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A HYBRID LOGISTIC REGRESSION MODEL WITH A BOOTSTRAP APPROACH TO IMPROVE THE ACCURACY OF THE PERFORMANCE OF JELLYFISH COLLAGEN DATA

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Abstract: The Logistic Regression Model (LRM) is successful in many fields due to its capability of predicting and describing the relationship between binary response variables and one or more independent variables. However, the prediction results of this model are still not accurate enough due to error terms, regardless of their existence in the model. To overcome this problem and, at the same time, produce more accurate and efficient predictive model values, the bootstrap approach was proposed. Unfortunately, this approach did not receive any attention, especially for this model. This study aims to introduce the bootstrap approach to LRM and investigate the performance of the proposed models using data on wound healing using jellyfish collagen. The results revealed that the proposed model generated smaller values of MSE and RMSE, as well as shorter confidence intervals, compared with the existing LRM. These results proved that the proposed model could produce an estimated value that is more accurate and efficient than those of the LRM. The results warrant a proper ecosystem management for the perpetual medicinal use and conservation of jellyfish, which is also related to the productive resources and services target by 2030 for SDG 14 involving marine life.

Keywords: Bootstrap logistic regression models, accuracy, jellyfish collagen, SDG 14.

Introduction

Nowadays, many types of diseases can cause harm to humans. Some disorders often start from a small wounds, but worsen when no treatment is given. Wound healing is a normal biological process in the human body, and it is a complex, and dynamic process consisting of four highly integrated, continuous, overlapping, and precisely programmed phases (Guo & DiPietro, 2010). Based on that, there are many factors that can affect wound healing, which interferes with one or more steps in this process, thus causing improper or impaired tissue repair. Among those are interruptions, aberrancies, or prolongation that can lead to delayed wound healing or a non-healing chronic wound. Scientists and doctors have struggled to find alternatives to treat scars in the shortest time possible. Laboratory investigation, together with clinical studies, have yielded a wealth of information on both healthy and impaired wound healing, and a great deal of research directed at understanding the critical factors that influence poorly healing wounds have been produced. Thus, it has become a challenge for the medical community to heal wounds, whether they are chronic or acute (Wilhelm, *et al*., 2017). One of the ways is by using the collagen of jellyfish (phylum

Cnidaria). Collagen is the main structure and function of proteins to the outer cells involved in the wound healing process. Collagen is a type of protein that is widely used in the human body, especially in the formation of bones (Tiago, *et al*., 2012; Silvipriya, *et al*., 2015; Meyer, 2019). The use of essential collagen biomaterials in tissue engineering has improved a lot since decades ago. However, collagen is a protein, which means that it is hard to sterilise without causing any alteration to its shape (Remi, *et al*., 2010).

The effects of jellyfish collagen on promoting wound healing were studied based on the model of rat skin wounds. In an experiment, the skins of rats were cut to create an injury, and the wounds were treated with collagen, and at the same time, Yunnan Baiyao was used as a positive control. According to Li, *et al*. (2019), it refers to a famous traditional Chinese medicine formula used for wound healing, and is useful for bleeding, haemostasis, pain relief, and apocatastasis. It is also widely used in hospital departments, like orthopedics, respiratory care, gastroenterology, and gynecology. The size of the wounds measured through cross measurement and the healing rates were calculated. The results showed that the optimal conditions of jellyfish collagen extraction obtained were as follows: extraction time was 62.64 hour, the solid-water ratio was1:23.6, and the acetic acid concentration was 0.562 moles/L. Animal tests showed that treatment with collagen could significantly accelerate re-epithelialisation and promote wound healing (Ding *et al.,* 2010).

Understanding wound-healing treatment that enables wounds to heal is crucial using wound-healing models. Among the models is the full-thickness wound model (Svensjo, *et al*., 2000; Hiroko, *et al*., 2007; Ruszymah, *et al*., 2014; Zhang, *et al*., 2015; Ali, *et al*., 2018) in-vitro model (Wilhelm, et al., 2017), incision model (Meena, *et al*., 2010; Daniela, *et al*., 2011; Vipin & Sarvesh, 2011; Rajesh, *et al*., 2013; Muqeem Nasir, *et al*., 2016) and lesion model (Crist, *et al*., 1992; Joerg, *et al*., 1999; Mikus, *et al*., 2001; Janet, *et al*., 2010; Gloria, *et al*., 2015; Guimei, *et al*., 2018)

It is also crucial for us to sustain the marine ecosystem's sustainability for jellyfish to make sure that its supply is sufficient. Thus, various research work can be found through literature study on the viability of marine ecosystem, specifically for jellyfish (Malej, 1989; Lucas, 2001; Hansson, *et al*., 2005; Lynam, *et al*., 2006; Doyle, *et al*., 2007; Pauly, *et al*., 2009; Brotz, *et al*., 2012; Lucas, *et al*., 2012; Bastian, *et al*., 2014; Condon, *et al*., 2014; Ceh, *et al*., 2015; D'Ambra, *et al*., 2018; Philip, *et al*., 2019). Recently, there has been an increasing interest in the analysis of jellyfish collagen using statistical or mathematical modelling (Tarzan, 1987; Berline, *et al*., 2013; Mary, *et al*., 2013; Florain & Jurgen, 2015; Philip, *et al*., 2019; Simon, *et al*., 2020). Besides, there are numerous statistical models that analyzes the sustainability of marine ecosystem data, particularly in the east coast of Peninsular Malaysia (Mazlan, *et al*., 2005; Mohd Zamri, *et al*., 2009; Mohd Zamri, *et al*., 2010; Muhamad Safiih, *et al*., 2018). However, no other study has looked into the modelling of jellyfish, specifically in the South China Sea. Thus, the Logistic Regression Model (LRM) was used in this study due to its ability to examine and describe the relationship between a binary response variable (in this study, the wound status, i.e., "healed = 0" or "not healed =1") and the set of predictor variables (Fitzmaurice and Laird, 2001). The LRM is as follows:

$$Y = \frac{1}{1+e^{-(\beta_0+\beta_1X_1+\beta_2X_2+\cdots\beta_nX_n+\varepsilon_i)}} = \frac{1}{1+e^{-(\beta_0+\sum\beta_iX_i+\varepsilon_i)}} \quad (1)$$

However, the prediction results based on the model in Eq. (1) is still not very accurate, as well as not efficient and not precise due to ε_i, i.e., the error term existence in the model. Hence, to make this model more reliable, efficient and precise, the bootstrap approach is used (Nur Amalina, *et al*., 2011; Nurul Hila, *et al*., 2016; Nurul Hila & Muhamad Safiih, 2016; Muhamad Safiih, *et al*., 2017a; Nurul Hila, *et al*., 2019). This approach also has been subjected by Muhamad Safiih, *et al*., (2017b). This approach will allow higher predictability to the success of wound healing using the jellyfish collagen. Unfortunately, this approach has never been subject to study, especially in terms of LRM, and hence, it becomes a novelty in terms of ways to improve the effectiveness of predicting models. Through this approach, the variables in Eq. (1), especially its error term, are mainly reconstructed to produce a smaller standard error and a shorter confidence interval. By doing that, it can provide estimated results that are close to the actual values. The aims of this study are twofold. First, to propose the hybridisation of the bootstrap approach into LRM to produce a more accurate model, coined as the Bootstrap Logistics Regression Model (BLRM). Second, to investigate the performance of these proposed models by comparing them with the existing LRM using jellyfish collagen.

Materials and Methods

Logistic Regression Bootstrap Model

The general form of the Logistics Regression Model with variables p covariates can be summarised as follows:

$$y(x) = \frac{e^{b_0+b_1x_1+\ldots+b_jx_p+e_i}}{1+e^{b_0+b_1x_1+\ldots+b_jx_p+e_i}} \tag{2}$$

with $y(x)$ being the probability of success with the likelihood $0 \le y(x) \le 1$ and β_j the parameter with $j = 1,2,..., p$. The bootstrap approach is implemented to the Logistic Regression Model. The algorithm of the LRM model using the bootstrap approach as proposed is as follows:

Step 1: Generate the input of wound healing using jellyfish collagen data.

Step 2: Estimate the prediction probability of success (P_i) using the logistic model (LR):

$$P_i = \{1 + e^{[-(\alpha+X_i\beta)]}\}^{-1}$$

where a is intercept term, $X_i = (X_{i1}, X_{i2}, X_{i3})$ is the set of covariate values for observation i, and $\beta_i = (\beta_1, \beta_2, \beta_3)$ is the set of corresponding values of the regression coefficients estimated from the full sample as shown in Step 1.

Step 3: Calculate the residual model for LR based on e_i = failure – P_i

Step 4: For every generated data, a residual value obtained by the LR model, as shown in Step 3 is calculated using the bootstrap method. Due to this, a new bootstrap value, is obtained, where i=1,…,m referring to the i^{th} time, and t=1,..,B. The notation B refers to the total bootstrap replication sets, i.e., 1000.

$$\hat{e}_i^{B(t)} = \begin{bmatrix} \hat{e}_1^{B(1)} & \cdots & \hat{e}_1^{B(999)} & \hat{e}_1^{B(1000)} \\ \vdots & & \vdots & \vdots \\ \hat{e}_{m-1}^{B(1)} & \cdots & \hat{e}_{m-1}^{B(999)} & \hat{e}_{m-1}^{B(1000)} \\ \hat{e}_m^{B(1)} & \cdots & \hat{e}_m^{B(999)} & \hat{e}_m^{B(1000)} \end{bmatrix}$$

Step 5: The estimation obtained in Step 4 is revaluated using the Step 3 formula. Thus, a bootstrap data set is obtained as follows:

$$x_i^{B(t)} = \begin{bmatrix} x_1^{B(1)} & \cdots & x_1^{B(999)} & x_1^{B(1000)} \\ \vdots & & \vdots & \vdots \\ x_{m-1}^{B(1)} & \cdots & x_{m-1}^{B(999)} & x_{m-1}^{B(1000)} \\ x_m^{B(1)} & \cdots & x_m^{B(999)} & x_m^{B(1000)} \end{bmatrix}$$

Step 6: A bootstrap sample, x_i^B, can be obtained by averaging each column of bootstrap data set in Step 5.

Step 7: Using the same calculation to estimate the value of parameter β using the bootstrap data in Step 6 and the MLR model, the BMLR hybrid model is subsequently formulated in this step.

Based on these developed algorithms, the Bootstrap Logistic Regression Model (BLRM) is now defined as:

$$y(x)^B = \frac{e^{(b_0 + b_1 x_1{}^B + ... + b_j x_p{}^B + e_i{}^B)}}{1 + e^{(b_0 + b_1 x_1{}^B + ... + b_j x_p{}^B + e_i{}^B)}} \quad (3)$$

The parameter β_i from the Bootstrap Logistic Regression Model, approximated using the Maximum Likelihood Estimation (MLE), will become $\hat{\beta}_j$ and the model for the Logistic Regression Bootstrap Model is shown as follows:

$$\hat{y}(x)^B = \frac{e^{(\hat{b}_0 + \hat{b}_1 x_1{}^B + ... + \hat{b}_j x_p{}^B + e_i{}^B)}}{1 + e^{(\hat{b}_0 + \hat{b}_1 x_1{}^B + ... + \hat{b}_j x_p{}^B + e_i{}^B)}} \quad (4)$$

This model uses the variables $x_1, x_2, ..., x_p$, which is dependant and has a natural correlation between variables. From this equation, the error in Logistic Regression is written as $\hat{\varepsilon}_i = y - \hat{y}$ and $i = 1, ..., N$, where N is the number of observation values. Generally, the bootstrap approach in the Logistic Regression Model starts after parameter approximation is done by MLE, and the real bootstrap error is obtained from the Logistic Regression Model. From the bootstrap error, the new data calculation for the Logistic Regression Bootstrap Model is established. Next, the findings of the original data and the new data are compared through the approximation statistics, such as the mean squared error (MSE) and root mean squared error (RMSE) based on Nurul Hila, *et al*., (2019), through the following:

$$MSE = \frac{\sum_{i=1}^{N} [\beta_i^B - E(\beta^B)]^2}{N-1} \quad (5)$$

$$RMSE = \sqrt{\frac{\sum_{i=1}^{N} [\beta_i^B - E(\beta^B)]^2}{N-1}} \quad (6)$$

The calculation of the confidence intervals for the normal distribution, *t*-distribution, and bias-corrected and accelerated (BCa) methods are written based on Eq. (7), Eq. (8), and Eq. (9), respectively.

$$[\hat{\theta}_B, \hat{\theta}_A] = \hat{\theta} \pm \hat{\sigma} \cdot z^{(\alpha)} \quad (7)$$

$$[\hat{\theta}_B, \hat{\theta}_A] = [\hat{\theta} - \hat{s} \cdot t_{n-1}^{\alpha}, \hat{\theta} + \hat{s} \cdot t_{n-1}^{\alpha}] \quad (8)$$

$$[\hat{\theta}_B, \hat{\theta}_A] = [\hat{\theta}^{\alpha_1}, \hat{\theta}^{\alpha_2}] \quad (9)$$

Where $\hat{s}$ and t_{n-}^{α} in Eq. (8) are the standard error and the critical value for student's *t*-distribution with *n*-1 degree of freedom. The standard error is calculated using statistical measurement based on Nur Amalina, *et al*., (2011), Muhamad Safiih, *et al*., (2017a) and Muhamad Safiih, *et al*. (2017b). The interval length of Eq.(8) is calculated based on the percentile of mean estimation of bootstrap replication, *B* with 100*α* – *th*, where *α* = 0.05 and 1 – *α* = 0.95. The upper and the lower limits of BP refer to the interval length from 50 – *th* through 950 – *th* replication. While α_1 and α_2 in Eq. (9) refers to the normal confidence interval with $\alpha_1 = \alpha$ and $\alpha_2 = 1 - \alpha$, respectively.

Descriptive Data

The effectiveness of the proposed model was studied using a set of secondary data obtained from the laboratory of the Institute of Marine Biotechnology, UMT, understudy of wound healing using jellyfish collagen. In this study, three variables are involved, which are the condition of the rat, the number of days where the thickness of the collagen is measured, and the thickness of the collagen during the healing process. The effects of jellyfish consumption on the wound contraction diameter rat were analysed, where the larger the size of wound contraction, the better the healing process. The effects of healing were observed on different days, i.e., days 7, 14, and 21 on lab rats (*Rattus norvegicus domestica*) that were not given any treatment, and lab rats receiving jellyfish treatment. The number of observations for this study is 300 observations. It consists of 100 sample sizes with three different days, i.e., day 7, day 14, and day 21, for standard and tested wound contraction of jellyfish, respectively, with 1,000 replications. For the formation of collagen, the value given is the value of collagen formed on the wounded skin. Eighteen (18) rats were involved in this experiment. The summary of the variables are shown in Table 1.

Results and Discussion

The results for both the error values of the LRM and BLRM models are shown in Table 2. Based on the results, the BLRM model has a small error value, compared with the LRM model. The decrease in the error value was also attained in all three variables: the condition of the rat, the number of days the readings recorded, and the thickness of the collagen formed. For example, for variable x, the error value obtained through LRM is 0.35180356 and 0.5931303 for MSE and RMSE, respectively. However, the error values obtained From BLRM are smaller, i.e., MSE and RMSE are 0.00922625 and 0.0960534. Hence, the BLRM model is proven to be more accurate than the LRM model. The effectiveness of the error values of the BLRM is plotted in Figures 1 and 2.

Figures 1 and 2 revealed that the BLRM model gives smaller error values than the LRM model. This finding is identified in every error values of MSE and RMSE, and also in all investigated variables. The values of normal distribution and t-distribution confidence intervals for all variables representing the BLRM model are shorter (Table 3). For example, X1, where the value for BLRM-N is 0.0284938 and BLRM-t, is 0.0306776, while in the LRM model, the value is longer, which is 17.6765000 for LRM-N and 19.0378800 for LRM-t. The normal distribution and t-distribution of confidence interval values are shown in Figures 3, 4, and 5. The lower, upper, and length values are the size of the percentile for the data treatment of wound healing using jellyfish collagen with a 95% confidence interval (CI). LRM-N, LRM-*t*, BLRM-N, BLRM-*t*, and BLRM-BCa refer to the normal confidence interval, the *t*-distribution confidence interval, a normal confidence interval for the bootstrap, the t-distribution confidence interval for the bootstrap and the bias-corrected and accelerated confidence interval all for the LRM, respectively.

Based on Figures 3, 4, and 5, it can be concluded that the BLRM model always gives a shorter interval range, compared with the LRM model. The comparison between the achievements of these two models provides

Table 1: List of variables

Variables	Representatative	Explanation
Condition of the rat	X_1	0 = Collagen applied, 1 = Not
Number of days measured	X_2	which is Day 7, 14, and 21
Thickness of collagen	X_3	The thickness of collagen during the healing process
Wound status	Y	0 = Heal, 1 = Not heal

Table 2: The measurement error in jellyfish data

P/U	Model	MSE	RMSE
X_1	LRM	0.07350789	0.2711234
	BLRM	0.05816027	0.2411644
X_2	LRM	0.35180356	0.5931303
	BLRM	0.00922625	0.0960534
X_3	LRM	0.52269337	0.7229754
	BLRM	0.15156211	0.3893098

Figure 1: The MSE performance of LRM vs BLRM for all variables

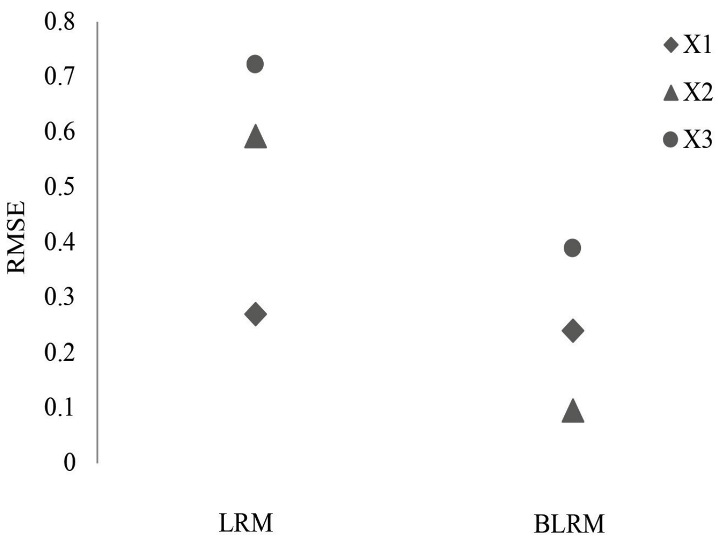

Figure 2: The RMSE performance of LRM vs BLRM for all variables

evidence that the model with the bootstrap approach produces shorter confidence interval value, and this illustrates that the BLRM model can give a more accurate and effective approximation.

Another method used, which is bias-corrected and accelerated (BCa) interval, also gives a shorter interval range value, as a matter of fact, shorter than the normal confidence interval and t-distribution. Based on Figure 6, the BCa interval is the shortest compared with other approximate confidence interval values. According to Davison and Hinkley (2003), and Micheal and Robert (2011), the BCa method would consider the accuracy and final point. Another advantage of this method is it would adapt accurately if the parameters were altered.

Table 3: The values of the confidence interval in Jellyfish data

Variables	Model	Lower	Upper	Length
X_1	LRM-*N*	3.9993790	4.2800050	17.6765000
	BLRM-*N*	1.8123070	1.6514540	0.0284938
	LRM-*t*	3.9886520	4.2907320	19.0378800
	BLRM-*t*	1.8184560	1.6453050	0.0306776
	BLRM-BCa	1.7230020	1.7407580	0.0031420
X_2	LRM-*N*	0.0771277	1.0754380	1.8510960
	BLRM-*N*	0.3458101	0.3371817	0.0061323
	LRM-*t*	0.0389641	1.1136020	2.0055730
	BLRM-*t*	0.3461399	0.3368518	0.0066011
	BLRM-BCa	0.3394397	0.3435521	0.0029227
X_3	LRM-*N*	5.6487260	6.3567250	292.4258000
	BLRM-*N*	2.6349560	2.0504430	0.0569558
	LRM-*t*	5.6216610	6.3837900	315.8197000
	BLRM-*t*	2.6573010	2.0280980	0.0614483
	BLRM-BCa	2.3596230	2.3257760	0.0032518

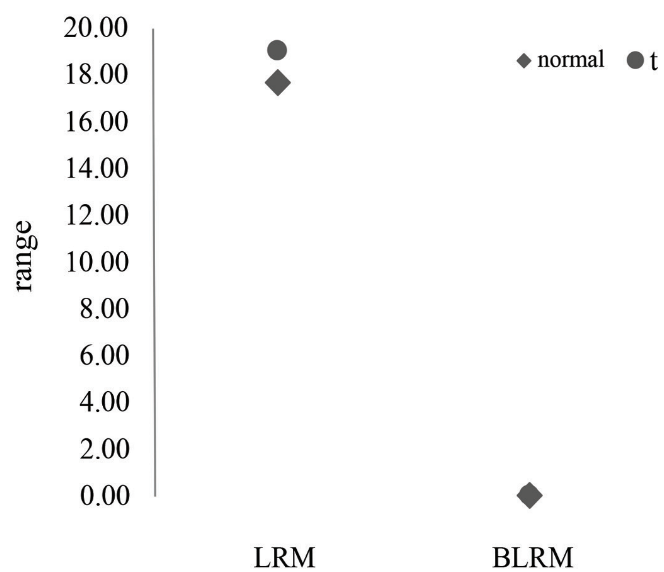

Figure 3: The CI of *t*-distribution for LRM and BLRM of X_1

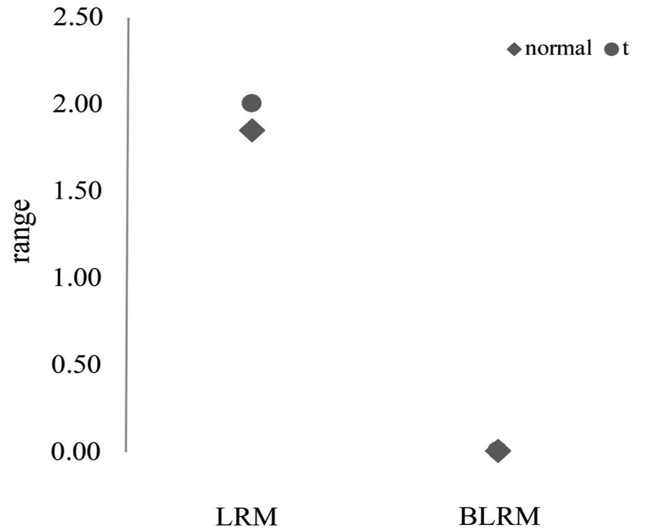

Figure 4: The normal and *t*-distribution for LRM and BLRM of X_2

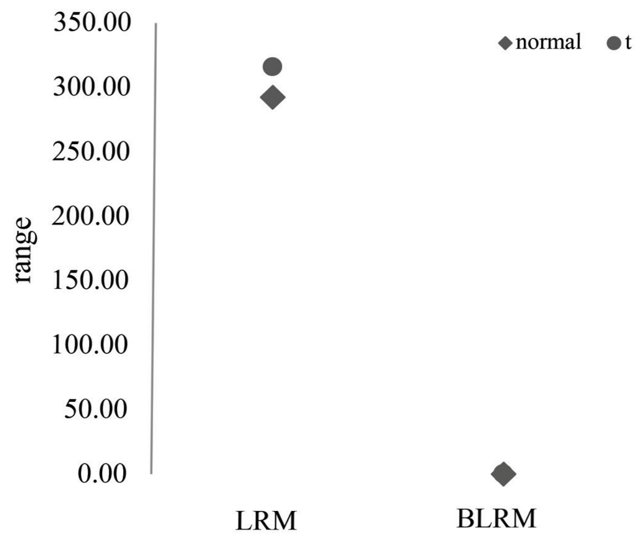

Figure 5: The normal and *t*-distribution for LRM and BLRM of X_3

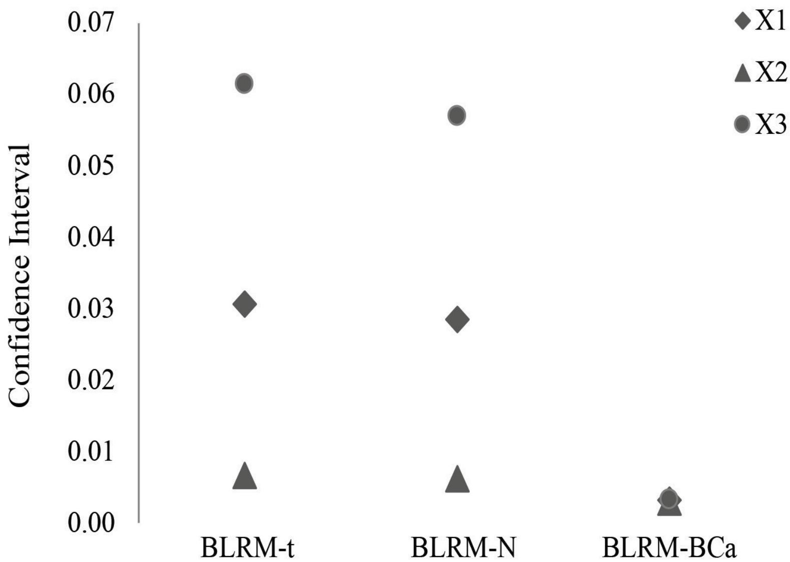

Figure 6: The plot of confidence interval in BLRM for all variables

A Logistic Regression Model that was produced in this research is:

$$y(x) = \frac{e^{(1.3686+4.1397x_1+0.5763x_2+6.0027x_3)}}{1+e^{(1.3686+4.1397x_1+0.5763x_2+6.0027x_3)}}$$

$$y(x) = 1.0003$$

A Logistic Regression <odel with the bootstrap approach produced in this research is:

$$y(x)^B = \frac{e^{(1.4659-1.7319x_1-0.3415x_2-2.3427x_3)}}{1+e^{(1.4659-1.7319x_1-0.3415x_2-2.3427x_3)}}$$

$$y(x)^B = 0.5161$$

The results show that the BLRM model is robust enough to give a better value of approaching 0, represented by a healed wound, while the value of the LRM model approaching 1 represents an unhealed wound.

Conclusion

The findings show that the BLRM model is more precise than the original model in terms of smaller error value and shorter confidence interval range for all variables. Therefore, ur model precision is higher because the onfidence interval is narrow for the variables. Ience, we have demonstrated that all variables ı this study, which are the conditions of the ıt, number of days for observation, and the ıickness of collagen, can significantly influence wound healing, which can be represented using the regression model implemented with the bootstrap approach. This study also shows that ıe use of jellyfish not only has a positive effect n the healing process, but we could even justify nproving the sustainability of the marine cosystem services (medicinal use) to preserve ıe jellyfish diversity related to the global targets ın SDG 14.

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