Texture Classification using Fractal Geometry for the Diagnosis of Skin Cancers

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Abstract

We present an approach to object detection and recognition in a digital image using a classification method that is based on the application of a set of features that include fractal parameters such as the Lacunarity and Fractal Dimension. The principal issues associated with object recognition are presented and a self-learning procedure for designing a decision making engine using fuzzy logic and membership function theory considered. The methods discussed, and the ‘system’ developed, have a range of applications in ‘machine vision’ and in this publication, we focus on the development and implementation of a skin cancer screening system that can be used in a general practice by non-experts to ‘filter’ normal from abnormal cases so that in the latter case, a patient can be referred to a specialist. The paper provides an overview of the system design and includes a link from which interested readers can download and use a demonstration version of the system developed to date.

Categories and Subject Descriptors (according to ACM CCS): F.2.2; I.5.4 [Analysis of Algorithms and problem complexity, Pattern Recognition]; Pattern matching, Computer vision

1. Introduction

Image analysis involves the use of image processing methods that are often designed in an attempt to provide a machine interpretation of an image, ideally, in a form that allows some decision criterion to be applied [Bla06], [Bla05]. Pattern recognition uses a range of different approaches that are not necessarily based on any one particular theme or unified theoretical approach. The main problem is that, to date, there is no complete theoretical model for simulating the processes that take place when a human interprets an image generated by the eye, i.e. there is no fully compatible model, currently available, for explaining the processes of visual image comprehension. Hence, machine vision remains a rather elusive subject area in which automatic inspection systems are advanced without having a fully operational theoretical framework as a guide. Nevertheless, numerous algorithms for understanding two- and three-dimensional objects in a digital image have and continue to be researched in order to design systems that can provide reliable automatic object detection, recognition and classification in an independent environment, e.g. [E.R97], [Fre88], [LG90], [SQ04].

In the work reported here, the object is analysed in terms of metrics derived from both a Euclidean and fractal geometric perspective, the output fields being used to train a fuzzy inference engine. The recognition structure is based on some of the image processing, analysis and machine vision techniques reported in [SHB99], for example. The approach considered is generic in that it can, in principle, be applied to any type of imaging modality for which there are numerous applications where self-calibration and learning is often mandatory. Example applications may include remote sensing, non-destructive evaluation and testing and other applications which specifically require the classification of objects that are textural. However, in this paper we focus on one particular application, namely, the diagnosis of skin cancer for screening patients through a general practice. The system

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reported is, in principle, just one of a number of variations which can be used for medical image analysis and classification in general. This is because the system includes features that are based on the textural properties of an image (defined in terms of fractal geometric parameters including the Fractal Dimension and Lacunarity) which is an important theme in medical image analysis.

2. Feature Detection and Classification

Suppose we have an image which is given by a function \( f(x, y) \) and contains some object described by a set of features \( S = \{s_1, s_2, ..., s_n\} \). We consider the case when it is necessary to define a sample which is somewhat ‘close’ to this object in terms of a matching set. This task can be reduced to the construction of some function determining a degree of proximity to the object to a sample - a template of the object. Recognition is the process of comparing individual features against some pre-established template subject to a set of conditions and tolerances. This process commonly takes place in four definable stages: (i) image acquisition and filtering (as required for the removal of noise, for example); (ii) object location (which may include edge detection); (iii) measurement of object parameters; (iv) object class estimation. We now consider aspects of each step. In particular, we consider the design features and their implementation together with their advantages, disadvantages and proposals for a solution whose application, in this paper, focuses on the problem of designing a skin cancer screening system. It is for this reason, that the examples given to illustrate the steps proposed, are ‘system related’.

The system discussed in this paper is based on an object detection technique that includes a novel segmentation method and must be adjusted and ‘tuned’ for each area of application. This includes those features associated with an object which fractal models are well suited [Blad06], [Blad08], [TBA98]. The system generates an output (i.e. a decision) using a knowledge database which generates a result (a decision) by subscribing different objects. The ‘expert data’ in the application field creates a knowledge database by using supervised training with a number of model objects [Zad75]. The recognition process is based on the following principal steps:

1. Image Acquisition and Filtering.
   A physical object is digitally imaged and the data transferred to memory, e.g. using current image acquisition hardware available commercially. The image is (Wiener) filtered to reduce noise and to remove unnecessary features such as light flecks.

2. Special Transform: Edge Detection.
   The digital image \( f_{m,n} \) is transformed into \( f_{m,n} \) to identify regions of interest and provide an input dataset for segmentation and feature detection operations [NBD86]. This transform is based on an edge detection filter designed specifically for the application considered here [BD08].

   The image \( f_{m,n} \) is segmented into individual objects \( \{f_{1,2}\}, \{f_{3,4}\}, ... \) to perform a separate analysis of each region. This step includes such operations as thresholding, morphological analysis and edge detection.

4. Feature Detection.
   Feature vectors \( \{x_{1,1}\}, \{x_{2,2}\}, ... \) are computed from the object images \( \{f_{1,2}\}, \{f_{3,4}\}, ... \) and corresponding transformed images \( \{f'_{1,2}\}, \{f'_{3,4}\}, ... \). The features are numeric parameters (as defined in Section 4) that characterize the object inclusive of its texture. The feature vectors computed consist of a number of Euclidean and fractal geometric parameters together with statistical measures in both one- and two-dimensions. The one-dimensional features correspond to the border of an object whereas the two-dimensional features relate to the surface within and/or around the object.

5. Decision Making.
   This involves assigning a probability to a predefined set of classes [Vad93]. Probability theory and fuzzy logic [Mam76] are applied to estimate the class probability vectors \( \{p_j\}, \{p'_j\}, ... \) from the object feature vectors \( \{x_{1,1}\}, \{x_{2,2}\}, ... \). A fundamental problem has been to establish a quantitative relationship between features and class probabilities, i.e.

\[
\{p_j\} \leftrightarrow \{x_k\}
\]

where \( \leftrightarrow \) denotes a transformation from class probability to feature vector space. A ‘decision’ is the estimated class of the object coupled with the probabilistic accuracy [San76].

The approach reported in this paper uses a number of new algorithms that have been designed to solve problems associated with the above steps, details of which lie beyond the scope of this publication but are available in [BD08]. For example, two new morphological algorithms for object segmentation have been considered which include auto-threshold selection. One of these algorithms - a contour tracing algorithm - extracts parameters associated with the spatial distribution of an object’s border. This algorithm is also deployed in the role of feature detection.

With regard to the decision making engine, the approach considered is based on establishing an expert learning procedure in which a Knowledge Data Base (KDB) is constructed using answers that an expert makes during normal manual work. Once the KDB has been developed, the system is ready for application in the field and provides results automatically. However, the accuracy and robustness of the output depends critically on the extent and completeness of the KDB as well as on the quality of the input image, primarily in terms of its compatibility with those images that have been used to generate the KDB.

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3. Segmentation

Segmentation is implemented by adaptive thresholding and morphological analysis. The adaptive image threshold is given by

\[ T = \begin{cases} T_x, & T_x \geq T_y; \\ T_y, & \text{otherwise.} \end{cases} \]

where

\[ T_x = \frac{1}{2} \left( \min \left( \max f(x, y) \right) - \left( \max f(x, y) \right)_y \right) \]

\[ + \left( \max f(x, y) \right)_y, \]

\[ T_y = \frac{1}{2} \left( \min \left( \max f(x, y) \right) - \left( \max f(x, y) \right)_x \right) \]

\[ + \left( \max f(x, y) \right)_x. \]

Here, \( \langle \cdot \rangle_x \) and \( \langle \cdot \rangle_y \) are the means within column \( x \) and row \( y \), respectively. This approach provides a solution for extracting the most significant features associated with a well-defined object in the image frame. Thus, if an object covers an extensive image space, then this ‘filter’ provides the fastest compact solution. For example, in the skin cancer screening application considered here, there is preliminary information based on the fact that there is just one object on the image (as shown in the example given in Figure 1). In order to obtain a clear boundary, the morphological analysis applied here selects objects with a predefined area.

![Figure 1: Example of object segmentation applied to a skin cancer screening system.](image)

4. Feature Determination

Features (which are typically compounded in a set of metrics - floating point or decimal integer numbers) describe the object state in an image and provides the input for a decision making engine. The features considered in this paper are computed in the spatial domains of the original image \( f_{m,n} \) and transformed image \( \tilde{f}_{m,n} \). Further, these features are extracted from different colour channels - Red (R), Green (G) and Blue (B) - captured by the CCD array. The issue of what type, and how many features should be used to develop a computer vision system, is critical in the design. The system considered here has been developed to include features associated with the texture of an object, features that are compounded in certain parameters associated with the field of fractal geometry. Texture is particularly important in medical image classification and of primary importance in the application (skin cancer screening) considered in this paper. The following features and their derivatives have been considered (primarily through numerical experimentation) in the recognition system reported in this paper:

**Average Gradient \( G \)**

describes how the intensity changes when scanning from the object center to the border. The object gradient is computed using the least squares method compounded in the following result:

\[ g = \frac{N}{\sum_{(m,n) \in S} r_{m,n} \tilde{f}_{m,n} - \sum_{(m,n) \in S} r_{m,n} \sum_{(m,n) \in S} \tilde{f}_{m,n}^2} \]

where \( N \) is the number of pixels defining an object of compact support \( S \) and \( r_{m,n} \) is the distance between \( (m,n) \) and the center \((m',n')\), i.e.

\[ r_{m,n} = \sqrt{(m-m')^2 + (n-n')^2}. \]

The center coordinates \((m',n')\) correspond to the local maximums of \( \tilde{f}_{m,n} \) within the cluster. The cluster gradient is the average of object gradients,

\[ G = \langle |r_i| \rangle_{i \in S} \]

where \( i \in S \) is the index object.

**Colour Composites \( \Upsilon \) and \( \Upsilon_D \)**

characterise the relationship between the R, G and B layers of the transformed image. The triangle formula

\[ r(a,b,c) = \sqrt{(s-a)(s-b)(s-c)}, \]

\[ s = \frac{1}{2}(a+b+c) \]

is applied to the ‘colour triangle’ RGB such that the following pixel colour composite is obtained

\[ \upsilon_{m,n} = r(a,b,c) \]

where

\[ a = \tilde{f}_{m,n}^R, \quad b = \tilde{f}_{m,n}^G, \quad c = \tilde{f}_{m,n}^B. \]
and \( y^D = r(a, b, c) \) with
\[
a = |f^R_{m,n} - f^G_{m,n}|, \quad b = |f^G_{m,n} - f^B_{m,n}|
\]
and
\[
c = |f^R_{m,n} - f^B_{m,n}|
\]
The average colour composites are then given by
\[
Y = \{\langle y^D_{m,n}\rangle \}_{(m,n) \in S}, \quad Y^D = \{\langle y^D_{m,n}\rangle \}_{(m,n) \in S}.
\]

**Fractal Dimension** \( D \)
determines the frequency characteristics of the object boundary and surface \([Bla06], [Bla05]\). It represents a measure of texture \([TBA98]\) and describes a random fractal signal, for example, with a power spectrum of the form \( P(k) = c|k|^{D-5} \) where \( k \) is the spatial frequency, \( c \) is a constant and \( 1 < D < 2 \). Both \( D \) and \( c \) can be computed using a least squares method \([TBA98]\). An example of the differences in the Fractal Dimension associated with the boundary of two objects is given in Figure 2) and Figure 3.

![Figure 2: Example of an object with a (boundary) Fractal Dimension \( D = 1.68 \)](image)

**Lacunarity (Gap Dimension)** \( \Lambda_k \) characterizes the way the ‘gaps’ are distributed in an image \([Bla05], [TBA98]\). The gap dimension is, roughly speaking, a measure of the number of light or dark regions in an image. It is defined for a degree \( k \) by
\[
\Lambda_k = \sqrt{\left\langle \frac{f_{m,n}}{(f_{m,n})^k} - 1 \right\rangle^k}
\]
where \( \langle f_{m,n} \rangle = \frac{1}{N} \sum f_{m,n} \) denotes the mean value. In the system described in this paper, an average of local Lacunarities of the degree \( k = 2 \) is measured.

**Symmetry Features** \( S_n \) and \( M \) are estimated by morphological analysis in a three-dimensional space, i.e. two-dimensional spatial coordinates and intensity. A symmetry feature \( S_n \) is measured for a given degree of symmetry \( n \) (currently \( n = \{2, 4\} \)). This value shows the deviation from a perfectly symmetric object, i.e. \( S_n \) is close to zero when the object is symmetric and \( S_n > 0 \) otherwise. Feature \( M \) describes the fluctuation of the centre of mass for pixels with different intensities; \( M = 0 \) for symmetric objects and \( M > 0 \) otherwise.

**Structure** \( \gamma \) provides an estimation of the 2D curvature of the object in terms of the following:
\[
\gamma < 0, \quad \text{if object bulging is less than a threshold},
\]
\[
\gamma = 0, \quad \text{if the object has standard bulging},
\]
\[
\gamma > 0, \quad \text{if object has a higher level of bulging}.
\]

**Geometrical Features** include the minimum \( R_{\min} \) and maximum \( R_{\max} \) radius of the object (or ratio \( R_{\max}/R_{\min} \)) object area \( S \), object perimeter \( P \) (or ratio \( S/P^2 \)) and the coefficient of infill \( S/S_R \), where \( S_R \) is the area of the bounding polygon which, in this application, is determined using the Convex Hull algorithm reported in \([BD08]\).

The present solution detects objects by computer analysis using mixed mode features that are based on Euclidean and fractal metrics. The procedure of object detection is performed at the segmentation stage and needs to be adjusted for each area of application. The recognition algorithm then makes a decision using a knowledge database and outputs a result by subscribing objects based on the features defined above. The ‘expert data’ associated with a given application creates a knowledge database by using the supervised training system with a number of model objects as described in the following section.
5. Object Recognition

In order to characterize an object, the ‘system’ has to know its mathematical representation. Here, this representation is based on the features considered in the previous section which are used to create an image of the object in the ‘electronic mind’. This includes the textural features (Fractal Dimension and Lacunarity) for the object coupled with the Euclidean and morphological measures defined. In the case of a general application, all objects are represented by a list of parameters for implementation of supervised learning in which a fuzzy logic system automatically adjusts the weight coefficients for the input feature set.

The methods developed represent a contribution to pattern recognition based on fractal geometry (at least in a partial sense), fuzzy logic and the implementation of a fully automatic recognition scheme as illustrated in Figure 4 for the Fractal Dimension D (just one element of the feature vector used in practice). The recognition procedure uses the decision making rules from fuzzy logic theory [Zad75, Mam76, San76, Vad93] based on all, or a selection, of the features which are combined to produce a feature vector $x$.

![Figure 4: Basic architecture of the diagnostic system based on the Fractal Dimension D (a single feature) and decision making criteria $\beta$.](image)

5.1. Decision Making

The class probability vector $p = \{p_j\}$ is estimated from the object feature vector $x = \{x_i\}$ and membership functions $m_j(x)$ defined in a knowledge database. If $m_j(x)$ is a membership function, then the probability for each $j^{th}$ class and $i^{th}$ feature is given by

$$p_j(x_i) = \max \left[ \frac{\sigma_j}{|x_i - x_{j,i}|} \cdot m_j(x_{j,i}) \right]$$

where $\sigma_j$ is the distribution density of values $x_{j,i}$ at the point $x_i$ of the membership function. The next step is to compute the mean class probability given by

$$\langle p \rangle = \frac{1}{J} \sum_j w_j p_j$$

where $w_j$ is the weight coefficient matrix. This value is used to select the class associated with

$$p(j) = \min \left[ \langle p \rangle, w_j - \langle p \rangle \right] \geq 0$$

providing a result for a decision associated with the $j^{th}$ class. The weight coefficient matrix is adjusted during the learning stage of the algorithm.

The decision criterion method considered here represents a weighing-density minimax expression. The estimation of the decision accuracy is achieved by using the density function

$$d_i = |x_{\text{max}} - x_i|^3 + \left| \sigma_{\text{max}}(x_{\text{max}}) - p_j(x_i) \right|^3$$

with an accuracy determined by

$$P = w_j p_j - \frac{2}{N} \sum_{i=1}^N d_i$$

5.2. Supervised Learning Process

The supervised learning procedure is the most important part of the system for operation in automatic recognition mode. The training set of sample objects should cover all ranges of class characteristics with a uniform distribution together with a universal membership function. This rule should be taken into account for all classes participating in the training of the system. An expert defines the class and accuracy for each model object where the accuracy is the level of self-confidence that the object belongs to a given class. During this procedure, the system computes and transfers to a knowledge database, a vector $x = \{x_i\}$, which forms the membership function $m_j(x)$. The matrix of weight factors $w_{j,i}$ is formed at this stage accordingly for the $i^{th}$ parameter and $j^{th}$ class using the following expression:

$$w_{i,j} = 1 - \frac{1}{N} \sum_{k=1}^N \left( p_{i,j}(x_{i,k}) - \langle p_{i,j}(x_{i,k}) \rangle \right) \cdot p_{i,j}(x_{i,k})$$

The result of the weight matching procedure is that all parameters which have been computed but have not made any contribution to the characteristic set of an object are removed from the decision making algorithm by setting $w_{i,j}$ to null.
6. Application to Skin Cancer Screening: ORSCSS

In this section, we describe the basis and operational performance associated with the Oxford Recognition Skin Cancer Screen System (ORSCSS) developed by Oxford Recognition Limited (ORL) in collaboration with Dublin Institute of Technology. A demonstration version of the system is available online at http://www.oxreco.com/setup.zip which includes information on the system and an instruction manual. Installation is initiated through setup.exe from the root folder in which the downloaded application has been placed (after unzipping the downloaded file setup.zip).

Malignant Melanomas are increasingly common and a potentially fatal form of skin cancer, the incidence of which is increasing at a rate greater than any other form of cancer. It is often difficult to visually differentiate a normal mole from abnormal and general practitioners do not usually have significant expertise to diagnose skin cancers. Skin cancer specialists can improve the identification rate by over 80% but are often severely overloaded by referrals from regional general practices. It is possible for a general practitioner to take a high quality digital image of the suspect region on a patient’s skin and email the result to a remote diagnosis center. However, this can also lead to a (remote) overload and it is for this reason that the system discussed here has been considered in response to developing a screening method that can ‘filter’ benign melanomas in a general practice.

The current system is composed of the following basic steps:

1. Filtering
   The image is Wiener filtered [Bla05] to reduce noise and remove unnecessary and obtrusive features such as light flecks.

2. Segmentation
   The image is segmented to perform a separate analysis of each object (moles and/or other skin features). Two segmentation modes are available:
   - Automatic Mode
     The software identifies a mole as the largest and darkest object in the image. This mode is applicable in most cases.
   - Manual Mode
     The area of interest is manually selected by the user. This is most useful in cases when multiple moles and/or foreign objects are present in the image with possible overlapping features, for example.

3. Feature Detection
   For each object, a set of recognition features are computed. The features are numeric parameters (as defined in Section 4) that describe the object in terms of a variety of Euclidean and fractal geometric parameters, colour components and statistical metrics in one- and two-dimensions. The one-dimensional features correspond to the border of a mole and the two-dimensional features relate to the surface within the object boundary. In addition, a recognition algorithm is used to analyse the mole structure as illustrated in Figure 5. This provides information on the possible growth of the object when an inspection is undertaken over a period of time.

4. Decision Making
   The system uses fuzzy logic to combine features into a decision. A decision is the estimated class of the object and its accuracy. In this particular application, the output is designed to give two classes: normal and abnormal. This provides the simplest output with regard to the use of the system in a general practice in which abnormal cases are immediately referred to a specialist.

![Figure 5: Analysis of the structure of a mole for comparative growth analysis.](image)

6.1. Key Advantages

The technology delivers high accuracy and automation which has been made possible by the following innovations:

**Fractal analysis**

Biological structures (such as body tissues) have natural fractal properties. Numeric measurements of these properties enable efficient and effective detection of abnormalities.
Extended set of detectable features

High accuracy is achieved when multiple features are measured together and combined into a single result.

Advanced fuzzy logic engine

The knowledge-based recognition scheme used enables highly accurate diagnosis and offers significant improvements over current diagnostic methods.

6.2. Knowledge Database

ORSCSS is a knowledge-based system and requires extensive training before clinical operation. The training process includes a review and probabilistic classification of appropriate images by experts. The minimal number of training images depends on the number of classes and the diversity of objects within each class. An example of the output generated by the system is given in Figure 6 which provides a decision as to whether the object is ‘normal’ or ‘abnormal’ together with an estimate of the associated precision.

![Figure 6: Example of the output generated by ORSCSS.](image)

6.3. Comparison with Other Approaches

There are a number of commercially available products which offer a range of aids and tools for skin cancer detection. Some of them use an extensive database to estimate the pathology and may require a relatively significant amount of time to make a decision. Other products calculate several properties and represent them graphically. Medical staff are then used to make a final decision. More interesting techniques involve the capture of images using different sensors or a multiplicity of different images. However, these systems are as yet, not approved for clinical diagnosis and are not a referenced form of dermatoscopy. The following list provides some of the more common products in the field: (i) MoleMAX - http://www.molechecks.com.au; (ii) DermLite - http://www.dermilite.com/nnmfoto.html; (iii) DermoGenius Lite - http://www.dermogenius.de; (iv) MelaFind - www.melafind.com. Comparing these products with the methods developed for this paper, it is clear that there are no other automatic recognition systems with self-adjusting procedures and self-controlled functions. The tests undertaken to date, have established the capacity for ORSCSS to be used in routine clinical conditions provided extensive training of the system has been undertaken.

7. Discussion

The methods discussed in the previous sections represent a novel approach to designing an object recognition system that is robust in classifying textured features, the application considered in this paper, having required a symbiosis of the parametric representation of an object and its geometrical invariant properties. In comparison with existing methods, the approach adopted here has the following advantages:

**Speed of operation.** The approach uses a limited but effective parameter set (feature vector) associated with an object instead of a representation using a large set of values (pixel values, for example). This provides a considerably higher operational speed in comparison with existing schemes, especially with composite tasks, where the large majority of methods require object separation. The principal computational effort is that associated with the computation of the features defined in Section 4.

**Accuracy.** The methods constructed for the analysis of sets of geometrical primitives are, in general, more precise. Because the parameters are feature values, which are not connected to an orthogonal grid, it is possible to design different transformations (shifts, rotational displacements and scaling) without any significant loss of accuracy compared with a set of pixels, for example. On the other hand, the overall accuracy of the method is directly influenced by the accuracy of the procedure used to extract the required geometrical tags. In general, the accuracy of the method will always be lower, than, for example, classical correlative techniques. This is primarily due to padding, when errors can occur during the extraction of a parameter set. However, by using precise parametrisation structures based on the features defined in Section 4, remarkably good results are obtained.

**Reliability.** The proposed approach relies first and foremost on the reliability of the extraction procedure used to establish the geometrical and parametric properties of objects, which, in turn, depends on the quality of the image; principally in terms of the quality of the contours. It should be noted that the image quality is a common problem in any vision system and that in conditions of poor visibility and/or resolution, all vision systems will fail. In other words, the reliability of the system is fundamentally dependent on the quality of the input data.

Among the characteristic disadvantages of the approach, it should be noted that: (i) The method requires a considerable number of different calculations to be performed and
appropriate hardware requirements are therefore mandatory in the development of a real time system; (ii) the accuracy of the method is intimately connected with the required computing speed - an increase in accuracy can be achieved but may be incompatible with acceptable computing costs. In general, it is often difficult to acquire a template of samples under real life or field trial conditions which have a uniform distribution of membership functions. If a large number of training objects are non-uniformly distributed, it is, in general, not possible to generate accurate results.

8. Conclusion

This paper has been concerned with the task of developing a methodology and implementing applications that are concerned with two key tasks: (i) the partial analysis of an image in terms of its fractal structure and the fractal properties that characterize that structure; (ii) the use of a fuzzy logic engine to classify an object based on both its Euclidean and fractal geometric properties. The combination of these two aspects has been used to define a processing and image analysis engine that is unique in its modus operandi but entirely generic in terms of the applications to which it can be applied.

The work reported in this paper is part of a wider investigation into the numerous applications of pattern recognition using fractal geometry as a central processing kernel. This has led to the design of a new library of pattern recognition algorithms including the computation of parameters in addition to those that have been reported here such as the information dimension, correlation dimension and multifractals [TBA98]. The inclusion or otherwise of such parameters in terms of improving vision systems such as the one considered here remains to be understood. However, from the work undertaken to date, it is clear that texture based analysis alone is not sufficient in order to design a recognition and classification system. Both Euclidean and fractal parameters (as well as other metrics such as colour composites) need to be combined into a feature vector in order to develop an operational vision system which includes objects that have textural properties such as those associated with medical imaging.

The creation of logic and general purpose hardware for artificial intelligence is a basic theme for any future development in terms of the applications to which it can be applied. The authors are grateful for the advice and help of Professor V Deviatkov and Professor A Chernikov (Moscow State Technical University), Professor Jonathan Brostoff (Kings College, London University), Dr Alastair Deery (Royal Free Hospital, London) and Professor Irina Shabalova (Russian Medical Academy of Postgraduate Education, Moscow).

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