Eli Peli, Reed Augliere, and George Timberlake, Fast Registration of Digital Retinal Images, Noninvasive Assessment of the Visual System Technical Digest, 87-4 (Optical Society of America, Washington, D.C. 1987) pp. [61]-[64].

Fast Registration of Digital Retinal Images

Eli Peli, Reed Augliere, and George Timberlake
Eye Research Institute, 20 Staniford Street, Boston, MA 02114

Registration, or alignment, of retinal images taken at different times is frequently required in image-processing applications. Images that need to be registered may be separated by a few years and may show slow changes in the retina. Such changes include drusen, nerve fiber layer damage, and changes in optic disc cupping and pallor. Registration may also be required for pictures taken only a fraction of a second apart, as in measurement of dilution curves in fluorescein angiography or at video rates required in fundus perimetry using the scanning laser ophthalmoscope (SLO).

Most researchers used the cross-correlation method for fundus image registration in the past (1,2). Preprocessing of the two images with high-pass filtering is usually required to obtain a sharp peak (1,3). However, this approach is computationally intensive and may require a lengthy calculation time even with fast main-frame computers (1). Various procedures to speed the calculation of the cross-correlation coefficient have been implemented (1,4). Because of the lengthy computations, numerous researchers have used manual techniques to register fundus images (2,5). In all of these applications, the operator used the vascular pattern of the retina as the main cue for registering the images. This selection is natural because the retinal background is fairly uniform, and the vessels occupying only a small percentage of the area are very distinct. A different registration method, sequential similarity detection (SSD), proposed by Barnea and Silverman (6), is up to 100 times faster than the correlation method. We have developed a feature-based modification of the SSD, which improved the speed and reliability of the registration by simulating the human operator's detection of vessels in the fundus images, registering the images quickly, and then refining the vessels' registration.

Featured-Based SSD

The process of matching a template in a search area is common to many registration techniques. A window $F_1(j,k)$ of size J x K is defined in one image as the template. Another window $F_2(j,k)$ of size M x N in a separate image is defined as the search area. The template window is then shifted across the search area, and a similarity measure is calculated. The point of maximal similarity is designated as the match position. The SSD method improves this process by using the sum of the absolute values of the differences (SAVD) as the similarity measure. The algorithm accumulates an error of normalized absolute values of differences:

$$E\,(m,n) = \sum_j \sum_k [F_1(j,k)-TT] - [F_2\,(j-m,\ k-m) + SS\,(m,n)] \qquad (1)$$

where TT is the average of the template's grey levels, and SS is the local average of a section of the template size within the search area. The summation of the cumulative error is taken only on the subgroup of the possible J x K template points for every position (m,n). If the cumulative error E (m,n) exceeds a predetermined threshold value before all points in the window are examined, the test is completed, the number of points tested up to this point- - called the count- - are recorded, and the window is shifted to the next position within the search. When all positions have been examined, the position with the maximal count, indicating the largest number of points that had to be examined to reach the threshold, is defined as the point of registration.

In the original SSD algorithm (6), the points selected for calculating the cumulative error in every template position are chosen randomly. This may be the best way to select those points without a priori knowledge of the image, but it is inefficient in the case of fundus photographs. Fundus photographs usually contain large areas of fairly uniform brightness representing the retinal background. The pattern of retinal vessels makes each fundus photograph unique and, thus, provides the most relevant information for the registration process. We have, therefore, modified the SSD algorithm to select points in a template used for calculating the accumulated error from the vessel position in the template window.

The operator can manually select vessel points using a cursor driven by a graphics bitpad or an automatic preprocesser. Selecting those points is required only for the template, not for the search area. For this reason, the preprocessing overhead in selecting the template is minimized. Vessel points in the template are detected automatically using an adaptive thresholding procedure (5).

Comparison of Registration Techniques

To evaluate the differences among the registration methods, the program was modified to display the similarity measure from each technique as a grey scale image. A series of different fundus images were then processed with all three techniques, and the resulting similarity surface images were compared visually.

Images selected for this study included routine fundus photographs, fluorescein angiograms, and SLO images. Two fundus photographs featured a patient with age-related maculopathy (Fig. 1) and with drusen in the macular area. One picture was taken in 1980, and the other in 1983. The images were then registered once with the standard SSD (Fig. 1C), using randomly selected template points, and again with the feature-based SSD, using the manually selected vessel points (Fig. 1D). The same images using the same template and search area were then processed according to the cross-correlation process (Fig. 1E). Fig. 1 represents the typical results of these experiments on the three types of images. The vascular pattern of the original search area was evident in the images representing all three similarity measures. However, these images clearly differed. Although the feature-based SSD method produced a sharp, well-delineated image of the vasculature in the search area, the standard SSD produced multiple reflections of a similar image at different phases. The vascular pattern was apparent also in the cross-correlation image, but this image was a blurred version of the feature-based SSD count surface. The line scans taken through the matching points illustrated the same difference, i.e., a smoother, less distinct peak for cross-correlation than for SSD, and an even sharper peak for the feature-based SSD than for the standard SSD. The line scans also demonstrated that the count at the match point was higher for the feature-based SSD than was the standard SSD.

The program was modified to run for each image pair at all integer threshold values between 1 and 300. A printed output was obtained with a threshold level, the corresponding coordinates of the selected matching point, and the count of points tested at the selected matching point. Both fundus photographs and SLO images were tested this way. The feature-based SSD was very reliable in that once correct detection was achieved, it was maintained for all higher threshold levels tested, but the standard SSD fluctuated between correct and grossly incorrect registrations for similar values of threshold.

Two-Stage Registration

Using the SSD algorithm, template positions that are likely candidates for match have a slow rate of error increase. This rate can be estimated simply by evaluating the count at different threshold levels. As each temporary threshold is passed, the count at that point is tested; a "high" count represents a "likely" candidate for matching. Since we found that the correct matching was included in the 10 most likely points even for very low threshold levels, using a two threshold-two stage technique to accelerate the feature-based algorithum further seemed safe. A two-stage algorithm was applied in the following way: A low threshold level was selected, such that the count at matching point and other likely points was fairly low: 1 to 2% of the template points. When this threshold was reached, the count was tested; if the count exceeded 1% of the points, the threshold for this template position was multiplied 4 times, and the process continued. Thus, more template points were examined, and the error continued to accumulate. When the new threshold was reached, the process was completed, and the template was shifted to the next search position. If the count was less than 1% of the template points when the initial threshold was reached, the position was considered an unlikely match, and the template was shifted to the next position. In this process, positions of unlikely candidates were determined by evaluating less than 1% of the template points. Likely candidates for high similarity measure was defined by the threshold elevation and the continuation of the feature-based SSD process. This process is analagous to manual processing whereby vessels are aligned quickly, and vessel positions in the two images are refined for accurate overlap.

Discussion

The standard SSD algorithm and the sum of absolute value of difference (SAVD) algorithm have been compared with other similarity measures (7,8). Both were found to be inferior because they had more erroneous registrations than the cross-correlation coefficient method (7) and the stochastic sign change (SSC) measures (8). However, in both cases, the non-normalized version of the algorithm was used rather than the normalized one. Although the non-normalized version is faster, it is prone to errors in registration, especially if the images differ significantly in illumination. Even with this version, the algorithm performed well in both tests; Svedlow et al (7) indicated that if computation time is examined, the non-normalized SSD is better than the cross-correlation coefficient algorithm. Although the normalized version of the SSD is more extensive computationaly, it is still up to 100 times faster than the cross-correlation method with proper programming (6). The overhead calculation cost for modifying the SSD algorithm by selecting the template first from the vessel was relatively low. This modification also increased the reliability of the registration. With the modified SSD algorithm, the two-stage approach was implemented successfully and maintained higher reliability while accelerating the calculation further.

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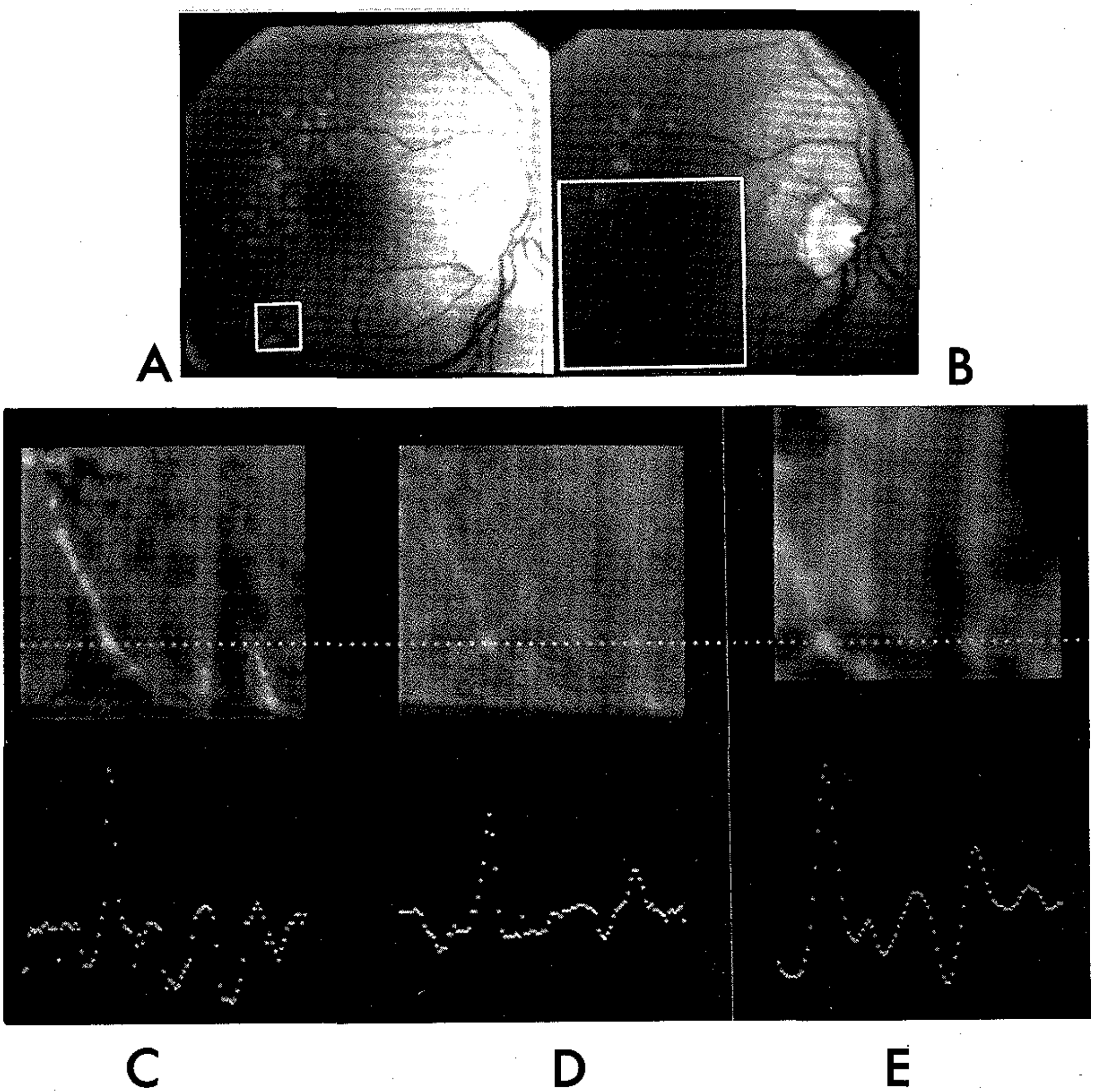

Fig. 1. Comparison of similarity measures used for registration.
A) Fundus photograph taken at 1980 with the template area marked. B) Same eye photographed at 1983 with search area marked. C) Count surface from feature-based SSD. Note clear appearance of vascular pattern. The curve (bottom) represents count measure across illustrated line. D) The count surface obtained with the standard SSD. Vascular pattern is less apparent, and peak at registration less sharp. E) The cross-correlation surface is a blurred version of the image in C.

This work was supported in part by grants R01-EY05450 and R01-EY03966 from the National Eye Institute.