A computerized system for the classification of chromosomes based on pattern recognition and image analysis techniques (Çankaya system)

Selim ESKİİZMİRLİLER[1,3], Aydan M.ERKMEN[3], A.Nur ÇAKAR[2], M.Sinan BEKSAÇ[1]

[1]Biomedical Engineering and Fetal Medicine Unit Dept. of Obstetrics and Gyneacology, [2]Dept. of Histology and Embryology Hacettepe University, [3]Dept. of Electrical Engineering, Middle East Technical University, ANKARA - TURKEY

Recently, automated cytogenetic analysis of fetal chromosome specimens, has become an important and efficient diagnostic approach in the prenatal diagnosis of chromosomal abnormalities. The objective of this study is to develop a chromosome recognition and classification system, heretofore named as ÇANKAYA SYSTEM, based on automated image processing and analysis techniques. In parametric representation of chromosomes we have used length, area (as a number of pixels) of chromosomes, centromere location and band patterns (such as number of bands, grey level mean in bands and size of bands) to describe and arrange chromosomes. Amniotic fluid is cultured and metaphase chromosome slides are prepared for this study. Giemsa-trypsin G-banding is used as a staining technique. Nikon Microphote fluorescence microscope, Nikon CCD camera and related computer environment are used for data acquisition.
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Key Words: Prenatal diagnosis, Automated cytogenetics, Image processing & analysing, Karyotyping

One of the most important goals of Maternal and Fetal Medicine in the prenatal diagnosis of chromosomal abnormalities to reduce the perinatal morbidity and mortality (1-2). Chromosomal disorders are accounted for a certain per cent of genetic problems and congenital malformations and fall into two main categories such as numerical and structural abnormalities. With the advent of technology in the field of cytochemistry and image analysis/pattern recognition studies semi-automated and automated systems were introduced into cytogenetics and fetal medicine (3-10).

Automated cytogenetics aims to reduce interpretative variations and failures due to conventional karyotyping and cytogenetic approaches. In this study, we have described a chromosome classification and recognition system, heretofore named as ÇANKAYA, based on automated image analysis.

MATERIALS AND METHODS

Patients and Clinical Data

Amniocentesis was performed on 25 pregnant women inbetween 16-19th gestational weeks. All patients delivered healthy babies without any chromosomal abnormality. The amniotic fluid is cultured and slides are prepared. Metaphase chromosomes are banded by using Giemsa-trypsin G-band procedures (11).

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Correspondence: M.Sinan BEKSAÇ
Biomedical Engineering and Fetal Medicine Unit, Department of Obstetrics and Gynaecology, Hacettepe University, 06100 ANKARA

Data Acquisition

Our Hardware & Software configuration for obtaining and filtering image files from chromosome specimens, consists of Nikon fluorescence microscope, Nikon CCD camera, Image Processing Unit (IPU-IAS25), General Image Analysis Software (GENIAS) designed by Joyce Loebl Ltd. A block diagram representation of our hardware structure is shown in Figure 1.

RESULTS

Image Analysis

This phase consists of two parts: *1) Image processing; 2) Object measurements.*

In the first step, images captured and digitized via special microscope-camera configuration are converted to standart computer format so that they can be read with IBM PC compatible computers. Subsequently different filtering algorithms are applied for the enhancement of image characteristics. In our case this can be summarized as differentiating band patterns of chromosomes from the background (12).

On the other hand, the separation of touching chromosomes / decomposition of overlapping chromo-

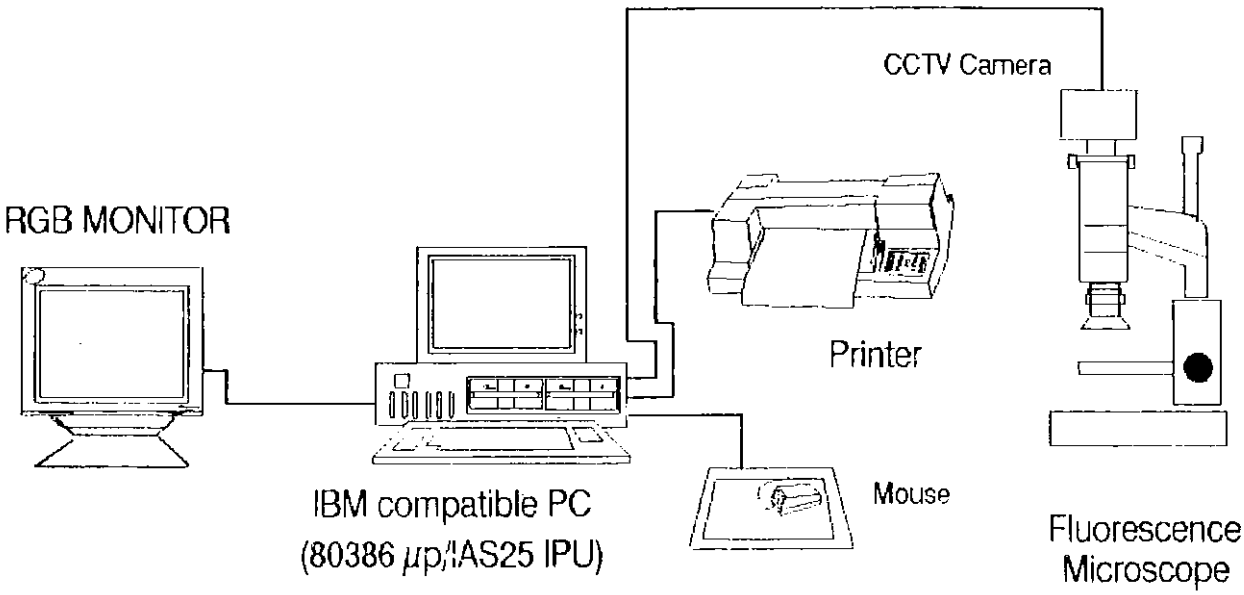


Figure 1. Block diagram o(our hardware structure (Çankaya System).

somes and annihilation of artifacts are performed by allowing user interference. Such a user interface is done by allowing the user to point such chromosomes and thus direct the program flow (13,14).

As a second step, Point measurements for grey level information of pixels, automatic object-chromosome detection, normalisation of their orientations, are automatically performed through our currently developed software. For this purpose, original object detection and object skeletonizing algorithms are developed (Figure 2).

Parametric respesentation used in the arrangement of chromosomes requires feature extraction. Our feature vector consists of length of chromosome (LC), number of pixels (NP), centromere location (CL), band patterns (number of bands (NB), grey level mean in bands (GLMBX), size of bands (SBX). In the last two components (GLMBX-SBX) we have decided to use the two bands before and after the centromere in order to minimize the effects of laboratory performance on banding chromosomes.

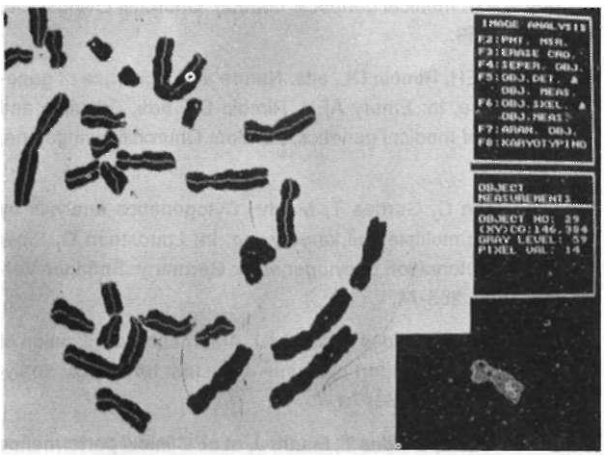


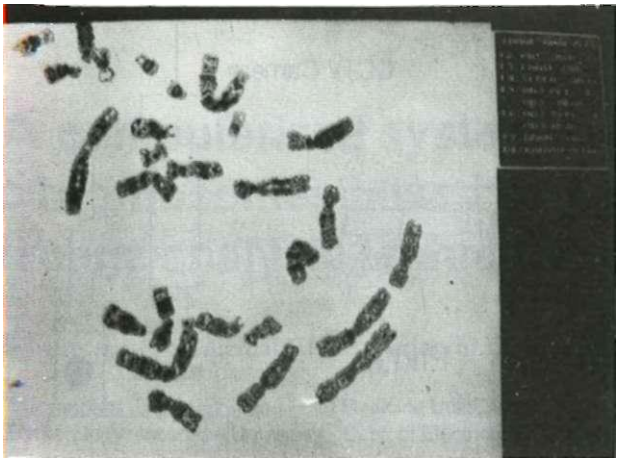
Figure 2. An intermediate step for object detection and object skeletonizing algorithms.

Moreover, our architecture allows the arrangement of detected chromosomes with respect to each measurement. Figure 3 shows an example for arrangement of 29 chromosomes within partial metaphase with respect to their object-area.

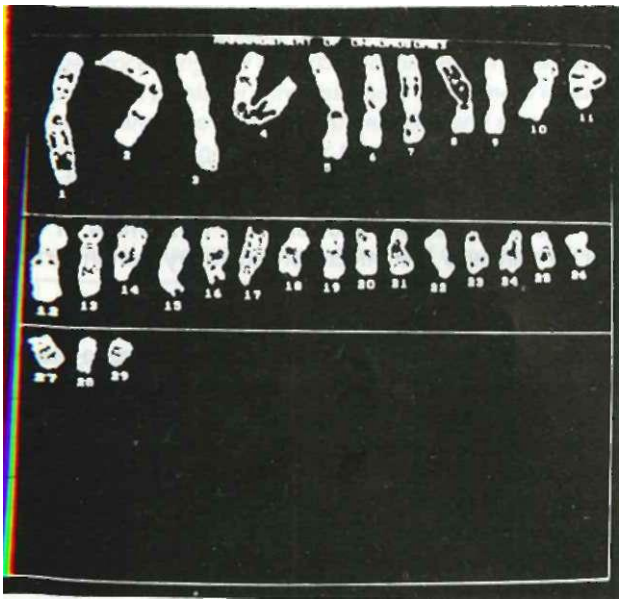
DISCUSSION

The detailed study of human chromosome morphology are the main tools of prenatal diagnosis of chromosomal abnormalities (1,10). High technology applications in the field of fetal medicine enable scientists to deal with automated cytogenetics (3,9). Automated cytogenetics aims to prevent the intra and inter individual variations and problems arising from visiual analysis (3-5). Various semi-automated and automated systems were introduced for metaphase finding and karyotyping procedures (3,10). However, further investigations are still necessary to obtain a good system.

In this study we have developed a chromosome recognition and arrangement system based on automated image analysis. Our system, heretofore named as ÇANKAYA, is consisted of two main phases: 1) Image Processing and Analysis, 2) Chromosome Recognition and Classification. Image analysis and pattern recognition is the main engineering approaches of automated cytogenetics (4,9). However, there is still not a considerable consensus on the exact methodology in the establishment of the systems (3). Different feature extraction and statistical classifi-



jag **figure** 3a. Partial metaphase image before Processing&Analy-



• gure 3b. Arrangement of 29 chromosomes with respect to :i-ieir object-area.

ition techniques were used in automated metaphase inding and karyotyping systems (3-10). In this study, 'e have used the length of chromosomes, number of •ixels (object area), centromere locations, band pat- •rns (e.g. number of bands, grey level mean in *ands, size of bands) to describe arrange the chromosomes.

Our future aim is the set a classical karyotyping tructure to persuade conventional cytogenticists for t"»e performance of the Çankaya System and to use it or decision making / diagnostic purposes via neural „C—"otworks. We believe that artificial intelligent system ^^•^vhich will be based on our chromosome classifi- iton is the most realistic approach in a diagnostic rogram.

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Otomatik görüntü analiz tabanlı bir kromozom tanıma ve sınıflandırma sistemi (Çankaya Sistemi)

Son zamanlarda, fetal kromozom slaytlarının otomatik sitogenetik analizi prenatal tanı açısından kromozom anomalilerinin belirlenmesinde önemli ve etkili bir tanı yöntemi haline gelmiştir. Bu çalışmanın amacı otomatik görüntü analiz tabanlı bir kromoz tanıma ve sınıflandırma sistemi geliştirmektir (ÇANKAYA SİSTEMİ). Sistemin görüntü analiz fazında yapay objelerin silinmesi, nokta ölçümleri, yapışık ve çakışık kromozomların ayrıştırması gibi problemler çözülmüştür. Kromozomların parametrik olarak gösterilmesinde ve düzenlenmesinde kromozomların boyları, sentromer lokalizasyonu ve bant sayısı, bantlara ait ortalama griton seviyeleri, bant boyutları gibi band paternleri kullanılmıştır. Bu çalışmada amnion sıvısı kültüründen elde edilen kromozom slaytları kullanılmış ve boyama tekniği olarak Giemsa-trypsin G-bantlama tekniği uygulanmıştır. Veri elde edilmesinde Nikon floresan mikroskop, Nikon CCD kamera ve bunlara bağlı çift monitörlü (RGB-VGA) bilgisayar ortamı kullanılmıştır.

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