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#### Introduction

The goals of image and signal processing fell into three main categories: - Visualization,

- -Recognition/Interpretation, and
- Integration.

The first stage is essential and strongly related to the development of measurement methods. The introduction of visualization techniques such as Computer Tomography (CT) and Magnetic Resonance Imaging (MRI) have made a major impact on the medical world. These methods succeeded in visualizing "unseen" objects. The first task of image and signal processing after such discoveries is to find ways to improve the signal-tonoise ratio, improve the spatial resolution, speed up the analysis time, etc. Studies of this type are still in progress. Finding methods to derive as much information as efficiently as possible from a given source is the goal of research in this category. The second stage is to develop image and signal processing methods to retrieve the information necessary to assist tasks such as diagnostics and choice of appropriate therapy. Automatic image segmentation or pattern recognition may fit in this category, as do most of the contributions reviewed in this synopsis. This may imply that the levels of technology of the first stage has reached a high standard and that people are now more interested in how to interpret or utilize visualized data by devel-

Yearbook of Medical Informatics 1997

### **Synopsis**

# **Image and Signal Processing**

oping sophisticated image and signal processing methods. This trend may continue until another revolutionary visualization or signal measurement method appears. The development of measurement methods and signal processing alternate. The third category is showing a promise. A vast knowledge database may be combined with the results of sophisticated image and signal processing for realizing powerful tools for monitoring, making diagnoses or performing therapy. I believe contributions in such a category may dominate before too long. This synopsis introduces six outstanding papers recently published in reputable journals. Five papers are on image processing and one is on time series analysis.

The first paper [1] deals with computer tomography (CT) image processing for efficient contour determination in order to derive useful pulmonary CT parameters, such as mean lung density (MLD) and the emphysema score (ESCR). The extensive evaluations made in this study confirms the reliability of the method.

The second paper [2] introduces a method for three-dimensional segmentation of bone structures from CT images. Gaussian smoothing followed by taking the second directional derivatives is successfully applied for identifying a small sheath surrounding different bone structures, which is helpful in accurate segmentation.

The third and fourth papers [3,4] deal with segmentation of brain images obtained by magnetic resonance imaging (MRI), positron emission tomography (PET) or single-photon emission tomography (SPET). Both studies utilize a model or atlas to find the region of interest. The third paper introduces the elastic transformation while the fourth paper proposes the construction of a probabilistic composite model of the target object in order to fit a priori morphological knowledge to the specific data. Introduction of models or a priori knowledge in image processing adopted in these studies may indicate the future direction of study in this area.

The fifth paper [5] proposes a new spectrophotometric method to estimate hemoglobin distribution over gastrointestinal mucosa for diagnosis and treatment of diseases such as ulcers or gastritis. An elegant estimation scheme utilizing the light absorbing characteristics of hemoglobin and known equations in optics are derived for the estimation. The method is promising for routine clinical use.

The final paper [6] compares four signal processing methods of electroencephalogram (EEG) for assessing the depth of anesthesia. An unsupervised clustering algorithm has been shown to be useful in deriving an index representing the depth of anesthesia. The study demonstrates that existing features, if properly integrated, can yield a consistent index for a specific purpose even in the case where each individual feature is insufficient as a satisfactory index.

#### **CT** Scans of the Lungs

Zagers et al. [1] propose a semiautomatic method of lung contour detection for accurate derivation of pulmonary CT parameters describing the disease state of emphysema. Although several methods are available for contour detection in a general image processing scheme, the authors have made an extensive validation of their method specifically for the CT lung image processing. Single slice CT images with 512 x 512 pixels, 12 bit density at and near the carina level were subjects for study. A total of 78 images were collected from emphysema patients. The method first finds a pixel that belongs to a non-lung body region near the center of whole pixels. An edge pixel in each left and right lung is chosen as the starting point of the contour tracing process. By tracing border pixels between lung and body region, the contour is extracted. The least total cost method was applied to find the septum. The method also removes the trachea or a bronchus automatically, yielding the final result. After the automatic contour extraction, manual correction of the contour can be made. In their study, 27.6% of the data needed manual correction, mainly for bronchi elimination from the lung. Extensive validation of the proposed method was conducted. The areas surrounded by semi-automatically and manually determined contours showed a good agreement, with a slight bias of less than 2.1%. The authors also evaluated intra- and inter-observer variability of the lung area determination using randomly selected image data. For intraobserver variability evaluation, the contours were manually and semi-automatically determined twice by the same radiologist at several weeks interval. The variations in the semi-automatic method are caused by different manual corrections made by the individual. The procedure continues until the radiologist is fully satisfied with the results of the contour determination. The intra-observer variability was shown to be much less in semi-automatic contour determination (0.3% on average for MSE) than manual (3.2%). Manual contour determination also showed significant bias for the same data, whereas no significant bias was observed with the semi-automatic method. For interobserver variability evaluation, the same image data were processed by another radiologist in the same manner as the first radiologist. The bias and MSE were evaluated. The results showed that the bias and MSE values were much higher in manual contour determination (-1.2% vs. 0.2% for bias; 3.7% vs. 0.3% for MSE). We tend to take manual determination as the gold standard for evaluating artificial systems. However, the results show that this is not the case, suggesting that the corrected contours started from automatically determined contours by the proposed method yield more consistent results than manually determined contours. Since parameters useful for the diagnosis of emphysema, such as the emphysema score (ESCR), are accurately estimated once the lung contours are determined, the proposed semi-automatic contour extraction method may be an efficient and reliable tool for making final diagnoses.

#### Three-Dimensional Segmentation for CT Images of Bone Structures

Van Cleynenbreugel et al. [2] describe a semi-automatic method for separating and identifying multiple 3D bone structures from the spiral CT image. The method is important in identifying bone structure in regions where multiple bone structures meets e.g. acetabulum and femoral head The goal of the proposed method is to disarticulate geometrically close but distinct bone structures with little manual interaction. Simple thresholding of the original image tends to cause fusion of such structures due to the partial volume effect. The proposed method is to be applied first to evenly spaced image slices, then extended along the axis perpendicular to the slice plane. For each slice, bone structure candidates are selected by simple thresholding, where the threshold value is determined manually. Then the sheath, connecting part of distinct bones, is detected utilizing Gaussian smoothing followed by taking the second directional derivatives. The derivatives are sensitive to the pixel intensity valley typically seen at the soft tissue separating bones. Knowing the bone boundary, two methods of 3D bone image reconstruction, which they call 2D connected component labeling (CCL) and adapted 3D CCL, are proposed. In CCL, the 3D bone region is constructed as the union of 2D slice regions obtained by the region growing algorithm starting from the user-defined seed pixel. In 2D CCL, the seed pixel is selected at each slice manually while in the adaptive 3D CCD, the seed position information propagates to the next slice, reducing the number of human interactions. A final procedure to remove isolated voxels yields the distinct 3D bone image. Validation was carried out on 10 spiral CT images. An average of 115 slices were processed for each image. The manual and semi-automatic disarticulation methods proposed in the paper and compared. In the manual method seve eral disarticulation lines had to be drawn on 313 slices, whereas much shorter lines had to be added to 64 slices in the semi-automatic method. Further, rendered surfaces appeared to be much smoother when the proposed method was applied compared to the manual method. Although some manual interactions are still necessary, the method could drastically reduce the processing time. With a high-end Unix workstation (IBM RS6000/370), the authors need on average only 30 min. for processing 250 slices.

#### Brain Atlas for Clinical PET/ SPETData

The following two contributions introduce a model or reference data hase in processing image data. Rizzo et al. [3] propose a method which flexibly associates images obtained by positron emission tomography (PET) or single-photon emission tomography (SPET) with the region of interest (ROI). For adequate interpretation (e.g. measuring blood flow at a specific brain region) of the functional PET or SPET images, correct mapping of individual data to a standard ROI atlas is inevitable. To achieve this goal the authors have introduced a method utilizing both MRI and PET/SPET images. The proposed method first uses MRI brain images to achieve slice-byslice correspondence between a standard atlas by Damasios' and PET/ SPET data. Then to achieve the warping of the atlas to the MRI-PET/SPET image, MRI contours of cortical and ventricles are determined by a semiautomatic one-pixel-wide edge detection algorithm. An elastic deformation method is next applied to match the MRI and atlas contours. The derived distortion rule is applied to the atlas to match the ROIs to individual MRI-PET/SPET data. The warping algorithm proposed by the authors based on MRI contour matching with the atlas needs less human interaction compared to the conventional method utilizing the neuroanatomical knowledge for identifying anatomical landmarks. Two examples demonstre the effec-

Yearbook of Medical Informatics 1997

tiveness of the proposed method. MRI and PET images were obtained from a patient (patient 1) in the early stage of Alzheimer's disease, and MRI and SPET images were obtained from a patient (patient 2) suffering from primary sclerosis. The number of slices and space resolutions for MRI, PET and SPET were 128 of 256 x 256; 14 of 128 x 128; 64 of 128 x 128 pixels, respectively. By the proposed elastic procedure, MRI contours are shown to be fitted with the atlas's contours much better than linearly resized atlas contours. Expected abnormalities in both patients were clearly visualized in the correct geometrical ROI after the warping, i.e. hypometabolism in the parietal cortical regions and in the middle and superior aspects of the temporal lobe in patient 1, and hypoperfusion in particular parietal and frontal associative areas in patient 2. These illustrative examples show that the proposed method is promising for clinical use.

#### Segmentation of MR Brain Images

Arrata and colleagues introduce a three-dimensional composite model for accurate segmentation of brain structure. Although the authors propose a general methodology, the method is outlined here in terms of the specific example of segmenting the ventricles and salci. The proposed method first performs initial segmentation of a set of MRI images on slice-by-slice bases for constructing a composite model of the ventricles. The proton density MRI images are subtracted from T2weighted MRI images to enhance the contrast between the cerebrospinal fluid (CSF) and gray matter. The region growing process is applied to each enhanced image for extracting the ventricle area with manual seed pixels selection. Manual corrections by experts were made on the ventricle region for accurate extraction of the ventricle. Lesions observed in some images are removed for accurate construction of ventricles model. Images are then registered by the principal axes registration method for normalizing brain volumes and matching orientations and centroids. A composite model of ventricles is now constructed as spatial probability distribution of the subvolume, i.e. the relative frequency of each pixel included in the ventricles is assigned to the pixel. The model may be regarded as an atlas describing the brain ventricles region taking individual variation into account. Once the model is constructed, model based segmentation yields accurate automatic segmentation for new image data. The model is fitted to the new scan by scaling, rotation and translation. For each slice of the new data, seed pixels (the number of seed pixels depends on the number of connected regions) for extracting ventricles are determined by choosing the pixels for which corresponding model pixels show the highest probabilities to be in ventricles. Then a weighted region growing process determines the ventricle region of the slice. Sulci segmentations are performed next after removing the ventricles from the image. The K-means clustering technique is applied for segmenting sulci. Three brightest clusters are classified as sulci. Validation was made by comparing the subvolume obtained by the model-based segmentation and manual segmentation in 10 cases which are not included in the model construction. A good agreement (less than 3%) was achieved by the comparison. To see the usefulness of the proposed method in practice, the method was applied to MRI images taken from 8 normal and 10 chronic alcoholic subjects. Relative ventricular and sulcus volumes with respect to the total brain volume were compared. Model-based segmentation was successfully applied and the human expert did not need to make any correction to

automatically segmented data. This accuracy may come from a priori morphological information given by the model. Without information of a priori spatial distribution, one would include many pixels with a similar gray level outside of the target region. The results showed that there was no significant difference between normal and alcoholic subjects in the ventricular volume, but the sulcus volumes of alcoholic patients were significantly larger than those of normal subjects implying the presence of cortical atrophy. The method may be effectively applied for such quantitative analysis of the brain pathology.

# Estimation of Hemoglobin in Gastroscopic Images

Englmeier et al. [5] present a new method to estimate the spatial hemoglobin distribution over the mucosa for assessing the blood flow condition, which is an important indicator for treating various diseases such as ulcers or gastritis. The method basically utilizes the fact that hemoglobin exclusively absorbs green light and spectrophotometric analysis enables the estimation. Color image of mucosa is obtained by CCD chips implemented in an endoscope. A single-layer neural network has been introduced for the initial segmentation. The neural network receives red, green and blue color values of each pixel together with surrounding color information, i.e. histograms of red, green and blue color values on the surrounding 17 x 17 pixel regions. The neural network was trained by 10 images with the size of 256 x 256 pixels to extract the region of interest for estimating the hemoglobin concentration excluding undesired image segments such as camera saturation, high light or too dark areas. Then, for the pixels thus chosen, spectrophotometric analysis is applied. First, the equation of estimating hemoglobin concentration was derived by combining the Kubelka-Munk equation and Beers' law. The equation needs the light intensity of reflected and radiated light, since hemoglobin strongly absorbs green light whereas all pigments in mucosa absorb red light weakly. The red and green light intensity could be approximately the measure of radiated light intensity and reflected light intensity for the measurement of hemoglobin concentration. The authors further introduced a transformation as post processing of the data to ensure the luminance independence of estimated hemoglobin concentration. At the bright area, the red-green intensity plot presents nonlinear bending due to the camera saturation which causes biases in estimating the concentration. Rotation of the intensity distribution for such high intensity regions solves the problem. Then applying another rotation of the whole resulting distribution yields the line intersection at the origin. This transformation is essential for deriving a consistent estimation independent from the luminance. The method was applied to 13 endoscopic images where hemoglobin distribution is supposed to be uniform on expert visual inspection. The uniform mean concentration values were obtained by the proposed method regardless of the illumination. Although further validation may be necessary for the method to be recognized as a standard method, the method is attractive and enables measurement in daily clinical practice.

#### Quantitative EEG for Assessing Anaesthetic Depth

Thomsen et al. [6] compare four time series data processing methods of the electroencephalogram (EEG) for assessing the depth of anesthesia. The first and second methods are to monitor single spectral parameters, i.e. the median and edge frequency. The third method, called cerebral function analyzing monitor (CFAM1), is to monitor several amplitude and frequency domain parameters. Amplitude parameters are the mean, 10th and 90th centiles, maximum and minimum amplitude, percent time of EEG suppression (<3 micro volts). Frequency domain parameters are frequency band energy of  $\beta_2(>20 \text{ Hz}), \beta_1(14.3-20)$ Hz),  $\alpha 2(10-14.3 \text{ Hz})$ ,  $\alpha 1(7.7-10 \text{ Hz})$ . θ2(5.3-7.7 Hz),θ1(3.5-5.3 Hz),δ2(2.0-3.5 Hz),  $\delta 1(1-2$  Hz) and very low frequency (<1 Hz), fast/slow EEG frequency ration  $(\beta 1 + \beta 2 + \alpha 2 + \alpha 1)/(\theta 2)$  $+ \theta 1 + \delta 2 + \delta 1$ ). These parameters are obtained for every two seconds. The fourth method called advanced depth of anesthesia monitor (ADAM), processes both amplitude and frequency domain parameters yielding a single parameter representing the depth of anesthesia. An unsupervised repetitive clustering algorithm was applied to form a set of reference patterns for each depth of anesthesia. Then, the algorithm estimates the class probability for a given data segment. A single numerical value index representing the depth of anesthesia is assigned based on this class probability distribution in such a way that the value six represents very deep anesthesia and value one indicates a drowsy state. EEG suppression time was used for modifying the index representing the depth of anesthesia. The above mentioned four methods were compared on the same 24 EEG data recorded from 24 normotensive subjects. Although some parameters showed high correlation with the depth of anesthesia, e.g. fast/ slow EEG power ratio or median frequency for anesthesia by Isoflurane, none of the time and frequency domain single parameters showed a good monotonic relation over the wide depth range of anesthesia. The index value of the depth of anesthesia obtained by the ADAM system showed good monotonic relation with the depth of anesthesia for both agents, Isoflurane and Halothane, tested in this study. Although the authors remark that inter-patient variability is still large, development of a such system integrating multiple features for the complex decision may be a future mend in the field of biosignal processing.

#### Conclusion

Judging from the number of contributions in journals addressing biomedicalimage and signal processing, image processing of CT, MRI, PET or SPET data seems to be a major concern of researchers and clinical practitioners. For automatic segmentation of a target region of a complex object such as the brain, the model-based approach as reviewed in this synopsis may be a promising direction of research. Extensive validations of the image processing methods, independently proposed and in different contexts at present, may lead us to a standard image processing scheme in the near future. Integration of a priori knowledge as well as a number of known parameters for designing sophisticated intelligent system may be a key notion not only for image processing but also in time series analysis, as indicated in the last article discussed here.

References

- 1. Zagers R, Vrooman HA, Aarts NJM, Stolk J, Schultze Kool LJ, Van Voorthuisen AE, Reiber JHC. Quantitative analysis of computed tomography scans of the lungs for the diagnosis of pulmonary emphysema. Invest Radiol 1995;30:552-62.
- 2. Van Cleynenbreugel J, Kratka D, Berben L, Smet MH, Marchal G, Suetens P. A semiautomatic three-dimensional segmenation method for disarticulation of bone structures on spiral computed tomography images. J Dig Imag 1995;8:156-61.
- Rizzo G, Gilardi MC, Pronster A, Grassi F, Scotti G, Cerutti S, Fazio F. An elastic computerized brain atlas for the analysis of clinical PET/SPET data. Eur J Nucl Med

1995;22:1313-8.

- Arata LK, Dhawan AP, Broderick JP, Gaskil-Shipley MF, Levy AV, Volkow ND. Three-dimensional anatomical modelbased segmentation of MR brain images through principal axes registration. IEEE Trans Biomed Eng 1995;42:1069-78.
- Englmeier KH, Herpers R, Jacoby RS, Zwiebel FM. A method for the estimation of the hemoglobin distribution in gastroscopic images. Int J Biomed Comput 1996;41:153-65.
- 6. Thomsen CE, Prior PF. Quantitative EEG in assessment of anaesthetic depth: Comparative study of methodology. Br J Anaesth 1996;77:172-8.

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