APPLICATION OF ARTIFICIAL INTELLIGENCE-BASED IMAGE ANALYSIS IN BIOINFORMATICS

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Abstract:

The collection of image data is an extremely common procedure in clinical practice today. Many of the diagnostic approaches generate such data – computed tomography (CT), X-ray radiography, magnetic resonance imaging (MRI), and others. This data collection process allows for the use of computer vision approaches to be applied with the goal of analysis and diagnostics. Artificial Intelligence (AI) based algorithms have repeatedly been shown to be the best performing computer vision algorithms, in many fields including medicine. AI-based – or more precisely machine learning (ML) based, algorithms have capabilities which allow them to learn the patterns contained in the data from the data itself. Among the best performing algorithms are artificial neural networks (ANNs), or more precisely convolutional neural networks (CNNs). Their pitfall is the need for the large amounts of data – but as it has been previously mentioned, the amount of data collected in today's clinical practice is large and ever increasing. This allows for the development of Smart Diagnostic systems which are meant to serve as support systems to the health professionals. In this paper first, the standard practices and review of the field is given – with the focus on challenges and best practices. Then, multiple examples of the research applying AI-based algorithm analysis are given – including diagnostics of various cancer types (bladder and oral) as well as COVID-19 severity diagnostics and image quality determination.

Key words: artificial intelligence, computer vision, machine learning, smart diagnostics

1. Introduction

The collection of patient data is a common occurrence in today's diagnostic procedures. Much of this data comes in shapes of images from different diagnostic procedures, such as endoscopy, x-ray, computed tomography (CT), magnetic resonance imaging (MRI), and others [1]. Such data is commonly stored in hospital databases, allowing for a relatively easy data extraction [2]. Amount of data collected through the years may be extremely high, and ease of data extraction from the databases – of not only images, but other supporting patient data, lend themselves to the application of data science (DS) and machine learning (ML) applications [3]. Such applications, allow for the development of various Artificial Intelligence (AI) models. ML is a set of methods within AI that is used to develop high precision models which are based on, and created using, existing data. ML algorithms, allow the creation of extremely precise models, but their main pitfall is the need for large amounts of data for proper functioning. But, as discussed previously, the amount of data is not necessarily an issue when it comes to medicine, provided a large enough patient group.

In this paper, the application of such techniques will be discussed. First, an overview of current trends will be given, followed by a series of examples of AI-based ML techniques being used in bioinformatics, more specifically – medicine.

2. Current Trends

Most of the image-based algorithms today are various architectures of convolutional neural networks (CNN) [4]. CNNs are a subtype of artificial neural networks (ANN). ANNs are algorithms which attempt to emulate the process of learning through the creation of neuron networks which consist of artificial neurons interconnected with weighted connections [5]. These artificial neurons are arranged in layers, with each neuron acting as the summator of weighted values of previous neurons [6], with the weights of the connections adjusted during the so-called training process. The adjustment of connection values is based on the error the network achieves on the known data, used for the training [7]. In CNNs, the neurons are replaced with matrices, and the connection weights are replaced with filter matrices [8]. Instead of the error of the network being addressed through the adjustment of singular weights, the filter values are adjusted [9]. The output is achieved through the performing of serial convolution between the input image and the filters, with the final image vectorized (flattened), and connected to an output neuron [10].

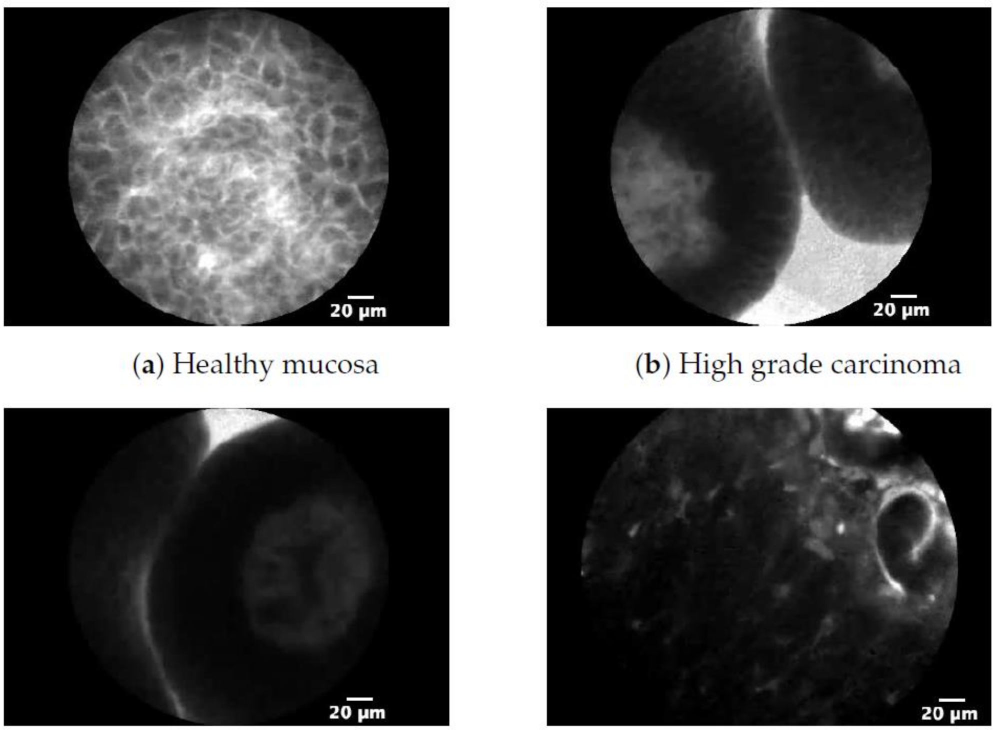
Many authors discuss the manner in which AI can be applied in medicine and bioinformatics. Precision medicine is one of the key topics. Johnson et al. (2021) [11] discuss the application of precision medicine for personalized health application, in which health care process can be adjusted to the individual patient based on their personal relevant metrics. Applications of AI in precision medicine are also discussed by Lin et al. (2021) [12], in which authors discuss the ever-growing trend of AI application in medicine and their positive impact. Bhinder et al. (2021) [13] also discuss the ever-growing application of AI, especially in the topic of cancer research. The authors demonstrate multiple points of use for cancer research using AI, and show multiple successful uses. Applications of AI are shown to be wide when current research is observed. Khan et al. (2021) [14] demonstrate the uses of AI in the chemical systhetization of plant-based drugs. Musulin et al. (2021) [15] demonstrate the wide use of the regression techniques in the determination of COVID-19 epidemiological spread. Still, many authors call for regulatory actions, such as Wegner et al. (2021) [16]. As discussed by Poon et al. (2021) [17] and Kundu (2021) [18], main concerns lie with the unexplainable models. The so-called, “black-box” models do not allow the determination of internal influences, meaning that the way the model concluded something cannot be known. CNNs are examples of such algorithms – but their high performance causes certain authors to determine that knowing the internal functions is not necessary and proof-of-quality through data-validation is enough, while others insist on the use of poorer performing, but explainable models such as Decision Trees (DT) [19].

3. Research examples

In this section, five examples of AI application on image-shaped data in bioinformatics are reviewed. The examples given focus on the application of the AI-based algorithms, namely the CNNs or similar ANN based algorithms in the medical applications within bioinformatics. The examples should illustrate the First, two applications connected to bladder carcinoma are given, followed by an application of quality assessment in radiographical images. Then, an example of severity diagnostics is given, finally followed by an application of CNNs in the oral carcinoma thematic.

3.1. Bladder Carcinoma Classification

Lorencin et al. (2020) [20] discuss the application of a multilayer perceptron (MLP) ANN. The authors aim to investigate the performance of such a method, which is relatively simple in comparison to deep learning convolutional neural networks (DLCNN), for the classification of bladder cancer data. The data is collected through the endoscopical procedure. The collected dataset consisted of 1997 images containing cancerous tissue and 986 images of a healthy (non-cancerous, but with the possibility of other diseases/inflammations) tissue. The classification of the images was not performed binary, but in four classes – healthy tissue, low-grade carcinoma, high-grade carcinoma and carcinoma in-situ, shown in Figure 1.



(**a**) Healthy mucosa (**b**) High grade carcinoma

(**c**) Low grade carcinoma (**d**) Carcinoma in-situ

Figure 1. Example of the different classified bladder carcinoma types [22].

The novelty of the paper lies in the application of edge-detector functions to perform image processing on the original image data. Application of edge detector functions can serve to simplify the task of image classification, allowing a simpler model – such as MLP, to be used. The quality of the classification was evaluated using Area Under Receiver Operating Characteristic Curve, a popular classification metric. Authors concluded that the developed algorithm, shown in Figure 2, achieves the best classification results [21].

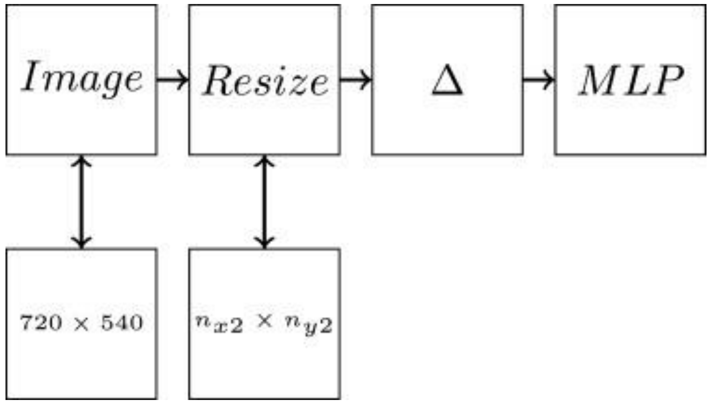


Figure 2. Flowchart of the algorithm developed by the Lorencin et al. during their research [20].

3.2. Bladder Carcinoma image generation

Lorencin et al. (2021) [22] demonstrate the application of Deep Convolutional Generative Adversarial Networks (DCGAN) for the purpose of image generation. Authors propose an algorithm consisting of two neural network – a discriminator and a generator. The generator generates fake images of bladder cancer in an attempt to fool the discriminator which has been trained to discriminate between real and fake images. Generator continually adjusts itself in order to generate better images, until the discriminator is fooled. This process is illustrated in Figure 3.

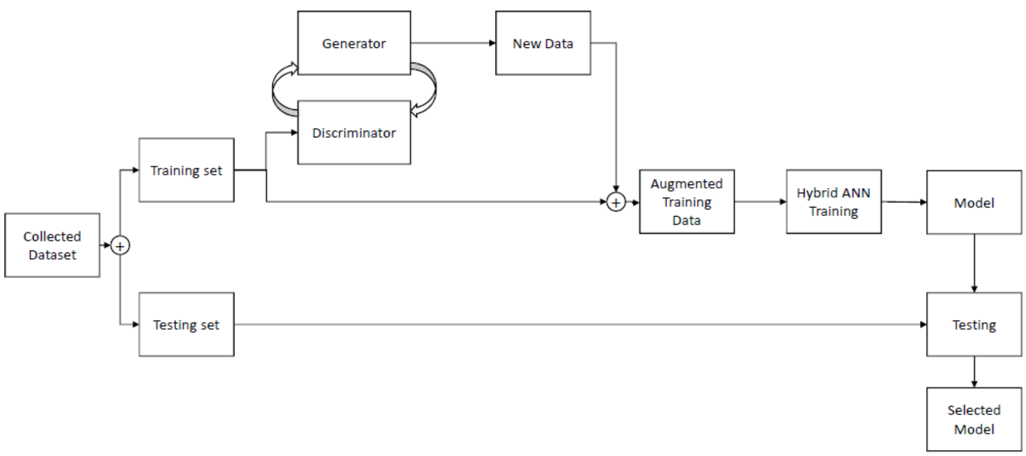
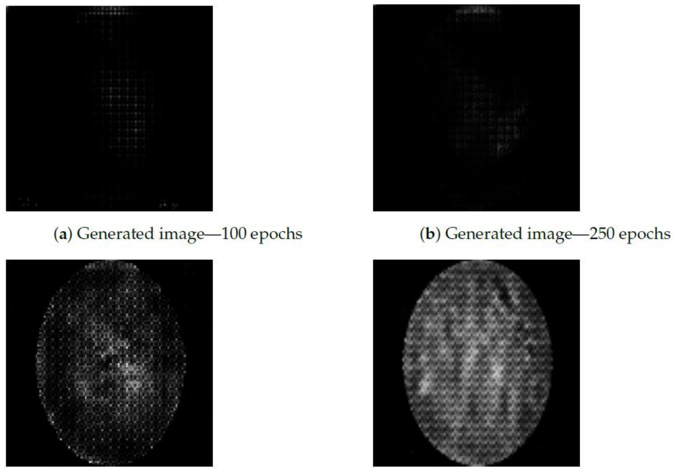


Figure 3. The discriminator-generator pair authors used in the research [22]

The images generated by the algorithm are shown in Figure 4. It is important to note that, while images may have noticeable artifacts visible to the human eye, the used neural networks do not perceive those artifacts, due to the nature of the convolution and filter sizes. When such images are used in the training dataset, an improvement in scores and generalization is shown, based on which the authors conclude that such methods may prove useful when low amounts of data are available.



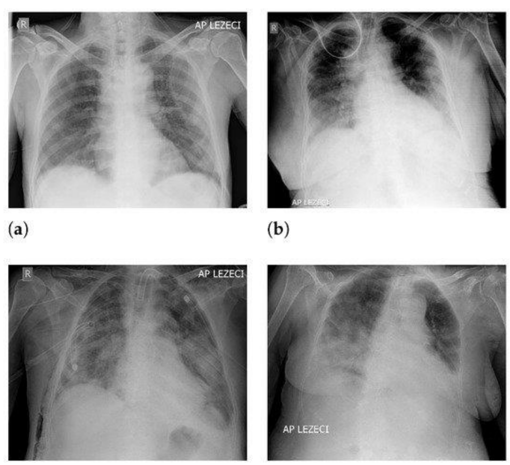
(a) Generated image—100 epochs (b) Generated image—250 epochs

(c) Generated image—500 epochs (d) Generated image—1000 epochs

Figure 4. An example of artificially generated bladder cancer images [22]

3.3 Viral disease severity diagnostics

One of the challenges experienced during the COVID-19 pandemic was accurate assessment of disease severity based on the patient data. This information was key to determine the patient needs. This posed a challenge, not only due to the complexity of determining the severity, but also due to the large amount of patients placing high amounts of stress on medical staff. Lorencin et al. (2021) [23] utilize a dataset consisting of x-ray lung images of COVID-19 patients. The dataset is split into four classes – mild, moderate, severe and critical, as shown in Figure 5.



(a) (b)

(c) (d)

Figure 5. An example of (a) mild, (b) moderate, (c) severe and (d) critical clinical image [23].

Due to the low amount of data, researchers applied an augmentation procedure, using deterministic augmentations – rotation, image mirroring and brightness adjustment. This allowed for a significant increase in the dataset, generating additional 11 images per each original one. It should be noted that only non-augmented data was used for the algorithm validation. Authors tested multiple neural network architectures – Alexnet, ResNet and VGG16. The results show that ResNet152, the largest network tested, has shown the best results when the layer-freezing process is applied.

3.4. Oral carcinoma segmentation and classification

Musulin et al. present an application of CNNs for the purpose of multiclass grading of oral squamous cell carcinoma and the segmentation of epithelial and stromal tissue. Authors use a dataset of biopsy acquired histopathology images to create a multi-stage AI-based system. First, the grade classification is performed on the images, with the segmentation of the oral squamous cell carcinoma within the images of epithelial and stromal tissue. Authors achieved the highest AUC rate with the integration of Xception network and stationary wavelet transformation on images, with AUCmacro score of 0.963 ($\sigma = 0.042$) and AUCmicro score of 0.966 ($\sigma = 0.027$). Segmentation part of the pipeline achieved the mIOU score of 0.878 ($\sigma = 0.027$) and F1 score of 0.955 ($\sigma = 0.014$). An example of the achieved predictions per different image grade is shown in Figure 6 – along with the used mask and preprocessed image of each type.

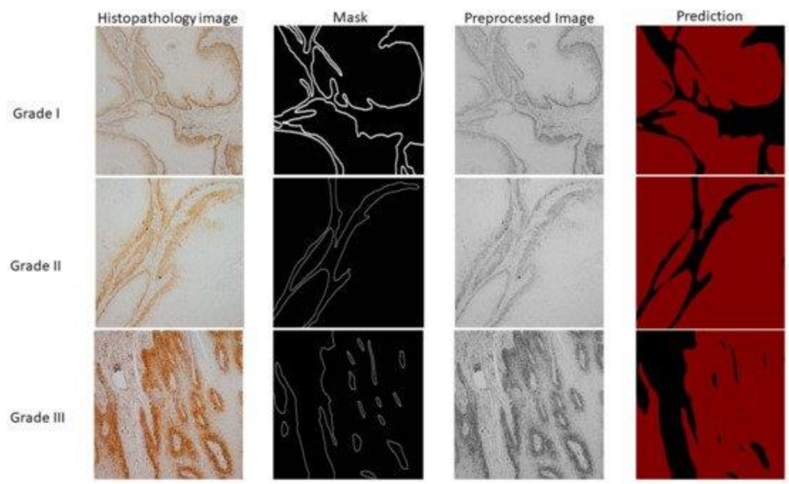


Figure 6. Example of achieved predictions

Based on the achieved scores the authors conclude that the developed system may have great potential in the diagnosis of this particular cancer type, being the first part of the tumor microenvironment (tumor-stroma ratio) analysis and microenvironment cell segmentation using AI-based algorithms.

3.5 RTG Image Quality Assessment

A common issue experienced by clinicians when using x-ray images is that some images are of unsatisfactory quality. This is usually not noticed by the technician performing the procedure and only noticed later by the doctor examining the image. This leads to the need for image to be re-taken. The repeated procedure lowers the patient satisfaction and puts additional strain on the hospital resources. Research by Lysdahlgaard et al. (2021) [25] tries to address this issue through the use of CNNs. The main idea is to have a model which will determine whether the image is of the satisfactory quality or not. The authors test five CNN architectures – ResNet50, ResNet101, ResNet152, Xception and Alexnet. To determine the robustness of models authors apply a five-fold cross validation on the dataset consisting of 1000 images of left knees and 1000 images of right knees (each consisting of 500 valid and 500 non-satisfactory images). Authors tested the application of the above listed CNNs on just left and right knees separately, or using a combined dataset – determining that the quality of achieved models is higher when a single orientation is used. Models were evaluated using AUC metric and the standard error, with the heatmaps of achieved models shown in Figure 7.

Figure 7. An example of achieved classification heatmaps [25].

4. Conclusion

The reviewed trends and research show a huge potential of image-based AI analysis application in bioinformatics. From the given examples, it can be concluded that a wide array of various applications exists for ML models in medicine and bioinformatics. Such methods may prove to be a perfect solution to the problems present in various fields, provided that large enough amounts of data either exist, or can be collected in a timely manner.

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