Statistical Sequential Analysis for Detection of Microcalcifications in Digital Mammograms

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***Abstract*—We formulate the problem of microcalcification detection in digital mammograms as a statistical change detection problem in the local properties of the image. First, we represent mammograms by two-dimensional autoregressive moving-average (2D ARMA) fields; thus uniquely characterizing the images by their reduced dimensionality 2D ARMA feature vectors. Texture changes in mammograms are then modeled as an additive change in the mean parameter of the PDF associated with the 2D ARMA feature vector sequence that describes the image. A generalized likelihood ratio test is used to detect theses changes and estimate the exact time (or space) where they occur. Our simulation results on the Digital Database for Screening Mammography hosted by the University of South Florida show that the decision functions of cancerous images present high peaks at the microcalcification locations, whereas they exhibit a uniform behavior for healthy mammograms. The proposed algorithm achieves a sensitivity and specificity of 96.9% and 97.8%, respectively.**

***Index Terms*—Breast microcalcification, mammogram, 2D-ARMA model, change detection algorithm.**

I. Introduction

The rapid expansion in number and volume of digital mammograms, the increasing demand for fast access to relevant medical data, the need for interpretation, and retrieval of medical information has become of paramount importance [1]. Mammography is the current standard for breast cancer diagnosis. Women 40 years of age or older are recommended to undergo a screening mammogram to check for breast malignancies every 6 months. Screening mammograms usually involve two x-rays of each breast. This process generates a huge amount of data that needs to be processed, interpreted and saved.

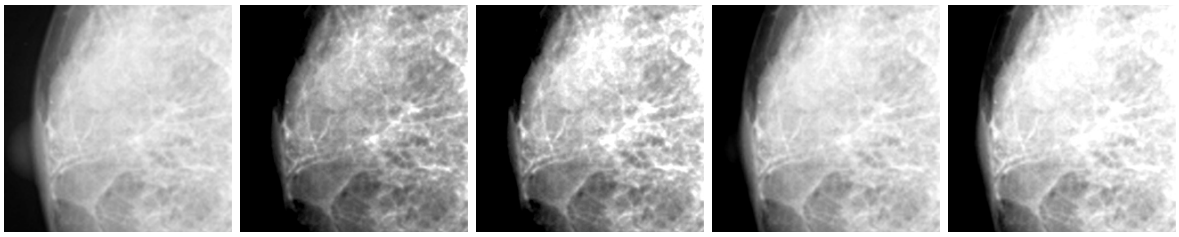
The presence of microcalcifications (tiny deposits of calcium) in the breast is an important sign for the detection of early breast carcinoma. Accurate and uniform evaluation of the enormous number of mammograms generated in widespread screening is a difficult task. 10-30% of breast carcinomas are missed by trained radiologists [2]. Mammograms are low contrast images, and the breast malignancies present a great diversity in shape, size and location, and low distinguishability from the surrounding healthy tissue.

In the last two decades, various computer-aided (CAD) systems have been proposed to help bring suspicious areas on the mammogram to the radiologist's attention. Many approaches were considered including denoising [3], segmentation [4], filtering [5], machine learning [6], [7] and artificial intelligence [5], mathematical morphology [8], time-frequency analysis and multiresolution techniques, and neural networks [2]. Despite their technical differences, these approaches share a common outline: they are all deterministic. They usually assume a small region of interest as a subject of recognition. Hence, their performance is contingent upon the natural variability of healthy and cancerous mammography images.

In contrast to deterministic methods, statistical methods take into account the noise in the digitized mammogram and the heterogeneity of its characteristics by considering an underlying probability distribution of the image features. It is, therefore, surprising that very few researchers have pursued this direction. Statistical analysis of mammograms was mainly considered in the context of textural information [9], [10]. In [9], the third and fourth order statistical moments, skewness and kurtosis, were estimated from the bandpass filtered mammogram. A region with high positive skewness and kurtosis is marked as a region of interest. In [10], a statistical model of the mammographic image, termed the "log-likelihood image", is generated from the original mammogram image. However, the method does not include any decision making, and the log-likelihood image has the same resolution of the original mammogram.

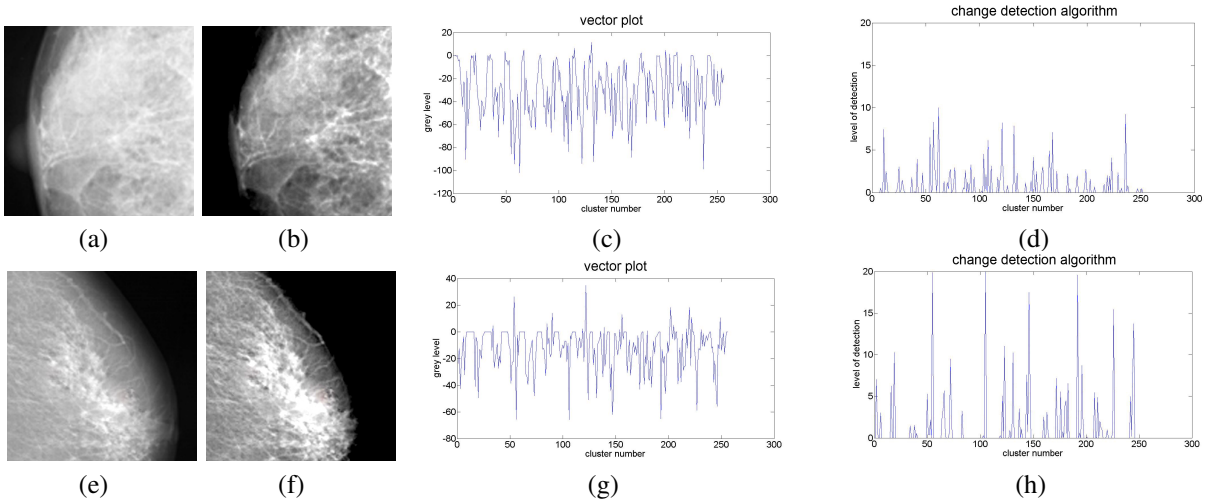
The challenge in breast carcinoma localization is that the detection algorithm must be able to handle all types of microcalcifications. Therefore, it is necessary to formulate the detection problem beyond the use of empirical observations about the type, shape, size or location of microcalcifications, which may or may not hold in all cases. In order to address these challenges, we pose the microcalcification detection problem in the context of statistical sequential representation and analysis of mammograms. A mammogram image is considered to be a realization of a stochastic process. We use statistical analysis to detect parameter changes of the stochastic process, which will indicate the presence of suspicious areas in the breast. In our approach, we achieve a decision-making CAD system through use of *dimensionality reduction* and *sufficient statistics*. We first show that mammograms can be accurately modeled as 2D autoregressive moving-average (ARMA) fields, and thus each image can be solely represented by its 2D ARMA coefficients.

In this paper, we consider a change detection framework based on additive modeling. Specifically, we detect changes



(a) (b) (c) (d) (e)

Fig. 1. 2D ARMA Modeling: (a) Original (healthy) mammogram; (b) 2D ARMA[2,2,2,2] model of (a); (c) 2D ARMA[3,3,3,3] model of (a); (d) 2D ARMA[4,4,4,4] model of (a); (e) 2D ARMA[6,6,6,6] model of (a).



(a) (b) (c) (d) (e) (f) (g) (h)

Fig. 2. Change detection algorithm (a) A normal (healthy) mammogram; (b) 2D ARMA[2,2,2,2] model of (a); (c) Plot of the average gray level of the 16×16 subimages in (a); (d) Plot of the decision function g_k for the image in (a); (e) Original cancerous mammogram; (f) 2D ARMA[2,2,2,2] representation of (e); (g) Plot of the average gray level of the 16×16 subimages in (a); (h) Plot of the decision function g_k for the image in (e). Observe that the plot of the gray-level values of the subimages does not discriminate between healthy and cancerous mammograms, whereas the proposed detection algorithm clearly pinpoints the location of microcalcifications in cancerous mammograms.

of the mean parameter of the PDF associated with the 2D ARMA feature vector sequence. The sufficient statistic used is based on the generalized likelihood ratio. Thus, the main steps used for detecting microcalcifications in mammograms are the 2D ARMA dimensionality reduction of the original image followed by change detection on the resulting feature vectors. In particular, no a priori assumptions are made about the specific nature of the microcalcifications (e.g., circular, smooth, etc.).

This paper is organized as follows. Section II presents the 2D ARMA field model. We show that the estimated 2D ARMA coefficients provide an accurate representation of the original image while reducing its dimensionality. The statistical carcinoma detection approach is discussed in Section III. Section IV shows the simulation results on mammograms from the digital database for screening mammography (DDSM at the University of South Florida). Concluding remarks and future work are presented in Section V.

II. 2D-ARMA Representation

We represent the breast image as a 2D random field $\{x[n,m],(n,m) \in \mathbb{Z}^2\}$ [11]. We define a total order on the discrete lattice as follows: $(i,j) \leq (s,t) \iff i \leq s$ and $j \leq t$ [11]. The 2D ARMA$[p_1,p_2,q_1,q_2]$ model is defined for the $N_1 \times N_2$ image $I = \{x[n,m] : 0 \leq n \leq N_1 - 1, 0 \leq m \leq N_2 - 1\}$ by the following difference equation

$$x[n,m] + \sum_{\substack{i=0 \\ (i,j)\neq(0,0)}}^{p_1} \sum_{j=0}^{p_2} a_{ij} x[n-i,m-j] = \sum_{i=0}^{q_1} \sum_{j=0}^{q_2} b_{ij} w[n-i,m-j], \quad (1)$$

where $\{w[n,m]\}$ is a stationary white noise field with variance σ^2, and the coefficients $\{a_{ij}\},\{b_{ij}\}$ are the parameters of the model.

A Two-stage Yule-Walker Least Squares parameter estimation method was proposed in [11]. First, the noise sequence $\{w[n,m]\}$ is assumed to be known. The ARMA parameter estimation problem is then reduced to a simple input-output system identification problem, which is solved by a least-squares (LS) method. The final estimate is then obtained by estimating the noise, using a truncated autoregressive (AR) model, and plugging it back in the Least Squares solution [11].

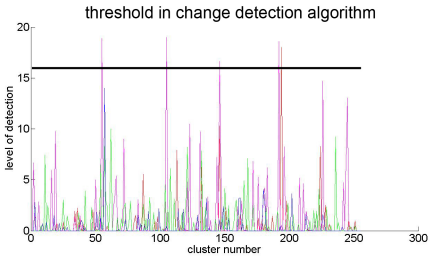
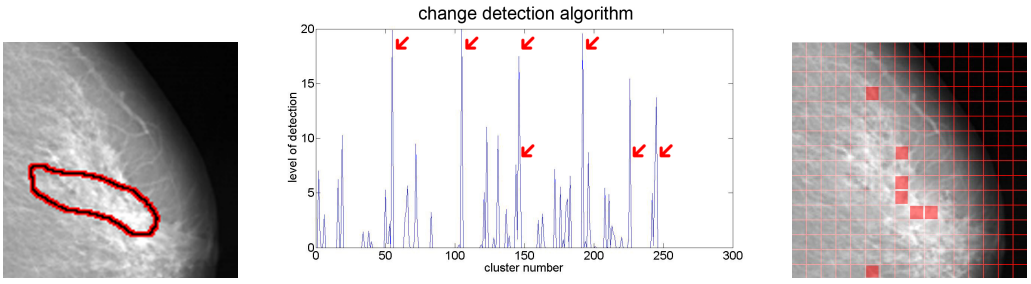


Fig. 3. The decision function g_k for four mammograms: cancerous in red/magenta and normal in blue/green. The value of the treshold is determined as the mean of the highest normal peak and the highest cancerous peak.



(a) (b) (c)

Fig. 4. Change detection algorithm: (a) Radiologist marked area of interest of the cancerous region; (b) Plot of the decision function of the mammogram. The arrows indicate the peaks above the threshold; (c) Marked 16×16 clusters that correspond to the detected peaks.

In practice the ARMA parameters are estimated using a window of size $N \times N$. The choice of the window size presents an inherent trade-off between the accuracy of the ARMA representation and the reliability of the classification. An image of size $L \times C$ is therefore represented by $s = \frac{LC}{N^2}(p_1 p_2 + q_1 q_2 + 4)$ ARMA feature vectors. Let $Y_k = [a_{ij}, b_{kl}]$; $0 \leq i \leq p_1$, $0 \leq j \leq p_2$, $0 \leq k \leq q_1$, $0 \leq l \leq q_2$ be the ARMA feature vector of the k-th block. The mammogram image is then compared to the $(LC)^2$ raw pixels of the unprocessed image. The 2D ARMA model presents a compressed representation of the image, which will lead to an efficient implementation of the CAD system. For instance, for $L = C = 256, N = 16, p_1 = p_2 = q_1 = q_2 = 1$, the 2D ARMA model represents a dimensionality reduction of more than 97% compared to the original image. Figures 2b and 2f show the 2D ARMA$[2, 2, 2, 2]$ models of a healthy and canceros mammograms respectively Section IV subsection IV-A discuss in detail the choice of the model degree parameters p_1, p_2, q_1, q_2.

The problem of tumor detection becomes one of detecting changes in the parameters of the probability density function (PDF) associated with the ARMA vector random process.

III. Change Detection Algorithm

The 2D ARMA feature vectors are assumed to form an i.i.d. (independent and identically distributed) sequence of r-dimensional random vectors $\{Y_k\}_{k \geq 1}$, with Gaussian distribution $N(\mu, \sigma)$ having PDF:

$$p_{\mu,\sigma}(Y_k) = \frac{1}{\sqrt{(2\pi)^r (det(\Sigma))}} e^{-(1/2)(Y_k - \mu)^T \Sigma^{-1} (Y_k - \mu)}, \quad (2)$$

Observe that the ARMA feature vectors are assumed to be independent. However the components of each ARMA feature vector are correlated with covariance matrix Σ. The independence of the ARMA feature vectors reflects an independence assumption between pixels in different NxN sub-blocks of an image. The tumor detection is modeled as a change in the vector parameter $\theta = \mu$ of the PDF characterizing the feature vector random process. Let the parameter $\theta = \theta_0$ be the value before the change, and $\theta = \theta_1$ the value after the change. In general, we have minimal or no information about the parameter θ_1 after change. Let us begin by discussing the scenario where there is a known upper bound for θ_0 and a known lower bound for θ_1. In this case, the change detection problem is equivalent to the following:

$$\begin{aligned} \mathbf{H_0} &= \{\theta : ||\theta - \theta_0||_\Sigma^2 \leq a^2, k < t_0\} \\ \mathbf{H_1} &= \{\theta : ||\theta - \theta_0||_\Sigma^2 \geq b^2, k \geq t_0\} \end{aligned} \quad (3)$$

where $||\theta - \theta_0||_\Sigma^2 = (\theta - \theta_0)^T \Sigma^{-1} (\theta - \theta_0)$, t_0 is the true change time and $a < b$. The case of interest where θ_0 is assumed to be known, and θ_1 unknown can be obtained as a limit case of the solution to the above problem, as we shall see in the sequel of the paper.

The solution to the detection problem formulated in 3 can be obtained by deriving the generalized likelihood ratio (GLR) test [12], where the unknown parameters are replaced by their maximum likelihood estimates. Thus, the generalized likelihood ratio for the sequence $\{Y_1, \cdots, Y_k\}$ is

$$S_j^k = \ln \frac{\sup_{||\theta - \theta_0||_\Sigma \geq b} p_\theta(Y_j, \cdots, Y_k)}{\sup_{||\theta - \theta_0||_\Sigma \leq a} p_\theta(Y_j, \cdots, Y_k)} \quad (4)$$

where p_θ is the corresponding parameterized probability density function. The sequential GLR algorithm is then given by

$$\begin{aligned} t_a &= \min\{k \geq 1 : g_k \geq h\} \\ g_k &= \max_{1 \leq j \leq k} S_j^k \end{aligned} \tag{5}$$

where k is the discrete time index, t_a is the alarm (detection) event, g_k is the test statistic, and h is a threshold.

Given the i.i.d. Gaussian assumption, S_j^k can be written as

$$S_j^k = \ln \frac{\sup_{||\theta-\theta_0||_\Sigma \geq b} e^{-(1/2)\sum_{i=j}^k (Y_i-\theta)^T \Sigma^{-1}(Y_i-\theta)}}{\sup_{||\theta-\theta_0||_\Sigma \geq a} e^{-(1/2)\sum_{i=j}^k (Y_i-\theta)^T \Sigma^{-1}(Y_i-\theta)}} \tag{6}$$

It can be shown that S_j^k can be rewritten as [12]

$$\frac{2}{k-j+1} S_j^k = \begin{cases} -(\chi_j^k - b)^2, & \chi_j^k < a; \\ -(\chi_j^k - b)^2 + (\chi_j^k - a)^2, & a \leq \chi_j^k \leq b; \\ +(\chi_j^k - a)^2, & \chi_j^k > b. \end{cases} \tag{7}$$

where

$$\begin{aligned} \chi_j^k &= [(\bar{Y}_j^k - \theta_0)^T \Sigma^{-1} (\bar{Y}_j^k - \theta_0)]^{1/2} \\ \bar{Y}_j^k &= \tfrac{1}{k-j+1} \textstyle\sum_{i=j}^k Y_i \end{aligned} \tag{8}$$

Observe that, for the current problem formulation, the data that are needed in Eq. (7) are the feature vectors Y_i, the covariance Σ, and the mean before the change θ_0.

In the more realistic case where the parameter before the change θ_0 is assumed to be known but the parameter after the change is assumed to be completely unknown, the change detection problem statement is as follows

$$\begin{aligned} \mathbf{H_0} &= \{\theta : \theta = \theta_0, k < t_0\} \\ \mathbf{H_1} &= \{\theta : \theta \neq \theta_0, k \geq t_0\}. \end{aligned} \tag{9}$$

Hence, the case where nothing is known about θ_1 can be considered the limit of the previous case when $a = b = 0$. Therefore, the GLR algorithm in (5) becomes:

$$\begin{aligned} t_a &= \min\{k \geq 1 : g_k \geq h\} \\ g_k &= \max_{1 \leq j \leq k} \{\tfrac{k-j+1}{2} (\chi_j^k)^2\} \end{aligned} \tag{10}$$

where (χ_j^k) is defined in (8).

In the above study, θ_0 is assumed to be known. In practice, θ_0 can be estimated using a number M of feature vectors at the beginning of each mammogram. The covariance Σ is estimated using the same feature vectors.

IV. Simulation Results

A. 2D ARMA Model

We test the proposed algorithm using the University of South Florida digital mammography library available online at: *http://marathon.csee.usf.edu*. The Digital Database for Screening Mammography (DDSM) is a resource for use by the mammographic image analysis research community. Each mammogram image is 256×256 pixels. The ARMA parameters were estimated using a window of size 16×16. Hence, each image is represented by 256 ARMA feature vectors $\{Y_k\}$. We find the optimal ARMA degree model (p_1, p_2, q_1, q_2) as the degree that minimizes the average square error between the original image and the predicted ARMA model. An exhaustive off-line search between the degrees $[1,1,1,1]$ and $[6,6,6,6]$ reveals that ARMA$[2,2,2,2]$ leads to the smallest average square error for most mammogram images in the DDSM library. Figure 1 shows 2D ARMA models of an original healthy mammogram.

B. Change Detection Algorithm

We can estimate the value of θ_0 (parameter before the change) as the sample mean of the first 10 feature vectors $\{Y_k\}$. An other approach is to estimate the value of θ_0 from the entire mammogram image. This method yields an estimation error not higher than the relative size of the microcalcifications in the image, i.e. about 1%. For both methods, estimation of the parameter θ_0 yielded similar values. The detection algorithm is based on the value of the threshold h, that was chosen experimentally. Figure 3 displays the decision function g_k of four sample mammograms including two cancerous and two normal. The cancerous images exhibit peaks that are twice as high, on average, than healthy images. Therefore, we found that a value of h equal to the mean of the highest cancerous peak and the highest normal peak achieves an optimal balance between false and missed alarms. Figure 2 shows a plot of the average grey level of the 16x16 sub-images of healthy and cancerous mammograms. It is seen that a simple plot of the grey level values of the mammograms does not discriminate between healthy and cancerous mammograms. However the proposed change detection algorithm leads to a decision function that is uniform for healthy mammograms and spiky for cancerous mammograms, where the spikes indicate the position of microcalcifications.

By lexicographical ordering of the image and its feature vectors, we are able to not only discriminate between normal and cancerous mammograms but also pinpoint the exact location of microcalcifications in the cancerous image. The peaks of the decision function can be easily traced back to the suspicious areas. Figure 4 shows a radiologist's marked area of suspicion, which is successfully detected as cancerous by our algorithm. Table I displays the performance of our algorithm based on 524 normal and cancerous digital mammograms from the DDSM library. Based on these statistically significant analysis, the results of the sensitivity and specificity of the proposed algorithm are 96.9% and 97.8%, respectively

V. Conclusion

In this paper, we introduced a new approach to the problem of malignancy detection in digital mammograms using statistical sequential analysis theory. The statistical approach inherently takes into account the noise in the image (from the imaging device and the digitization) and the great variety of healthy and cancerous mammograms by considering an underlying probability distribution of the image characteristics. For increased efficiency, the dimensionality of the original images is reduced using 2D-ARMA modeling, which is shown to accurately represent mammograms. The change detection algorithm is applied to the low-dimensional 2D ARMA feature

TABLE I
PERFORMANCE OF THE CHANGE DETECTION ALGORITHM IN 524 NORMAL AND CANCEROUS MAMMOGRAMS

	True	False
Positive	96%	4%
Negative	97%	3%

vectors compared to the pixels of the raw image. Tumor detection is defined as changes in the mean parameter of the random process describing the 2D ARMA feature vectors. No a priori assumptions were made about the nature, shape, size, or location of the microcalcifications. Such assumptions would limit the scope of a detection algorithm given the variability of microcalcifications and healthy tissues in mammograms.

In our ongoing and future work, we will investigate the effect of non-additive changes in the ARMA feature vectors on the performance of the proposed CAD system for mammograms and ultrasound breast images.

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