B(t))^2 \quad (11)$$

Where,  $t$  is the threshold value,  $\sigma^2(t)$  is the between-

class variance,  $P_F(t)$  and  $P_B(t)$  are the probabilities of pixels in foreground and background respectively computed using cumulative distribution function,  $\mu_F(t)$  and  $\mu_B(t)$  are the mean intensities of foreground and background respectively for the given threshold  $t$ . Differential and Gaussian mutations, two mutation operators influenced by Gaussian distributions, are used in the optimization process of this proposed work, GNDO. The purpose of these mutations is to effectively explore the search space and identify the ideal threshold value that minimizes the goal function—in this example, the between-class variance. By creating new candidate solutions through mutation operations and choosing the best solutions based on their fitness (in this case, the between-class variance), the method iteratively improves the threshold values. Until the stopping requirement is satisfied, this process is repeated a certain number of times in Figure1.[15] The algorithmic steps are as given below:

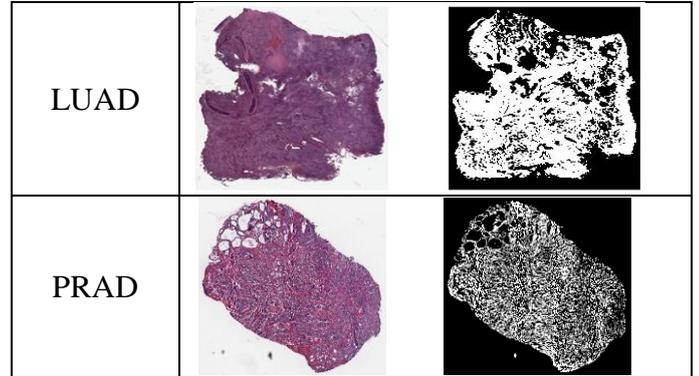
- The algorithm is initiated with input image, the number of iterations, lower and upper bounds for the threshold values, and the population size.
- Population of thresholds is chosen randomly within the specified bounds and their fitness using the objective function is evaluated.
- The population for a certain number of iterations using the GNDO algorithm is updated, which involves selecting individuals from the population, generating new candidate solutions, and evaluating their fitness.
- The GNDO algorithm uses differential evolution and Gaussian mutation to explore the search space and potentially improve the fitness of the thresholds.
- Finally, the best threshold found is used to create a binary image by thresholding the input image, and the threshold value is normalized to the range [0, 1].
- The objective function computes the objective value, which is the sum of the between-class variances for the binary image created using the current threshold [16].



**Figure 1** Flowchart Depicting GNDO Algorithmic Steps (Khan Et Al. 2020)

### 3. Results and Discussion

The experiments are carried out in MATLAB 2023B. The proposed methodology is validated on lung adenocarcinoma (LUAD) and Prostate adenocarcinoma (PRAD) images which were obtained from The Cancer Digital Slide Archive (CDSA n.d.). The CDSA was developed by researchers at Emory University to support the browsing of imaging data related to the Cancer Genoma Atlas. The image and its corresponding ground truth is given in Figure 2 [17].



**Figure 2** WSI with Their Ground Truth

The histopathology images are first tiled in smaller sized images and then processed further. The tiles are then subjected noise reduction using adaptive histogram method for enhancing the segmentation efficiency. The quality of the hence obtained images are measured using Peak Signal to Noise Ratio (PSNR) and Structural Similarity Index (SSIM). PSNR validates the similarities between the original and enhanced image using the root mean square error (RMSE) of each pixel. They are calculated as:

$$PSNR = 20 \log_{10} \left( \frac{255}{RMSE} \right) \text{ dB} \quad (12)$$

$$RMSE = \sqrt{\frac{\sum_{i=1}^{r_0} \sum_{j=1}^{c_0} (I_{og}(i,j) - I_{seg}(i,j))^2}{r_0 \times c_0}} \quad (13)$$

where  $I_{og}$  is the primary image,  $I_{seg}$  is the segmented image, while  $r_0$  and  $c_0$  are the maximum number of rows and columns of the images, respectively. SSIM is another measure for checking the similarity between the original and segmented image. It is given as:

$$SSIM(I_{og}, I_{seg}) = \frac{(2\mu_o \mu_{seg} + c_1)(2\sigma_{o,seg} + c_2)}{(\mu_o^2 \mu_{seg}^2 + c_1)(\sigma_o^2 + \sigma_{seg}^2 + c_2)} \quad (14)$$

where  $\mu_o$  and  $\mu_{seg}$  are the mean intensities of the actual image and the segmented image,  $\sigma_o$  and  $\sigma_{seg}$  are the standard deviations of actual image and the segmented image.  $\sigma_{o,seg}$  is the covariance of actual image and the segmented image, and  $c_1$  and  $c_2$  are constants. The mean PSNR and SSIM values for the considered WSIs are tabulated in Table 1. The results obtained for these metrics show that the pre-processing was completed successfully [18].

**Table 1 Quality Measurement Metrics After Preprocessing**

Image	PSNR	SSIM
LUAD	41.68	0.86
PRAD	42.48	0.82

**3.1. Comparative Analysis**

The proposed GNDO algorithms efficiency is established through measuring various performance metrics such as Dice coefficient, Jaccard coefficient and F-measure with traditional Otsu thresholding method. Dice similarity coefficient is widely used for measuring the performance of segmentation. Jaccard coefficient compares segmented images with ground truth images by calculating the similarity between them. All the metrics used here are calculated as given below:[19]

$$\text{Dice Coefficient} = \frac{2A \cap B}{A+B} \quad (15)$$

$$\text{Jaccard coefficient} = \frac{A \cap B}{A \cup B} \quad (16)$$

$$\text{Recall} = \frac{TP}{TP+FN} \quad (17)$$

$$\text{Precision} = \frac{TP}{TP+FP} \quad (18)$$

$$\text{F Measure} = 2 \times \frac{\text{Precision} \times \text{Recall}}{\text{Precision} + \text{Recall}} \quad (19)$$

where, the number of pixels that are accurately predicted to constitute a region of interest (ROI) is known as true positive (TP) pixels, true negative (TN) is the number of pixels that are correctly predicted as background pixels, false positive (FP) is the number of background pixels that are incorrectly predicted as ROI pixels and false negative (FN) is the number of nuclei pixels that are incorrectly predicted as background pixels. Table 2 and 3 gives the segmentation performance metrics result for the images considered in this work. Table 2 shows the segmentation results of algorithms applied on the LUAD dataset. From the table, it is observed that the proposed GNDO algorithm gives a high Jaccard coefficient of 0.72, a dice value of 0.79, and an F-measure value of 0.79. The segmentation results given by the Otsu algorithm are comparatively very low. Furthermore, the proposed GNDO algorithm performed well with PRAD dataset, giving high values of 0.87, 0.82 and 0.86 for Dice coefficient, Jaccard coefficient and F measure value which is given in Table 3. Figure 3

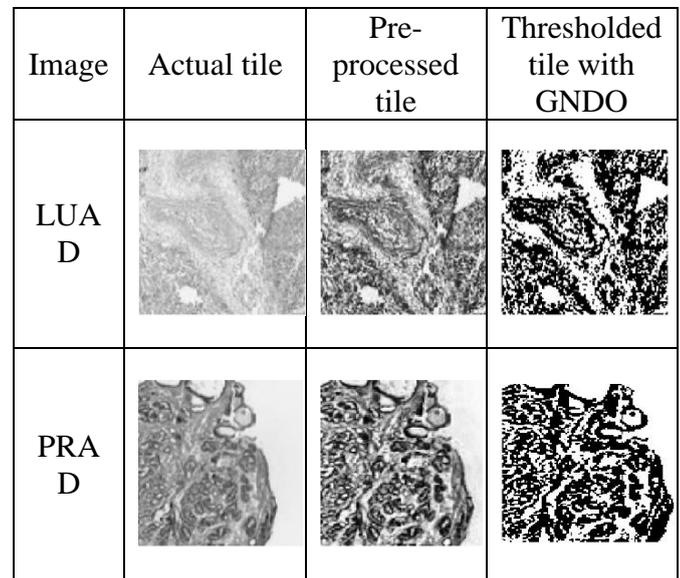
shows a sample segmented image obtained for after preprocessing and GNDO algorithm application with optimal threshold value. From the results, it is observed that, the proposed GNDO algorithm performed well for the two types of datasets considered with better segmentation results [20].

**Table 2 Segmentation Results for LUAD Dataset**

	Dice coefficient	Jaccard coefficient	F measure
Otsu Thresholding	0.50	0.49	0.50
GNDO	0.79	0.72	0.79

**Table 3 Segmentation Results for PRAD Dataset**

	Dice coefficient	Jaccard coefficient	F measure
Otsu Thresholding	0.48	0.48	0.48
GNDO	0.87	0.82	0.86



**Figure 3 Segmented Images with GNDO**

**Conclusion**

This paper presents an innovative approach to image thresholding using the Generalized Normal Distribution Optimization (GNDO) algorithm. The experimental results underscore the superiority of GNDO over conventional methods in achieving accurate and adaptive image segmentation. Two

types of whole slide images are tested for validating the proposed methodology. Additionally, the proposed method is compared against traditional Otsu thresholding method. The better segmentation performance was observed with GNDO algorithm which was measured through various metrics.

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