

# Automatic Evaluation of the Progress of Bacterial Pulmonary Infections in Temporal Radiographic Image Sequences

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**Abstract**— Pulmonary radiographs are essential tools to the evaluation and diagnosis of suspected infections of the lower respiratory system. Interpretation of a radiograph in the clinical context is a valuable diagnostic adjunct to the selection and the management of a specific clinical protocol for therapy. The key element in the proper diagnosis of a bacterial pulmonary infection is the analysis of the radiographic data accumulated over time. A dynamic consultation system that captures the progress of a disease over time can prove a valuable means to patients' monitoring and follow-up. The aim of this work is to provide an initial framework which can be used to describe the progress of a bacterial pulmonary infection based on the spatial variation of its radiographic manifestation in temporal image sequences. This is realized by the unsupervised discrimination of inflammatory areas from normal lung parenchyma in chest radiographs and their quantitative evaluation over time. Inflammatory areas, which are visually discriminated by their relative opacity within the lung fields, are identified by using an hierarchical cluster merging scheme based on successive non-negative matrix factorizations (NMF) of radiographic patterns of intensity and texture. The experimentation results validate the effectiveness of the proposed methodology along with its advantage over standard supervised methodologies where the need for feature normalization between the diverse images is prevalent.

## I. INTRODUCTION

BACTERIAL infections represent a major threat to the patients' safety and a diagnostic challenge for intensive care physicians [1]. Lower respiratory tract infections are among the most common infectious diseases in humans [2]. Despite the careful hygienic measures and the existing guidelines in antibiotic prescription, the changes in the characteristics of the population along with the high levels of pathogen multidrug resistance have increased the number of individuals at risk. The early detection of such infections as well as the choice of the appropriate antibiotic treatment can be life-saving especially for the critically ill patients.

Routine chest radiographs are a major source of information regarding the differential diagnosis and the assessment of the extent of pulmonary infections. More

importantly, when obtained in a follow-up basis they can provide significant evidence about the progress of the infection over time, and they are seriously considered in decisions related to patients' therapy and management [3]. Therefore, the implementation of a computational solution able to capture the temporal progress of the infection can prove a valuable tool to patient safety and aid to the expert.

Up to now computational approaches coping with the analysis and assessment [4]-[9] of the lung fields have mainly focused on radiographs that represent static time instances. In terms of the assessment of temporal image sequences, the use of recursive least squares technique for image registration has been proposed for the analysis of temporal radiographic sequences [10], whereas a framework for spatio-temporal modeling using segmentation and thin-plate spline interpolation for the segmentation and registration of pulmonary cancer nodules in pMRI image sequences has been proposed in [11]. In general the concept of the temporal pattern has been used by various authors in the medical domain. In [12],[13] diseases are described by using a graph in which the temporal constraints of the associated manifestations are specified and expressed through qualitative temporal relations. In [14] an approach to the temporal model based diagnosis is proposed that presents the diagnostic solution in the form of a causal network and makes use of ontologies for the modeling of temporal information and possibility theory for the hypotheses evaluation.

In this paper we propose a novel unsupervised approach to monitor the progress of a bacterial infection over time by being based on the spatial variation of its radiographic manifestation. The most common radiographic manifestation of bacterial pulmonary infections is foci of consolidation, which are visually discriminated by their relative opacity within the lung fields. The proposed computational approach to the discrimination of the consolidations from the normal lung parenchyma is based on the non-negative matrix factorization (NMF) of radiographic patterns of intensity and texture. Radiographic image opacities are represented by grey-level histograms, whereas image texture is represented by Gabor energy features [15].

By using an unsupervised methodology to assess the extent and the evolution of an infection we manage to avoid the need for feature normalization between images, which can be quite complicated and roughly approximative when it comes to the analysis of diverse sets of chest radiographs acquired with different settings.

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The rest of this paper consists of three sections. Section II describes the proposed methodology, section III presents the results of its experimental evaluation on a set of time-series high-resolution chest radiographs, and section IV summarizes the conclusions of this study.

## II. METHODOLOGY

Non-negative matrix factorization (NMF) has been shown to be a useful technique in the approximation of high dimensional data where the data are comprised of non-negative components [16]. The NMF of a  $m \times n$  non-negative matrix  $\mathbf{V}$  is a linear approximation  $\bar{\mathbf{V}}$  to  $\mathbf{V}$  formed by the product of a  $m \times r$  matrix  $\mathbf{W}$  and a  $r \times n$  matrix  $\mathbf{H}$  where  $r$  ( $r < \min(m, n)$ ) is the rank of the factorization:

$$\mathbf{V} \approx \bar{\mathbf{V}} = \mathbf{W} \times \mathbf{H}, \mathbf{W} \in \mathfrak{R}^{m \times r} \text{ and } \mathbf{H} \in \mathfrak{R}^{r \times n} \quad (1)$$

NMF was proposed as a means to find a set of basis functions to represent image data where the basis functions enable the identification and classification of intrinsic “parts” that make up the object being imaged by multiple observations [16]. We may think of  $\mathbf{W}$  as the matrix containing the NMF basis and  $\mathbf{H}$  as the matrix containing the non-negative coefficients (or encodings) that exhibit a one-to-one correspondence with the data that consist  $\mathbf{V}$ .

In order to quantify the similarity between the data matrix  $\mathbf{V}$  and the model matrix  $\bar{\mathbf{V}}$  we use as an objective function the Kullback-Leibler (KL) divergence measure  $\mathbf{D}(\mathbf{V} \parallel \mathbf{W} \times \mathbf{H})$  [17] since it is better adapted to real applications where the data manifold is not always flat:

$$\mathbf{D}(\mathbf{V} \parallel \mathbf{W} \times \mathbf{H}) = \sum_{ij} \left[ \mathbf{v}_{ij} \otimes \log \frac{\mathbf{v}_{ij}}{(\mathbf{W} \times \mathbf{H})_{ij}} - \mathbf{v}_{ij} + (\mathbf{W} \times \mathbf{H})_{ij} \right] \mathbf{H} \geq \mathbf{0} \quad (2)$$

where  $\mathbf{W}, \mathbf{H} \geq \mathbf{0}$

This optimization problem is solved by using the following multiplicative update rules:

$$\mathbf{W}_{ir} \leftarrow \mathbf{W}_{ir} \otimes \frac{\sum_j \mathbf{H}_{rj} \times \mathbf{v}_{ij}}{\sum_j (\mathbf{W} \times \mathbf{H})_{ij}}, \mathbf{H}_{rj} \leftarrow \mathbf{H}_{rj} \otimes \frac{\sum_i \mathbf{W}_{ir} \times \mathbf{v}_{ij}}{\sum_j (\mathbf{W} \times \mathbf{H})_{ij}} \quad (3)$$

where  $\otimes$  denotes the element-wise product and  $\times$  denotes the matrix product. NMF can be considered as an alternative clustering technique [18]-[20] since given a normalized solution  $(\tilde{\mathbf{W}}, \tilde{\mathbf{H}})$  of NMF,  $\tilde{\mathbf{H}}^T$  can be interpreted as the cluster posterior and thus the normalized encodings matrix  $\tilde{\mathbf{H}}_{ij}$  represents the posterior probability that  $\mathbf{v}_j$  belongs to the  $r$ -th cluster. In this paper the normalization approach described in [18] was adopted.

Among other algorithms, Fuzzy C-Means (FCM) has been proposed as a method to initialize NMF [20]. More specifically, for a given number of clusters, the NMF basis matrix  $\mathbf{W}$  is initialized by the cluster centroids obtained after FCM convergence, whereas factor matrix  $\mathbf{H}$  is initialized by the fuzzy membership values assigned to each data vector. Since,  $\mathbf{W}$  and  $\mathbf{H}$  correspond to a clustering result after their initialization, certain restrictions are enforced on them and NMF can be regarded as the method to improve this result in a sense that it cannot pull the factorization out of a centroid-

related local minimum. This leads to a more concrete cluster structure [20].

In this paper, we apply the FCM-NMF clustering approach to discriminate consolidation from normal patterns in plain chest radiographs following an Hierarchical Cluster Merging scheme that extends the one proposed in [9] and targets into the assessment of the spatial evolution of the consolidation over a temporal sequence of radiographic images. It is assumed that the lung fields are isolated in regions of interest (ROIs) defined either manually or with a pre-processing lung field boundary detection algorithm [6] and the all the image analysis operations are applied only in these ROIs. A block diagram of the proposed methodology is given in Fig. 1.

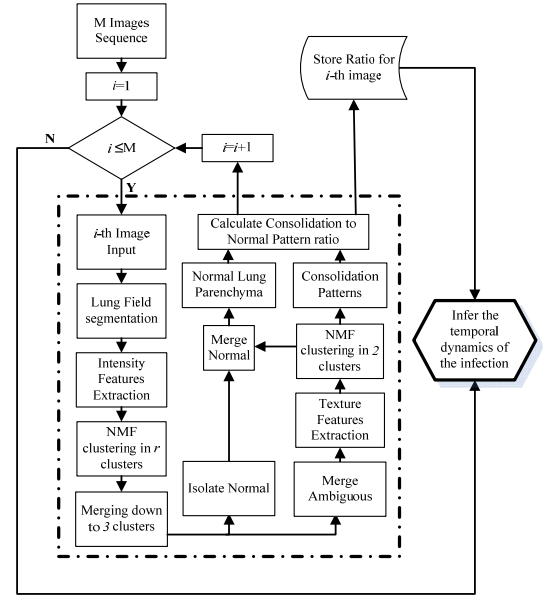


Fig. 1. Block diagram of the proposed methodology.

Considering that the radiographic opacities are evaluated first in the reading of a chest radiograph by the experts [21] as a first step in the proposed methodology,  $N$  local grey-level histogram signatures capturing image intensity information are extracted from an equal number of overlapping square sub-images raster-sampled from the lung area. These signatures are subsequently clustered into  $r$  clusters where  $r$  is properly chosen so as to achieve well separated clusters. By splitting the feature space into many small clusters, we expect that some of them will be formed from patterns of normal lung parenchyma, others from consolidation patterns, and fewer from both normal and consolidation patterns. The clusters comprising of normal patterns will be characterized by smaller intensity values than the rest ones, since the lungs are normally filled with air, which has the smallest radiographic density. As demonstrated in [9], by choosing directly  $r=2$  clusters, the resulting clusters are not well separated, since cluster shapes in this case are limited to hyperellipsoids. This would be a reasonable choice if the target clusters were also hyperellipsoids.

Based on that observation, the  $r$  clusters are dyadically merged down based on the similarity of their centroids, which are derived from factor  $W$ . Since the signatures are intensity histograms the similarity is evaluated by the histogram intersection metric [22]. Dyadic merging takes place by merging, in each iteration, the two clusters whose centroids exhibit the maximum similarity. Ideally the number of the merged clusters would be equal to two, since the patterns are expected to be either normal or abnormal. However, a perfect discrimination of the patterns in two clusters is usually infeasible due to limitations mainly posed by the feature extraction as well as other sources of

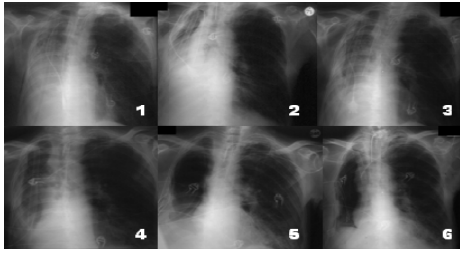


Fig. 2. An indicative temporal image sequence that demonstrates the progressive treatment of the patient.

ambiguity such as intensity signatures extracted from superimposed structures, such as the ribs that exhibit intensity values similar to those of the consolidation patterns. The ambiguity is usually higher for higher intensity levels, i.e. one cannot be certain that a histogram signature with very high grey-levels represents a consolidation; however, the certainty of a histogram signature with very low intensity levels to belong to the normal lung parenchyma, is higher. Therefore, if the number of merged clusters is greater than two, it will be more likely that a cluster of normal patterns is formed and the rest clusters to contain ambiguous patterns. Experimentation demonstrated that a number of three merged clusters lead to a better performance.

The methodology proposed in [1] is extended here by merging the ambiguous clusters into a sole cluster that is subsequently sampled. Feature extraction of textural features from the corresponding sub-images takes place. The extracted features are formed by the energies estimated from the outputs of two Gabor filter banks; one with symmetric and one with anti-symmetric Gabor kernels [1],[1]. The textural features are subsequently clustered into two clusters that correspond to the consolidation patterns on the one hand, and to the remainder normal patterns on the other. Afterwards, the image regions with the consolidations will be comprised of the sub-images corresponding to the discovered consolidation patterns, whereas the image regions of the normal lung parenchyma will be comprised of the normal patterns discovered in both the first and the second step of the proposed methodology.

The previously mentioned process is repeated for every image in the sequence, and finally, the ratio  $\omega$  of the pixels corresponding to the consolidation patterns to those corresponding to the total lung patterns is calculated. Since the consolidation patterns are always a subset of the total lung patterns extracted from a particular radiograph, this

ratio is invariant to translation, scaling and rotation of the lung fields, which can occur due to changes in patient's posture in the different chest radiographs acquired over time. This way the need for application of complex image registration techniques to align the different radiographs of the same patient is avoided. The diminishment or the spreading of the infection is inferred by the way that this ratio changes as a function of time. Thus, a decreasing function demonstrates a progress towards the treatment of the infection, whereas an increasing function indicates that the patient's treatment should probably be reconsidered.

### III. EXPERIMENTAL RESULTS

For the experimental evaluation of the methodology proposed, a collection of twenty seven radiographs spanning to five sequences of three to nine images per sequence were used. Radiographs in the dataset came from patients with diagnosed bacterial pulmonary infections hospitalized in an intensive care unit. The infections in all radiographs were manifested as foci of consolidations. The radiographic images were 8-bit grayscale with a size of  $2K \times 2K$  pixels. The lung fields were isolated by manual delineation by an expert and were further sampled using  $32 \times 32$ -pixel sliding window, with a sliding step equal to 8 pixels. Comprehensive experiments were conducted to investigate the performance of the proposed methodology towards the assessment of the evolution of the infection over time.

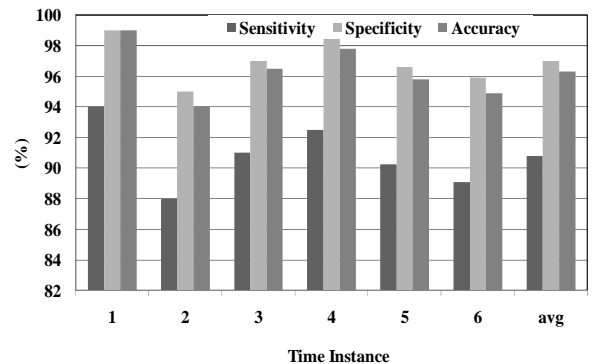


Fig. 3. Experimental results of a temporal sequence of six radiographs (1-6) and the sequence's average (avg).

Whereas, the performance measures considered in this study are sensitivity (SE), specificity (SP) and accuracy (AC) [1]. For each radiographic image, the different measures were calculated from the number of pixels classified as true positive  $TP = GTP \cap PCLA$ , true negative  $TN = GTN \cap NCLA$ , false positive  $FP = GTN \cap PCLA$ , and false negative  $FN = GTP \cap NCLA$ , where PCLA (positive cluster lung area) is the area corresponding to the patterns considered as consolidations, NCLA (negative cluster lung area) is the area corresponding to the patterns considered as normal lung parenchyma, and GTP and GTN are the ground truth areas of consolidations and normal lung parenchyma, respectively.

The results from the application of the proposed approach on the temporal image sequence of Fig. 2 are illustrated in Fig.3, whereas Table 1, shows the average results regarding the discrimination of the consolidation patterns from the normal ones, estimated from the application of both the proposed approach and the supervised  $k$ NN approach [1] on the whole dataset. As for the later, both intensity and textural features were used, where the performance

TABLE I  
AVERAGE CLASSIFICATION RESULTS

	Proposed	$k$ NN
Accuracy (AC)	91.0%	88.0%
Sensitivity (SN)	97.3%	87.1%
Specificity (SP)	96.5%	78.2%

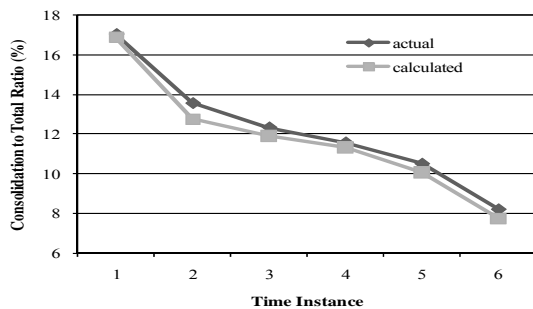


Fig. 4. The actual and calculated, by the proposed methodology, percentage ratio  $\omega$  of the consolidation to total patterns for the sequence of Fig. 2.

measures were estimated by 10-fold cross validation. It can be noticed that the accuracy the  $k$ NN approach is inferior to the one obtained with the proposed methodology.

Moreover, as regards the ratio  $\omega$ , Fig. 4 demonstrates that there is only a small deviation in the ratios calculated after the application of the proposed methodology from the actual ones as it is shown for the image sequence of Fig. 2. This result is also verified by the average error, between the actual and calculated ratios, estimated for all the image sequences in the dataset that equals to about 1.5%. From Fig. 4 it is also inferred that the infection is diminishing. This observation is in accordance with the opinion of the experts.

#### IV. CONCLUSION

We proposed a novel computational approach for monitoring the progress of bacterial pulmonary infections through the analysis of chest radiographic image sequences obtained from patients in a follow-up basis. According to this approach each radiograph is analyzed by a novel hierarchical cluster merging scheme based on NMFs evaluating successively both the intensity and the texture of the lung fields. The experiments showed that the proposed clustering scheme can be effectively used as a “second opinion” tool for a) the assessment of the extent of the radiographic manifestations of the infection, and b) the evaluation of the progress of the infection when applied to time-series radiographs

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