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Coordinate-based versus structural approaches to brain image analysis

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Abstract

A basic issue in neurosciences is to look for possible relationships between brain architecture and cognitive models. The lack of architectural information in magnetic resonance images, however, has led the neuroimaging community to develop brain mapping strategies based on various coordinate systems without accurate architectural content. Therefore, the relationships between architectural and functional brain organizations are difficult to study when analyzing neuroimaging experiments. This paper advocates that the design of new brain image analysis methods inspired by the structural strategies often used in computer vision may provide better ways to address these relationships. The key point underlying this new framework is the conversion of the raw images into structural representations before analysis. These representations are made up of data-driven elementary features like activated clusters, cortical folds or fiber bundles. Two classes of methods are introduced. Inference of structural models via matching across a set of individuals is described first. This inference problem is illustrated by the group analysis of functional statistical parametric maps (SPMs). Then, the matching of new individual data with a priori known structural models is described, using the recognition of the cortical sulci as a prototypical example.

Keywords: Brain mapping; Structural models; Model inference; Matching with a model; Markovian random fields; Random graph; Cortical sulci

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1. Introduction

The brain complexity often leads neurosciences to employ a reductionist strategy that focus on elementary cerebral processes and their interactions. Each high level cognitive system is then supposed to result from the cooperation of a set of modules, each module relying on neural computations performed in a specific brain area. Assuming that the brain architecture is deeply related to this distributed organization, a number of investigations intend to put forward architectural and cognitive structural models to discuss their possible relationships [10,20,33,62,63,71,79] (see Fig. 1). Most of these attempts, however, have been restricted to animal studies. Architectural subdivisions, indeed, are not yet accessible non invasively. Therefore, while some of the putative modules of the structural cognitive

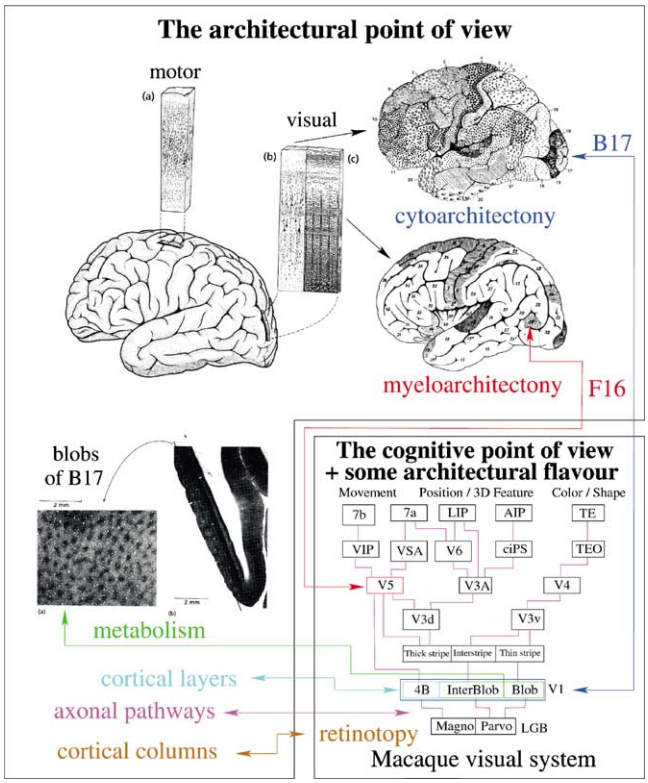

Fig. 1. Relationships between the cortex architecture and the macaque visual system [20,71]. The modules of the lowest levels of the cognitive model correspond to areas of the cortical surface parcellations related to variations of the micro-architecture (types of neurons, development of the myelin around axons, etc.), or to subdivisions of these areas related to cortical layers, metabolism or connectivity differences [4,6,23,50,61,73,79]. Furthermore, some of these modules are endowed with a retinotopic organization, namely an isomorphism between the underlying cortical surface patch and the retina surface, which is discretized by cortical columns orthogonal to the cortex surface [47]. Finally, communication between these modules relies on the connectivity induced by axonal pathways, that have been mapped for the macaque [50,55,62].

models specific to the human brain have been given a gross localization, thanks to functional imaging technologies, their architectural substratum remains unclear.

In this paper, we use the term ''structural model'' to refer to a set of entities linked by various relations (brain areas linked by fiber bundles, cognitive modules linked by communication means, etc.). It should be noted that the term ''structural'' is also often used in the neuroscience field to mean ''related to brain architecture''. This confusion in wording that we will try to avoid simply stems from the fact that brain architecture is a huge structural network made up of neurons and synaptic connections. While the structural models aiming at describing this network may often rely on oversimplifications, they seem necessary to underpin thought on brain organization.

The discussions concerning the nature of psychological phenomena and their neurobiological bases invariably make reference to the notion of levels. For instance, brain architecture can be described at different scales: synapses, neurons, columns, maps, and systems. A host of neuroscience techniques have led to some structural models of the highest levels of organization, which are of interest for neuroimaging studies. For instance, such models consist of cortical surface parcellations in various areas according to differences in cyto-architectony (types of neurons), myelo-architectony (axon local organization), connectivity and metabolism tracers [4,6,23,50,61,73,79]. These models provide also information about forward and backward connections between areas for several animal species, thanks to invasive tracer studies [50,62].

It has to be understood, however, that these structural architectural models are far from providing an exhaustive description of the brain organization. The micro-structure of the cortex, indeed, may embed a lot of additional subdivisions, which is a subject of intensive research [29]. Moreover, an area may be homogeneous relative to microstructure but include sub-areas involved in different processing because of different connectivity. Hence a lot of further subdivisions may stem from a detailed study of the brain connectivity, which is still to be done for the human brain [50]. Finally, the current strategy used to represent the brain architecture may fail for putative cognitive modules corresponding to neural networks distributed throughout the whole brain rather than inside a localized area.

While a flurry of objections can be raised against the current oversimplified architectural models, they have provided invaluable **reference systems for neuroscience studies**. These brain segmentations and their connectivity, indeed, are supposed to be reproducible across individuals of the same species and are endowed with important similarities across species. This opens the door to comparative studies and attempts to understand the mammalian brain evolution [48,52]. Therefore, a number of neuroscientists try to match their putative structural cognitive models to these structural architectural referentials, which are used as the natural basis of brain mapping.

The primary objective of this paper is to highlight the gap between this structural point of view of standard neurosciences which is based on invasive animal studies, and the coordinate-based image analysis methods that have been put forward in the neuroimaging community during the last decade. The second objective is to show that the structural strategies common to the field of computer vision may allow the development of another family of brain image analysis methods that would fit better with the standard neuroscience point of view. We develop this idea using several examples related either to the inference of

new structural models via matching across a set of individual data, or to the matching of new individual data with a priori known structural models.

2. Iconic spatial normalization

Unfortunately, most of the architectural information underlying the reference systems used in standard neuroscience can not be accessed in the living human brain. Therefore, the neuroimaging community has designed its own reference system in a very different way [65,66] (see Fig. 2). This system, which was required to compare functional images across individuals and across experiments [24], relies on 3D coordinates indicating a location in a template, and is called the proportional system. Each new brain is endowed with this coordinate system through spatial normalization, namely a 3D deformation that aligns the individual macroscopic anatomy with the template brain anatomy [13,26]. The simplest approaches rely on affine transformations only, while modern registration techniques can now provide complex warping relying on a large number of degrees of freedom, that are supposed to improve the normalization. In the following, we will call "**iconic spatial normalization**" this kind of processing.

The iconic spatial normalization paradigm, originally introduced to overcome the poor statistics of positron emission tomography (PET) data, has made a tremendous impact on brain mapping strategies [19,44,25]. Thanks to the large diffusion of free softwares, the proportional system is now a standard which allows dense communication inside the

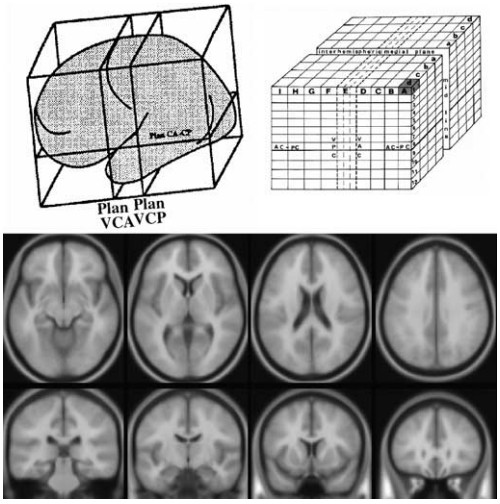

Fig. 2. The 3D proportional coordinate system used by the brain mapping community was introduced before the advent of modern neuroimaging for neurosurgery purposes [65,66]. A few landmarks were used to orient and scale any brain into a standard stereotactic grid (up). The modern approach relies on automatic registration with a template made up of the average of a large number of brains manually aligned with the proportional system [13,26]. The usual template (down), based on 305 different brains, has been provided by the Montreal Neurological Institute [18].

community [13,26]. The coordinate-based approach, indeed, is very versatile: brain images from any imaging modality can be simply compared across individuals on a voxel by voxel basis. Nevertheless, it has to be noted that the normalization approach fathers some frustrations when one tries to link neuroimaging results with standard neuroscience knowledge. For instance, no one to one translation can exist between the proportional coordinates and the Brodmann architectonic areas, because of the remaining inter-individual variability of brain architecture after iconic spatial normalization [5,6,35].

The advent of functional MRI has largely increased the frustrations induced by the proportional system. Indeed, this modality allows easy detection of the individual brain activations induced by cognitive experiments. Therefore, since the iconic normalization framework is no longer required for detection purpose, its well-known weaknesses with regard to inter-individual matching of sulco-gyral structures (the cortical surface folds) give rise to continual questioning [5,31] (cf. the blurred template of Fig. 2). For instance, it seems rather difficult to perform reliable coordinate-based group studies without spatially blurring the data, when the number of subjects is small (see Fig. 3). Alternatively, the new application of the iconic normalization framework that compares grey and white matter densities across different populations on a voxel by voxel basis often involves hundreds of subjects, which is unfortunately more difficult to achieve for functional experiments [1,30,74].

Before discussing further strengths and weaknesses of iconic spatial normalization, we have to become aware of a very surprising fact: a number of different normalization algorithms are used throughout the world, each one leading to different results [16,32]. Even statistical parametric map (SPM) software proposes a lot of alternatives related to the deformation parameters or to the choice of the template [26]. This observation means that what is called spatial normalization is far from being clear simply because nobody really knows how to match brains. Furthermore, nobody knows today to which extent matching two different brains with a continuous deformation makes sense from a neuroscience point of view. Nevertheless, the brain mapping community needs methods to compare brains, even if they are not perfect. An important question remains: what is the best way to design a spatial normalization procedure overcoming as far as possible the problems induced by the complexity of the cortex folding patterns?

It seems reasonable to think that the weights given to the various macroscopic anatomical landmarks used to drive the iconic spatial normalization should be related to their architectural value. This idea calls for instance for an accurate matching of each basal ganglia (groups of neurons located inside the brain) boundary with the corresponding boundary of the template brain. However, what remains largely unclear is the best way of dealing with cortical folding. Indeed, while some major sulci are usually considered as good indications of architectonic or functional transitions, few people postulate that this property can be extrapolated to all cortical folds [56,76,80]. Furthermore, this question is very difficult to address because a lot of the cortical sulci look different across individuals [49].

3. Future of iconic normalization

A number of teams try to overcome current difficulties via more sophisticated iconic normalization procedures [68]. In our opinion, without a better understanding of the

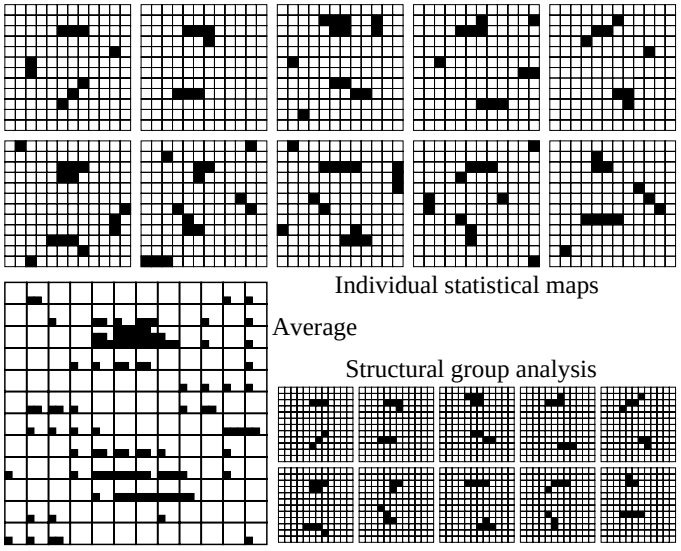

Fig. 3. This figure provides a caricature-like illustration of the problem induced by a coordinate-based approach during the analysis of an experiment involving several subjects. The top 10 images correspond to simulated thresholded statistical parametric maps (SPMs) obtained from 10 different subjects [27]. These maps provide for each voxel a probability of activation induced by the cognitive experiment. Each map includes two clusters supposed to correspond to the interesting activated areas and a few spurious clusters. The upper activation has a relatively stable localization in the coordinate system, while the lower one has not a very precise position. Bottom left: The 10 maps have been averaged (the black zone of each pixel is proportional to the number of subjects with black pixel at the same place). Note that in real studies, the averaging process occurs before thresholding individual maps. The lower activation is difficult to distinguish from noise using a simple threshold and a pixel by pixel approach. In real applications, spatially smoothing the initial data, performing a cluster analysis in the average map or increasing the number of subjects partly overcomes the problem [53]. Bottom right: The result of an ideal structural group analysis [15] detecting two clusters in each individual map. The comparison of the individual maps is performed on a cluster basis rather than on a pixel basis. More or less sophisticated distances between clusters, possibly relying on the coordinate system, are used to match them. An individual cluster is selected if a close cluster can be found in a number of other individual maps.

inter-individual variability of the cortical folding patterns, most of these works are bound to drift toward pure **morphing approach** without consistent architectural justification. It should be noted, however, that some teams have chosen to impose some constraints in the morphing procedures leading to match explicitly some of the cortical sulci [9,11,67]. In our opinion, this direction of research is much more reasonable than a blind morphing procedure only driven by image grey levels, even if some progress have to be made with regard to the automatic identification and the choice of the sulci to be matched.

To overcome some of the problems induced by the standard volumetric approach, several teams have proposed new methods dedicated to the cortical surface [22,40,72]. This new point of view consists in using the 2D topology of the cortex to create **2D reference systems**, like latitude and longitude on earth. This approach simplifies the matching of the main cortical folds, although a lot of issues remain open. Most of the 3D applications find a 2D analogue. For instance, voxel-based morphometry becomes coordinate-based cortical

thickness analysis [21,40]. However, the structural point of view is not embedded in this 2D approach, which is still coordinate-based. Hence, while the surfacic approach improves the analysis of cerebral cortex related data, the weaknesses induced by the lack of architectural information behind the coordinate system remain.

As a consequence of the coordinate system paradigm, a lot of the studies reported in the brain mapping community are called "**probabilistic maps**", which are providing the remaining variability in the localization of various features after spatial normalization. Some projects focus on atlases of cytoarchitectonic areas [59,60], other ones are interested in various cortical macroscopic features like sulci or cortical thickness [45,69], finally most of the functional results stem from some averaging in the proportional system, which amounts to the same kind of maps [19,25].

Although the idea of coordinate-based map has led to a lot of interesting neuroscience results, the spatial normalization behaviour leads usually to fuzzy maps that disturb the meta-studies looking for relationships between the architectural and functional maps. Moreover the variability intrinsic to the spatial normalization process is mixed up with the variability of the feature under study. Finally, the averaging process is bound to hide various information related to subpopulations, variability in cognitive strategies during experiments, etc. Of course, the methods embedding the normalization framework will be refined in the future, but in our opinion, an interesting structural alternative may be found for most of the standard treatments.

4. Emergence of structural methods

The idea of using the 2D topology of the cortex for MR image analysis was not proposed initially to design a new coordinate system, but to perform "**retinotopic mapping**" of the primary visual areas [70]. The inner organization of primary visual areas, isomorphic to the retina, allows the design of fMRI experiments leading to a parcellation of the visual system, which is used as a referential for further study. This approach, which discards the usual neuroimaging point of view, is deeply relying on the structural reference systems of standard neuroscience. This referential for the visual system is not only a parcellation, but embeds also the knowledge of the fiber related isomorphism between areas [20,71,79].

The retinotopic coordinate system used inside each visual area is a convenient way of representing the general connectivity based architecture of the visual system. Hence, the retinotopic system is essentially different from the neuroimaging global coordinate systems. A rapid mapping of well-known functional areas performed as a preliminary step before any new study would be a powerful way of developing reference systems based on functional landmarks. Unfortunately, an exhaustive parcellation of the whole cortical surface is far beyond our current understanding of the cortical organization. Therefore, the development of this approach will lead to a mixture between the structural approach and various local coordinate systems.

While retinotopic mapping is the perfect example of a brain image analysis procedure driven by neuroscience structural a priori knowledge, this approach relies mainly on functional experiments. The foreseeable progress of anatomical MRI could rapidly lead to much more architectural information. For instance, the possibility to segment the cortical

surface into **architectony related patches** has been recently shown with high resolution post mortem scans [34]. High field magnets could rapidly provide such a high resolution in vivo in reasonable time. Another rapidly developing area is diffusion MRI, which provides a lot of information about tissue microstructure [36]. This imaging modality gives for instance the hope to track the main **fiber bundles connecting brain areas**, which is a way of parcelling the cortex [14,46,54], or of segmenting the thalamus into nuclei [77].

5. Computer vision structural methods

5.1. Inference of structural models

While additional functional or anatomical individual data are required to infer the structural referentials mentioned above, the structural point of view can also lead to alternative methods with standard data. In this section, we will address the inference of structural models via the comparison of data stemming from a group of individuals. We have chosen to illustrate the approach with an application dedicated to functional data, but this direction of research is **generic** and could be applied to anatomical data, which will be detailed further.

It is interesting to note that emerging groups in fMRI not familiar with the iconic normalization paradigm often choose a very different approach to perform group analysis, namely to compare functional images across subjects. The images to be compared are called statistical parametric maps. They provide for each voxel the probability of being activated by the cognitive experiment [27]. While the common strategy consists in comparing these maps on a voxel-by-voxel basis, these newcomers in fMRI analysis apply first a common statistical threshold to the individual SPMs in order to define activated voxels. Then, they try to match connected clusters of such voxels across the group individuals according to vague anatomical considerations (see Fig. 3). This matching is supposed to yield a synthesis of the experiment, namely the activated areas stable across individuals. While this approach may appear naive at first glance, it overcomes the problems induced by the coordinate-based inter-individual comparison. Dealing with clusters rather than voxels is justified by the idea that each cluster may represent the activation of a cognitive module.

In our opinion, this **transition from voxels to clusters** is the first important step towards the development of structural analysis methodologies closer to the standard neuroscience points of view. For instance, the neuroscientist deals freely with the anatomical constraints used to guide the cluster pairing: invariant localization relative to surrounding sulco-gyral anatomy [75], loose localization in one specific lobe [17], emergence of two distinct types of individual activation patterns corresponding to two different populations or two different strategies to perform the cognitive task, etc. This versatility is today required to overcome the weaknesses of the normalization framework and the lack of knowledge about the localization power of the cortical folds.

The neuroscientist's approach mentioned above introduces a very common strategy in computer vision: dealing with various features extracted from the images rather than with the images themselves. This is exactly what the neuroscientists are doing when they think

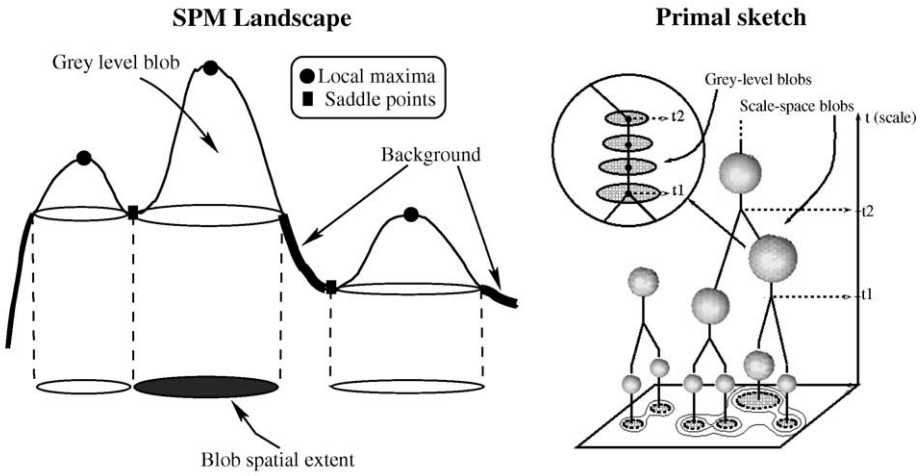

Fig. 4. Computer vision provides a powerfull method to represent the landscape of any SPM. This structural representation called a scale-space primal sketch [37,38] stems from the following stages. (1) Add a smoothness/scale dimension to the SPM using for instance the heat equation. The scale can be viewed as the time of the heat equation, which amounts to convolve the initial SPM with a Gaussian, whose width increases with time. (2) At each level of smoothness, compute the ''grey level blobs'', which are the hills of the SPM landscape defined by a maximum and a saddle point (left). (3) Track the hills across the scales in order to create ''scale-space blobs'', namely the hills surviving for a while during the smoothing process, between two bifurcations (some local structural changes in the landscape shape like the merge of two hills) (right). The sampling of the scale direction is performed with an adaptive strategy in order to get access to enough information to detect all the bifurcations. This structural representation overcomes the threshold problem when defining the connected clusters of the SPM (see Fig. 3). Any SPM's hill, indeed, is represented by a scale-space blob, which can be described further by various feature like the integral volume across scales of the underlying grey level blobs.

over a thresholded SPM as a set of connected clusters. The main problem underlying this approach is the threshold choice. The topology of the thresholded image, indeed, may be very dependent on the chosen threshold. For instance, an activated area, that appears as a hill of the SPM, could be represented by a cluster or not if its summit is above or under the threshold.

Computer vision provides a threshold free solution to this problem, which consists of an abstract hierarchical description of the SPM landscape called a scale-space primal sketch [37,38] (see Fig. 4) that can be used to perform an automatic ''structural group analysis'' [15]. Each individual SPM is transformed first into this structural representation, without any thresholding. Then an automatic exploratory method can be designed to compare individual representations in order to give an answer to questions like:

- For a given pairing tolerance in terms of distance in the proportional system, are some clusters reproducible across numerous individuals?
- For a given parcellation of the cortical surface into gyri, are some clusters in the same gyral subdivision across numerous individuals?

The method proposed in [15] introduces a Markovian random field framework, which defines the answer to the first question as the labelling maximizing a Gibbs distribution

[3,28]. Each label is supposed to correspond to a reproducible activation, yielding an acceptable trade-off between two constraints:

- Each labelled individual cluster has to correspond to high *P*-values in the underlying individual SPM (here, high *P*-value does not mean above the usual statistical thresholds used by the community).
- When two clusters share the same label, they have to be close to each other. The distance between clusters can stem from pure localization or from more sophisticated similarity measures including for instance shape descriptors.

The two kinds of potentials, which embed these constraints into the Gibbs distribution, are tuned in such a way that a label can survive only if it can be found in a large number of different individuals. It should be noted that this **structural group analysis** does not question the main stream of statistical methods used to infer individual SPMs, but differs in the way of comparing these maps across individuals. The goal is to detect activated areas reproducible across subjects without imposing a strong localization constraint relative to the coordinate system.

A number of other approaches could be designed to tackle this structural model inference problem, which is commonly addressed in artificial intelligence [64]. The example mentioned above is very simple, since the inferred model is just a list of labels, each label standing for a cognitive module. Other examples mentioned further will describe some problems involving graph inference. It is interesting to note that the neuroimaging problems seem easier to address than the problems in computer vision, because the volumetric nature of the data eliminates the need for stereovision. Furthermore, the existence of the proportional coordinate system means that all the brain images can be approximately aligned without great difficulties, which overcomes another difficult problem of computer vision. Brain structural model inference is nevertheless a difficult challenge, facing for instance the problem of data under or over segmentation during the initial computation of the structural representations. This last problem can be overcome if the structural representations can be questioned and modified during the inference process. This approach which could be related to active vision leads unfortunately to a large increase in complexity. In our opinion, nonetheless, the strategy inspired by computer vision advocated in this paper may sometimes yield better inference hypothesis than what can be proposed by a human neuroscientist, because human vision does not provide simple ways of visualizing large sets of volumetric data.

5.2. Matching individual data with a structural model

The transition from voxel to image features introduced above can be done for any kind of images. As far as SPM images were concerned, a primal sketch extracting hills at different scales was sufficient to describe the data. Brain anatomical images, however, require more dedicated processing to be converted into some interesting structural representations. Then, a lot of a priori anatomical knowledge about brain shapes can be embedded into the process, which simplifies further computations. Therefore, while general purpose computer vision approaches build structural representations from generic features like edges or corners [2], brain image dedicated approaches can rely on more specific anatomical

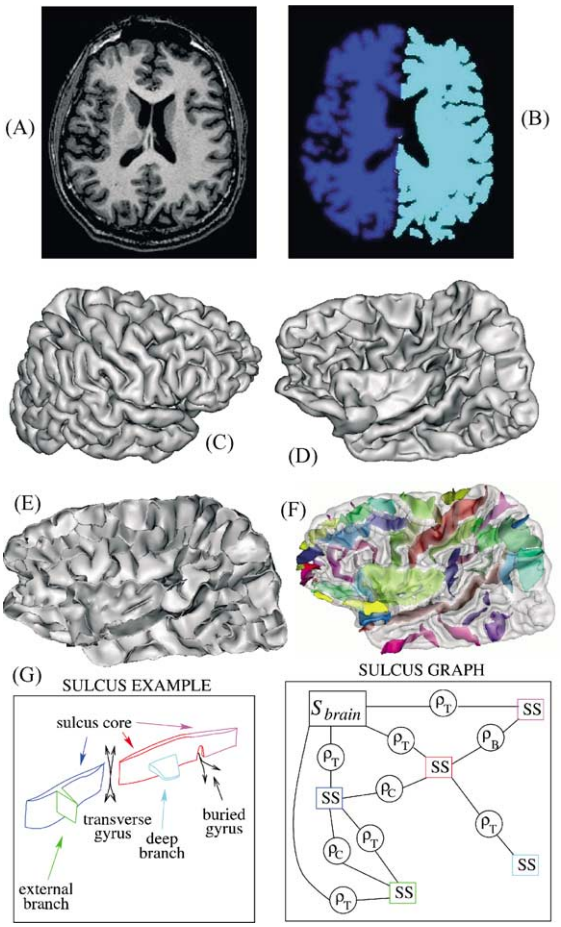

Fig. 5. Computation of a structural representation of the cortical folds from a raw T1-weighted MR image [41,58]: (A) raw MR slice; (B) brain hemisphere segmentation; (C) right hemisphere cortex external surface; (D) right hemisphere cortex inner surface (interface between grey and white matters); (E) skeleton of the (cortex + cerebro spinal fluid) object; (F) segmentation of the skeleton using discrete topology and labelling of the main sulci with colors (several folds can be gathered in the same sulcus); (G) an example of the attributed subgraph representing a sulcus. Each node SS is a piece of the surfacic skeleton while S_{brain} represents the brain hull. Three kinds of relations are used: topological junction ρ_T, neighbor geodesic to the brain hull ρ_C, split induced by a buried gyrus ρ_B. Semantic attributes like size, length, depth, etc. are added to nodes and relations for recognition purpose.

features like cortical folds [58] (see Fig. 5), cortical surface maximal depth points [39,57], or pieces of fiber bundles [54].

The brain anatomy can be split into a hierarchy of different entities supposed to play a different architectural role. The usual approach to segment the brain according to this hierarchy is iconic normalization, which consists in warping an iconic template endowed with a manual segmentation (often called an atlas) [12]. This strategy is successful for brain areas with a stable organization, for instance for basal ganglia, provided that some clues

about the anatomical boundaries can be extracted from the image intensities. Otherwise, for instance for thalamus subdivisions, a perfect segmentation can not be guaranteed. The iconic normalization strategy is much more problematic for cortical gyri because of the large inter-individual variability of the folding patterns (see Fig. 7). One of the difficulties is the fact that the deformations may easily get trapped in a local minimum of the intensity based energy driving the warping, because of the very local point of view embedded in the underlying similarity measure.

To overcome this problem, we have developed an approach that may be considered as a **symbolic version of the deformable atlas** approach [58]. The framework is made up of two stages. An abstract structural representation of the cortical topography is extracted first from each new T1-weighted MR image (see Fig. 5). This representation is a graph supposed to include all the information required to identify the sulci (the structural model of the folds according to human anatomists). The graph nodes are the cortical folds and the graph relations represent various kinds of neighborhood relationships. Finally various attributes like size, orientation or depth are attached to the graph nodes and relations.

A contextual pattern recognition method is then used to identify automatically the cortical sulci. This method can be interpreted as a graph matching approach (see Fig. 6). The usual iconic template, indeed, is replaced by an abstract template graph. The vertices (nodes) of this template graph are the cortical sulci defined in anatomical nomenclature, and the arcs (links) correspond to pairs of sulci close to each other on the cortical surface. Because of frequent sulcus branches and interruptions, a given sulcus is represented by a different subgraph in each individual brain (see Fig. 5). Unfortunately, the origin of this variability is not understood today, which explains why no gold standard exists about the sulcus identification. Therefore, the approach developed for the sulcus recognition has been based on a learning strategy using a set of manually labelled brains. The one to many matching between the template vertices (the sulci) and the nodes of one individual

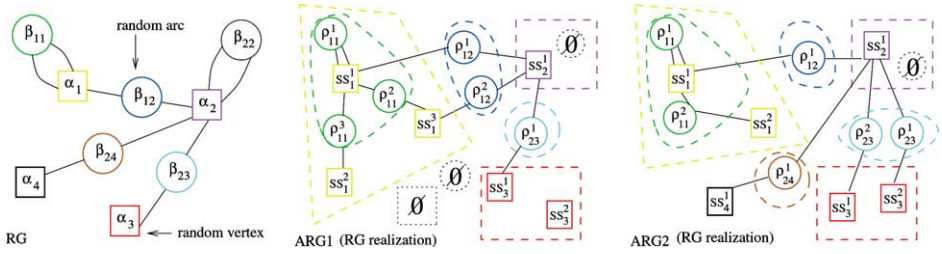

Fig. 6. The template graph used as a model of the cortical folding is endowed with a Random Graph (RG) structure, made up of random variables representing vertices (α_i) and arcs (β_{ij}) [43]. A random vertex's realization is a set of nodes (SS_i^k) representing folds. A random arc's realization is a set of relations (ρ_{ij}^k) representing various relationships between folds. Thus, the RG's realization is an attributed relational graph yielded by the method described in Fig. 5. The link between the random graph and its realization is a homomorphism, namely a labelling of the ARG's nodes with the RG's vertices. A multi-layer perceptron is defined for each random variable (vertices and arcs). The a posteriori probability of a labelled ARG is given by a Gibbs distribution $(1/Z)\exp\{-\sum_e P_e(l)\}$, where Z denotes a normalization constant, l the labelling, and P_e the weighted output of a perceptron. The sulcus automatic identification amounts to maximizing this a posteriori probability.

structural representation (the elementary cortical folds) is simply a labelling, which has been done manually by our human neuroanatomist to constitute a learning database of 26 brains.

This cumbersome manual labelling of the folds was relying on the standard sulcus nomenclature [49]. It should be noted that this nomenclature stems from a structural model inference belonging to the generic class of approaches mentioned in the previous section. This inference has been performed manually by the first neuroanatomists. In the future, we plan to design a method to perform this inference automatically to try to obtain a refined nomenclature dealing with the inter-individual variability.

While the example of group analysis of a set of SPMs described in the previous section led only to a list of activations, the inference of the template graph of the cortical sulci requires also relational information. The neighborhood relationship added to the standard sulcus nomenclature, in fact, is inferred automatically from the learning database in order to build the links of the template graph. Such a link is created for each pair of sulci whose instances in the learning database are sometimes connected. The contextual information used to drive the recognition will rely on this neighborhood. Since the a priori knowledge used by the human expert to identify the sulci is only contextual, the Markovian random field framework is used to develop the pattern recognition method [3,28]. Hence, the automatic labelling of the folds of any new brain is driven by the minimization of a global function made up of local potentials (see Fig. 6).

Each local potential is a measure of the likelihood of the labelling of a restricted cortex area. This potential is given by a virtual expert in this area made up of a multi-layer perceptron trained on the learning database (see Fig. 7). Then, each expert has a field of view, which is learned from the database, and corresponds to a domain of the standard proportional system. These fields of view and the neighborhood inferred from the learning base endow the congregation of experts with a corticotopic organization, which shares some similarities with the retinotopy of the visual system. The artificial neuroanatomist embodied by the congregation of perceptrons, however, is tuned to the cortical surface spherical topology.

Two kinds of experts are used. One expert is in charge of the shape of each sulcus, and one expert is in charge of the shape of each pair of sulci neighbors in the template graph. Each expert's contribution to the global energy is weighted by an estimation of its reliability obtained from a second learning base. The perceptrons are feeded by a fixed set of synthesized attributes that can be viewed as descriptors of the subgraph to be evaluated (defined by one or two labels). Some attributes are more syntactic, like the number of connected components of the subgraph; some other are semantic, like the total size of the folds included in the subgraph. It is important to understand that the standard coordinate system is used to define the fields of views, or to provide normalized localization and orientation information to the perceptrons.

While the complexity of the preprocessing stage required by our method may appear as a weakness compared to the straightforward use of warping, it results in a fundamental difference. While the evaluation of the functions driving continuous deformations is expensive in terms of computation, the function used to drive the symbolic recognition relies on only a few hundred labels and can be evaluated at a low cost. Hence **stochastic optimization** algorithms can be used to deal with the problems induced by local minima.

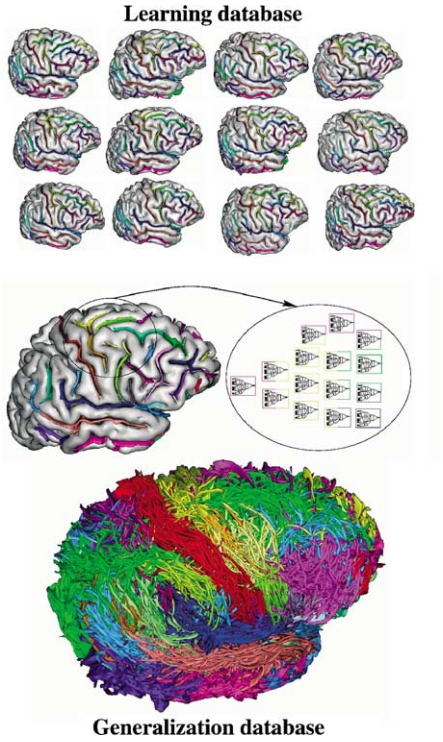

Fig. 7. The matching of the model of the cortical sulci with any new brain is performed according to a learning strategy. Top: 12 brains of the learning database with manual labelling of some sulci. This database is used to train a congregation of 500 multi-layer perceptrons [58]. Each perceptron is in charge of a local anatomical feature like the shape of a sulcus, or the shape of a pair of neighboring sulci. The automatic sulcus recognition is then performed via the minimization of the sum of the expert outputs, relatively weighted by their reliability on a test database. The result is obtained using simulated annealing. Down: 50 brains not used for learning, which have been automatically labelled by our method and aligned with the proportional system for visualization purpose.

The sulcus recognition is performed using a heuristics based on simulated annealing. This heuristics introduces dedicated explorations of the configuration space, which aims at modifying the labels of connected component of nodes in a constraint way. This approach, which consists in creating some paths between configurations that differ by more than one label, decreases the depth of local minima and improves the stochastic minimization behaviour. While the results are comparable to the manual ones for most of the brains, a lot of questions remain open in the most variable cortical areas. Therefore, the future work will consist in trying to improve the template model using automatic inference.

The current artificial neuroanatomist can be downloaded from ‘‘http://anatomist.info’’. The system is still at the beginning of its education. It has been trained from 26 manually labelled brains, including 10 brains used as a test base preventing overlearning. The automatic recognition results decrease from 85% of accordance with the manual labelling on the learning base, to 75% on a generalization base, which calls for increasing the size of the learning base. It should be noted, however, that these results do not mean 25% of errors.

Because of the large inter-individual variability of the folding patterns, indeed, no gold standard exists to evaluate the percentage of correct labelling. The training of the 500 multi-layer perceptrons on this base of 26 brains lasts about 12 h on a network of twenty recent Pentium processors. The stochastic minimization leading to the automatic labelling last one hour for one hemisphere with a 2 MH processor and the default tuning of the temperature decreasing. The framework has been applied with about 500 brains stemming from different laboratories.

The structural approach to the recognition of the cortical sulci is much closer to the way neuroanatomists are thinking to the folding patterns than any iconic normalization based approach. Therefore, the underlying tools are also used to assist the **study of the cortical folding process**, from antenatal to adult stage, which is in our opinion mandatory to understand better the inter-individual variability. One of the aims of our research is to favor the emergence of new anatomical descriptions relying on smaller sulcal entities than the usual ones. According to different arguments that would be too long to develop in this paper, these units, the primary cortical folds that appear on the fetal cortex, are stable across individuals; an architectural meaning is probably attached to them [9,56]. During ulterior stages of brain growth, some of these sulcal roots merge with each other and form different patterns depending on the subjects. The more usual patterns correspond to the usual sulci.

In our opinion, some clues about these sulcal root fusions can be found in the depth of the adult sulci and detected from the curvature of the cortical surface (see Fig. 8). Therefore, a structural representation of this 2D curvature map has been developed using the primal sketch idea (see Fig. 9) and will be used to try to perform **inference of a structural model of the cortical folds** using a set of brains covering the whole brain growth [7]. It should be noted

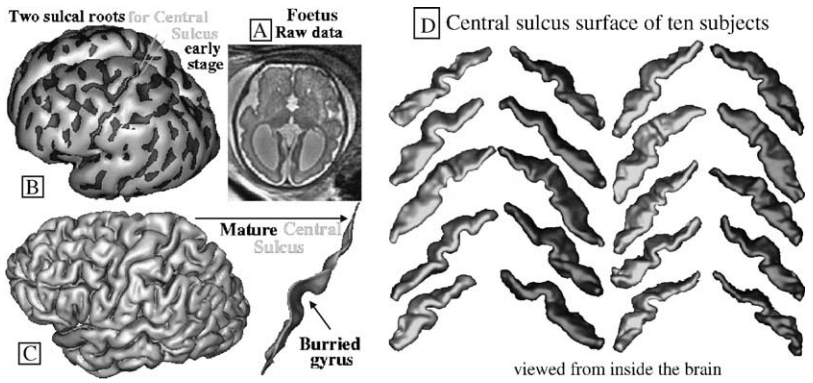

Fig. 8. A better understanding of the cortical folding inter-individual variability may stem from longitudinal studies. (A) Antenatal MR images provide a window on the beginning of the folding process. (B) The reconstruction of the fetus cortical surface highlights the sketch of the future sulci as high mean curvature areas. For instance, central sulcus is made up of two sulcal roots. (C) The following stages of brain growth lead usually to a merge of the two sulcal roots, which can be associated to a gyrus buried in the depth of the adult central sulcus. (D) A visualization of the inner cortical surface located in the central sulcus shows the almost systematic presence of this buried gyrus. For a few brains, however, two different gyri seem to appear, which may be explained by the fact that the underlying gyral folding is a tripod connecting one gyrus in the parietal lobe with two gyri in the frontal lobe. For some individuals, the frontal split of the buried gyrus may reach the bottom of the central sulcus.

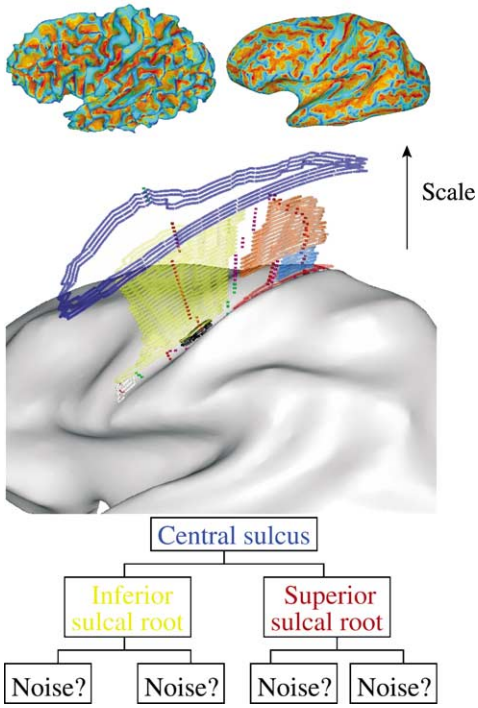

Fig. 9. A primal sketch of the central sulcus stemming from the mean curvature of the cortical surface [7] (see Fig. 4). Top: Mean curvature mapped on the white matter surface and on an inflated version of the same surface in order to show buried gyri. Middle: a geodesic implementation of the heat equation allows the computation of a primal sketch from curvature extrema and saddle points. This sketch is supposed to include scale-space blobs corresponding to sulcal roots, which is illustrated here with the example of the central sulcus. The support of the grey leel blobs is moved away from the brain surface according to the scale. The different colors correspond to the different scale-space blobs. Red points are extrema, purple and green points are two kinds of saddle points. Down: An abstract representation of the primal sketch of the central sulcus on scale-space blobs and bifurcations.

that while brain growth studies are becoming a very attractive part of neuroimaging research [51], the iconic normalization of small children brains seems to raise a lot of difficulties [78]. A structural approach to brain growth study could be much more informative.

5.3. The brain mapping structural framework

Each of the previous examples of the structural approach to brain image analysis relies on homogeneous structural data: primal sketch of blobs or graph of cortical folds. More ambitious projects should **mix several kinds of data** into a more complex structural representation. This merging process may sometimes involve some computation leading to additional links between the nodes of the different representations. For example, cortical folds and activation related blobs should be mixed to study the potential localization power of the sulco/gyral patterns. This could call for the development of new structural representations

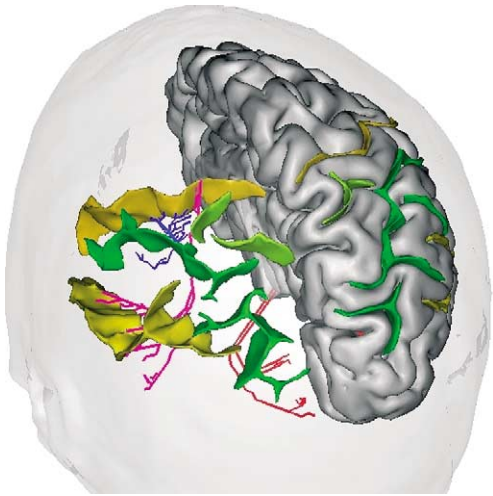

Fig. 10. Toward the inference of the matrix of connectivity of the main cortical gyri using MRI (green to orange: cortical sulci stemming from T1-weighted images [58]; blue to red: putative fiber bundles stemming from diffusion-weighted images connecting two different gyri [54]).

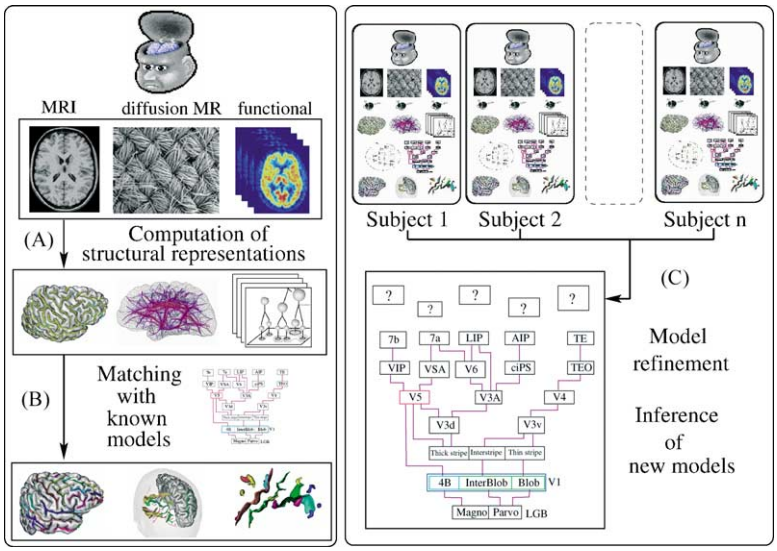

Fig. 11. A possible scheme for a structural brain mapping strategy. (A) Raw anatomical and functional individual images are converted first into structural representations. (B) Each structural representation is matched with the syntactically corresponding structural model in order to use previous knowledge as a referential: the main sulci are identified, standard functional areas related to fast cognitive experiments are localized, the usual fiber bundles are tracked, etc. (C) The different individual representations are compared in order to infer new similarities across subjects that will refine the current models: stable links between some sulci and some activated areas, new activated areas, stable sulcus branches, stable fiber bundles, etc.

of the cortical surface based on gyral rather than sulcal elements [8]. Another very attractive example consists in using MR diffusion data to infer the connectivity between activated clusters, or between cortical gyri [14,42,46,54] (see Fig. 10).

In fact, the structural approach can allow the development of computer vision's method, which mimic most of the ways neuroscientists manually explore their data to infer some new models. The hope motivating the framework advocated in this paper is to provide a way to address the same questions using huge brain datasets, while the human brain can hardly do an efficient synthesis of a few volumetric images. Hence, a complete structural framework can be proposed for brain mapping relying on a few generic ideas:

(1) Convert raw images into structural representations.
(2) Merge several representations coming from the same individual.
(3) Match each new structural representation with one syntactically corresponding structural model. This model could stem from a database of the current knowledge, which could include concurrent points of view.
(4) Infer new similarities across a set of individuals to improve the current structural models.

An illustration of a possible resulting scheme is proposed in Fig. 11.

6. Conclusion

This paper has advocated for a larger development of structural approaches to the analysis of brain images. In our opinion, this is the best way to bridge the gap between the current neuroimage analysis techniques and the standard neuroscience point of view. The underlying goal is the design of artificial intelligence methods performing the structural model inference supposed to stem from brain imaging experiments. Such methods would rely on a specific kind of computer vision dedicated to volumetric images of the brain. They could greatly support human neuroscientists that have unfortunately not been endowed with a captor for volumetric images.

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