PROPOSAL FOR AN AUTOMATED SYNTHESIS OF MORPHOMETRICS AND IMAGE ANALYSIS FOR SOLID MEDICAL IMAGES

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Abstract: We review recent developments in morphometrics and image analysis with an eye toward their synthesis. Over the last decade, it has become possible to apply all the usual methods of biometric statistics to configurations of landmark points. Hitherto this information has been used for the description of form without further reference to pictorial content, which is typically analyzed separately for densities, lucencies, abnormal textures, and other visual anomalies. We propose a synthesis of these two traditions of analysis, one which will support, for instance, a distinction between a diagnosis of "wrong texture" associated with an appropriate structure. Statistical comparisons of a single patient's surface form with the mean and range of a large normative data base will make possible a systematic approach to the semiautomatic detection of disease states.

Introduction

Our interest is not in rendering one image at a time but in quantitative image understanding taken many at a time. Recent advances in this sort of medical image analysis have dealt with highly constrained subsystems: for instance, the beating heart. We propose to extend to studies of moderately constrained static anatomy (the contents of the skull, or of the pelvis) the sort of technology that has proved successful in applications to more strongly constrained dynamic systems. It is time that the technology of CT and MR anatomical imaging was turned to the measurement of what the clinicians look to these images to report, namely, the presence or absence of disease, and its characterization.

The key to the formalization of diagnosis that we are exploring here is the notion of a landmark configuration, a set of individually labelled points ("bridge of the nose," "tip of the chin") that can serve as guide for the deformation of one whole medical image onto another. The main advantage of landmarks is the existence of a complete statistical method for analysis of data in either two or three dimensions. (For reviews, see Bookstein, 1991a; Rohlf and Bookstein, eds., 1990, Goodall, 1991) Techniques available for routine application include the description of differences between groups, the computation of classification probabilities for cases into groups, the description of systematic effects such as age, dose, or extent of surgery upon form, and the extraction of statistically efficient components or factors underlying all of this information. Nevertheless, the sampling of a medical image by its landmark point locations omits considerable information about the curving of edges and, in three dimensions, of surfaces, and even more information about the grey levels at picture points "in-between the geometry."

At present this missing information may be used to supplement the biometrics of the landmark locations by one of two devices. In one approximation, edge points that are not landmarks are extracted from the differential information and then treated as if they had anatomical meaning. Examples of these include centers of structures and vertices (extrema of curvature) and inflections on curves or surfaces. In the other approach, points are selected arbitrarily upon regions of curves or surfaces as traced according to gradients of grey level, and then treated as if they were landmarks, except in that the statistical computations are instructed to ignore information known in advance to be arbitrary. Usually this discarded information takes the form of one or more coordinates of such pseudolandmarks. We call these coordinates deficient. In either of these techniques, all the pictorial information not somehow concentrated into the geometric
An interesting combination of these techniques is the notion of the ridge curve (Bookstein and Cutting, 1988). Many anatomical surfaces incorporate extended three-dimensional curving lines away from which the surface falls off relatively sharply on both sides. We call such lines ridge curves; they are the same as the "ridges" of Koenderink (1990). Examples from the human head include the orbital rims and the lower border of the mandible. Our current operational definition of curves like these makes no reference to any biological information. Rather, on an automatically detected bony surface, an algorithm weights the purely geometric information about curvature at appropriately sampled surface loci and links up candidate points into connected curves. It is surprising how often curves detected almost purely automatically in this way include recognizable points having a clear anatomical identity. Examples of such hybrid landmarks include the "corners" of the orbital rim and the angle of the lower jaw on the mandibular border ridge. These points serve as landmarks for the ridge curve itself, from which they can be extracted automatically by some further differential geometry (for instance, as curvature or Darboux curvature maxima of smoothed models).

Curves on form, whether these ridge curves or instead true biological features like center lines of vessels, have one deficient coordinate at every point that is not itself a landmark (endpoint, branch point, or one of the extrema of curvature mentioned above). Continuing up the hierarchy of dimension, we might wish to treat points on surfaces in-between ridge curves as if they had two deficient coordinates that correspond to the traditional (u,v)-parameterization from classic differential geometry. The only coordinate with a biological identity is that in the direction of the surface normal; the others are deficient, in that they do not include information relevant to the comparison of one form to another.

Points of ridge curves thus have one fewer deficient coordinate than have neighboring points on the surface. Other ways of making additional coordinates of surface points meaningful include the quantification of surface texture (as along sutures) and the direct extraction of landmarks from surfaces by properties of the curvature tensor. (For instance, Nasion, the bridge of the nose, is a "saddle point" of extreme negative Gaussian curvature.)

Finally, points inside homogeneous volume regions may be considered to have three deficient coordinates, that is to say, no morphometric significance at all. Their grey levels contribute not to an understanding of the geometry of form but only to the various integrals and derivatives that make up the analysis of pictorial content.

In this way, the grey levels of a solid medical image may be decomposed, point by point, into a combination of geometric and pictorial information totalling, at all points, three dimensions in addition to the original grey level. (For multispectral images, the count of dimensions of content is to be altered appropriately.) The typical point inside a volume has no geometric information but three coordinates' worth of pictorial information (i.e., the gradient of grey level there). A surface point has one geometric coordinate that is not deficient (that along the surface normal) plus two dimensions' worth of pictorial information inside the surface. A typical point on a space curve has two coordinates and one pictorial dimension (for instance, its gradient along the curve). Finally, a landmark has fully three Cartesian coordinates, but no information about image fields, only a single (scalar) grey level at that point.

A literature is just beginning to emerge combining morphometric information with grey-level information according to this complementarity. In this approach, which is presently limited to the consideration of landmarks and ordinary (wholly deficient) points only, any landmark configuration is used to define an "unwarping" of the image at hand onto a typical or average configuration. The shape standardization of the landmarks by a statistically convenient interpolation (Bookstein and Jaynes, 1990; Bookstein, 1991b; Evans et al., 1991) applies to every pixel of the original image to produce a new picture which presents the patient's pixel values in the standardized places. In the standardized image we can then proceed to compute averages, discover correlates of function or treatment, trace averaged gradients, and so on. However, the statistical properties of these standardized images are not at present being used to aid
in the complex task of image analysis that produced the detected empirical features (so far only points, but in principle curves and surfaces as well) on which the morphometric and pictorial statistics are based. In our view, the reversion of morphometric statistics so as to improve the image analysis that ostensibly precedes would represent a major leap forward in the analysis of form, of pictorial density, and of their combination, which is the detection of medical anomalies in images. At present this crucial contribution of the physician's eye to the comprehension of a medical scene lacks automation almost entirely. The next section informally advances a research paradigm to explore automatic modelling of this process.

**A Research Programme**

We propose to pursue the following series of thrusts as they apply to single solid medical images in the presence of a normative data base.

1. **Find** topologically connected surfaces around easily identified homogeneous solids within the form (e.g., bone, ventricles). Current three-dimensional image processing methods seem competent to this end. Some surfaces will separate two different volumes, while others will bound only one. "Homogeneous" is, of course, a fuzzy notion; eventually data bases will provide statistical criteria (e.g., gradients and their standard errors) tissue by tissue.

2. **Extract** features from these topologically connected solid boundaries: identify diverse geometric landmark structures—discrete points, ridge curves, and center lines. Many of these extrema will prove to incorporate biological landmarks in the usual sense. Whenever the processing to this point is in parallel, "blackboard" methods can automatically sort out features according to appropriately coded normative schemes. (E.g., of all the Gaussian curvature maxima of the heart, the apex is the one at the bottom; of all the saddle-point landmarks on the skull, the bridge of the nose is the highest.)

3. **Interpolate** the correspondence of landmarks to as to apply to all voxels. (Properly speaking, the role of landmarks is to serve as a discrete sample from these maps, which are called homology maps; landmarks sample the homology map, not the individual picture.) The interpolation function ought to incorporate as many pseudolandmarks as possible, so as to map curves onto biologically corresponding curves, and surfaces onto surfaces, within some geometric criterion of adequate fit. An immediate technical question arises as to whether textures are copied unchanged or instead are altered by the Jacobian of the transformation implied.

At this stage of the procedure, the match of warped structures from the normative data to detected edges and surfaces of the patient data should usually be close enough to label regions of the patients with names from the atlas. Now we switch our attention from the geometric to the pictorial coordinates of our voxels:

4. **Delineate** homogeneous volumes and textures of the solid regions whose bounding surfaces have been identified in the preceding step. The notion of "texture" may be a simple as grey-level itself (Besl and Jain, 1988) or may extend to more complex volume textures such as bone marrow or lung, the output of arbitrary neighborhood-based computations, multispectral syntheses, and the like. In the language of biology, we are attempting to detect organs or tissues by their histological characteristics now that we have exhausted information about the geometry of their boundaries.

5. **Recursion.** These four steps should be recursive, beginning with homogeneous volumes (like cortical bone) that are easily segmented and proceeding to volumes that are progressively more difficult to identify without prior knowledge of anatomical form and its variability. In particular, the determination of boundaries as "limits" of homogeneous texture is a function of "where you are". Tentative boundaries computed locally, in step 4, will thereby be interrelated with topologically global aspects of thresholds. For example, the orbital rim ridge curve, step 2, needs to be extended over the inner margin along the surface of the relatively flat lamina papyracea of the ethmoid bone; afterwards, the orbital socket needs to be integrated into a topological cone over the various pseudoforamina that arose as a result of the thinness of these facial bones. As another example, the expected geometric relation between kidney and ureter is different between left and right kidneys,
even though they have the same texture.

6. Diagnose. At the "termination" of the conceptual algorithm of paragraphs 1-5, all regions of homogeneous volume texture will have been detected and bounded by topologically connected surfaces separating solids. The human body is then represented as a hierarchy of non-intersecting shells partially ordered by inclusion. (For a different approach to this same sort of decomposition, see Gauch, 1991.) From this hierarchy of solids and textures we propose to pass to a categorization of a range of previously identified disease states, as follows:

a. Topological discrepancy between the patient's and the normative data set. These include "extra volumes" cysts, foreign bodies, tumors and the like-and "missing volumes" such as unilateral renal agenesis. Also included under this heading are volumes that are misarranged with respect to their surroundings, such as bones in the vicinity of a fracture.

b. Statistically significant deformation of the configuration of landmarks, curves, and surfaces of one or more solid regions. These are the classic deformities, here detected as deformations of normal outside convenient statistical bounds given by analysis of normative data sets. Examples include hydrocephalus, craniofacial malformations, liver enlargement, cardiomegaly, various stenoses, and many others.

c. Statistically abnormal textures within otherwise "normal" volumes. These are image-processing abnormalities, i.e., "picture problems." Examples include fibrosis of the lung, osteoporosis, Binswanger's disease, and many others.

Conclusion

Our argument terminates prematurely because the two traditions we are proposing to connect have hitherto been kept quite separate. Thus, there is a considerable literature of geometric morphometrics, and a considerable literature of texture analysis, but relatively little interplay between them; the only counterexample that seems well-developed is the topic of optical flow. Beyond that, the simple tradeoff (geometric against textural) regarding degrees of freedom at a point, the tradeoff spurring on the project sketched here, has not hitherto been exploited for the automatic and semiautomatic conversion of medical images into near-diagnoses. In the presence of steadily cheaper parallel hardware and the adaptation of artificial intelligence techniques to exercise the wonderful redundancy generated thereby, we believe that breakthroughs are possible in regard to algorithms that see "what physicians see" in the cortex, not merely on the retina. The combination of modern tools of morphometrics, image analysis, and texture analysis is ripe for exploitation at this time.

Acknowledgements

Preparation of these comments was supported in part by NIH grants DE-09560 to C.B.C. and CM-37251 and NS-26529 to F.L.B.

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