Determination of molds isolated from the patient materials, based on their microscopic morphological characteristics

Mina Milanović, Aleksandar Milosavljević
Faculty of Electronic Engineering, University of Niš, Serbia
mina.milanovic@elfak.rs, aleksandar.milosavljevic@elfak.ni.ac.rs

***Abstract*—Based on literature data in recent years the incidence of invasive fungal infection (IFI) caused by molds is on the rise. Diagnostics of those infections can sometimes be inefficient; they require a longer period of time in laboratory procedures and sometimes may lead to late diagnosis or misdiagnosis, which can result in patient's critical condition or even mortality. Goal of this research is to train a classifier, a neural network model that can be used for classification of molds from patient materials, which can drastically improve the process of diagnosis and prevent fatal cases. Using a ResNet-50 deep convolutional neural network (CNN) and images obtained from Department of Microbiology and Immunology, Medical faculty, University of Niš, Serbia, archives, a classifier has been developed, displaying promising results, which show that with wider dataset it will be possible to train a model that can be used in diagnostics.**

Keywords: <molds identification, fungal infection, convolutional neural networks, deep learning>

I. INTRODUCTION

Numerous authors consider an ability of fungus to start a pathological process in the host organism as a specific phenomenon, because, excluding groups of dermatophyte molds and tropical fungi, these microorganisms do not need pathogenicity for their dissemination and survival in nature [1]. Nevertheless, among 400.000 species known in the nature, around 50 kinds can cause IFI that are characterized by very high morbidity (serious clinical case) and mortality. So far, incidence of IFI caused by molds is constantly growing. Numerous reasons have contributed to the increase of number of infected. The most important are complex procedures and medical interventions, intensive treatments with antibacterial drugs, cytostatics, immunosuppressant; longer lifespan of a humans, increase in the number of patients at high risk due to primary diseases and treatment, the appearance of resistance in fungi and certainly the establishment of mycological analyzes and higher diagnostic efficiency, i.e. more successful diagnostic procedures in a microbiology [2].

Fungi are eukaryotic microorganisms. In nature can be identified thousands species of fungi, they are widespread, living in soil and water, on organic materials as saprophytes, as symbionts or parasites of animals, plants, or human [3]. Based on the structure, all fungi can be primarily divided into yeasts -unicellular fungi with basal cell blastoconidia (blastospora) and multicellular fungi (molds) with a basic hypha cell. Molds classification was performed on the basis of structure, ie macroscopic and microscopic morphological characteristics. Based on the differences between the morphology of molds, hypha structure, production of different conidiae (spores), it is possible in diagnostic procedure to identify them. However, the process of isolation and identification of molds is often time-consuming and generally conventional mycological analyses have low sensitivity. Moreover, microscopic examination necessary to determine morphological characteristics requires an expert's knowledge and experience. Despite numerous microbiological laboratories, a small number of them has mycologist-experts who would ensure rapid and accurate determination of IFI mold- pathogens. The lack of this diagnosis can result inaccurate diagnosis or misdiagnosis which drastically affects beginning of the appropriate therapy, which gives time to infection to progress, can have drastic consequences sometime and fatal outcome. The goal of this project is to develop a neural network model that will perform identification of molds, and thus accelerate the process of diagnostics.

Since no similar projects, involving determination of molds or their morphological characteristics, could been found during our research, the main purpose of this solution, considering the early stages of sample collection, was to come to the conclusion is developing a classifier possible.

Dataset collection has been rather limited and needed manual preparation, as described in chapter II. Prepared dataset had to be expanded before training and ResNet50 convolutional neural network (CNN) has been used for developing and training the model, which makes the core of the classifier, as presented in chapter III. Results and discussion of the results, that are rather promising and show significant accuracy for this stage of the project, have been shown in chapter IV. Conclusion and planned further steps have been described in chapter V.

II. DATASET

A. Dataset description

According to literature, yeast of genus *Candida* and *Aspergilus* spp. molds are causing around 80% of IFI in

the world [4], so number of quick and efficient tests that can determine these fungal infection are designed [5].
For the rest of the 20% of the cases, diagnostics is really poor and no efficient tests exist. Quick and precise diagnostics is sometimes crucial for patients condition, especially because there are some species of fungi that are resistant to antifungal drugs. For example, *Mucorales* fungi and *Fusarium* spp. are resistant to majority of anti-fungal medicaments and if in mycological analyses they're misdiagnosed, it can lead to wrong, pointless therapy [6].

In this paper, we will concentrate mainly on some main IFI molds pathogens. These significant molds are determined from their microscopic morphological characteristics. Once the patient material is obtained in the laboratory, it is inoculated on nutrient media, which is used for cultivation of fungi-molds. This process results in material ready to be examined on microscope, and which would be used as input once our classifier is made. morphological differences. Once the patient material is obtained in the laboratory, it is put on nutrient media, which is used for fungi cultivation. This process results in material ready to be examined on microscope, and which would be used as input once our classifier is made.

B. *Morphologial differences of fungi*

Knowledge of morphological characteristics of fungal structure allows their differentiation and identification to the level of genus or species during microscopic examination [7].

Microscopic morphology of some fungal genera is:

i) ***Aspergillus*** spp.: Septate hyphae with unbranced conidiophores which ending with swollen vesicule that is covered with flak-shaped phialides on which are chains of mostly round sometimes rough conidia;

ii) ***Fusarium*** spp.: Septate hyphae with formation of canoe shaped or sickle shaped multiseptate macroconidia that are produced from phialides on unbranched or branched conidiophores;

iii) ***Trichoderma*** spp. : Septate hyphae, , short and branched at wide angles conidiophores, flask-shaped phialides also form at wide angles to conidiophores on which oval, unicellular cluster together at the end of each phialide;

iv) ***Cladosporium*** spp.: Dark and septate hyphae with lateral and terminal conidiophores of various sizes, which produces long, branching chains with oval dispersed conidioconidiae;

v) ***Alternaria*** spp.: Septate, dark hyphae with septate conidiophpores and formation of large macroconidiae which have transverse and longitudinal septations;

vi) ***Mucor*** spp.; Wide and practically non-septate hyphae, speorangiophores are long, often branched and bear terminal round spore-filled sporangia (Figure 1).

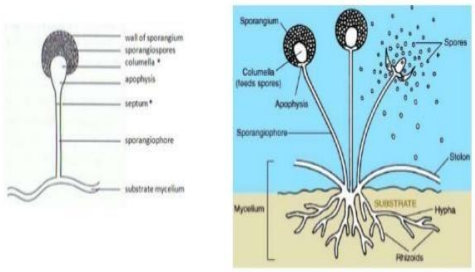

Figure 1. Mucor morphology

C. *Preparation of dataset images for training*

For a human being, it is easy to classify what is on a picture, but for a machine this can be a rather hard job. Machine sees a picture as an array of pixels and numbers. Also, human can determine what is on the picture even if brightness is not the best or if angle of camera changes, or if there is only a part of an object on the image, which can be troubling for the machine.

For the first model, we extracted examples of six fungal genera, which had the biggest dataset, which are *Aspergillus* spp., *Fusarium* spp., *Trichoderma* spp., *Alternaria* spp., *Cladosporium* spp. and *Mucor*spp. (Figure 2). Images have been made at the Department of Microbiology and Immunology, Medical faculty, University of Niš, Serbia, where molds have been isolated from patient materials, examined on microscopes and then photographed.

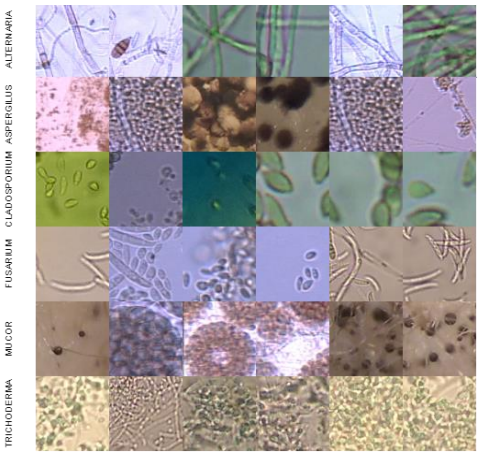

Figure 2. Examples of the dataset images

After preparing the images, which included cutting high resolution samples into smaller, training suitable images, and excluding ones without mold samples, it is necessary to determine which percentage of them will be used for training, and which for evaluation, since these sets have to be different so results of evaluation can be regular. We used around 80% of images for training, (total of 884 images of all 6 classes of fungi obtained after preparation) and the rest of the images (20%) for evaluation (total of 221 images of all 6 classes of fungi). In Table I, details of dataset used for training are presented.

TABLE I
Details of used dataset

Number of classes	Number of samples	Number od samples per class	Number of images after preparation	Images used for training	Images used for validation
6	25	3-6	1105	884	221

III. METHOD DESCRIPTION

For a neural network to learn to recognize certain patterns in images, it is necessary to create examples so it can learn from them. Since our dataset was limited during the work on this first solution, it was necessary to cut original images into the set of smaller images, suitable for training. Even after cutting the images, and manually eliminating the ones that don't contain mold samples, the dataset was insufficient.

Operations that are used on the images to widen the dataset are called augmentations [8]. These functions use random zoom, rotation and translation, to get more similar images from one image (Figure 3). In the end of this process, dataset became multiple times bigger and it could be used for training.

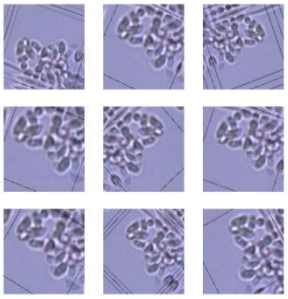

Figure 3. Augmentation of an image gives more images for training

Problem of image classification is present in wide specter of fields, and traditional approach to this problem is making a feature extractor that can be used for training a classifier [9-12]. Major advantages in this area have been made in recent years with introduction to convolutional neural networks (CNNs) [13], substituting earlier solutions which used artificial neural networks (ANNs) [14]. CNNs represent an aggregation of three architectural ideas, local receptive fields, shared weights and spatial subsampling, which makes them more consistent in terms of translation and distortion [15].

There are many types of neural network architectures, but the one that's showing as a most promising in this solution is ResNet50 (Figure 4) [16]. ResNet50 is a very deep and innovative neural network, convenient for classification of images because of its convergent layers, which calculate average, maximum or minimum data of each part of the image, making then the data for model training smaller and compact [17].

Resnet50 architecture model makes the core of this solution. After training of this model, feature vectors are obtained, which are then used to form a classifier. Classifier can then be used to determine which of 6 classes of molds new input images belong to. Diagram of current solution is shown in Figure 5.

For training the model, programming language Python [18] and library Keras have been used. Keras library [19], implemented in Python, has an interface which can be used for creating and training neural network models. Keras is a deep learning API, running on top of the machine learning platform TensorFlow [20]. They were developed with a focus on enabling fast experimentation.

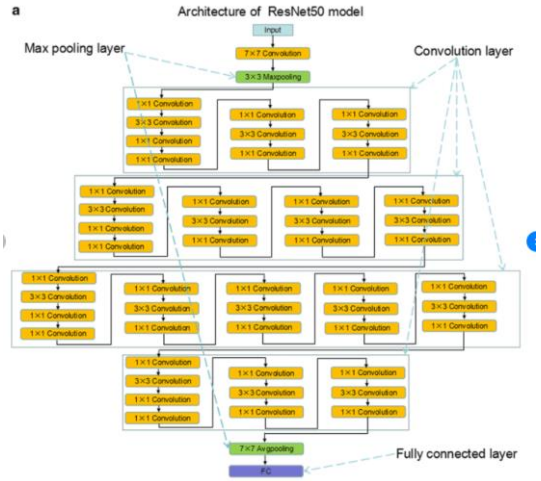

Figure 4. ResNet50 architecture

Model has been compiled with *Adam* algorithm for optimization (optimizer modul), *categorical_crossentropy* type of error (losses modul), and the only parameter of metric during learning has been set as accuracy.

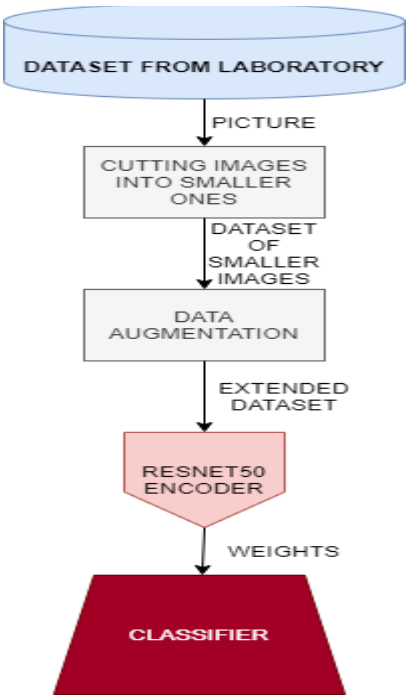

Figure 5. Solution diagram

Adjusting parameters of Keras functions and starting the training with different number of epochs, preliminary results at these phase of the project show that the trained model after nine epochs gives the best results, with 92,19% accuracy in classification of images.

IV. Results and Discussion

In Table II, average results based on samples and standard deviation has been presented. Because of specific nature of the dataset, model has not been tested and compared with other models.

TABLE II
Average accuracy and standard deviation of classified samples

Subset number	Accuracy [%]	Standard deviation [%]
1	92,19	0,24
2	91,98	0,32
3	92,05	0,23

After validation of the model, it has also been tested manually, showing that the results for most images are accurate. The most problems have been detected for *Fusarium* spp. genera, for which we had the least number of images, which points out that more images have to be obtained so better accuracy can be achieved.

Since misdiagnosis of fungi infections can lead to critical conditions of a patient, precision got is not yet sufficient for use in diagnosis, but current model and validation results show a promising base for future development, pointing out that developing a classifier that can be used for diagnostics can be done.

V. Conclussion

Classification of images described in section III presents a very good platform for building a model that can be used in diagnostics. Results of the primary method present promising results, showing that even the standard architecture and very small dataset give solid results.

Future development of the model and application for diagnostics will consist of collecting more images and using more augmented images. Larger dataset will provide more flexibility for running tests and provide the model enough data for training, which will lead to more precise results.

Once the model reaches needed precision, the decision it makes will be opted to be a result of many smaller images provided in a larger input image. Once the large resolution image is given to the model, it will be divided to a set of smaller images, and the decision of the category will be determined for each of the smaller images, making the final decision as a ruling of the mayor. This approach will give even more precise results needed in diagnostics.

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