

Data Balancing using Deep Convolutional Generative Adversarial Networks (DCGAN) in Patients with Congenital Syndrome by Zika Virus

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Keywords: Congenital Syndrome, Zika, Generative Adversarial Networks, GAN, DCGAN.

Abstract: Class imbalance is a common health care problem and often affects the performance of machine learning algorithms. Unfortunately, the minority class, generally the one with the most significant interest, has their learning affected to the detriment of the majority class. This article proposes using Deep Convolutional Generative Adversarial Networks (DCGAN) for minority class oversampling, generating synthetic instances. For this, the 'RESP-Microcephaly' database was used, which records suspected cases of congenital alteration due to Zika virus (ZIKV) infection. The database presents unbalanced data with 2904 and 7606 instances with and without congenital alteration, respectively. To evaluate the performance of DCGAN, we compared this method with an undersampling and an oversampling approach, using SMOTE with three classification algorithms. The use of DCGAN for balancing demonstrates a significant improvement in classification indices, especially about the minority class.

1 INTRODUCTION

In recent years, machine learning techniques have been applied to several domains, especially in the health area such as breast cancer, thyroid disease, Parkinson's disease, predict mortality rate, and life expectancy (Tomar, 2013) (Herland et al., 2014) (Japkowicz, 2000a) (Batista et al., 2004) (Alsharqi et al., 2018) (Weng et al., 2017) (Green, 2018) (Esteva et al., 2017).

However, these healthcare datasets often suffer from "rare class" issues, which result in unbalanced classes in the training datasets (Batista et al., 2004) (Chawla, 2005) (Milovic and Milovic, 2012). That is, most health datasets generally have very few cases of the target disease compared to the number of healthy patients in the dataset (Chawla, 2005) (Japkowicz, 2000b). In the binary classification for medical diagnosis, the rare minority class refers to the positive instances or target class. In contrast, the majority class is represented by the negative cases in the dataset.

Although unbalanced data is frequent in machine learning tasks, this is a very challenging task for classification algorithms (Chawla et al., 2003). This is because traditional machine learning methods applied to unbalanced problems usually have a bias in favor of the majority class, with unsatisfactory performance in the minority class. This takes place during train-

ing; the minority classes collaborate less towards the minimization of the objective function (Chawla et al., 2002).

There are traditional techniques for working with class imbalance. One approach is subsampling, which involves excluding majority class instances to balance instances in each class. Unfortunately, despite repairing the disproportion, the classifier loses the majority of information and is also likely to make sampling errors on small data sets (Japkowicz, 2000a). Another technique is oversampling, in which instances of the minority class are augmented so that the classes are uniform. This solves the balance problem but may cause the classifier to generalize less to the minority class because the particulars of the minority class data become more usual (Japkowicz, 2000a).

An example of a widely used algorithm that uses this approach is the SMOTE (Chawla et al., 2002) (Chawla et al., 2003). It increases the number of instances of the minority class by creating synthetic examples. First, a sample belonging to the minority class is randomly selected to generate new instances, considering its neighbors. Then, from this neighborhood, a new sample is built with the interpolation of neighboring points. For this, lines are drawn between the examples that make up the neighborhood. On these lines, synthetic points belonging to the minority class are generated (Chawla et al., 2002). Thus, al-

though these new instances may not accurately reflect the actual distribution of the data, they tend to be close enough to encourage generalization and increase the accuracy of the overall classification (Chawla et al., 2002). On the other hand, deep learning methods have been used very efficiently, as is the case of Generative Adversarial Networks (GANs) (Mariani et al., 2018) (Mullick et al., 2019).

The GANs were inspired by game theory; the generator (G) and the discriminator (D) complement each other until reaching the Nash equilibrium in the training process (Goodfellow et al., 2014). Both are neural networks with different responsibilities. The discriminator is a network responsible for evaluating whether certain content is real or generated. The generator produces the content itself. The relationship between these two components is performed in an adversarial way. At the same time, the discriminator is enabled to distinguish the real from the fake, and the generator is trained to deceive the discriminator through the content it is producing. Through the training of both, networks develop together to determine their responsibilities (Goodfellow et al., 2014).

This article uses a synthetic oversampling approach called DCGAN (Deep Convolutional Generative Adversarial Network), a GAN type that explicitly uses convolutional and convolutional transpose layers in the discriminator and generator (Salimans et al., 2016).

Generating artificial data through data augmentation (DA) techniques can be an alternative to improve classification. Several works have already applied DA and obtained improvement in their results (Hussain et al., 2018), (Wang et al., 2017) and (Yu et al., 2017). We used GAN's to perform AD and tested it on a set of tabular data from the Public Health Event Registry RESP-Microcephaly¹, which presents an imbalance of classes in the order of 1:2.6. There is a majority class with 72.37% (without syndrome), much more frequently than the minority class (with the syndrome) 27.63%

In addition to the two oversampling balancing methods, SMOTE and GANs, we also compared the *Random Under Sampler* (RUS). The RUS undersampling method removes the majority class samples at random; in the end, the majority class has the same number of samples as the minority class.

¹The RESP-Microcephaly is an online form developed by DATASUS-Brazil, instituted by the Ministry of Health (MS), since November 19, 2015, to record cases and deaths suspected of changes in growth and development related to infection by the Zika virus and other infectious etiologies (Brasil et al., 2015). Available at: <http://www.resp.saude.gov.br/microcefalia>

Thus, this work aims to investigate data balancing methods in diagnosing newborns and children with congenital syndrome caused by ZIKV infection. Regarding classifiers, we use three algorithms: Random Forest, Decision Tree, and Bagging.

This work is structured as follows: Section 2 brings the background used in the research. Section 3 presents the works related to the topic investigated. Section 4 describes the materials and methods used in the experiments. Finally, in Section 5, the results and Discussions, and Section 6 presents the final considerations and proposals for future work.

2 BACKGROUND

2.1 Congenital Zika Syndrome

On March 31, 2016, the World Health Organization (WHO) announced Zika virus infection (ZIKV) as an emergency public health problem worldwide due to the association of this arbovirus with the occurrence of congenital Zika syndrome.

ZIKV is mainly transmitted by the vector *Aedes aegypti*, which resides in tropical and subtropical regions, as well as by *Aedes albopictus*, the inhabitant of the European Mediterranean (Carvalho et al., 2019).

Mothers can transmit the Zika virus to embryos or fetuses during pregnancy or at birth time (Zanluca et al., 2017).

Children born to women infected with ZIKV during pregnancy showing varying degrees of nervous system impairment, such as microcephaly and other neurodevelopmental lesions (Boeuf et al., 2016).

In additional observational studies, a set of congenital anomalies was identified and linked to ZIKV infection in the uterus, called Congenital Zika Syndrome (CZS). This syndrome includes, in addition to microcephaly, craniofacial disproportion, irritability, spasticity, seizures, feeding difficulties, visual abnormalities, and hearing loss, as well as calcifications, cortical disorders, and fetal cerebral ventricle dilatation (Lima et al., 2019).

This article aims at improving CZS classification by balancing GAN's by improving classification methods to improve early diagnosis and prevention.

2.2 Generative Adversarial Networks - GAN

The Adversary Generative Networks (GANs), proposed by (Goodfellow et al., 2014), are deep neu-

ral network architectures composed of two networks placed against each other. The authors call this model adversary networks and training both models using only the backpropagation and dropout algorithms, being highly successful.

GANs are a kind of differentiable generator network, which is, we can use backpropagation to train with a descending gradient (Goodfellow et al., 2014). This type of model transforms samples from a latent vector z into examples x using the smooth function $g(z, \theta)$ (Goodfellow et al., 2014). Essentially, differentiable generator networks are computing procedures for generating samples.

A typical architecture for GANs is illustrated in Figure 1. The generator is an G differentiable function. When z is sampled from some previous simple distribution, $G(z)$ yields a sample of x (Goodfellow et al., 2014).

The generator input is a random noise vector Z , usually a uniform or normal distribution. The noise is mapped to a new data space via the G generator to obtain a false sample, $G(z)$, which is a multidimensional vector (Goodfellow et al., 2014) (Pan et al., 2019).

The generator is G differentiable function. When z is sampled from some previous simple distribution, $G(z)$ produces a sample of x (Goodfellow et al., 2014).

The generative network tries to produce samples that resemble the original data, $x \text{ yes } P_{data}$, according to the series of transformations that can be described by the function $x = g(z; \theta_g)$.

The D discriminating is a binary classifier. It takes an accurate sample from the dataset. The false piece generated by the G generator as input and the output from the D discriminator represents the probability that the example is authentic.

The discriminating network, in turn, produces the likelihood of x being false or real, which is given by a function $d(x; \theta_d)$. D is trained to maximize the probability of a hit of a sample being genuine or false (coming from G), and while G is trained to minimize the likelihood of being discovered, $[\log(1 - D(G)(z))]$.

In practice, Goodfellow et al. (2014) have observed that minimize $[\log(1 - D(G)(z))]$ makes gradients converge to zero quickly and maximizing $\log(D(G)(z))$ is equivalent and allows for gradients with higher values. Consequently, the optimization problem of GANs is transformed into the objective function presented in Equation 1.

$$\begin{aligned} \min_G \sim \max_D V(D, G) &= \\ = E_{x \sim data}(x) [\log D(x)] + E_{z \sim p(z)} [\log(1 - D(G)(z))], & \quad (1) \end{aligned}$$

So the game between Generator and Discriminator is established, the function $V(D, G)$ will reach its maximum value when the Nash equilibrium is reached, that is, when neither of the two can improve its performance. Thus, the above function will be used as the trouble loss function.

Thus, in its simplest form, given the two players (discriminator and generator), the GAN's learning problem is solved as a zero-sum game, when the gain obtained by one participant is equivalent to the loss by the other participant, where the function $r(\theta_d; \theta_g)$ determines the reward for one of the networks and $-r(\theta_d; \theta_g)$ for the other.

As the game is zero-sum, in Nash's unique equilibrium you will have:

$$g^* = \arg \min_g \max_d r(g, d) \quad (2)$$

where g^* is the generating network at the convergence point, optimally capturing the data distribution. The standard choice for r is

$$r(\theta_d; \theta_g) = E_{x \sim P_{data}} \log(d(x)) + E_{x \sim P_{model}} [\log(1 - d(x))] \quad (3)$$

We can separate the cost function of each one of the networks, for the discriminator we would have

$$L_g = \frac{-1}{m} \sum [\log(d(x))] + [\log(1 - d(g)(z))] \quad (4)$$

The second term, $\log(1 - d(g)(z))$, concerns the incorrect classification of false samples. The equation 5 gives the cost to be optimized by the network generator.

$$L_g = \frac{1}{m} \sum [\log(1 - d(g)(z))] \quad (5)$$

Intuitively, these cost functions make it the objective of the discriminating network to maximize the correctness of the classification of samples into false and accurate; the generating network will try to minimize these hits.

3 RELATED WORKS

Adversary Generative Networks (GANs) have currently been used in machine learning problems in unbalanced (Japkowicz, 2000a) databases. We will present below the main works that used GAN's for oversampling of the minority class in several areas of knowledge.

Mehta et al. (2019) used GAN's to help improve the images of those who suffered a stroke. Han et al. (2019) investigated magnetic resonance (MR) images

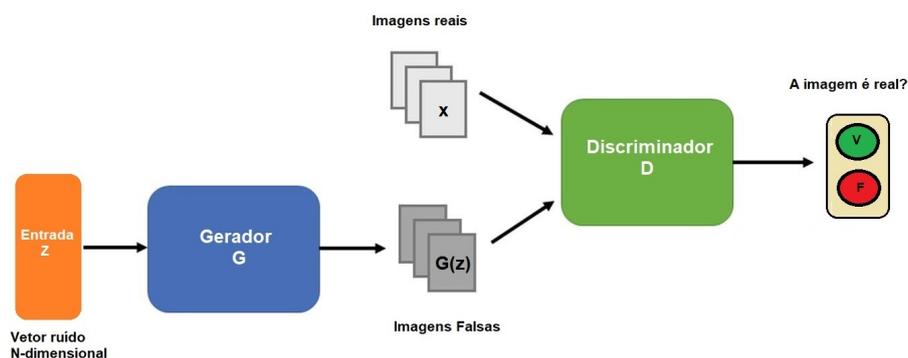


Figure 1: GANs architecture. Source: Based on (Goodfellow et al., 2014).

for tumor detection. Bhagat and Bhaumik (2019) created synthetic chest X-ray images of pneumonia patients to improve the accuracy of the image classification. Bailo et al. (2019) augmented the blood smear microscopic image datasets, which are images of blood taken with a microscope, where a thin layer of blood is placed on a microscope slide (Bailo et al., 2019). Asvestopoulou et al. (2019) augmented the speech dataset to improve DysLexML's dyslexia screening tool ranking. Sheng et al. (2019) created datasets to improve speech recognition in children under noisy conditions (Hu et al., 2018). (Haradal et al., 2018) and (Fahimi et al., 2020) increased the biosignal dataset (electrocardiogram and electroencephalogram) to improve ranking.

All works obtained promising experimental results, even with few original data, implying that the generated data can be used as extended samples to increase a database to improve classification tasks in the most diverse applications.

It was also observed that GAN performance is sensitive to model parameters such as learning rate, number of epochs, and others (Karadağ and Erdaş Cicek, 2019).

Data augmentation with GANs is sensitive to the size of the dataset because when the number of images increases to more than 60,000, the synthetic images generated by the GAN do not contribute to the classification performance and may even cause a reduction in performance (Karadağ and Erdaş Cicek, 2019).

4 MATERIALS AND METHODS

This section presents the materials and methods used in this work. As well as an overview of the RESP-Microcephaly database that records suspected cases of genetic alteration due to Zika virus (ZIKV) infection. A descriptive analysis of the database is also

presented, in addition to its pre-processing.

4.1 RESP Database

Initially, the database had 17451 instances. As the interest of the work is to classify children born with genetic alterations due to Zika virus infection, we work with the notifications of newborns and children². We also excluded all subjects with laboratory confirmation for syphilis or toxoplasmosis³.

The instance selection process summarized in Figure ref Selection. Initially, there were 14,144 cases and confirmed cases with syphilis and toxoplasmosis excluded. We only work with congenital changes due to ZKV and not other causes. At the end of the selection process, we have 10,510 instances, 2,904 children with genetic alterations, and 7,606 children without alterations.



Figure 2: Selection of instances from the RESP.

²These children already had Microcephaly before the Zika outbreak and were included in the RESP under the guidance of the Secretary of Health to follow up on cases (Brasil et al., 2015).

³Microcephaly may be associated with various environmental and genetic factors. Among the environmental factors there is fetal distress, congenital STORCH infections. The acronym is composed of the pathogens most frequently related to diseases: Treponema Pallidum bacteria that causes syphilis (S), the protozoan Toxoplasma Gondii that causes toxoplasmosis (TO) and the rubella virus (R), cytomegalovirus (C), herpes virus simple (H) (Ribeiro et al., 2018).

Thus, the RESP database had 10.510 instances and 43 attributes, organized into nine (9) categories:

1. *Notification*: Displays the classification of suspected cases of congenital infection (newborn, child, fetus at risk, miscarriage, or stillbirth) and the date it notified
2. *Pregnant Woman's Data*: age, race/color, and state of residence (UF)
3. *Information about Live Births*: sex, date of birth, weight (grams), and length (centimeters)
4. *Data on Pregnancy and Childbirth*: types of congenital changes, when the change was detected (in pregnancy or after delivery), gestational age at detection of microcephaly, type of pregnancy, classification of live birth, head circumference, and date of head circumference measurement. The type of pregnancy that defined as preterm (gestational age less than 37 weeks of gestation), the term (gestational age between 37 and 41 weeks of gestation), post-term (gestational age greater than 42 weeks)
5. *Mother's Clinical, Epidemiological Data*: date of onset of symptoms, type of symptoms (fever, rash, itching, conjunctivitis, headache, and neurological involvement), Syphilis/Toxoplasmosis test and result, Zika test results, history of arboviruses, and congenital malformations
6. *Information about Imaging Tests*: ultrasound, transfontanellar ultrasound, computed tomography, and magnetic resonance
7. *Data about the Health Establishment*: municipality and state
8. *Data on Disease Evolution*: death and date of death
9. *Fields Restricted to the Manager*: Final classification of the suspected case of Congenital alterations and Confirmation criteria through laboratory tests performed (Zika, Dengue, Chikungunya, Syphilis, and Toxoplasmosis, others and image)

These categories, together with their attributes, are shown in Figure 3.

The occurrences registered in the RESP confirmed congenital ZIKV infection peaked in 2016 with more than 1600 records. As of May 2016, there is a drop in the number of cases, a behavior observed in subsequent years, as shown in Figure 4.

The cases are distributed throughout the Brazilian territory, as shown in Figure 5. The ten states that presented the highest number of positive diagnoses were: Bahia, Pernambuco, Rio de Janeiro, Paraíba, Maranhão, Ceará, Sergipe with, respectively: 490,

452, 259, 193, 166, 146, 134 cases; in addition to the states of Alagoas and Rio Grande do Norte, both with 130 cases.

About the pregnant women's region, 60.8% of the records are from the Northeast region, 24.9% from the Southeast, 6.7% from the Midwest, 4.3% from the North region, and only 3.3% from the Southern region.

4.2 Preprocessing

Before applying the classification algorithms effectively, simple pre-processing strategies were adopted to obtain a more consistent and impartial model. The database processing phases were:

- *Attribute Binarization*: The original RESP was composed of numerical (13%) and categorical (87%) attributes. We perform one-hot coding to binarize all categorical attributes. At the end of the process, the database had 56 attributes.
- *Inconsistent Data*: There were 95 instances in which the pregnant woman's age was with values 2 and 3. As this is a physiologically incompatible age for a conception, we excluded these values and left them blank.
Two instances had the brain circumference value measuring 323.3 cm, not corresponding to an actual value. These literature reports refer to a mean head circumference of 34.61 cm in typical male NBs, ranging between 32.14 and 37.08 cm, and an average of 34.05 cm in normal female NBs. with variation between 31.58 and 36.52 cm (Brasil et al., 2015). As these values do not correspond to values found in the literature, we excluded these values, leaving them absent.
- *Missing Data*: Missing data is common in health databases. Therefore, the use of proper methods becomes essential to reduce the impact of information loss. The original database was about 30 % missing data. We deal with missing data by imputing the data via the mean and median.
- *Sampling Methods*: There are two types of sampling methods: undersampling and oversampling. Undersampling removes elements from the majority class while oversampling seeks to include elements from the minority class.

Random oversampling was implemented using the RandomOverSampler class in Python. The class used the sampling strategy argument set to "minority" to balance the minority class with the majority class automatically.

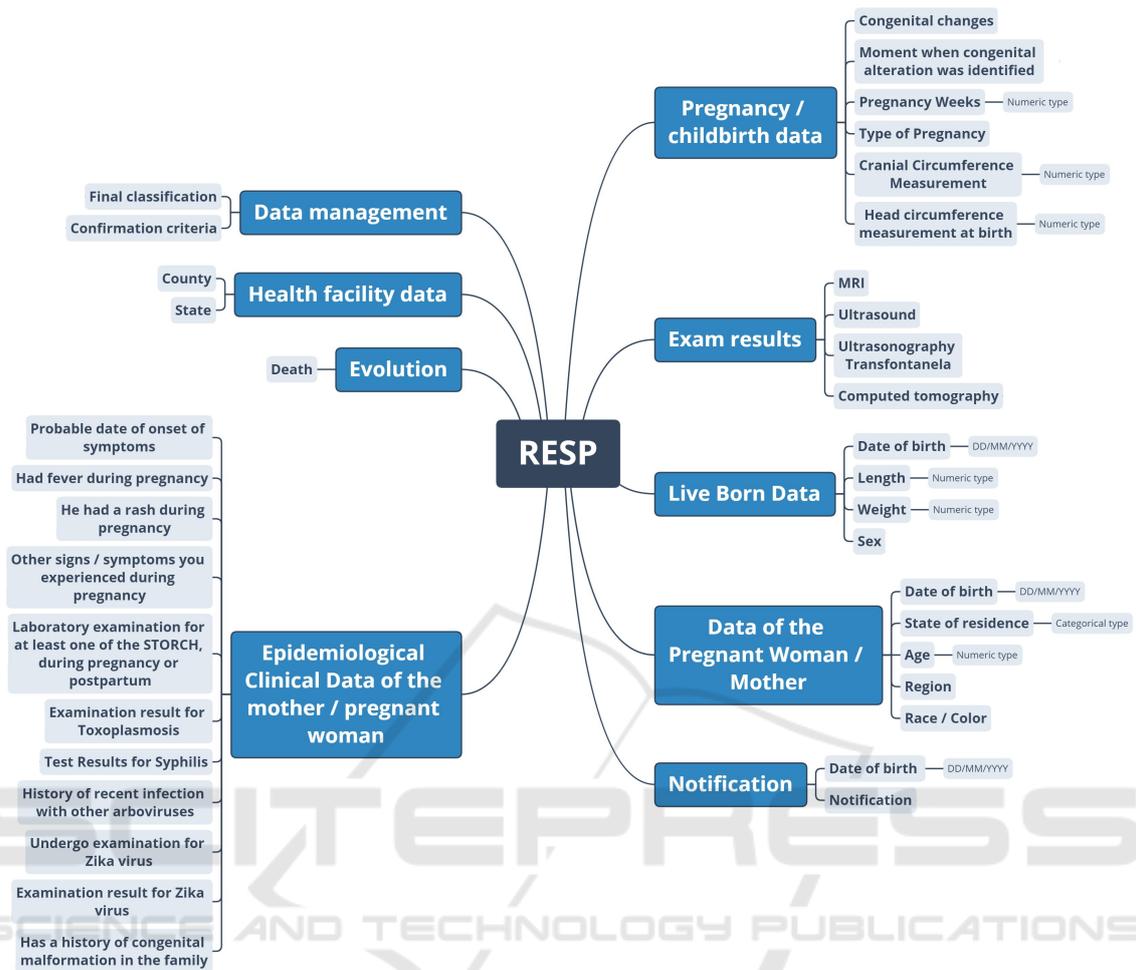


Figure 3: Categories and their respective attributes Registration of Public Health Events - RESP.

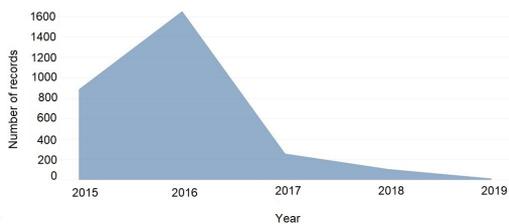


Figure 4: Confirmed cases of congenital infection due to Zika Virus in Brazil between 2015 and 2019.

In work we use two oversampling methods: 1) SMOTE (*Synthetic Minority Over-sampling TEchnique*), which generates synthetic cases for the class of interest from existing data. The new data are generated in the neighborhood of the minority class data to increase the decision space of this class and increase the generalization power of the obtained classifiers (Chawla et al., 2002); 2) GAN, in which the architecture used was a DCGAN (Deep Convolutional Generative Adversarial Network) that allows training



Figure 5: Brazil - Cases of congenital infection due to Zika Virus.

a pair of deep convolutional networks: generator and discriminator.

DCGAN is a GAN model that uses deconvolution layers in the generator and convolution layers in the discriminator to extract characteristics from the data

and build a model to generate the synthetic data.

The first layer of the generator receives an evenly distributed N -dimensional noise as an input to a fully connected network. Then, the result is remodeled in a series of four convolutions with fractional steps (512, 256, 128, 64), according to Figure 6.

DCGAN combines the deep learning stage as the key to GAN training. These techniques include the fully convolutional network and Batch Normalization (BN). Batch normalization is a technique initially introduced by (Ioffe and Szegedy, 2015). Batch normalization is a solution to speed up the training phase of deep neural networks by introducing internal normalization of input values in the neural network layer.

The first emphasizes magnified convolutions (rather than grouped layers) for both: increasing and decreasing the spatial dimensions of the feature. Second, normalizes feature vectors to have zero mean and unity variance across all layers, helping to stabilize learning and handle underweight startup problems.

The generator network has four convolutional layers. All followed by BN (except for the output layer) and rectified linear activation (ReLU). In addition, the generator receives as input a random z vector (obtained from a normal distribution).

The discriminator is also a 4-layer CNN with BN (except its input layer) and leaky RELU triggers. Many enablement functions will work fine with this basic GAN architecture. However, leaky ReLUs are very popular because they help gradients to flow more easily across the architecture.

A regular ReLU function works by truncating negative values to zero, blocking the flow of gradients across the network. However, instead of the function being zero, leaking RELUs allow a small negative value to pass. That is, the function calculates an immense value between resources and a smaller factor.

The generator output corresponds to the 55 resources of the dataset, plus an extra neuron to enable class discrimination. In the discriminator, the final convolution layer is flattened and then fed to a single sigmoid output.

4.3 Assessment Metrics

In this work, the following performance evaluation measures were used: precision, recall and F-Score.

Precision (Equation 6) identifies, among all instances classified in a given class, those that are actually of the class in question.

$$Precision = \frac{TP}{TP + FP} \quad (6)$$

wich: TP = True positive, TN = True Negative, FP = False positive, and FN= False Negative.

Recall (Equation 7) measures the hits in a given class. That is, among all the instances of a given class, how many actually the classifier classified as being of the class.

$$Recall = \frac{TP}{TP + FN} \quad (7)$$

F-Score is a harmonic mean between precision and recall and indicates the overall quality of the model, given by Equation 8.

$$F - Score = \frac{2 * precision * recall}{precision + recall} \quad (8)$$

5 RESULTS AND DISCUSSIONS

To evaluate the performance of using GANs, we compared this method with two traditional balancing methods: Undersampling and SMOTE, and with the results with unbalanced classes.

We split the dataset into 80% for model creation and 20% for testing. 10-fold cross-validation was used to create the models.

The unbalanced dataset had 2904 instances of the class “yes” and 7606 instances of class “no”. In the sub-sampling, the data of the majority class were reduced so that, in the end, the data set was composed of 2336 instances of each class. To avoid a biased model, the oversampling method was applied in cross-validation. In other words, for every nine training folds, the oversampling method was used.

In addition, we use three learning algorithms: Bagging, Random Forest, and Decision Tree. The results obtained are shown in Figure 7.

Analyzing the results, we see that the highest precision for the ‘Yes’ class was 94% with data balancing with GAN using the Random Forest classifier. This means that only 6% of the data were classified as false positives, that is, individuals who were identified as having the congenital syndrome but actually did not have the alteration.

Regarding the precision for class ‘No,’ the best results were also balanced with GAN in which the three classifiers had the same 90% performance; this represents that 10% of the instances were classified as not having the syndrome, but actually they were.

Regarding the Recall rate, the best index for the ‘Yes’ class was 90% for balanced data with GAN with Random Forest. This result represents that 10% of the patients were classified as not having a congenital alteration and were carriers. For the ‘No’ class, the best

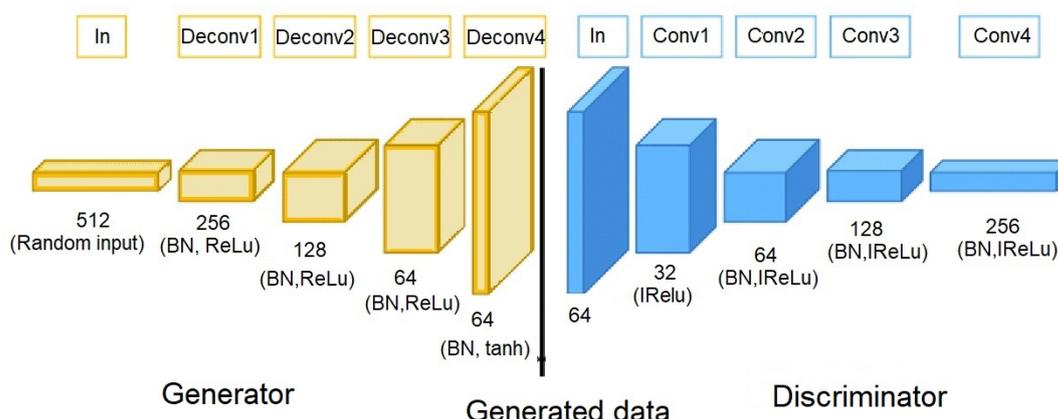


Figure 6: Structure of the deep convolutional generator for DCGAN.

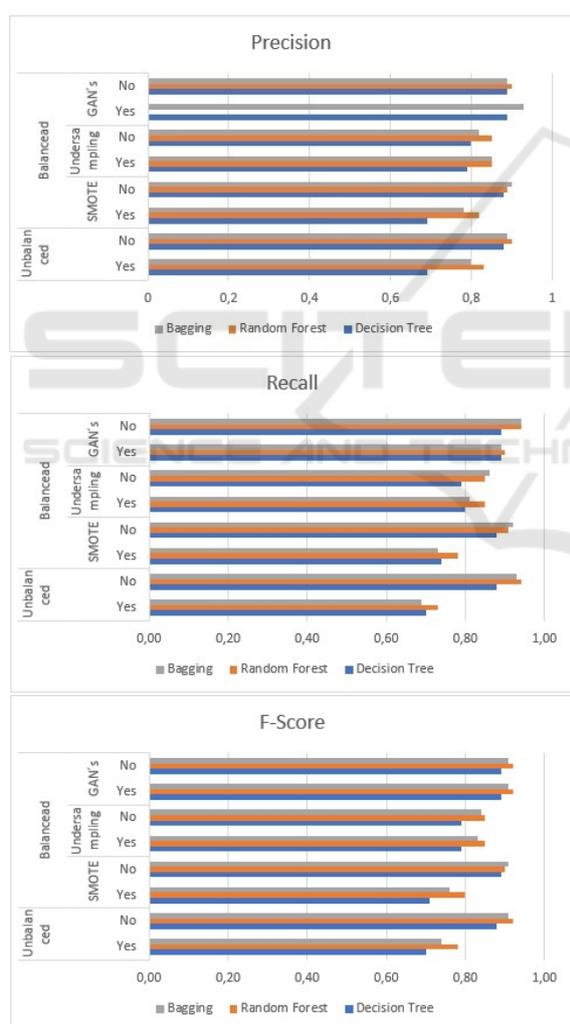


Figure 7: Classification metrics with balanced and unbalanced datasets.

rate was 94% for unbalanced and balanced data with GAN, for Bagging and Random Forest. This means that 6% were false negatives; that is, individuals classified as having congenital alterations, but on the contrary, they didn't have it.

For the F-Score metric, for both classes, the best rate was 92% in balancing with GAN using Random Forest classifier.

Regarding the unbalanced data, we found that the algorithms ranked the majority class better (not), which was expected to happen, as there is a significant difference between the classes.

When we work with SMOTE, there are a slight improvement in the "yes" class results. When we compare the "no" class results, all metrics improve for all algorithms.

Therefore, we can conclude that the undersampling method significantly improves the classification of the 'yes' minority sample, which is expected since we took samples from the majority class. With SMOTE, there is a slight improvement for the minority class, but it continues to rank the majority class better. Finally, with GAN's there was a significant gain in all metrics for both classes.

It is noted that balancing data with GAN showed a significant improvement in the indices, especially concerning the minority class 'Yes,' as with the creation of synthetic data with GAN, the minority class gains more importance, and the bias on the class majority is slight.

6 FINAL CONSIDERATIONS

This work uses Adverse Generative Networks to synthesize data to oversample minority classes in unbalanced datasets and compares the results with other balancing algorithms. The results suggest that GAN

can increase the classifier performance for all evaluated metrics since, in all metrics (accuracy, recall, and F-Score), for all classification algorithms, the values were above 90%.

Observed that there is a significant improvement, especially about the minority class, as with the creation of synthetic data, there was an increase in the representation and density of the data.

As most classification models are designed to work with balanced datasets, GANs for data balancing add a greater generalization power of the algorithms, detecting rare and essential patterns that discriminate the classes of the problem by establishing a reliable decision threshold.

Another point worth mentioning is that data on CZS are rare data since, since 2019, the Federal Government has considered the data as confidential and no longer makes this information available to researchers and the general public⁴.

Therefore, this detailed analysis of this dataset and, above all, the significant improvement in the classification process, add the importance of using GANs for balancing tabular datasets and, above all, for generating synthetic data from rare and restricted data as it is our case.

Furthermore, the approach presented in this article has the potential for early diagnosis of congenital syndrome associated with Zika virus infection. Early diagnosis increases prevention, speeds up treatment, and reduces the devastating consequences of this illness for mothers and children.

In future works, we suggest the refinement of the model proposing the application of deep learning techniques to the GAN architecture to deal with different data types and performing statistical analysis and uncertainty analysis of the results obtained.

ACKNOWLEDGEMENTS

The authors thank the National Council for Scientific and Technological Development of Brazil (CNPq), the Coordination for the Improvement of Higher Education Personnel - Brazil (CAPES), the Foundation for Research Support of Minas Gerais State (FAPEMIG) and Pontifical Catholic University of Minas Gerais (PUC Minas).

⁴The report is available in a way that has already been processed by state and is available at: <https://datasus.saude.gov.br/aceso-a-informacao/registro-de-eventos-em-saude-publica-resp-microcefalia/>

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