This thesis describes a set of image analysis tools developed for the purpose of quantifying the distribution of chromatin in (light) microscope images of cell nuclei. The distribution or pattern of chromatin is influenced by both external and internal variations of the cell environment, including variations associated with the cell cycle, neoplasia, apoptosis, and malignancy associated changes (MACs). The quantitative characterisation of this pattern makes possible the prediction of the biological state of a cell, or the detection of subtle changes in a population of cells. This has important application to automated cancer screening.

The majority of existing methods for quantifying chromatin distribution (texture) are based on the stochastic approach to defining texture. However, it is the premise of this thesis that the structural approach is more appropriate because pathologists use terms such as clumping, margination, granulation, condensation, and clearing to describe chromatin texture, and refer to the regions of condensed chromatin as granules, particles, and blobs. The key to the structural approach is the segmentation of the chromatin into its texture primitives. Unfortunately all of the chromatin segmentation algorithms published in the literature suffer from one or both of the following drawbacks: (i) a segmentation that is not consistent with a human’s perception of blobs, particles, or granules; and (ii) the need to specify, a priori, one or more subjective operating parameters. The latter drawback limits the robustness of the algorithm to variations in illumination and staining quality.

The structural model developed in this thesis is based on several novel low-, medium-, and high-level image analysis tools. These tools include: a class of non-linear self-dual filters, called folding induced self-dual filters, for filtering impulse noise; an algorithm, based on seeded region growing, for robustly segmenting chromatin; an improved seeded region growing algorithm that is independent of the order of pixel processing; a fast priority queue implementation suitable for implementing the
watershed transform (special case of seeded region growing); the adjacency graph attribute co-occurrence matrix (AGACM) method for quantifying blob and mosaic patterns in the plane; a simple and fast algorithm for computing the exact Euclidean distance transform for the purpose of deriving contextual features (measurements) and constructing geometric adjacency graphs for disjoint connected components; a theoretical result establishing an equivalence between the distance transform of a binary image and the grey-scale erosion of its characteristic function by an elliptic poweroid structuring element; and a host of chromatin features that can be related to qualitative descriptions of chromatin distribution used by pathologists.

In addition, this thesis demonstrates the application of this new structural model to automated cervical cancer screening. The results provide empirical evidence that it is possible to detect differences in the pattern of nuclear chromatin between samples of cells from a normal Papanicolaou-stained cervical smear and those from an abnormal smear. These differences are supportive of the existence of the MACs phenomenon. Moreover the results compare favourably with those reported in the literature for other stains developed specifically for automated cytometry. To the author’s knowledge this is the first time, based on a sizable and uncontaminated data set, that MACs have been demonstrated in Papanicolaou stain. This is an important finding because the primary screening test for cervical cancer, the Papanicolaou test, is based on this stain.