Model-driven parameterization of the cortical surface for localization and inter-subject matching

C. Clouchoux, D. Rivièrè, J.-F. Mangin, G. Operto, J. Régis, O. Coulon

Abstract

In this paper we present a generic and organized model of cortical folding, and a way to implement this model on any given cortical surface. This results in a model-driven parameterization, providing an anatomically meaningful coordinate system for cortical localization, and implicitly defining inter-subject surface matching without any deformation of surfaces. We present our cortical folding model and show how it naturally defines a parameterization of the cortex. The mapping of the model to any given cortical surface is detailed, leading to an anatomically invariant coordinate system. The process is evaluated on real data in terms of both anatomical and functional localization, and shows improved performance compared to a traditional volume-based normalization. It is fully automatic and available with the BrainVISA software platform.

Introduction

Cerebral localization is a key point in neuroimaging. It is needed in order to assess anatomo-functional correlations, to communicate results from functional studies, and implicitly to match structures between subjects. Indeed, the major concern in group studies is the large variability occurring within a set of individuals, and even between hemispheres for a single subject (Thompson et al., 1996, 2001; Toga and Thompson, 2003; Kennedy et al., 1998; Fillard, 2008). However, extracting anatomical similarities between brains has been shown to be a hard task (Zilles et al., 1997) and is still an open problem.

The usual approach of neuroimaging studies is to consider the brain in its 3D acquisition volume. It is then possible to give each voxel of a MRI scan a unique coordinate set, using the canonical parameterization of the 3D domain. A number of methods aim at matching different brain 3D volumes, using various affine or elastic registration techniques (Christensen, 1999; Davatzikos, 1996; Thompson and Toga, 1996; Vercauteren et al., 2007; Crivello et al., 2002; Pennec et al., 1999; Collins et al., 1998; Ashburner and Friston, 1997; Ashburner, 2007; Klein et al., 2009). The process is often designated as “spatial normalization” and maps brain volumes to a reference target. For instance, the Talairach coordinate system offers a way to do this using a few anatomical markers (Talairach et al., 1967; Talairach and Tournoux, 1988). A more recent way is to use complex non-linear registration techniques to register brain volumes to a standard atlas such as the MNI305 (Ashburner, 2007; Hellier et al., 2003). Although this kind of method is widely used and was shown efficient for inter-subject matching and functional localization, its precision is poor for cortical features (Devlin and Poldrack, 2007; Van Essen et al., 1998).

It has been shown that considering the cortex as the reference for inter-subject studies is of great interest (Van Essen et al., 1998; Fischl et al., 1999a). However, this leads to some very specific problems, such as surface normalization, in order to match different cortices. There are different existing answers to this problem, which conform to the point of view that has been defined by the volume-based methods: a standard domain is defined, that is a canonical surface such as the unit sphere, and cortical surfaces are mapped to this domain, on which registration is later performed (Van Essen, 2005; Sereno et al., 1996; Fischl et al., 1999b; Tzisari and Leahy, 2000; Tosun et al., 2004). This registration approach to the inter-subject matching is still limited by the ill-defined problem of homologies between different cortices: what to match and what not to? In the absence of a clear and generic model of the cortex, registration has to compromise between stable but coarse features and dense but unreliable information. In contrast, we propose to tackle the inter-subject matching problem as a localization one and advocate for the fact that if one had a “map” of the cortex (i.e., a generic description of cortical features and their organization) the problem would be solved by answering the question: where are we? In other words, having an anatomical localization of any point or feature on the cortex implicitly solves the inter-subject matching problem.
The approach proposed in this paper therefore takes this localization point of view, and performing matching via the direct construction of an anatomically-constrained coordinate system on the original cortical surface of each individual hemisphere. A key point of the method is that this parameterization is driven by a generic model of cortical anatomy and provides an implicit cortical surface normalization without any explicit spatial transformation. Next section reviews different approaches developed to address the cortical surface matching problem. The **Cortical organization** section presents the anatomical model we based our method on, describing a model of cortical organization. The **Model-driven parameterization: method** section focuses on the parameterization algorithm. Then, the **Experiments and discussion** section discusses the possible applications of this method, as well as experiments and results with real anatomical and functional data, followed by a discussion.

### Inter-subject surface matching

Multi-subject studies aim at analyzing specific anatomical areas, measuring and understanding their variability, or correlating functional activity across subjects, in order to extract models of anatomical or functional organization. When working at the group level, it is then necessary to have a reference domain on which each subject’s information can be mapped. This is for instance the MNI 3D template after volume-based spatial normalization. With surface-based approaches, such a domain does not exist naturally, each cortex having its own geometry. This is why existing methods map cortical surfaces to a standard geometry such as a sphere. This mapping is either isometric (e.g., Fischl et al., 1999b) or conformal (e.g., Wang et al., 2007). Individual information such as geometrical features or anatomical landmarks can then be transported on the new geometry via the mapping. On the new reference domain, inter-subject registration can then be performed. Spherical registration can use either several anatomical landmarks or a dense field of geometrical information such as depth, curvature, or compliance, as detailed below.

The first category of methods relies on local landmarks, typically stable cortical folds manually identified (Van Essen, 2005; Toro and Burnod, 2003; Tosun et al., 2004; Miller et al., 1993; Drury et al., 1996; Van Essen et al., 1998). Limits of such approaches are twofold: landmarks are manually identified, with all the consequences on precision and reproducibility, and they are limited in number. Indeed, automatically identifying and extracting folds is a difficult task and few methods are available (Riviére et al., 2002). Besides, the variability of the sulcal patterns implies that a ‘one-to-one’ transformation is impossible. We point out that some methods perform both the spherical mapping and the landmarks matching at once (Shi et al., 2007).

The second type of methods uses dense geometrical information on the surface. For instance, Fischl et al. (1999c) use the convexity of the original cortical surface, a feature that characterizes all folds, with a stress on the deep stable ones. This measure is weighted by the variance of the convexity through a pool of subjects, giving more weight to deep sulci (such as central sulcus or insula) than to more superficial and variable folds. This approach is proven useful but is limited by the reproducibility of the convexity map in various cortical areas. Similarly, a diffeomorphic approach to the problem is presented by Yeo et al. (2009) that uses the same convexity-based similarity measure.

In both cases, there is little prior about information that should be matched across subjects. A tradeoff has to be reached between precision and robustness, dealt with by the number of features used to perform registration and by the level of rigidity of this registration process. Moreover, the resulting coordinate system after registration does not embed any anatomical information and has an arbitrary orientation and origin. However, it is now thought that the cortex has a geometrical organization and that this organization naturally defines a referential. This issue has been tackled by Toro and Burnod (2003), where a geometric atlas of the cortex is proposed. This atlas has been built upon anatomical observations and theories and provides a generic scheme of organization for cortical structures. This scheme describes a natural orthogonal organization of the main folds. The two main directions are organized around two natural poles: the insula and the corpus callosum. Secondary and tertiary folds are organized following the two main directions, according to the “minimal radial distortion” described by Todd (1982). A similar organization has been described by Lohmann et al. (2008) for specific deep parts of sulci, showing that those “sulcal pits” are not only organized but also stable across subjects, confirming the ideas presented earlier by Régis et al. (1995, 2005) Using such organized and reproducible models of the cortex is a way to overcome at least partially the variability of the folding schemes across individuals. The method presented in this paper is based on such an idea. In the next section, we describe explicitly the cortical model used to drive our localization and inter-subject process.

### Cortical organization

Historically, the first cortical observations were post-mortem, and fold descriptions were based on visual observation (Broca, 1878; Cunningham and Horsley, 1892). They showed a great variability of sulci schemes, mostly because they were based on the superficial shape of the sulcal lines. The apparition of MRI techniques then allowed in-vivo studies, giving access to buried information. This information, the deep cortex, led to alternative descriptions, as well as to new organization schemes (Régis et al., 1995, 2005; Lohmann and Von Cramon, 1999; Toro and Burnod, 2003) that exhibit a structural stability of the cortical folds.

Considering deeply buried cortical structures allows a new vision and comprehension of sulcal patterns (Cunningham and Horsley, 1892; Gratiolet, 1954; Régis et al., 1995), considering that the surface of the buried cortex is 2.5–3 times greater than the superficial cortex surface (Von Economo, 1929; Zilles et al., 1997; Van Essen, 1997; Elias, 1971). Actually, buried cortex shows a smaller variability than the visible one, and deeply buried structures are more stable than superficial ones, like the superficial sulcal lines (Toro and Burnod, 2003; Régis et al., 2005; Lohmann and Von Cramon, 1999; Lohmann et al., 2007; Fischl et al., 2007). This has been corroborated by artemiographic studies (Szikla et al., 1977) and quantitative studies that showed that deep cortical structures are more stable than others, advocating for a greater genetic influence than for the surface (Régis et al., 1995; Le Goualher et al., 1999; Lohmann and Von Cramon, 1999).

In order to establish correspondences between subjects, an appropriate approach is to consider not only a set of anatomical landmarks, but also to include prior knowledge, such as relations between these landmarks. This has been used to propose structural representations of the cortical anatomy (Mangin et al., 2004; Felleman and Van Essen, 1991; Chicurel, 2000; Kotter, 2001; Stephan et al., 2000).

The first geometric representation of the cortex was based on several mammalians cortices observations, simpler than human anatomy (Todd, 1982). It describes a natural orthogonal system formed by the principal curvature lines, based on canid brain studies, showing the “minimal radial distortion” principle, where folds will follow the direction of minimal curvature, due to mechanical action of radial glial and neuronal fibers. This organization has been refined and described in human brains in more recent works (Régis et al., 1995. Based on this, a geometric atlas of the cortex has been proposed as well, describing the cortex as an organized surface (Toro and Burnod, 2003). An interesting point of this work is that it exhibits an orthogonal organization of the main sulci. An underlying theory is that the proposed markers are closely related to connective,..
functional and architectonic regionalization, observed in small mammals (Woolsey, 1963; Welker, 1989) and human primary sensitive areas, but not clearly established in associative cortical areas (Zilles et al., 1997).

In Régis (1994) and Régis et al. (2005), an original approach brings elements to explain cortical organization. Unlike the geometric atlas proposed by Toro and Burnod (2003), it relies on deep cortical structures, the sulcal roots. A key idea of this model is that the spatial stability of the deep sulcal cortex is greater than that of the superficial image of the sulci. This point leads us to consider not only sulci, but also deeply buried subparts of sulci, the so-called sulcal roots, corresponding to the first folding location during antenatal life. During brain growth, sulci appear around the sulcal roots. This step is one of the cause of the sulcal pattern variability, where different orientation, size and shape of folds can occur from one individual to another (Régis et al., 2005). Fig. 1 shows an illustration of the sulcal roots model.

Another major idea of this model is that these entities are naturally organized, according to two major orthogonal directions and two poles, in a latitude/longitude manner. Main folds are organized following these two directions, sulcal roots being the “anchor points” around which the folding process occurs. Although resulting folds may seem variable from an external point of view, their deepest parts remain stable across growth and individuals. In the theoretical organization scheme, each sulcal root is a crossing point between a meridian and a parallel. The two poles are specific anatomical structures (Mesulam, 2000; Welker, 1989; Toro and Burnod, 2003; Régis et al., 2005). The first one is the insular pole, defined by the paleocortical core, and describes a “polar circle” at the delimitation between the insula and the rest of the neocortex. The other pole is the
cingular pole, the archeocortical core, and describes another “polar circle” following the limbic circumvolution. From a geometric point of view they are natural poles of the orthogonal system since all meridians in the system converge to those. Moreover, the specific nature of the cortex (paleocortex and archeocortex) in those areas, and their very early appearance during the developmental process differentiate them from the rest of the cortical surface. Fig. 2 shows a description of the poles.

The model also suggests that cortical organization is closely related to a certain degree of functional organization. Although it has been shown that sulci are not entirely reliable when dealing with functional delimitations (Zilles et al., 1997), the deep cortex is supposed to carry some functional value. This statement is derived from the protomap model, which proposes that cells of the embryonic vesicle carry programs for species-specific cortical regionalization (Racik, 1988). Hence, the protomap stability across individuals should imply stability of the folding process during gestation (Turner, 1948). This leads us to hypothesize the existence, at the adult stage, of progyral and prosulcal maps embedded in the protomap. This implies that sulcal roots related folds are bound to occur at the boundaries between cortical areas. It also raises the fact that sulcal roots are aligned along axes that delimitate functional areas. For instance, an axis going from the central sulcus to the frontal cortex describes a modal gradient. Also, the central sulcus itself is an axis that separates primary sensory and motor areas and describes a vertical somatotopic gradient. Hence, sulcal roots are thought to be crucial information for both anatomical and functional organization of the cortical surface.

In practice, automatic segmentation of sulcal roots is not available, and very few methods are available to automatically extract structures smaller than sulci (Mangin et al., 1995; Lohmann and Von Cramon, 1999; Lohmann et al., 2007). However, the study of the theoretical model and the observation of many subjects led us to define a generic folding pattern. This folding model, shown on Fig. 3, is derived from the sulcal roots model (Régis et al., 2005) and proposes a generic organization based on sulci or subparts of sulci, i.e., entities that can be segmented automatically (Rivièere et al., 2002, Mangin et al., 1995). Folds in the model were chosen since they could be identified in any subject and since their orientation with respect to the parallel and meridian directions was stable across subjects. The model uses 34 sulci per hemisphere, aligned according to 4 axes in the latitude orientation and 6 axes in the longitude orientation. Tables 1 and 2 present the sulci used in the model and their respective alignments.

Fig. 2. Cingular and insular pole zones. Top: on an inflated cortical surface, showing the zones delimited by polar circles (grey), the insular core (red dot), and cingular core (black). Bottom: a flattened representation of both poles.
Beside the implicit inter-subject matching and the anatomy-based localization, the advantages of such a parameterization lie in the fact that some remarkable meridians and parallels are supposed to embed functional information and naturally delimitate functionally consistent areas (see for instance Clouchoux et al., 2006).

We present in this section the parameterization itself. Fig. 5 presents a global scheme of the process, in which the model of the cortical organization is used to constrain the resulting coordinate system.

### Feature extraction

Sulci in the model, as well as the two poles, need to be extracted from data (typically an anatomical T1 MRI) in order to be used as constraints.

All data are preprocessed using the T1 MRI toolbox of the BrainVISA software platform (http://brainvisa.info). The first stage of the method, which has been described by Riviere et al. (2002), automatically provides the identification of the main sulci, each sulcus being represented by a set of voxels obtained from a skeleton segmentation. Another outcome of this preprocessing stage consists of two smooth meshes of the cortex hemispheres endowed with a spherical topology (Mangin et al., 1995), each mesh corresponding to the interface between the gray and white matter. It is this representation of the cortical surface that will be parameterized for each hemisphere.

### Poles

The insular pole (insular paleocortical core) is segmented using the projection onto the cortical mesh of the insular 3D structure as
segmented by the above-mentioned method. The limit of the segmented area corresponds to the insular polar circle, separating the mesocortex (defining insular paralimbic lobe) and the neocortex. The pole itself, the paleocortical core, is defined as the cortical mesh node in the insular area that is the closest (in terms of geodesic distance) to the cingular pole, according to anatomical statements (Mesulam, 2000). Fig. 2 shows a scheme of the poles, for a clearer comprehension.

The cingular pole is segmented by using a template volume, encapsulating the cingular pole. This template volume (see Fig. 6) has been defined from a set of several brains, normalized with ICBM-152 template. After an affine registration of the template volume with the T1 MRI, the intersection of the template volume and the cortical mesh allows to label all the vertices of the mesh belonging to the cingular pole. Finally, a geodesic closing of the resulting set regularizes its boundary.

**Origin meridian**

The model defines two orthogonal directions, longitude and latitude. Latitude spreads between the two poles, defining parallels, from 0° for the cingular pole up to 180° for the insular pole. The longitude is a cyclic parameter. Meridians are defined from 0° up to 360°, each meridian going from one pole to another. Then, the definition of an origin meridian, comparable to the Greenwich meridian, is mandatory (Brechbuhler et al., 1995). This meridian will have both 0° and 360° values. The central sulcus is particularly fitted to this role. First, it is one of the most stable sulci. Moreover, it almost naturally links the two poles of the system. The link between the two poles, going through the central sulcus, is artificially closed using a geodesic shortest path algorithm on the cortical mesh.

**Table 1**

Sulci used in the model for the latitude direction.

<table>
<thead>
<tr>
<th>Sulcus</th>
<th>Axis</th>
<th>Latitude</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.Call.</td>
<td>Cingular polar circle</td>
<td>30</td>
</tr>
<tr>
<td>F.C.M.ant.</td>
<td></td>
<td>55</td>
</tr>
<tr>
<td>F.C.M.asc.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F.C.M.AMS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.IntraCing.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.I.P.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F.Coll.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.F.sup.</td>
<td>2</td>
<td>81</td>
</tr>
<tr>
<td>S.O.T.lat.post.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.Olf.</td>
<td></td>
<td>92</td>
</tr>
<tr>
<td>S.T.inter</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.T.I.ant.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.T.S.ter.asc.post.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.T.post.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.T.i.post.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.F.inter</td>
<td>4</td>
<td>106</td>
</tr>
<tr>
<td>S.T.S.ter.asc.ant.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.T.s.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insula</td>
<td>Insular polar circle</td>
<td>150</td>
</tr>
</tbody>
</table>

**Table 2**

Sulci used in the model for the longitude direction.

<table>
<thead>
<tr>
<th>Sulcus</th>
<th>Axis</th>
<th>Longitude</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.C.</td>
<td>Origin</td>
<td>0/360</td>
</tr>
<tr>
<td>S.Cinf.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.Csup.</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>SPW.Csup.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.Pe.Cinf.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.Pe.Cmedian</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F.C.L.asc.</td>
<td>2</td>
<td>40</td>
</tr>
<tr>
<td>S.Pe.marginal</td>
<td>3</td>
<td>61</td>
</tr>
<tr>
<td>S.Forbitaile</td>
<td>4</td>
<td>281</td>
</tr>
<tr>
<td>F.CalAnt.-Sc.Cal.</td>
<td>5</td>
<td>297</td>
</tr>
<tr>
<td>F.P.O.</td>
<td>5</td>
<td>339</td>
</tr>
<tr>
<td>F.P.O.inf.</td>
<td>6</td>
<td>106</td>
</tr>
<tr>
<td>S.PoC.sup.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F.F.PoC.inf.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F.F.PoC.sup.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Minimizing $E(S)$ then optimizes a tradeoff between three criteria: a minimum distance between the snake and the sulcal projection; a maximum curvature at the snake location; and a regularized minimum-elasticity shape of the snake.

Minimization is performed via a multi-resolution scheme as follows: the snake is initialized with the two extremities of the sulcus projection; those points keep their position during the whole process to avoid shrinkage of the snake due to elasticity minimization; then a point is added halfway between the two first ones (in the middle of geodesic path between the two points); its position is optimized by minimizing the energy using a greedy algorithm (maximum decrease of energy amongst the neighbors, iteratively until convergence); then two new points are added halfway between each pair of consecutive snake points; positions of the whole resulting point set is optimized with the same greedy algorithm; then new points are added and so on. The algorithm has converged when the snake is formed of a succession of neighboring points on the mesh. At this point, resolution cannot be increased, and the snake has reached its optimal position.

This process provides a single connected regularized sulcal bottom line, fitting with the local anatomy, while satisfying depth and curvature constraints. The multi-resolution algorithm is illustrated on Fig. 7, while results for different sulci are shown on Fig. 8.
Parameterization

The method presented in this paper interpolates the coordinate values between the sulcal bottom lines using an implementation of the heat equation with an additional data-driven term. More precisely, we adapted a method inspired from the closed surface parameterization method proposed by Brechbuhler et al. (1995).

Coordinate propagation

After sulcal bottom lines have been obtained (see above), they are divided in two sets, latitude and longitude. Each sulcal bottom line is attributed a longitude or latitude, always the same, according to our cortical model. Using these sets the two coordinate fields, latitude and longitude, are propagated over the whole cortical mesh. This is performed via a heat equation with an additional data-driven term as shown below:

$$\frac{\partial I}{\partial t}(r, t) = \Delta I(r, t) + \beta(r).I(r, t) - C(r)$$  \hspace{1cm} (2)

Where $I(r, t)$ stands for the coordinate value at node $r$ and iteration $t$. $C(r)$ is a function that equals 0 everywhere except on the sulcal bottom lines and their direct neighboring nodes, where it equals the assigned coordinate value. $\beta(r)$ is a regularizing function that equals 0 where $C(r)=0$, a constant value $\beta$ on the sulcal bottom lines (where $C(r) \neq 0$), and $(\beta/2)$ in the direct neighborhood of the sulcal bottom lines. The role of $\beta(r)$ is to regularize and reduce the discontinuities of the data-driven process and improve the process stability.

Fig. 4. Set of sulci used in the cortical organization models, shown on a particular brain. Top: longitude. Bottom: latitude.
Such process forces coordinates to be close to their desired value at the sulcal bottom lines (with the data-driven part of Eq. (2)), while ensuring a smooth and minimal interpolation of the coordinate field between the lines (with the Laplacian part of Eq. (2)).

Numerically, Eq. (2) is solved using the following iterative scheme until convergence:

\[
I(r, t + dt) = I(r, t) + dt \cdot \left( I(r, t) + \beta(r) \cdot (I(r, t) - C(r)) \right)
\] (3)

The coordinate Laplacian \( \Delta I \) is computed at each node using a finite element method proposed by Chung and Taylor (2004). The process behavior is illustrated on Fig. 12.

An example of the resulting coordinate fields is presented in Fig. 9 with the corresponding coordinate grid on Fig. 10.

**Sulcal bottom lines coordinate values**

In order to solve Eq. (2), we must define the values that are given to each of the sulcal bottom lines used as constraints, in order to define the function \( C(r) \). The issue is to have a distribution of longitude and latitude that minimizes metric distortions (Fischl et al., 1999b). In other words, we want coordinate between the sulcal lines to be as proportional as possible to the distribution of a geodesic distance between the same constraints of an average anatomy. Fig. 11 shows the effect of non-optimal coordinate distribution.

---

Fig. 5. Scheme of the process of parameterization. (A) Original cortical surface, with segmented and labeled sulci. (B) Selected anatomical features. (C) Projected sulcal bottom lines. (D) Resulting parameterization. (E) Model of cortical organization.

Fig. 6. Left and middle: cortical mesh with registered Cingular pole template volume. Right: resulting cingular pole after projection and geodesic closing.
To do so, we performed the coordinate propagation on 15 hemispheres, using Eq. (2) without any anatomical constraint, except the poles and the origin meridian. All the anatomical features defined above were then projected on the resulting coordinate systems. For each sulcal line, the mean coordinate value for each sulcal line across the 15 subjects was then chosen as the optimal constraints values. The resulting values for each sulcal line are given in Tables 1 and 2.

Experiments and discussion

In this section we present and discuss results of the process presented in the Model-driven parameterization: method section. For all experiments, parameters have the same values, which have been chosen as follows.

\textbf{Parameters}

The snake algorithm behavior is directed by the three parameters $a_1$, $a_2$, and $a_3$ (Eq. (1)). If $a_1$ has a high value, the sulcal bottom line will be very close to the original sulcal projection. If $a_2$ has a high value the line will fit with high curvature locations on the mesh, and if $a_3$ has a high value the snake rigidity will increase and will minimize its overall length, as illustrated in Fig. 12 for the calloso-marginal sulcus. Each one of those values has been defined empirically, after a range of tests on different sulcal projections. We set $a_1 = 20$, $a_2 = 500$ and $a_3 = 800$. The algorithm showed a good behavior in all cases, even though sulcal projections are very variable in length, shape, and topology. Although we chose this simple solution, it would be possible to introduce more prior information on sulcus geometry by setting specific values for each sulcus.
The other parameter in the process is $\beta$. It acts as a weight on the data-driven term in the coordinate propagation (Eq. (2)). A low value will lead in a low data-driven parameterization, which would result in an imprecise localization system. However, a high value leads to a coordinate system that complies exactly to the sulcal lines, whatever their geometry, and would result in an irregular and locally distorted coordinate field. Therefore, $\beta$ acts as a weight that balances out precision and robustness, and we empirically found a good tradeoff with $\beta = 0.2$.

Anatomical localization

Using these parameters, we applied the whole process to a set of 15 subjects from the ICBM database. Fig. 13 shows the result of the parameterization on 4 of those subjects (left and right hemispheres). It is visible that meridian and parallel lines comply with the cortical geometry. To estimate the localization power it is possible to look at geometrical or anatomical information across subjects.

On Fig. 14, an average of the surface mean curvature across the 15 subjects is shown. On the main sulci that are part of the model, one can see that the fit across subjects is very good. A dark blue color shows a consistent negative curvature across subjects, e.g., for the central and pre-central sulci, the superior and inferior frontal sulci, and the post-central sulcus on the external surface, or for the calloso-marginal sulcus, the parieto-occipital sulcus, the calcarine sulcus, or the callosal sulcus on the internal surface. Indeed, such a match is expected considering that the corresponding sulcal bottom lines are the elements that define the inter-subject homology. Nevertheless, it is interesting to note that sulci are not the only location where a good match can be observed: dark red areas on Fig. 14 show a consistent inter-subject matching of positive high curvature areas, i.e., gyri. Many gyri have a good match, such as the temporal, post- and pre-central, and cingular gyri, or the gyrus above the superior frontal sulcus. This shows that the interpolation provided by the Laplacian part of Eq. (2) performs well on those gyri.

The quality of the process highly depends on the underlying cortical folding model. Although it could be an issue in terms of localization, recent studies advocate for the legitimacy of this model, bringing elements towards a natural orthogonal organization of the deep cortex, along specific axes (Lohmann et al., 2007; Toro and Burnod, 2003; Braak, 1980; Pandya and Yeterian, 1985). Although the link between the macroscopic (especially the sulci) and the microscopic anatomy has been widely debated (see Zilles et al., 1997 for instance), new studies are suggesting that a link between the cortical folding and the cyto-architectony could be extracted at some level (Fischl et al., 2007). Such considerations enhance the capabilities
of our approach, based on the cortical folding process to localize areas on the cortical surface, giving then immediate access to information of interest, such as anatomical and functional parcellation (Clouchoux et al., 2006).

Still, one issue is that the density of landmarks used in the model is not equally distributed over the whole surface. In particular, one can see on Fig. 4 that there are very few longitude sulcal landmarks in the temporal and frontal lobes. Similarly, the occipital lobe lacks latitude sulcal landmarks. This predicts a lower localization power in the parietal and occipital areas. The lack of landmarks can be explained in two ways:

- the model still needs to be refined, and our dependence on a cortical model will force us to improve our understanding of cortical variability. Fig. 5 in Régis et al. (2005) shows a good number of sulcal roots in the occipital lobe. Nevertheless we fail at identifying stable folds in this area. This is partly because folding around sulcal roots in this area is a lot more variable and occurs with various orientations, meaning that folds are in the latitude direction for some subjects, and in the longitude direction for others. Detecting one situation or the other would help to improve the process and add landmarks but would also force the issue of homologies between subpopulations with different folding patterns.
- the sulcus extraction process by Rivière et al. (2002) fails at segmenting properly the sulci. Some folds need to be divided in units as close as possible to the sulcal roots in order to show intersubject stability. They also can take two different directions in our model. For instance the intra-parietal sulcus has the longitude orientation in its anterior part and the latitude orientation in its posterior part. It is therefore necessary to segment both parts properly.

The lack of landmarks in some areas also suggests that additional information, such as geometry could be used. Convexity (FISCHL-99) or curvature maps could be used in a hybrid system to improve intersubject matching and add robustness in areas where sulcal landmarks are lacking. Indeed, it has been shown for the spatial normalization of volumes that combining model-free intensity information and model-based sulcal information improves performances (Cachier et al., 2001).

Functional localization

In order to estimate the functional localization power of the system, we applied the parameterization on a set of 12 subjects that took part in a localizer fMRI study (Pinel et al., 2007). All structural T1 MR images were processed according to the methods presented in the Model-driven parameterization: method section, in order to get a parameterized mesh of both hemispheres. A surface-based structural group analysis of functional data was performed using the method presented by Operto et al. (2008). We analyzed a specific contrast, “motor–cognitive,” because it showed different functional activations.
in various cortical areas. Specifically, 5 activations were detected at the group level, in the following areas: post-central gyrus (S1), pre-central gyrus (M1), supplementary motor area, temporal lobe, and parietal lobe. Additionally, the individual representation of these group activations was made available by the structural analysis (Operto et al., 2008). Besides, anatomical data were also normalized to the ICBM152 template with affine transformations, using the SPM5 software (Ashburner et al., 1999). The resulting transformation for each subject was applied to the hemisphere mesh in order to get a normalized mesh. Finally, for each individual representation of a group activation, the peak of activation was identified and 2 sets of coordinates were computed:
- The 2D coordinates \((l, L)\) from the method presented in this paper, where \(l\) stands for the longitude and \(L\) for the latitude.
- The 3D coordinates \((x_N, y_N, z_N)\) in the normalized ICBM152 space.

In order to estimate the functional localization power of the method, we computed the inter-subject dispersion as the mean distance (geodesic distance for 2D coordinates, Euclidean distance for...
3D coordinates) between each pair of individual occurrences of the activation. This distance was directly computed in the 3D normalized space:

$$d_{3D,i} = \frac{1}{66} \sum_{i=1}^{11} \sum_{j=i+1}^{12} \sqrt{(x_i - x_j)^2 + (y_i - y_j)^2 + (z_i - z_j)^2}$$

where \((x_{i,N}, y_{i,N}, z_{i,N})\) stands for the 3D normalized coordinates of the activation peak for subject \(i\). For the 2D coordinates, there is no reference domain (like ICBM152 in the 3D space) on which to compute distances. Dispersion was then computed on each subject’s surface, then averaged across subject as follows, to avoid the bias introduced by a single subject:

$$d_{2D} = \frac{1}{12} \sum_{i=1}^{12} d_{2D,i}$$

with \(d_{2D,s}\) the dispersion computed on the cortical surface of subject \(s\):

$$d_{2D,s} = \frac{1}{66} \sum_{i=1}^{11} \sum_{j=i+1}^{12} g_s(l_i, l_j).$$

Where \((l_i, l_j)\) stands for the 2D coordinate of the activation peak for subject \(i\), and \(g_s(,\,)\) stands for the geodesic distance computed on the cortical surface of subject \(s\).

In order to compare our method to another surface-based normalization technique, all cortical surfaces were normalized using the Freesurfer software (Fischl et al., 1999a,b, http://surfer.nmr.mgh.harvard.edu/) and resampled in order to have a node-to-node inter-subject matching. The exact same measurements were performed in the Freesurfer referential.

All measurements are given in millimeters. Table 3 gives results for each of the 5 activations, as well as the mean across activations.

For 3 foci (in the parietal, pre-central, and post-central areas) our method and Freesurfer give equivalent results, Freesurfer being better for two of them, and our method being better for one. For the supplementary motor area (SMA) and the temporal activation focus, our method outperforms Freesurfer. The SMA has been reported as a supplementary motor area (SMA) and the temporal activation focus, for two of them, and our method being better for one. For the parietal activation, the dispersion is mostly in the latitude direction, which can also be explained by the lack of precision in neighboring areas. For the post-central activation, dispersion is mostly in the latitude direction, which can also be explained by the lack of precision in neighboring areas.

Table 3 Dispersion in the 2D, 3D, and normalized 3D spaces (in mm) for each activation focus, and mean across foci.

<table>
<thead>
<tr>
<th></th>
<th>Pre-central</th>
<th>Post-central</th>
<th>SMA</th>
<th>Temporal</th>
<th>Parietal</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>(d_{2D,\text{BrainVISA}})</td>
<td>10.98</td>
<td>17.42</td>
<td>9.10</td>
<td>15.47</td>
<td>15.63</td>
<td>13.72</td>
</tr>
<tr>
<td>(d_{2D,\text{Freesurfer}})</td>
<td>9.44</td>
<td>19.73</td>
<td>14.55</td>
<td>29.25</td>
<td>14.68</td>
<td>17.53</td>
</tr>
<tr>
<td>(d_{2D,\text{Freesurfer}})</td>
<td>14.24</td>
<td>14.22</td>
<td>10.85</td>
<td>17.21</td>
<td>11.10</td>
<td>13.52</td>
</tr>
</tbody>
</table>

The local curvature and depth patterns used by Freesurfer to perform matching. On the other hand, this sulcus is used as a constraint in our system which guarantees a greater stability of the matching in this area. The ‘temporal area’ focus is on the inside of the Sylvian fissure. On Fig. 15, one can see the dispersion of foci across subjects, plotted on a cortical mesh. It suggests that in the Freesurfer referential, there is a stronger variability along the Sylvian fissure. Those results have to be interpreted carefully on a small group like the one we used, especially in an area where segmentation is difficult and can artificially disturb depth and curvature measurements. A small number of subjects could be locally misaligned and deteriorate measurements. On the other hand, the Sylvian fissure is close to the insular polar circle, an area where several main axis of our system (defined by folds located farther on the surface) converge, adding some constraints in this area. For a more extensive comparison of landmark-based and geometry-based methods, the reader can refer to Pantazis et al. (2009).

For 3 activation foci, our 2D parameterization performs better than the 3D normalized space. For the parietal and post-central activations it performs worse than the normalized 3D space. The overall performances are equivalent (see Table 3). For the comparison between 2D and 3D spaces, one has to keep in mind that geodesic distance have to be greater than Euclidean distances, which let us think that performances of the system are actually better than what they appear. The poor performances in the parietal area can be explained by the lack of landmarks of the model in this area, mainly because the posterior part of the intra-parietal sulcus is not used (see Fig. 4), and by the lack of landmarks in the occipital lobe that induces a lack of precision in neighboring areas. For the post-central activation, dispersion is mostly in the latitude direction, which can also be explained by the lack of latitude information of the model in the temporal and parietal area. As already stated in the previous section, this lack of landmarks has to be solved by refining our model or adding dense information such as curvature or depth to locally compensate for the lack of structures.

Conclusion

In this paper we presented a generic and organized model of cortical folding, and a way to implement this model on any given cortical surface. This results in a cortical parameterization constrained by the model. This parameterization provides a meaningful coordinate system for cortical localization, and implicitly defines an inter-subject surface matching. Such system leads to surface-based group studies of anatomical characteristics (e.g., cortical thickness) or functional data (as in Operto et al., 2008). The process is fully automated and is available in the Cortical Surface toolbox of BrainVISA (http://brainvisa.info).

Because the parameterization is driven by our cortical folding model, some specific meridians and parallels of the coordinate system correspond to anatomical feature alignments and functional axes. This exhibits the notion of cortical orientations (as already pointed out by
Régis et al., 1995; Toro and Burnod, 2003; Régis et al., 2005) and leads for instance to parcellations of the cortex based on remarkable axis of the system, as shown by Clouchoux et al. (2006).

Finally, having a model of cortical organization and a way to map any cortical surface to this model opens the door to functional meta-analysis (Toro et al., 2008) in order to understand functional organization and anatomo-functional correlations.

Acknowledgments

The authors would like to thank Bertrand Thirion, Alan Tucholka and Cyril Poupon for providing some data used in this manuscript.

References


Cunningham, D.J., Horsley, V., 1892. Contribution to the surface anatomy of the cerebral hemispheres. Academy, Royal Irish.


