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# Automatic Pipeline for the Identification of Ground Glass Opacities on CT Images of Patients Affected by COVID-19

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Academic Year 2019/2020

# Abstract



# Contents

**Abstract**

**Introduction**

## **1 Ground Glass Identification Pipeline**

1.1	Pipeline Description . . . . .	
1.1.1	Color Quantization for Image Segmentation . . . . .	
1.1.2	Pipeline Structure . . . . .	
1.2	Pipeline Implementation . . . . .	
1.2.1	ITK and OpenCV . . . . .	
1.2.2	Lung Extraction . . . . .	
1.2.3	Training . . . . .	
1.2.4	Labeling . . . . .	

## **2 Results**

2.1	DataSet Description . . . . .	
2.1.1	Sant'Orsola . . . . .	
2.1.2	MOSMED . . . . .	
2.1.3	ZENODO . . . . .	
2.2	Time Performances . . . . .	
2.3	Accuracy Comparison . . . . .	

## **3 Review on Image Segmentation techniques**

3.1	Review on Image Segmentation Methods . . . . .	
3.1.1	Thresholding . . . . .	
3.1.2	Region Growing Approach . . . . .	
3.1.3	Classifiers Approach . . . . .	
3.1.4	Clustering . . . . .	
3.1.5	Markov Random Field . . . . .	
3.1.6	Artificial Neural Networks . . . . .	
3.1.7	Deformable Model . . . . .	



# Introduction



# Chapter 1

## Ground Glass Identification Pipeline

Since the end of 2019, COVID-19 has widely spread all over the world. Up to now the gold standard for the identification of the pathology is the RT-PCR even if it is reported that its sensitivity might not be enough for COVID-19 identifications [1], moreover it is time consuming. Several chest CT scans collected from COVID-19 patients shown bilateral patchy shadows or ground glass opacity (GGO) in the lung [1] [7], which makes this technique suitable to help diagnosis, monitoring the course of the disease and check the recovery of healed patients, since the GGO pattern may change according to the status of the disease. Austin in Glossary of terms for CT of the lungs [2] define the Ground Glass Opacities as hazy increased attenuation of lung, with preservation of bronchial and vascular margins caused by partial filling of air spaces, interstitial thickening, partial collapse of alveoli, normal expiration, or increased capillary blood volume. This kind of lesion is not exclusive of COVID-19 but can be associated to many other pathologies but the study of its particular pattern in combination with other techniques may help early diagnosis of this pathology and the monitoring of the recovery, has shown by [3].

So the identification and quantification of this kind of lesions is very important to help diagnosis, monitor the recovery and understand infection pathogenesis. Up to know the identification of these lesions is made by manual or semi-automatic segmentations, both of them are time consuming, error prone and subjective, since require the interaction of specialized operators. To overcome this issues an automatic way to obtain these information is desirable, since allows to obtain measures that do not depend n operator subjectivity; moreover it is desirable to obtain segmentation results in a small amount of time, which is not compatible with manual or semi-automatic segmentation.

In this chapter I will describe in details the implementation of a segmentation pipeline which allows a fast and automatic segmentation of GGO.

### 1.1 Pipeline Description

As I've said before to overcome the time and subjectivity issues, the developed pipeline must have the following characteristics:

- **Fully Automated:** to remove the dependency from an external operator, and so the subjectivity of the segmentation;
- **Fast:** in order to compete with certified software and to provides a segmentation in few minutes.

During the developing, the first problem we have to face was the lack of information: since COVID-19 is new disease, there aren't much data available. I've worked mainly on



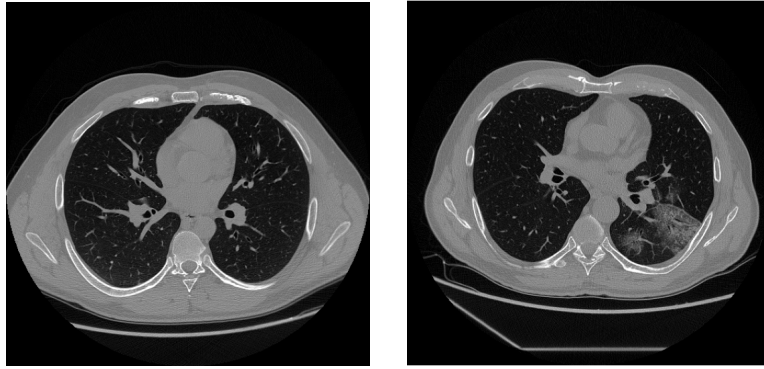


Figure 1.1: CT scan of torax for an healthy patient(left) and a COVID-19 affected one(right) in which we can observe a huge amount of GGO in the right lung



Figure 1.2: Place Holder

CT scans of 83 different patients provided by sant'Orsola hospital with manual segmentation, but also public dataset like MOSMED and ZENODO where used as benchmark. For each patient was available a manual segmentation, but even if some label seem to be of good quality and accurate, some other will present some errors and misclassified areas. In the end low number of patients and the quality of labels have discouraged us to use a supervised learning approach like classifiers or neural networks, an other reason is that a supervised approaches like Artificial Neural Network are computationally expansive and requires a lot of hardware resources and time.

In the end a completely unsupervised technique was used, which doesn't requires to provides already segmented images as prior knowledge.

An other thing to takes into account during the developing, is that the lesions may have different patterns according to the stage of the disease or the patients, and usually these patterns are spatially disconnected, so to perform the segmentation a pixel classification techniques was used.

In the end the basic idea was to use the Color Quantization as medical imaging segmentation , which aims to to identify the different type of tissue and lesions by grouping them by color similarity. In particular we aims to assign to each structure inside the lung a characteristic colors and label each voxel by identify it as belonging to the tissue with the most similar characteristic color. This approach is justified since exist a relation between the kind of tissue and the color used to display it in a CT scan, given by Hounsfield Unit. Since it is unlikely to find a structure with a single voxel extension, I've used the multi-channel characteristics of digital images to takes into accounts also the neighbouring voxels.

In this section I will describe how color quantization works for image segmentation, how the color space was build in order to incorporate also neighbouring information and the final structure of the segmentation pipeline.

## 1.1. PIPELINE DESCRIPTION

so we have to associate each pixel color to a particular tissue and, as we will see in the section below this will be done by using the Hounsfield Unit. In particular we will find the characteristic color of each lung tissue and assign each pixel to the tissue of the most similar characteristic color.

In this section I will discuss have applied the color quantization and I will describe the main structure of the developed pipeline.

### 1.1.1 Color Quantization for Image Segmentation

Color quantization is the process of reducing the number of colors in a digital image. The main objective of quantization process is that significant information should be preserved while reducing the number of colors in an image, in other word quantization process shouldn't cause significant information loss in the image. Color quantization, accepted as a pre-processing application, is used to reduce the number of colors in images with minimum distortion such that the reproduced image should be very close to the original image visually, as in Figure 1.1.1.



Figure 1.3: *Color quantized RGB image. We observe the original image, a 16 color image which look similar to the original one, a 8 colors image and 4 colors image*

Color quantization play an important role in many filed of applications such as segmentation, compression, color texture analysis, watermarking, text localization/detection, nonphotorealistic rendering and content-based retrieval [4].

As I've said before I have used this technique to segment medical images by grouping each tissue by color similarity. The relation between the kind of tissue and the voxel color is given by and the Hounsfield Units(HU) : Pixels colors are proportional to HU, which are defined as a linear transformation of the linear attenuation coefficient( $\mu$ ). HU normalize the  $\mu$  of a particular tissue according to a reference one, usually water( $\mu_{H_2O}$ ), ss we can see in equation 1.1 :

$$HU = \frac{\mu - \mu_{H_2O}}{\mu_{H_2O}} \quad (1.1)$$

In the end each color results proportional to the linear attenuation coefficient, different

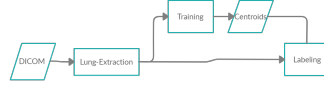


Figure 1.4: Flow chart of the main structure of the developed pipeline. The training process, which allows the estimation of the centroids, is performed only one time.

from each tissue, so exist a relation between the GL and the tissue type which is exploit by its intensity, that makes this techniques available.

Up to now we have discussed about single voxel intensity, but its also possible to exploit informations about neighbouring pixels, by building a suitable color space: this is useful since lesions areas involves many closed voxels. In digital image processing, images are represented with a 3D tensor, in which the first two dimensions represent the height and width of the image and the last one the number of channels. Gray scale images requires only one channel, so each pixel has a numeric values whose range may change according to the image format. On the other hand color images requires 3 channels, and the value of each channel represent the level of the primary color stored in this particular channel, so each color is represented by 3 different values, according to Young theory.

In our case we have decided to use more than 3 channels and each one of them incorporates different information like edges information or neighbouring pixels information. In the end we have build a color space of several dimensions in which each color is represented by different image features like edges and median neighbouring intensity.

To find the characteristic color of each tissue, which is a centroids in the color space, I've used a simple kmeans clustering, since it provides a suitable segmentation with good time performances, since it is efficiently implemented for multi-channel images in OpenCV. Kmeans clustering requires a prior knowledge on the number of cluster, which in our case is given by the anatomical structure of the lung, so each cluster will correspond to a different anatomical structure:

- Total lung parenchima
- Bronchial and vessels
- **GGO**
- Eventual noise

### 1.1.2 Pipeline Structure

In the end the pipeline structure is divided in three main blocks as displayed in Figure 1.1.2 :

- Pre-Processing and lung extraction
- Training
- Labeling

#### Pre Processing and Lung Extraction

Before starting with the actual segmentation, some pre-processing steps are required. First of all we have to manage the input HU to remove all the unwanted regions and manage some artifacts like metallic one. Once we have pre-processed the input volume, we can isolate the lung regions, by removing all the body regions and the extra lung organs, like heart and intestine, which are included into the CT scan. In this way it is possible to focus the segmentation only on the region of interest, avoiding the creation of false positives.

## 1.2. PIPELINE IMPLEMENTATION

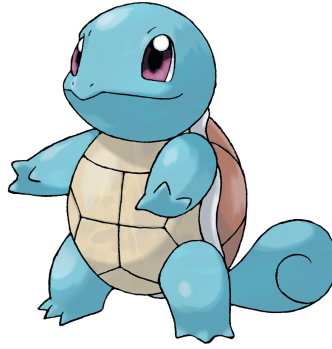


Figure 1.5: Placeholder

### Training

This step is the most time consuming and computational expansive of the whole pipeline, but it will be run only one time. This step involves the estimation of the centroids for each of the lung structures. It will be run on a lot of different patients in order to obtain a statistical rapresentation, but some results have shown that we can obtain similar results by performing the training only on one image in which each structure is represented by a suitable amount of pixels. Once we have estimated the centroids matrix, this process will not be performed again, so doesn't appears on the pipeline of the actual segmentation and doesn't affect the segmentation time.

### Labeling

This step involves the actual segmentation. The script which perform it requires as inputs the image after the lung extraction, and the previously estimated centroids. This block of the pipeline simply assign each voxel to the cluster corresponding to the nearest centroids. and the end of the procedure only the cluster corresponding to the GGO are provided. In this way we are performing a pixel classification thechniques by assign regions to a particular labels according only to intensities information, without exploiting spatial information: this allow us to group on the same cluster objects that are spatially disconnected as often happen in medical imaging field

So in the end, once we have estimated the centroids, the segmentation pipeline will results of only two steps, as shown in Figure 1.1.2 , in which we can observe the flowchart of each step with an image that shown the partial results.

## 1.2 Pipeline Implementation

In this chapter I will go into details about the actual pipeline implementation. First of all I will brifly describe the developing enviroment and the libraries used for the code implementation. After that I will describe how each step of pipeline is achieved.

The whole pipeline was implemented by using python, which is an high level object oriented programming language. The whole code is open spurce and available on github. The pipeline installation is automatically tested on both windows and linux by using Appvey-orCI and TravisCI([Insert link](#)). The installation is managed by setup.py, which provides also the full list of dependencies. The code documentation was generated by using sphinx and its available at ... . Bash and powershell scripts are available to allows the segmentation on multiple patients simultaneously.

The whole pipeline is organized into three scripts, which performs the main tasks of the pipeline :

- lung\_extraction
- train
- labeling

For the image processing tasks, like filter application, or morphological operations, I've used itk and OpenCV libraries, which are thdescribed below. The pipeline was developed in order to takes as input CT scans in medical image format like DICOM, Nifti and NRRd, and will return as output the labels in NRRD format, which can be easily read as a segmentation by medical software like 3D slicer.

### 1.2.1 ITK and OpenCV

To perform image processing operations, like application of blurring filters or morphological operations, and to perform the color quantization I've used two different libraries, which provides a large collection of optimized tools for medical image processing and computer vision. Each tool was optimized, so it will help to takes the segmentation times as short as possible.

#### OpenCV

OpenCV, acronym for Open Source Computer Vision, is an open source computer vision and machine learning software library. OpenCV was built to provide a common infrastructure for computer vision applications and to accelerate the use of machine perception in the commercial products. I've used the tolls from this library to perform all the processing that involves the single image and, most important, to perform the color quantization, since the kmeans implementation offered by the library allows to perform the color quantization, by performing the kmeans clustering on a multi channel image.

#### ITK

Insight Tool Kit (ITK) is an open source library which provides an extensive suite of tools for image analysis, developed since 1999 by US National Library of Medicine of the National Institutes of Health. This library provides tool useful to works also with N-dimensional images. During the developing of the pipeline I've used this library to read and write images in medical image format with meta-data preservation, and to perform operations on the whole image stack, like the detection of the connected components in 3 dimensions.

### 1.2.2 Lung Extraction

The lung extraction is the first step of the pipeline which aims to isolate the region of interest and to remove the non-lung regions on CT scan. This purpose is achieved by the following steps :

1. Pre-Processing
2. De-Noising
3. Global Treshold
4. Reconstruction of wrongly removed lung regions
5. Selection of the largest connected region

## *1.2. PIPELINE IMPLEMENTATION*

### **1.2.3 Training**

### **1.2.4 Labeling**



## Chapter 2

# Results

### 2.1 DataSet Description

#### 2.1.1 Sant'Orsola

#### 2.1.2 MOSMED

#### 2.1.3 ZENODO

### 2.2 Time Performances

### 2.3 Accuracy Comparison





## Chapter 3

# Review on Image Segmentation techniques

Image segmentation consist in the partitionng of an image into non overlapping, consin-  
sistent regions that are homogeneous respect to some characteristics such as intensity or  
texture [5]. Nowadays several non-invasive medical imaging techniques are available, such  
as Computed Tomography(CT), Magnetic Resonance Imaging (MRI) or X-Ray imaging,.  
that provides a map of the subject anatomy. Image segmentation plays a crucial role  
in many medical-imaging applications by automating or facilitationg the delineation of  
anatomical structures and other regions of interest [5]. Manual segmentation is possible,  
but is time consuming and subject to operator variability; making the results difficult to  
reproduce [8], so automatic or semi-automatic methods are preferable.

A major difficulty of medical image segmentation is the high variability in medical images.  
First and foremost, the human anatomy itself shows major modes of variation. Furthermore  
many different modalities (X-ray, CT, MRI, etc.) are used to create medical images [6].  
The results of segmentation can be used to perform feature extraction, that provides  
foundamental information about organs or lesion volumes, cell counting, etc. If the patient  
perform several analysis during time, image segmentation is a useful tool to monitor the  
evolution of particular lesions or tumors during, for example, a therapy.

This chapter contains a brief introduction on medical digital images and a brief review  
on the image segmentation techniques shuch as clustering or thresholding.

### 3.1 Review on Image Segmentation Methods

During the years, several segmentation methods have been developed based on a lot of  
different approaches These metods can be categorized in several way, for example we can  
divide them into *supervised* or *unsupervised* if they requires or not a set of training data, or  
can be classified according to the used information type, like *Pixel classification methods*,  
which use only information about pixel intensity, or *Boundary following* methods, which use  
edge information, etc. In this section I will provide a brief review on the main segmentation  
methods, organized in the same way as in [5] that divides the methods in 8 categories:

1. Thresholding,
2. Region growing,
3. Classifiers,
4. Clustering,

5. Markov Random Fields models,
6. Artificial Neural Networks,
7. Deformable Models,
8. Atlas guided approaches.

### 3.1.1 Thresholding

Thresholding approach is very simple and basically segments a scalar image by creating a binary partitioning of image intensities [5]. It can be applied on an image to distinguish regions with contrasting intensities and thus differentiate between tissue regions represented within the image [8]. Figure 3.1.1 show an histogram of a scalar image with two classes, threshold based approach attempts to determine an intensity value, called *threshold* which separate the desired classes [5]. So to achieve the segmentation we can group all the pixels with intensity higher than the threshold in one class and all the remaining in the other class.



Figure 3.1: Caption

The threshold value is usually setting by visual assesment, but can also be automatized by algorithm like otsu one.

Sometimes may happen that more than two classes are present in the image, so we can set more than one threshold values in order to achieve this multiclass segmentation, also in this case there are algorithms to automatized this process, like an extension of the previous one called *multi otsu threshold*.

This is a simple but very effective approach to segment images when different structures have an high contrast in intensities. Threshold doesn't takes into account the spatial characteristic if the image, so it is sensitive to noise and intensity inhomogeneities, that corrupt the image histogram of the image and making difficult the separation [5]. To overcome these difficulties several variation of thresholding have been proposed based on local intensities and connectivity.

Threshold is usually used as initial step in sequency of image processing operations, followed by other segmentation technique that improve the segmentation quality. Since threshold use only intensity information, can be considered a pixel classification technique.

### 3.1.2 Region Growing Approach

Region growing approach allows to extract connected regions from an image. This algorithm start at seed location in the image(usually manually selected) and check the adjacent pixels against a predefined homogeneity criterion [8], based on intensity, and/or edges. If the pixels met the criterion, they are added to the region. A continuous application of the rule allow the region to grow.

Like thresholding, region growing is used in combination with other image segmentation operations, and usually allows the delineation of small and simple structures such as tumor and lesions [5].

Regions growing can also be sensitive to noise so extracted regions may have holes or even

### 3.1. REVIEW ON IMAGE SEGMENTATION METHODS

become disconnected. May also happen that separate region becomes connected due to partial volume effect.

When we use this approach we have to consider that for each region we want to segment a seed must be planted. There are some algorithm, related to region growing, that does not require a seed point, like split and merge one. Split and merge operates in a recursive fashion. The first step is to check the pixel intensity homogeneity, if they are not homogeneous, the region is splitted into two equal sized sub-regions. This step leads to an oversegmentation, so a merging step is performed, which merge together adjacent regions with similar intensities [8].



Figure 3.2: Caption

#### 3.1.3 Classifiers Approach

Classifiers approaches use statistical pattern recognition techniques to segment images by using a mixture model that assume each pixels belonging to one of a known set of classes [8]. To assign each pixel to the corresponding classes, use the so called *feature space*, which is the space of any function of the image like intensity. An example of 1D feature space is image histogram.

The feature of each pixel form a pattern that is classified by assign a probability measure for the inclusion of each pixel in each class [8].

This approach assume a prior knowledge about the total number in the image and the probability of occurrence of each class. Generally this quantity aren't known, so we need a set of training data to use as reference.

There are different techniques which use this approach:

- **k-Nearest Neighborhood** : each pixel is classified in the same class as the training data with the closest intensity;
- **Maximum likelihood or Bayesian** : Assume that pixel intensities are independent samples from a mixture of probability distributions and the classification is obtained by assign each pixel to the class with the highest posterior probability.

This approach requires a structure to segment with distinct and quantifiable features. It is computational efficient and can be applied to multichannel images. This approach doesn't consider a spatial modelling and need a manual interaction to obtain the training data that must be several since the use of the same training set for a large number of scans can lead to biased results.

#### 3.1.4 Clustering

Clustering approach is similar to classifiers one but in an unsupervised fashion, so doesn't require a training dataset. Clustering iteratively alternate between segmenting the image and characterizing the properties of each class. In this way we can say that clustering approach train itself by using the data available information.

We can identify 3 main clustering algorithms:

- **k-means clustering:** that iteratively compute a mean intensity for each class and segmentats the image by classifying each pixel in the class with the closest mean;
- **Fuzzy C-means:** this algorithnm generalize the K-means clustering in order to achieve soft- segmentation;
- **Expectation Maximization:** use the same clustering principle as k-means by assuming that the pixel follows a Gaussian mixture model. It iterates between posterior probability and compute the the Maximul Likelihood estimates for the means, co-variances and mixing coefficients of the mixture model.

This approach doesn't requires training data, but suffer to an high sensitivity to the initial parameters and do not incorporates spatial model, so it is a pixel classification technique [5].

### 3.1.5 Markov Random Field

Markov Random Field(MRF) is not a proper segmentation method but its a statistical model that's used within segmentation methods that model the spatial interaction between neighbouring pixels. It's often incorporated in clustering algorithms such as K-means with a Bayesian prior probability.

This model is used because most pixels belong to the same class as their neighbouring pixels, this means that any anatomical structure that consist of only one pixel has a very low probability of occourring [5].

A difficulty of this model is that it is very sensitive to the parameters that controls the strenght of the spatial interactions. An other MRF disavvantage is that requires computationally intensive algorithms. However, despite these disavantages, MRF are widely used to model segmentation classes and intensity inhomogeneities [5].

### 3.1.6 Artificial Neural Networks

Artificial Neural Networks are formed by using artificial neurons derived from physiological models [8]. Neural Networks are made by nodes that simulate a biological learning. Each node of the network it is able to perform an elementary operation.

### 3.1.7 Deformable Model

Deformable Model use an artificial, closed, contour/surface able to expand or contract over time and conforme to a specific image feature [8]. This approach is physically motivated model-based thechnique for the detection of region boundaries [5].

The curve/surface is placed near the desidered boundary and it is deformed by the action of internal and external forces that act iteratively. The external forces are usually derived from the image.

This approach has the capability to directly generate closed parametric curves or surfaces from images and an also incorporate smootness constraint that providesrobustness to noise and spurioous edges.

However this approach requires a manual interaction to place the appropriate set of parameters.

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