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1 Larger seems twistier : Spectral Analysis of Gyrfication
2 patterns (SpAnGy) applied to adult brain size
3 polymorphism.

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13 **Abstract**

14 *Keywords:*

15 **1. Introduction**

16 The description of human cortical folding remains a major challenge for
17 neuroimaging due to its great complexity and variability. On the one hand,
18 a better knowledge of cortical folding would allow us to devise more precise
19 methods for inter-individual comparisons, on the other one, cortical folding
20 is interesting in itself as research reveals subtle correlations with typical and
21 pathological functioning (Fischl et al., 2007; Cachia et al., 2008). Sulci have
22 been traditionally classified from a developmental point of view into primary,
23 secondary and tertiary (Chi et al., 1977) according to their order of appear-
24 ance during fetal life and early childhood. But cortical folding is probably
25 a more continuous process than suggested by this classification (Armstrong
26 et al., 1995), and successive folding phases may impact on each other (?)
27 [PAUS, 1995, DON'T FIND THE ARTICLE] in a way that morphological
28 features resulting from different phases can intricate into the same given fold.
29 This interaction leads to a geometric complexity well described for the central

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30 sulcus (White et al., 1997): sulci are not straight objects but show ramifica-
31 tions, digitations, nodes, dimples, etc. This complexity is associated with an
32 important inter-individual variability (Yousry et al., 1997; Régis et al., 2005)
33 which complicates the construction of folding atlases, even at a large-scale
34 level. Eventually, as soon as mature gyrification is achieved, it is very difficult
35 to attribute, based on morphological features alone, a primary, secondary or
36 tertiary character to a given piece of a cortical fold (Fig. 1).

37 In the general population, human brain size is also highly variable, with
38 the largest adult brains having up to 2 times the volume of the smallest ones
39 (?Whitwell et al., 2001) [MILNER, 1990, DON'T FIND THE ARTICLE]. As
40 for many biological objects, the relationship between cortical surface geome-
41 try (shape) and brain volume (size) is not simply homothetic: there are shape
42 modifications coming with size variations (allometry). Across mammals, cor-
43 tical surface area appears to scale proportionally with brain volume, whereas
44 an isometric relationship would predict a scaling exponent of $2/3$ (Prothero
45 and Sundsten, 1984). A similar allometric scaling can be observed among
46 humans, with scaling exponents in the order of 0.8 to 0.9 (Im et al., 2008;
47 Toro et al., 2008). Indeed, large brains show a relative excess of cortical
48 surface, which is accommodated by an increased folding. Several gyrification
49 indexes have been proposed at hemispheric (Zilles et al., 1988) or local level
50 (Schaer et al., 2008; Toro et al., 2008). They measure the proportion of corti-
51 cal surface buried by folding, but are unable to distinguish an increase in the
52 depth of the folds from an increase in the number of folds or in ramification.
53 Such a modification of the complexity of cortical folding pattern (CFP) with
54 brain size is nonetheless suspected: larger brains seem twistier (Fig. 1b). So
55 far, attempts to propose a more descriptive assessment of gyrification com-
56 plexity have provided rather preliminary results and there is no consensual
57 measure, even at hemispheric level (Luders et al., 2004; Yotter et al., 2011).
58 From a theoretical perspective, several models suggest that folding in an ex-
59 panding domain should lead to the development of branching with doubling
60 of the spatial frequency patterns (Fig. 1a). This phenomenon is observed
61 with reaction-diffusion (Crampin et al., 1999; Striegel and Hurdal, 2009) and
62 mechanical models (Mora and Boudaoud, 2006), but also with fractal ap-
63 proaches (Thompson et al., 1996; Yotter et al., 2011). Thus, the study of
64 the spatial frequencies of CFP should provide us an interesting new measure
65 of gyrification complexity.

66 The grey/white matter interface of a brain hemisphere can be viewed
67 as a closed surface of zero-genus (Dale et al., 1999) on which it is possible

68 to map scalar functions estimating surface characteristics such as curvature
69 or sulcal depth. These oscillatory functions can be seen as proxies of the
70 hemispheres gyrification pattern. The properties of CFP could then be stud-
71 ied through the analysis of its spatial oscillation frequencies. This spectral
72 approach could be used to produce a power spectrum representative of the
73 spatial frequencies composition of a cortical surface. The study of the eigen-
74 functions of the Laplace-Beltrami Operator (LBO) provides a natural method
75 to obtain spectral decompositions of surfaces or, more generally, Riemannian
76 manifolds (Berger, 2003). The methods necessary to apply this mathemati-
77 cal theory to the analysis of discrete meshes have been recently described by
78 (Reuter et al., 2006) and (Lévy, 2006). One interest of this approach com-
79 pared with the more traditional spherical harmonics decomposition is that
80 it can be directly used with native data, without the non-linear alignment
81 and spherical parametrization steps required by spherical harmonics decom-
82 positions (Chung et al., 2008; Hübsch and Tittgemeyer, 2008). Since folding
83 wavelengths in the native surface are often projected onto the sphere with
84 a different wavelength, such a parametrization necessarily induce a certain
85 level of distance or angular distortions (Gu et al., 2004; Kruggel, 2008). In re-
86 turn, LBO-based spectral analysis requires to devise an appropriate strategy
87 to compare individually defined decompositions (Knossow et al., 2009).

88 In this article, we propose an original method for the Spectral Analysis of
89 Gyrification (Spangy) which produces a morphologically relevant band power
90 spectrum of CFP. We also report on the interest of Spangy for the study of
91 the variability of CFP complexity with brain size in the comprehensive cohort
92 of young healthy adults of the ICBM MRI database (Mazziotta et al., 1995;
93 Watkins et al., 2001). Firstly, we present theoretical and numerical aspects
94 of the LBO-based analysis, along with relevant Spangy design choices such
95 as definition of curvature function, spectral bands or spectral segmentation
96 of CFP. Next, we derive the measuring and describing properties of Spangy
97 from our numerical and anatomical results in the ICBM database. Finally,
98 we establish the relationship between spectral composition of CFP and brain
99 size through allometric scaling. In the field of cortical surface study, LBO-
100 based spectral analysis has been previously used only as a tool for surface
101 smoothing (Vallet and Lévy, 2008). To our knowledge, this is the first time
102 that this approach is used to provide a relevant signature of CFP and assess
103 gyrification complexity.

104 2. Materials and Methods

105 2.1. Population

106 2.2. Subjects

107 We analyzed the 152 normal volunteers of the ICBM MRI database
108 (Watkins et al., 2001). Each subject had a T1-weighted scan (3D fast field
109 echo images, 140 to 160 slices, 1 mm isotropic resolution, TR = 18 ms, TE
110 = 10 ms, flip angle = 30, Phillips Gyroscan 1.5T scanner). One scan was
111 excluded because of its lesser quality, leading to artifacts in the automatic
112 segmentation step. Of the remaining 151 subjects, 86 were males and 65 were
113 females. Ages ranged from 18 to 44 years (mean age: 25 years, standard de-
114 viation: 4.9 years). 128 subjects were right-handed, 14 were left-handed, and
115 handedness was unknown for the remaining 10.

116 2.3. Brain segmentation and morphometric parameters

117 T1-weighted images were automatically segmented with BrainVISA T1
118 segmentation pipeline (BrainVisa Software) to obtain topologically spherical
119 mesh reconstructions of the left hemispheric hull (morphological closing of
120 the hemispheric mask) and grey-white interface. The reconstructions were
121 visually inspected for segmental disruption or excess of surface spicules, lead-
122 ing to the exclusion of one subject. The hemispheric volume (HV) i.e. the
123 volume inside the hemispheric hull and the hemispheric surface area (HA)
124 i.e. the area of the grey-white interface were computed for each left hemi-
125 sphere using the BrainVISA Morphometry toolbox. The mean curvature of
126 the grey-white interface (H) was computed using the non-parametric esti-
127 mator implemented in the BrainVISA Surface toolbox, which is based on the
128 method introduced by (Desbrun et al., 1999).

129 2.4. Laplace-Beltrami operator and spectral theory

130 Given a compact Riemannian manifold (\mathcal{M}, g) , where g is a metric tensor,
131 we introduce $L^2(\mathcal{M}) = \{u : \mathcal{M} \rightarrow \mathbb{R} / \int_{\mathcal{M}} u^2 < +\infty\}$ and the scalar product
132 $\langle u, v \rangle = \int_{\mathcal{M}} uv$. The spectrum of the *Laplace-Beltrami operator* (LBO)
133 $\Delta_{\mathcal{M}} = \text{div} \circ \nabla_{\mathcal{M}}$ is discrete (Berger, 2003). We denote $\lambda_0 = 0 \leq \lambda_1 \leq \dots$
134 the *eigenvalues* of $-\Delta_{\mathcal{M}}$ and ϕ_0, ϕ_1, \dots an associated orthonormal basis of
135 eigenfunctions in $L^2(\mathcal{M})$ that satisfy:

$$-\Delta_{\mathcal{M}}\phi_n = \lambda_n\phi_n. \quad (1)$$

136 Given an eigenfunction ϕ_n , the nodal set of ϕ_n is defined as $\{x \in \mathcal{M}, \phi_n(x) =$
 137 $0\}$. The connected components of the complement of the nodal set are called
 138 *nodal domains*. The Courant Nodal Domain Theorem ensures that if ϕ_n is
 139 not the first eigenfunction, the number of nodal domains is at least 2 and
 140 at most n . Moreover any function $u \in L^2(\mathcal{M})$ can be decomposed in the
 141 previous basis:

$$u = \sum_{i=0}^{+\infty} u_i \phi_i, \text{ with } u_i = \int_{\mathcal{M}} u \phi_i. \quad (2)$$

142 The Parseval's formula which will be useful for normalization states that :

$$\int_{\mathcal{M}} u^2 = \sum_{i=0}^{+\infty} u_i^2. \quad (3)$$

143 It is possible to compute eigenfunctions on a mesh \mathcal{M}_h that approximates \mathcal{M}
 144 using a weak formulation of the eigenvalue problem and the finite elements
 145 method. If u and λ are solutions of $-\Delta_{\mathcal{M}} u = \lambda u$ then:

$$\int_{\mathcal{M}} g(\nabla u, \nabla v) = \lambda \int_{\mathcal{M}} uv, \forall v \in L^2(\mathcal{M}). \quad (4)$$

146 We use the finite elements framework to derive a matricial expression of
 147 this weak formulation. We consider the mesh \mathcal{M}_h composed of N vertices.
 148 For each vertex i of the mesh we have a function $w_i : \mathcal{M}_h \rightarrow \mathbb{R}$ which is
 149 continuous, linear on each triangle of the mesh and satisfying the property
 150 $w_i(j) = \delta_{ij}$. Any function continuous and linear on each triangle can be
 151 decomposed on this basis $u = \sum_{i=1}^N u_i w_i$ where u_i are real coefficients. So
 152 the equation (4) can be rewritten in the discrete setting, taking $v = w_j$ for
 153 all $j \in [1 : N]$. And the discretized problem becomes to find a vector
 154 $[U] = (u_i)_{i=[1:N]}$ and a scalar λ such that:

$$[\nabla][U] = \lambda[M][U], \quad (5)$$

with the stiffness and mass matrices given by :

$$[\nabla] = \left(\int_{\mathcal{M}_h} \nabla w_i \cdot \nabla w_j \right)_{i=[1:N], j=[1:N]}, \quad [M] = \left(\int_{\mathcal{M}_h} w_i w_j \right)_{i=[1:N], j=[1:N]}.$$

155 More details on the computation of these two matrices are given in (Desbrun
 156 et al., 1999). The eigenvalue problem (5) can be solved for example with

157 the Lanczos method as in (Arnoldi Package) since the matrices involved are
 158 sparse and symmetric positive.

159 In practice, we computed several thousand eigenfunctions (5000) such that
 160 the spatial wavelength reaches a reasonable spatial resolution (see Appendix
 161 B). Recent strategies could be investigated to compute sequentially an in-
 162 creasing list of eigenvalues (Vallet and Lévy, 2008) until obtaining the re-
 163 quired resolution.

164 2.5. Curvature decomposition

165 We used the mean curvature H of the cortical surface to represent its
 166 folding pattern. The mean curvature is the average of the two principal
 167 curvatures or equivalently half of the trace of the second fundamental form
 168 (Petitjean, 2002). Whether in theory we could have used the intrinsic Gaus-
 169 sian curvature, we preferred to use the mean curvature instead because, being
 170 an extrinsic measure (dependent on the embedding of the surface in space), it
 171 may add supplementary information to the LBO-based decomposition which
 172 is already intrinsic to the surface.

173 The mean curvature can be decomposed in the eigenfunction basis through
 174 formula (2). We will denote $H_n := \int_{\mathcal{M}} H \phi_n$ the coefficients of the cur-
 175 vature in the eigenfunctions basis ϕ_n and call *raw spectrum* the sequence
 176 $RS_H(n) := H_n^2$. We define also a normalized spectrum of curvature:

$$NS_H(n) := \frac{H_n^2}{\int_{\mathcal{M}} H^2} \quad \forall n \geq 0. \quad (6)$$

177 which satisfies:

$$\sum_{n=0}^{+\infty} NS_H(n) = 1 \quad (7)$$

178 thanks to Parseval's formula (3).

179 We call *Total Folding Power* the quantity:

$$TFP_H := \sum_{n=0}^{+\infty} H_n^2 = \int_{\mathcal{M}} H^2 \quad (8)$$

180 This dimensionless parameter is independent of homothetic brain size
 181 variation. Namely, if one has a scaling coefficient λ between \mathcal{M}_1 and \mathcal{M}_2
 182 then $H_{\mathcal{M}_2} = \frac{1}{\lambda} H_{\mathcal{M}_1}$ and a small quantity of surface becomes $dS_2 = \lambda^2 dS_1$,

183 and then:

$$\int_{\mathcal{M}_2} H_{\mathcal{M}_2}^2 dS_2 = \int_{\mathcal{M}_1} H_{\mathcal{M}_1}^2 dS_1 \quad (9)$$

184 See Fig. 2 for computation steps.

185 2.6. Spectral frequency bands design

186 In the following, we will call $F(n)$ and $WL(n)$ the theoretical frequencies
 187 and the wavelengths associated to the n^{th} eigenfunction (see Appendix A for
 188 further development on spatial frequencies):

$$F(n) = \frac{\sqrt{\lambda_n}}{2\pi} \quad WL(n) = \frac{2\pi}{\sqrt{\lambda_n}} \quad (10)$$

189 As a consistency check we compared these theoretical frequencies with eigenfunction-
 190 derived quantities of the same dimension, which can be intuitively considered
 191 as empirical frequencies and can be computed based on the number of nodal
 192 domains through the formula:

$$WL2(n) = \sqrt{\frac{\text{Surface of } \mathcal{M}}{\text{Number of nodal domains of } \phi_n}} \quad (11)$$

193 The raw spectrum of curvature is a very complex type of data, challeng-
 194 ing to analyze and even to visualize because of its several thousand points.
 195 Moreover, since the eigenfunction bases are defined on a per-individual ba-
 196 sis, there is no mathematically exact matching of eigenfunctions of the same
 197 n -order (Knossow et al., 2009; Lombaert et al., 2011). Hence, as a dimen-
 198 sional reduction and smoothing step, we merged levels of successive orders
 199 into superior grouping levels defined by a sequence of spatial frequency $F(n)$
 200 marking interval limits. The sequence was chosen in order to fulfill a model
 201 of branching with doublings of spatial frequency. The spatial frequency asso-
 202 ciated with the 1st non-constant eigenfunction was considered as the subjects
 203 reference frequency $F(1)$. The following interval limits were the spatial fre-
 204 quencies $2^k F(1)$. This merging strategy allowed us to define a band power
 205 spectrum (than could be later normalized or not) defined as:

$$BS_H(0) = H_0^2 \quad (12)$$

$$BS_H(k) = \sum_{n=n_1^k}^{n_2^k} H_n^2 \quad \text{with} \quad (13)$$

$$n_1^k = \arg \min_n |F(n) - 2^{k-1}F(1)| \quad (14)$$

$$n_2^k = \arg \min_n |F(n) - 2^k F(1)| \quad (15)$$

206 As we computed around 5000 eigenfuntions, this merging strategy allowed
 207 us to define 7 bands, numbered from B0 to B6. See Fig. 3 for band design
 208 step.

209 *2.7. Spectral segmentation of CFP*

210 We define a CFP map as the binary map where sulci correspond to regions
 211 of negative curvature and gyri correspond to regions of positive curvature.
 212 Based on the properties of spectral decomposition, band-by-band spectral
 213 synthesis of curvature can be performed in a cumulative or non-cumulative
 214 way. Non-cumulative synthesis is equivalent to band-pass filtering, and can
 215 be used to show the specific contribution of each spectral band. Cumulative
 216 synthesis, is equivalent to low-pass filtering, and can be used to show the
 217 effect of the gradual addition of higher frequency components to the map.
 218 From these 2 types of synthesis, we derived 2 segmentations of CFP:

- 219 • First, a segmentation according to the locally dominant frequency band:
 220 we used non-cumulative synthesis to label each vertex with the number
 221 of the band that contributed the most to its curvature value. See Fig.
 222 4 for computation steps.
- 223 • Second, a segmentation according to the locally patterning frequency
 224 band: we used cumulative synthesis to label each vertex with the num-
 225 ber of the band that determined whether it belong to the sulcal or the
 226 gyral pattern. We assessed the differential contribution of each fre-
 227 quency band to the CFP by subtraction between the CFP maps of two
 228 consecutive levels of cumulative synthesis. See Fig. 5 for computation
 229 steps.

230 Extensive formulations for these 2 types of segmentation are given in
 231 Appendix C. For the sake of clarity, they can be both visualized with a
 232 gyral pattern mask, hence restricting the image to the sulcal pattern. Due to
 233 their large preponderance in patterning (see Results), second segmentation
 234 is restricted to the last three frequency bands.

235 For each label, we computed the surface area and the number of parcels,
 236 i.e. sets of connected vertices that have the same considered label. The seg-
 237 mentation according to the locally dominant band is rather noisy due to the

238 use of a truncated spectrum (number of eigenfunctions < number of vertices),
239 which produces very small parcels (mainly isolated vertices) related to non-
240 computed bands (very high frequencies). We used an adaptive-threshold
241 filter to remove these noisy parcels before computation (see Appendix B).
242 Conversely, for the segmentation according to the locally patterning band,
243 the number of parcel related to each label had been directly computed on
244 the intermediary subtraction step.

245 *2.8. Statistical analysis and allometric scaling*

246 We performed an ANOVA to assess the effect of age, sex, and hemispheric
247 volume on hemispheric surface area and spectral parameters. The correla-
248 tions between cortical surface parameters (hemispheric surface area, total
249 folding power or spectral band power) and brain size (hemispheric volume)
250 were tested assuming a power law:

$$Y = bX^a \tag{16}$$

251 We compared the scaling factor a in the equation with the value it should
252 have when the scaling is isometric, i.e., presuming that 1 or 2 dimensional
253 parameters scale with hemispheric volume as the 1/3 or 2/3 power respec-
254 tively and that folding power is constant. The estimation of a and b was
255 performed using log-log linear fit.

256 All statistical analyses have been performed using SPSS version16.0.

257 **3. Results**

258 *3.1. Measuring properties: size and power*

259 *3.1.1. Wavelength for domain sizing*

260 The measuring properties of the proposed band power spectrum rely on
261 the association of each LBO eigenfunction of the basis with a well-defined
262 spatial frequency. Eigenfunctions of increasing order (i.e. smaller associated
263 eigenvalue) show an increasingly scattered nodal domain pattern, consistent
264 with the expected increase of their associated spatial frequency (Fig. 3a).
265 The consistency between the empirical wavelength estimated through the
266 number of nodal domains and the theoretical wavelength derived from the
267 eigenvalue is confirmed by the strong linear correlation between the two
268 values. For low orders, the empirical computation is not precise, due to its
269 sensitivity to domain shape, coalescence and irregularity, but from the 10th

270 order on, the relationship becomes almost exact (mean fit for ICBM database:
 271 $0.87x + 4.51$, $R = 1$), and after the 100th order, there no longer seems to be
 272 any difference ($0.97x + 0.56$, $R = 1$). In spite of a certain variability, the mean
 273 shape for the nodal domains of an eigenfunction looks like a spot scaled by
 274 its theoretical wave length (Fig. 3b). The wavelength not only depends on
 275 the order of the eigenfunction but also on the size of each individual brain.
 276 Being a one-dimensional parameter intrinsically derived from the grey/white
 277 surface, the theoretical wavelength is expected to scale as $HA^{1/2}$, which is
 278 almost exactly what we observe in the ICBM database: $1.74GWI^{0.495}$, R
 279 $= 0.938$. This result validates the possibility of computing frequency band
 280 statistics in the ICBM database (Table 1).

281 *3.1.2. Spatial resolution concerns*

282 The spatial resolution of our spectral analysis is limited intrinsically by
 283 the mesh resolution, and extrinsically by the number of eigenfunctions com-
 284 puted in the decomposition basis. The density of vertices in the surfaces
 285 that we used is not homogenous and changes locally depending on the sur-
 286 face geometry. The mean number of vertices in our surface reconstructions
 287 was 21418 ± 2268 , and the mean triangle edge length was $2\text{mm} \pm 0.5\text{ mm}$, i.e.,
 288 a mean resolution of 3mm^2 . The mean wavelength of the last eigenfunction
 289 necessary to compute the proposed 7 bands is 7mm , i.e. a mean resolution
 290 of 9 mm^2 (see Table 1 for values, Fig. 3b for illustration, and Appendix B
 291 for computation). Hence, in our analyses the spatial resolution of the de-
 292 composition basis was slightly larger than that of the surface meshes. This
 293 allowed us to consider a minimal pattern element of around 3 contiguous
 294 vertices. This resolution is reasonable given that the patterns of interest in
 295 a cortical surface are hardly to be found below half a centimeter, and also to
 296 avoid variation due to inaccuracies in surface segmentation and reconstruc-
 297 tion. To assess the robustness of our results with respect to the number of
 298 vertices of the meshes, we compared the spectrum computation before and
 299 after mesh refining (doubling of the number of vertices) , and we did not find
 300 any significant differences (data not shown).

301 *3.1.3. Band power proportions*

302 By construction, the proposed band power spectrum gives a partition
 303 of the total folding power in intervals of doubling spatial frequencies (i.e.
 304 spectral bands). The band power spectrum normalized by the total folding
 305 power provide a spectral proportion, or in other terms, the relative weight

306 of each spectral band. However, the decomposition basis necessary for the
307 computation of 7 bands cannot account for the full total folding power since
308 part of it is contained in the higher frequency levels that we do not compute.
309 The normalized 7 bands spectra of all ICBM database subjects shows that on
310 average, our analysis concerns around 2/3 of the total folding power (mean
311 65.8%, SD 1.45%, Fig. 6). More precisely:

- 312 • B0 (the constant band) accounted for 0.35% (SD 0.14%),
- 313 • B1, 2 and 3 (the first 3 oscillating bands) accounted for 4.39% (SD
314 0.79%),
- 315 • B4, 5 and 6 (the last 3 oscillating bands) accounted for 61.2% (SD
316 1.43%).

317 This shows the quantitative predominancy of the last 3 bands, which account
318 for a large proportion of the total folding power and almost the totality of
319 the analyzed folding power (92.8%).

320 *3.2. Describing properties : anatomo-spectral correlations*

321 We now show the utilization of Spangy to categorize and quantify pattern
322 elements back on the original cortical surface, on the basis of spatial frequency
323 properties.

324 *3.2.1. Global shape vs folds patterning*

325 Low-pass and band-pass filtering provide a first insight into the link be-
326 tween spectrum and cortical folding through the sequential visualization of
327 the contribution of each band to the curvature value (Fig. 4) and the CFP
328 (Fig. 5). B0 does not account for any pattern since the 1st eigenfunction
329 does not oscillate. B1 and B2 bands account for patterns that are not cor-
330 related with folding but rather with the global brain shape, like the slight
331 concavity of the medial hemispheric side (B1) and the bottom of the sylvian
332 fissure (B2), the global convexity of the lateral hemispheric side (B1), or the
333 convexity of the polar regions (B2). B3 contributes mainly to the global brain
334 shape with the transition between lateral and medial sides of the hemisphere
335 or the sylvian banks, but also to initiate the fundi of several primary sulci,
336 such as the posterior part of the superior temporal sulcus or the medial part
337 of the intra parietal sulcus. As we shown previously, whatever the qualitative
338 contribution to the CFP of the first three non-constant bands may be, they

339 are quantitatively very weak. Thus, patterns consistent with cortical folding
340 appear with B4 (Fig. 4, Fig. 5) and most substantial contributions to the
341 CFP are produced by B4, B5 and B6. These 3 bands will be further referred
342 as the folding bands.

343 3.2.2. *Dominant vs patterning band for segmentation of CFP*

344 The 2 types of spectral segmentation of CFP (Fig. 4 and Fig. 5) are pre-
345 sented in Fig. 7 on 5 brains of increasing size (restricted to sulcal pattern):
346 the segmentation according to patterning band in the 2nd column, and the
347 segmentation according to dominant band in the 3rd column. They provide
348 complementary information about the contribution of each folding band. The
349 segmentation according to patterning band sums up the observations made
350 on low-pass filter series and provides a clear image of the progressive rami-
351 fication of the sulcal pattern produced by the addition of higher frequency
352 bands. The segmentation according to dominant band shows a similar phe-
353 nomenon but with significant differences in surface labeling which show that
354 a vertex can be added to sulcal or gyral pattern by one band, whereas its
355 curvature value is mainly determined by a higher frequency band. These dis-
356 crepancies between a locally patterning frequency band and locally dominant
357 frequency band are particularly visible around the polar regions. Besides, as
358 previously explained, the segmentation according to dominant band is noisy
359 and we applied a band-adapted minimum threshold for size before the quan-
360 tification of surface area and number of sulcal parcels. This threshold had
361 a very mild effect on the regions labeled by B4, B5 and B6, leading to a
362 mean area reduction of respectively 6.9%, 1% and $< 0.1\%$ (SD 1.5%, 0.2%
363 $< 0.1\%$). Nonetheless, it was sufficient to rub out most of the irrelevantly
364 small spots, particularly for B4 band, rejecting an average of respectively
365 118, 45 and 3 spots (SD 19, 11 and 2), with a mean spot area 2 times below
366 the threshold. Finally, we found a strong linear correlation between B4, B5
367 and B6 spectral power and labeled surface area, respectively: $335x + 3660$
368 ($R = 0.783$), $396x - 96.3$ ($R = 0.917$), $403x + 884$ ($R = 0.961$), showing
369 that the segmentation according to dominant band gives a faithful picture
370 of the band power spectrum. The correlation was equally good between the
371 normalized band power and the labeled surface area reported to hemispheric
372 surface area.

373 *3.2.3. Anatomical correlates of spectral segmentation of CFP*

374 The sulcal pattern of the low-pass filtered CFP map at B4 level consists
375 in a limited set (21 elements ± 3) of large smooth sulcal parcels with few
376 ramifications (Fig. 7, 1st column). These spectrally defined folding fields
377 embed the main primary folds of the literature (Fig. 8a, (Chi et al., 1977))
378 and are refined by B5 and B6 to produce a more irregular and branched CFP.
379 Thanks to the proposed spectral segmentations, the CFP can be divided
380 into 1st, 2nd and 3rd order elements associated respectively with frequency
381 bands B4, B5 and B6. A segmentation considering only the folding bands
382 is supported by the restriction of lower frequency band labeling exclusively
383 to B3 for a few deep sections of the superior temporal sulcus, intra parietal
384 sulcus or insula, covering a very small percentage of the total sulcal area
385 ($< 5\%$). The anatomical correlates of this division are well illustrated by the
386 analysis of the pericentral region in 3 reference brains of increasing size (Fig.
387 8). The figure shows the straight course of the 1st order central element,
388 the 2 or 3 loops corresponding to 2nd order elements and the small dimples
389 associated with 3rd order elements, which are much more accentuated in the
390 larger brain. The increasing order for pattern elements in ramifications is
391 also visible in the post central sulci. The impression of extension of B4 or
392 even B5 labeling into higher ramification is drawn by the fact that gyral
393 pattern elements are masked on most of the presented segmentations (due to
394 legibility concerns for figures). Indeed, the same anatomical correlation can
395 be observed for gyral pattern and yet, for the whole CFP (Fig. 8c). Hence, we
396 show that the distribution of 2nd and 3rd order elements of pattern is neither
397 random nor homogeneously underlying the limits of lower order elements,
398 but rather parsimoniously matches the gradual ramification of CFP from the
399 previously defined 1st order folding fields.

400 *3.3. Spectral composition of CFP as a function of brain size*

401 *3.3.1. Surface area and folding power scaling*

402 We used the hemispheric volume (HV) as a brain size parameter. In
403 our dataset, HV ranged from 445 cm³ to 759 cm³, i.e., a 1.7-fold varia-
404 tion (Table 1). The hemispheric surface area showed a positive allometric
405 scaling: $HA = 0.209HV^{0.961}$ ($R = 0.950$, $p < 0.001$, confidence interval
406 $[0.935, 0.987]$), i.e. large brains had disproportionately more cortical sur-
407 face than smaller brains. We found the same variation with brain size for
408 the sulcal pattern area and the gyral pattern area, showing the absence
409 of allometric modification of sulcal versus gyral proportions: sulcal pattern

410 area= $0.127HV^{0.951}$ ($R = 0.953$, $p < 0.001$, confidence interval [0.926, 0.976])
411 ; gyral pattern area= $0.0828HV^{0.972}$ ($R = 0.898$, $p < 0.001$, confidence interval [0.934, 1.012]). Total folding power also showed a positive allometric
412 scaling, consistent with the fact that large brains are not simply scaled-up
413 versions of smaller ones: total folding power= $8.16 \times 10^{-3}HV^{0.781}$ ($R = 0.784$,
414 $p < 0.001$, confidence interval [0.73, 0.832]). We used these allometric expo-
415 nents as references for the scaling exponents we found for subdivisions of
416 the hemispheric surface (1st, 2nd and 3rd order elements of CFP) and total
417 folding power (B4, B5 and B6).
418

419 *3.3.2. Spectral allometry: different brain size means different spectral pro-* 420 *portions*

421 As they accounted for more than 90% of the analyzed folding power,
422 we limited the following analysis to the folding bands. The largest propor-
423 tion of the variance in spectral band power was related to brain size vari-
424 ation ($R^2=61\%$ in a centered model) with no significant effect of age, sex,
425 or handedness. Normalized band spectrum revealed a significant effect of
426 brain size on spectral proportions (Fig. 6c). Large brains (standard score for
427 $HV > Mean + 1SD$) showed a significantly larger proportion of B6 high spatial
428 frequencies than small brains (standard score for $HV < Mean - 1SD$)
429 and conversely, they showed a smaller proportion of B4 low spatial frequencies
430 ($p < 0.001$ in both cases). The proportion of B5 medium spatial frequen-
431 cies was not significantly different between the large and small brains. To
432 further investigate the relationship between brain size and curvature band
433 power spectrum we compared the scaling of each spectral band power with
434 the scaling of total folding power. We found no correlation between brain
435 size and folding power for B4, an allometric exponent similar to that of total
436 folding power for B5 (0.753 ± 0.052 versus 0.781 ± 0.051) and a higher allo-
437 metric exponent of for B6 (1.213 ± 0.061 versus 0.781 ± 0.051). This shows
438 that in large brains the larger proportion of B6 spatial frequencies compared
439 with B4 and B5 is due to an increased contribution of these high frequencies
440 to CFP rather than a decrease of B4 ones (Fig. 9 b). It also explains the
441 stable proportion of B5 frequencies since total folding power is the normal-
442 ization constant. In other terms, B4 contribution to the CFP is independent
443 of brain size i.e. isometric scaling, B5 contribution follows the average in-
444 crease of folding power with brain size i.e. positive allometric scaling, and
445 B6 contribution increase faster than average i.e. the positive allometry is
446 stronger for the higher spatial frequencies.

447 3.3.3. *Complexification of CFP with brain size*

448 How do the different behaviors of each folding band translate in terms
449 of CFP? The computation of surface area and number of sulcal parcels for
450 each label of the segmentation according to dominant band is presented in
451 Fig. 9c, d. The variation of surface area with brain size for each order
452 of CFP elements showed a specific behavior similar to that of frequency
453 band power: increase of area with brain size is very slow for 1st order (B4
454 label), parallel to surface extension for 2nd order (B5 label) and faster than
455 expected for 3rd order (B6 label). This result was robust and not sensitive
456 to filter suppression. The number of parcels was independent of brain size
457 for 1st and 2nd order i.e. constant in spite of surface extension, whether
458 the number of parcels increased for 3rd order (Fig. 9d). This result was
459 sensitive to filter suppression but we found the same behavior for each order
460 with the segmentation according to patterning band that provides an even
461 clearer image of the progressive ramification and do not require filtering (Fig.
462 9e). We found no significant differences between the analysis confined to the
463 sulcal pattern and that of the whole CFP. Hence, in terms of CFP, the
464 proposed spectral segmentation allows a characterization and quantification
465 for complexification with brain size demonstrating that it consists in a high
466 frequency ramification already suspected by visual comparison of smaller and
467 larger brain of the dataset (Fig. 7 and Fig. 8).

468 4. Discussion

469 The proposed Spectral Analysis of Gyrfication (Spangy) methodology
470 achieves a categorical and quantitative analysis of cortical folding pattern
471 (CFP) both in the frequency domain through a band power spectrum and in
472 the image domain with an anatomically relevant spectral segmentation. The
473 computation is directly carried on native data without the need for spherical
474 parametrization or template normalization. The choice of the mean cur-
475 vature of the grey-white interface for CFP depiction could be questioned.
476 Theoretically, any other continuous scalar function defined on a cortex de-
477 rived surface mesh could have been elected. Does any other would give a
478 more accurate rendering for folds? Actually, the mean curvature defines two
479 gyral and sulcal patterns of almost equal area on the grey-white interface,
480 but not on external cortical surface (i.e. pial surface) where the CFP is very
481 unbalanced. Future application of Spangy should probably try to analyze
482 this external surface or even an intermediate surfaces **such as proposed by**

483 **Van Essen (?) [Ref ?]**, It would also be of interest to look for invariants
484 between spectra computed on the same brains but with different choices of
485 surface or folding proxy (gaussian curvature, sulcal depth, etc.). Besides, the
486 choice of the surface and its computation could affect the spatial resolution
487 of the analysis. Indeed, if secondary mesh refinement (computational vertex
488 density augmentation) does not seem to impact much on results, a primary
489 higher mesh resolution could bring new spatial frequencies components out
490 of the background noise, requiring an expansion of the eigenfunction basis to
491 avoid aliasing.

492

493 The properties of Spangy rely on our frequency bands design and fre-
494 quency modeling choices. The a priori definition of band limits starting
495 from the first non-null frequency appeared to us as the simplest strategy.
496 First, merging the raw spectrum into bands of doubling spatial frequency
497 provides an objective method to compare different subjects. However, in-
498 ter subject matching between eigenfunctions of the same order is a difficult
499 problem, which complicates full ordinal comparison between extended raw
500 spectra (Knossow et al., 2009; Lombaert et al., 2011). This discrepancy exists
501 both for nodal domain pattern and exact associated wavelength. Nonethe-
502 less, the proposed large frequency bands realize a large scale smoothing in
503 the frequency space resulting in a strict inter subject frequency matching
504 between bands of the same order. It is worth noting that this matching is
505 up to a proportional factor given by the wavelength associated with the first
506 non-null eigenvalue ($WL(1) = 1/F(1)$). This factor, which is proportional to
507 $HA^{1/2}$, can be seen as the geodesic length of the hemisphere (Lefèvre et al.,
508 2012) and could be used as a surface based normalization factor of eigen-
509 function basis associated wavelength. In other terms, Spangy depicts CFP
510 with a scale of brushes adapted to object size: larger touches are required for
511 larger brains. Furthermore, analytic effects of the merging strategy strongly
512 depend on the frequency model chosen for band splitting. We could have
513 elected an arbitrary sequence of bands, such as quadratic sequences (limits
514 associated with $k^2F(1)$), but we found few obvious anatomical correlations
515 for the resulting spectra (data not shown). The proposed $2^kF(1)$ sequence
516 presents at least 3 very convenient properties :

517

- it allows a good degree of compaction.

518

- it segregates the folding bands that clearly contribute to CFP from those that seem to account for global shape.

519

520 • it leads to a segmentation of pattern ramifications.

521 The first property was obviously expected from high growth rate of $2^k F(1)$
522 sequence.

523 The second one could not be anticipated and we still have no model for sulcal
524 pattern apparition with B4, that is to say $2^3 F(1)$ to $2^4 F(1)$ spatial frequency
525 range. Since this range is quantitatively large and the density of eigenfunc-
526 tion still rather low in this zone of the spectrum, the matching is probably not
527 exact and there is probably no exact frequency threshold above which CFP
528 arises. This uncertain area concerning exact delineation of spectral folding
529 frequency domain pleads for future implementation of intelligent models such
530 as machine learning algorithm for CFP fundamental frequency assessment or
531 for frequency clustering, with or without anatomically labeled learning data
532 base (i.e., in a supervised or unsupervised way). Nonetheless, the present
533 strategy designs a convincing first folding band from which models of fre-
534 quency doubling makes sense. Our primary interest in CFP analysis should
535 not overshadow the clear emphasis of low frequency bands association with
536 curvature variations related to global shape. Though quantitatively small
537 compared with the folding bands, recent works suggest that the informa-
538 tion gathered into these low frequencies may be neuroscientifically relevant,
539 at least for global shape classification (Niethammer et al., 2007; Lai et al.,
540 2009).

541 As for the third property, it results from the main hypothesis of the frequency
542 model, namely, the doubling of frequency with pattern extension. Our results
543 in terms of spectral segmentation of CFP clearly show that this hypothesis
544 is consistent with true anatomical data. Interestingly, the bandwidth of the
545 folding bands may partially accommodate the variation of dominant wave-
546 length of same order elements of pattern between different regions of the
547 brain, such as polar regions where the patterns seem to be tighter and cen-
548 tral where they seem wider. At least it seems true with the segmentation
549 according to the locally patterning frequency band. With Spangy native data
550 strategy, this classical phenomenon on a surface with spherical topology is
551 accurately revealed and not artificially accentuated by spherical parametriza-
552 tion.

553

554 The accuracy and consistency of the spectral segmentation of CFP that
555 we obtained is indeed an important concern. Apart from the frequency dou-
556 bling hypothesis, the segmentation proposed is free from anatomical or de-

557 velopmental a priori. Labeling is then based only on spatial frequency char-
 558 aracteristics of local curvature variations, or more precisely on how this local
 559 variation integrates into the whole pattern since spectral analysis is not a
 560 local analysis. The results of our analysis of the central region show that we
 561 can distinguish two types of gradual contribution of the folding bands: firstly
 562 the termination of elongated elements of pattern, secondly the ramification
 563 of pattern both from an existing element and de novo. Termination label-
 564 ing is of little anatomical meaning and rather due to later discussed strong
 565 impact of depth on surface based wavelength. Conversely, ramification label-
 566 ing is an interesting achievement. Indeed, starting from spectrally defined
 567 primary folding fields, Spangy segmentation categorizes 2nd and 3rd order
 568 of ramification or complexification of CFP in a way that only developmen-
 569 tal longitudinal follow-up had authorized up to know (Chi et al., 1977). To
 570 our knowledge, no other strictly morphological analysis achieved this type of
 571 result. Recent closely related mathematical tools such as fractal modeling
 572 (Yotter et al., 2011) allows to estimate at global, regional and local scales,
 573 a fractal dimension of the cortical surface thanks to spherical harmonics but
 574 the authors have not applied their methodology to the characterization of
 575 normal CFP. More intuitively, Laplacian smoothing has been presented sev-
 576 eral times as a possible tool for categorization of elements of sulcal pattern
 577 since supposedly tertiary fold seems to disappear earlier in the process than
 578 secondary, and so on (Cachia et al., 2003). Unfortunately, it is a continuous
 579 process depending on a scale parameter t whose relevant values vary from
 580 a fold to another and across subjects. It is interesting also to note that
 581 this process is not mathematically equivalent to filtering even if smoothing
 582 a map u till time t can be expressed from eigenvectors and eigenfunctions of
 583 Laplace-Beltrami Operator:

$$S(u)(t) = \sum_{i=0}^{+\infty} u_i e^{-\lambda_i t} \phi_i \quad (17)$$

584 which is different from a truncated expression of equation (2):

$$F(u)(N) = \sum_{i=0}^N u_i \phi_i \quad (18)$$

585 Besides, many regions are much more intricate than the central region
 586 where categorization of CFP elements is probably unattainable locally, at

587 least in the image space. This is another advantage of the proposed spectral
588 analysis, which integrates the whole pattern information in the frequency
589 space for band power spectrum computation, but returns part of it locally
590 in the image space with the segmentation according to the locally dominant
591 frequency band. Hence, we are able to propose a spectral based segmenta-
592 tion even in a more difficult region such as prefrontal cortex. On that matter,
593 regional implementation of our spectral strategy on a patch of mesh corre-
594 sponding to a lobe or a functional area (Broca for instance) is of possible
595 interest. Nonetheless, further demonstration of concordance between spec-
596 tral and developmental labeling for elements of CFP still exceeds the aim
597 of the present work and certainly need more investigation, for instance on
598 longitudinal data. Indeed, it is of important concern to try and validate on
599 real biological data the different folding models proposed in the literature
600 (Thompson et al., 1996; Mora and Boudaoud, 2006; Striegel and Hurdal,
601 2009; Yotter et al., 2011). To a certain extent, the anatomical consistency of
602 Spangy spectral segmentation brings a new point to the models that predict
603 a frequency doubling with folding extension.

604

605 Besides its categorial properties, Spangy provides two types of quantita-
606 tive information.

607 Firstly, the wavelength intervals associated with B4, B5 and B6 give a size
608 for 1st, 2nd and 3rd order elements of CFP that can be seen as a surface-
609 based or geodesic wavelength. Such a surface-based measure depends both
610 on the local depth and the local width of the associated fold. Very few
611 object-based morphometric data are available for cortical folds. The Brain-
612 VISA morphometric toolbox allows maximum and mean depth assessment
613 for well validated sulci models but provides no ramification-based segmen-
614 tation. Nevertheless, the magnitude order for central sulcus is consistent
615 with B4 associated wavelength range (Mangin et al., 2004). Object-based
616 definition and computation of other size parameters such as volume-based
617 (Euclidian) or surface-based (Riemannian) wavelength would be of great in-
618 terest to compare with the measures provided by Spangy. Indeed, accurate
619 CFP morphometry could open the field to a new quantitative characteriza-
620 tion of folding during development or in congenital malformation such as
621 lissencephaly (too few, too large folds) of polymicrogyri (too many, too tight
622 folds) (Richman et al., 1975). But these two examples also emphasize that
623 sizing of CFP elements is not enough for such a characterization, one needs
624 to be able to give the global composition of CFP for each category.

625 This is precisely the second quantitative information provided by Spangy.
626 Each folding band power is probably the best assessment of each spatial fre-
627 quency interval to the CFP since spectral segmentation goes with certain
628 loss of information: locally, an element of pattern can only be related to one
629 band even if several folding orders are intricate. Nonetheless, back in the
630 image, useful ramification count is allowed by CFP spectral segmentation.
631 Here again, a regional analysis could be proposed by looking for lobar or
632 functional area dominant frequency variations.

633
634 In this work we propose a first application of this new insight provided by
635 Spangy to the question of the relationship between brain size polymorphism
636 and CFP complexity variation. The allometric relationship between brain
637 size (hemispheric volume) and hemispheric surface area has been already re-
638 ported (Toro et al., 2008). Some results even suggest that this allometry
639 is not spatially homogenous and that local gyrification indexes seems to in-
640 crease more in some brain regions than in others, prefrontal area for instance
641 (Toro et al., 2008; Schaer et al., 2008). Gyrification indexes inform us on the
642 amount of buried cortical surface but give no information about CFP. About
643 this concern, hemispheric total folding power behaves as hemispheric gyri-
644 fication index: they are highly correlated but both equally blind to shape
645 and gyrification pattern ($R = 0.8$). The band power spectrum provided
646 by Spangy precisely unwraps this black-box to reveal 3 orders of pattern
647 elements of 3 increasing spatial frequency bandwidth which behave differen-
648 tially with brain size and total folding pattern increase. Complexification of
649 gyrification can be seen as an extension of CFP both by ramification and
650 addition of disconnected new elements of pattern. Our results show that this
651 type of complexification occurs with increasing brain size since the contri-
652 bution to CFP of B4 low spatial frequencies is constant in terms of spectral
653 power and number of pattern elements, the one of B5 medium spatial fre-
654 quencies increase with the same allometric exponent than total folding power
655 but with a number of pattern elements still constant, and the one of B6 high
656 spatial frequencies shows both a much higher allometric exponent and an
657 augmentation of number of pattern elements. To our knowledge, this is the
658 first objective and quantitative demonstration of this allometric phenomenon
659 suspected from radiological observations. Large brains are definitely twistier
660 because of an increased number of barbells, dimples and kinks of high spatial
661 frequency that accommodate the allometric increase of cortical surface to be
662 buried.

663 **5. Conclusion**

664 At the end.

665 **Appendix A. Definition of spatial frequencies**

666 In one dimension, the eigenvalue problem (1) becomes

$$u''(x) = -\lambda u(x) \quad \forall x \in [0, L] \quad (\text{A.1})$$

667 and the solutions are obtained through the sine and cosine functions de-
668 pending on boundary conditions (Dirichlet or Neumann for instance). An
669 eigenfunction can be expressed on the form $\cos(\frac{\pi n x}{L})$ or $\sin(\frac{\pi n x}{L})$ with n an
670 integer that gives the number of oscillations of the eigenfunction and the cor-
671 responding eigenvalue is $\lambda_n = (\frac{\pi n}{L})^2$. The frequency is classically defined as
672 the inverse of the period or wavelength $\frac{2\pi}{\pi n/L}$ and therefore equals $\frac{\sqrt{\lambda_n}}{2\pi}$. In two
673 dimensions we can have explicit formula in the case of a rectangular domain
674 of size L and l and the eigenfunctions can be expressed in a decoupled way,
675 for instance for Neumann boundary conditions:

$$\cos\left(\frac{\pi m x}{L}\right) \cos\left(\frac{\pi n y}{l}\right) \quad \forall (x, y) \in [0, L] \times [0, l] \quad (\text{A.2})$$

676 and the corresponding eigenvalue is $\lambda_n = (\frac{\pi m}{L})^2 + (\frac{\pi n}{l})^2$. Even if the concept of
677 spatial frequency is ambiguous in 2D and depends on the oscillations along
678 each direction x and y , we will consider that $\sqrt{\lambda_n}$ has the dimension of a
679 spatial frequency.

680 **Appendix B. Computation of resolution and thresholds**

681 For a given spatial resolution of a mesh, let d be the average edge distance
682 between two contiguous vertices. Then, the average sign inversion spot (an
683 isolated point of different sign than its neighbors) is around $\pi(d/2)^2$ mm²
684 large (small disc of d mm diameter). For a given eigenfunction basis spatial
685 resolution, let WL be the wavelength associated with last eigenfunction of
686 the basis. Then, it is associated with an average size spot of $\pi(WL/4)^2$ area
687 (small disc of $WL/2$ mm diameter).

688
689 For the adaptative thresholding in 2.7, we have made a similar reasoning:
690 a noisy parcel in band k is roughly approximated by a circular shape of radius
691 R_k . So we have the relation for the characteristic size :

$$2R_k < \frac{1}{2} \frac{WL(1)}{2^k} \quad (\text{B.1})$$

692 which implies that the area of the parcels satisfies:

$$A_k < \frac{\pi^2}{16} \left(\frac{WL(1)}{2^k} \right)^2 \quad (\text{B.2})$$

693 The adaptative threshold for each spectral band k is therefore given by the
694 right term in the previous equation.

695 **Appendix C. Extensive formulations of the spectral segmentations**

696 We give here the formula for the segmentation according to the locally
697 dominant frequency band:

$$MBC(p) = \arg \max_{k>0} \left(\text{sign}(H(p)) \sum_{n=n_1^k}^{n_2^k} H_n \phi_n(p) \right) \quad \forall p \in \mathcal{M} \quad (\text{C.1})$$

698 The sign of the curvature indicates whether we are in a gyrus or a sulcus.

699

700 For the segmentation according to the locally patterning frequency band,
701 we start by computing the differential contribution of each frequency band
702 to the CFP by subtraction between the CFP maps of two consecutive levels
703 of cumulative synthesis :

$$\forall p \in \mathcal{M} \quad SM_k(p) = a - b \text{ where} \quad (\text{C.2})$$

$$a = 1 \text{ if } \sum_{n=1}^{n_2^k} H_n \phi_n(p) > 0 \text{ else } a = 0 \quad (\text{C.3})$$

$$b = 1 \text{ if } \sum_{n=1}^{n_2^{k-1}} H_n \phi_n(p) > 0 \text{ else } b = 0 \quad (\text{C.4})$$

704 Then, we follow the procedure explained graphically in Fig. 5: We start
705 from SM_k for $k = 6$ (third row, first column) which counts 3 labels -1 (blue),
706 0 (gray) or 1 (red). A vertex with label l will be assigned another label $3l$.
707 Then we consider SM_k for $k = 5$ (third row, second column) and to each
708 vertex with label l not previously re-labeled we assign the label $2l$. The last

709 step is achieved for $k = 4$ where all vertices not re-labeled previously will
710 keep their label l . Finally, the resulting segmentation is represented with a
711 gyral mask (last row) and counts 3 labels: -3 (green), -2 (cyan) and -1 (dark
712 blue).

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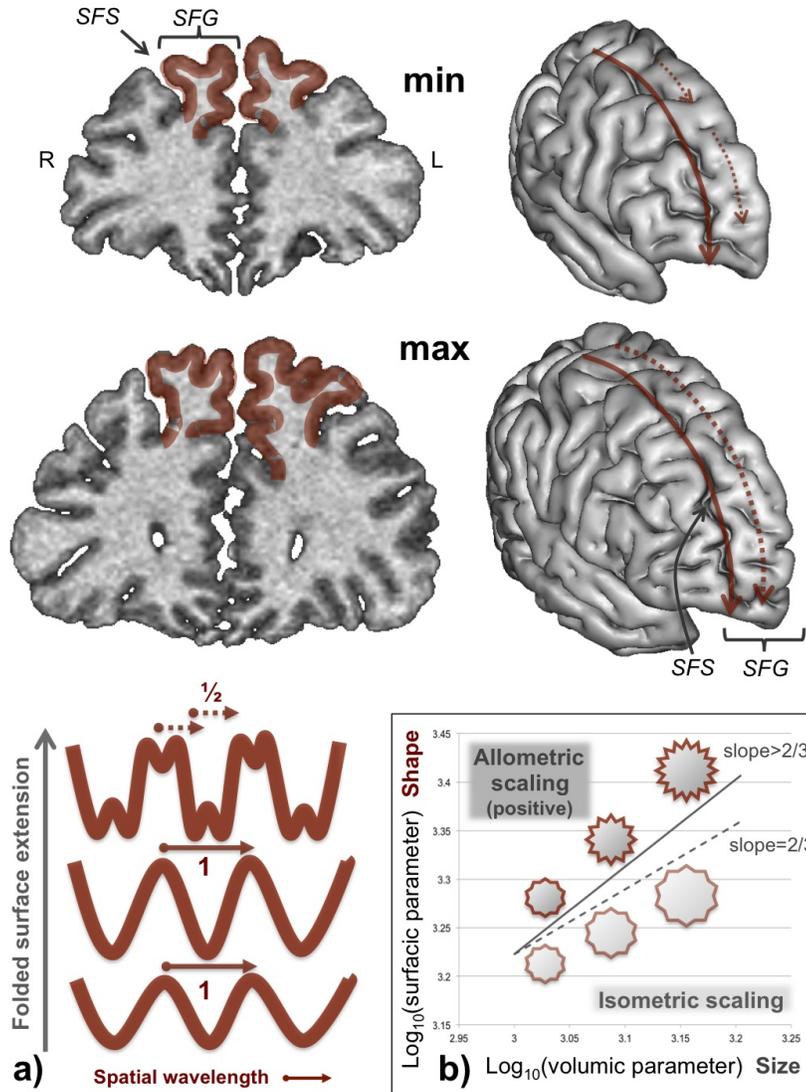


Fig 1: Modeling framework for cortical folding.

a) The doubling frequency hypothesis. 1st row: brain of minimum size of the database
 2nd row: brain of maximum size of the database, more folded cortical surface in the SFG
 3rd row: theoretical model extrapolated from (Mora and Boudaoud, 2006). Left column: coronal section perpendicular to the ACPC line and tangential to the genu of the corpus callosum (T1-weighted images) Right column: pial surface of the right hemisphere SFS: superior frontal sulcus, SFG: superior frontal gyrus, R: right, L: left.

b) Allometric scaling for cortical folding.

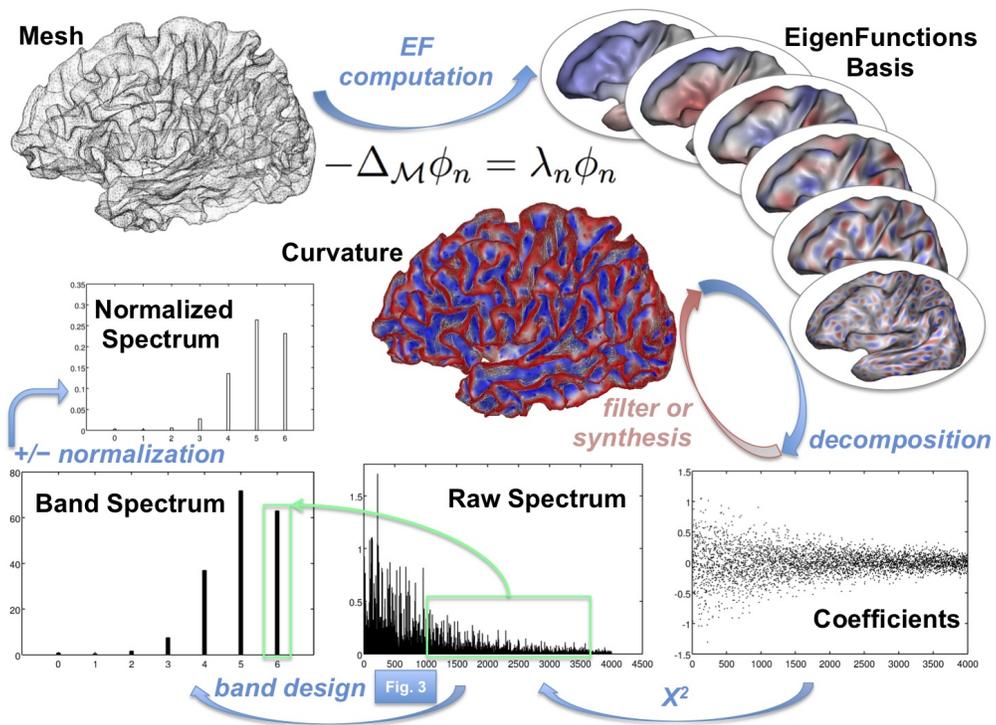


Fig 2: Spangy process

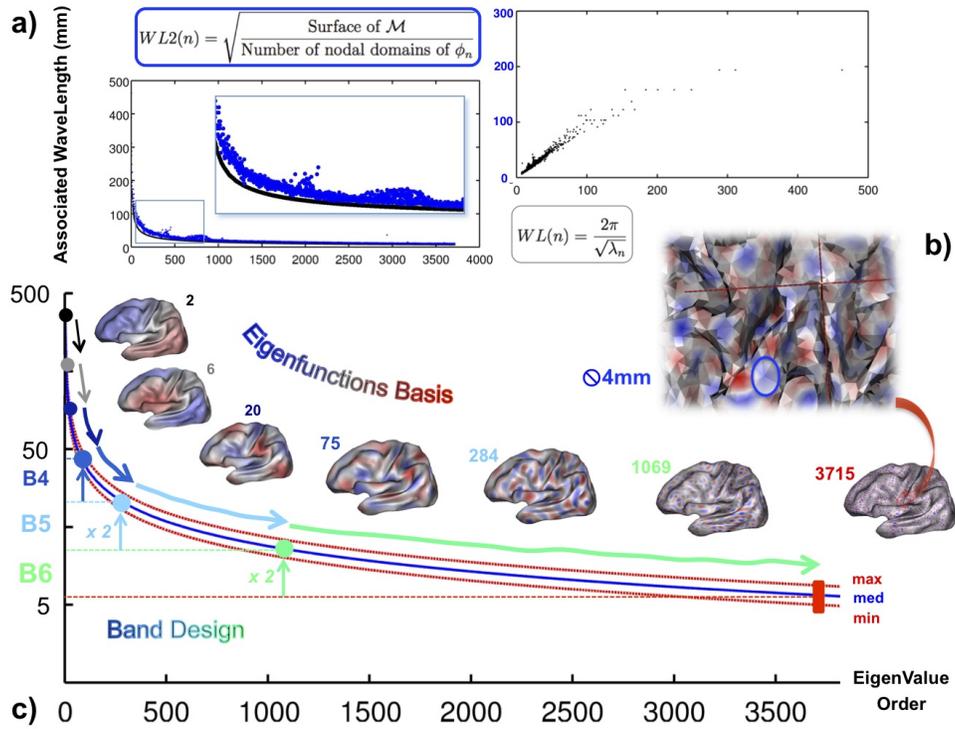


Fig 3: Spectral band design.

- a) Eigenfunction associated wavelength (WL). Comparison between theoretical wavelength (black) and empirical one (blue).
- b) Spatial resolution. Visualization of the nodal domains of the last eigenfunction of the basis for the median size brain of the database.
- c) Spectral bands: limits of the frequency intervals according to the doubling frequency hypothesis. Log-linear plot. min, med, max: brain of minimum, median and maximum size of the database.

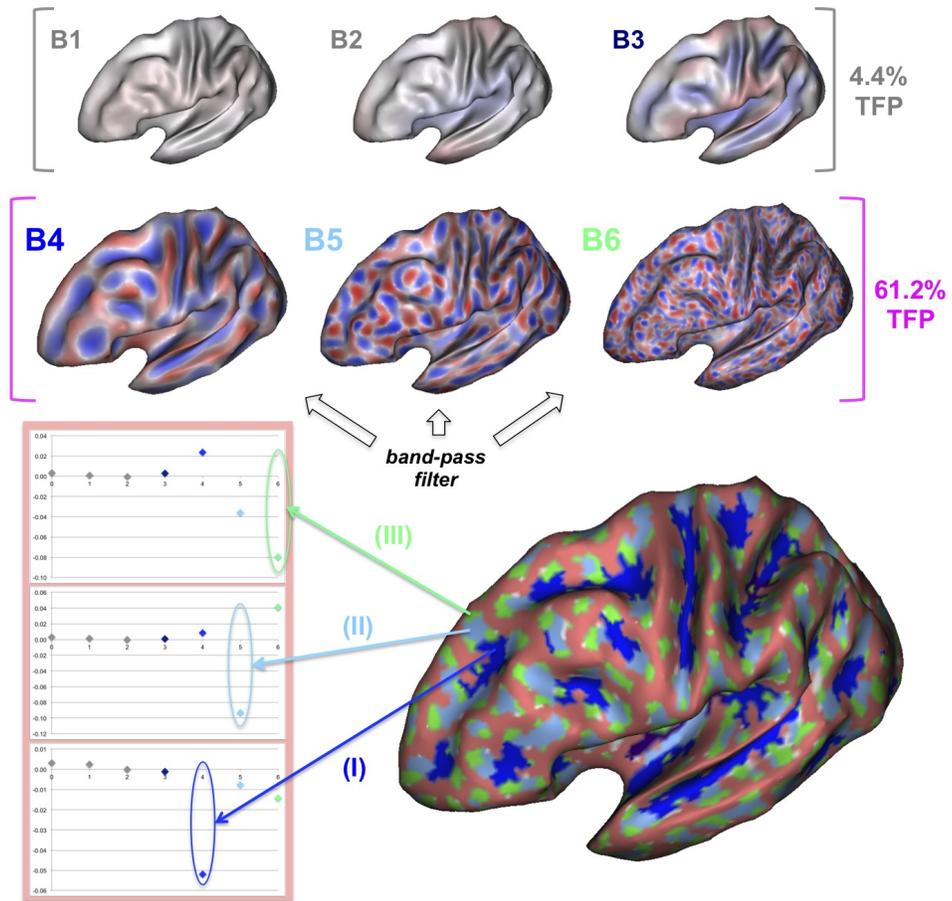


Fig 4: Segmentation of CFP according to the locally dominant band.

1st and 2nd row show the series of band-pass filtered curvature. Plots show the decomposition of curvature at point (I) (II) or (III). CFP segmentation is presented for median size brain on a smoothed anatomy with a gyral mask (salmon red). TFP: total folding power.

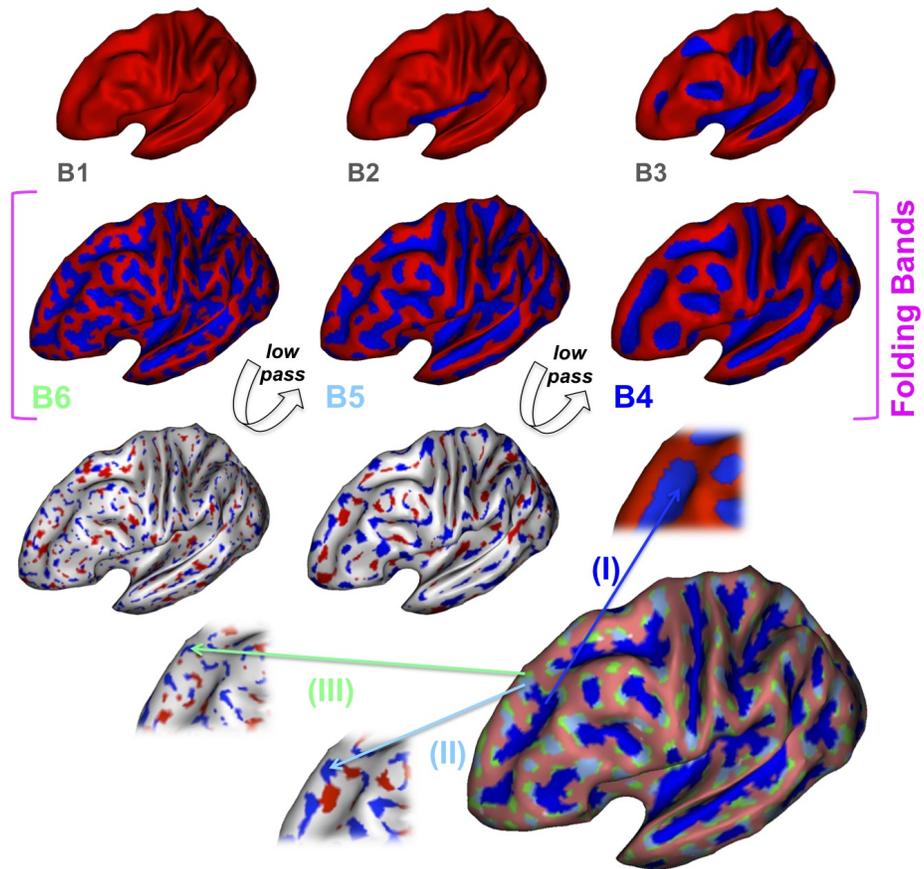


Fig 5: Segmentation of CFP according to the locally patterning band.

1st and 2nd row show the series of low-pass filtered cortical folding pattern. Local magnifications show the subtraction step between two consecutive levels in the neighborhood of points (I) and (II). CFP segmentation is presented for median size brain on a smoothed anatomy with a gyral mask (salmon red).

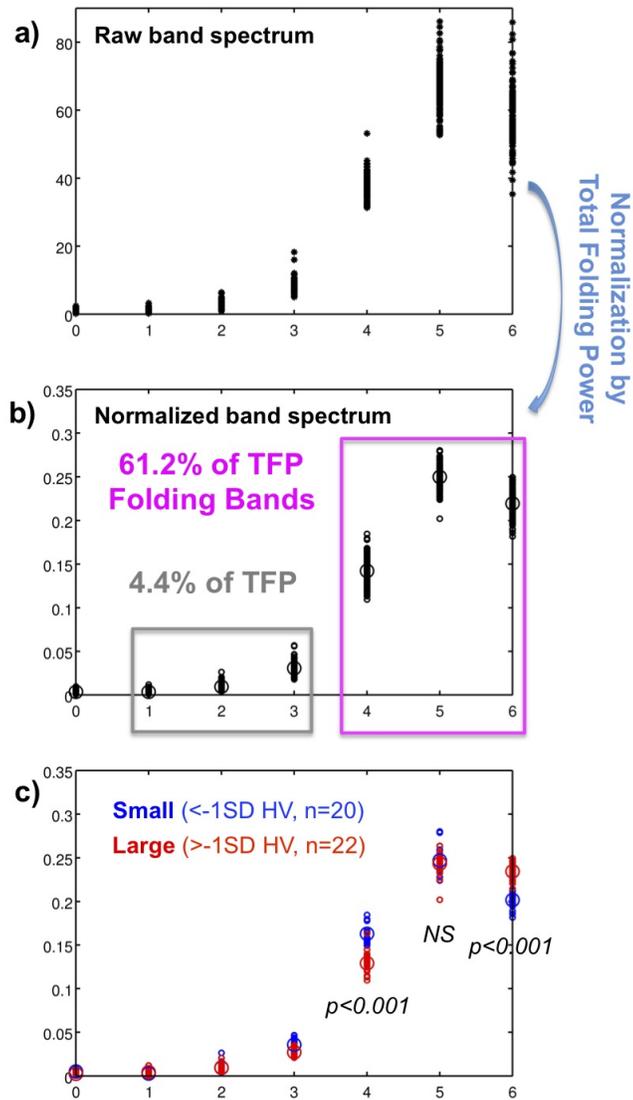


Fig 6: Spectral proportions.

- a) Raw band spectrum for the whole dataset.
- b) Normalized band spectrum i.e. spectral proportions for the whole dataset TFP: total folding power.
- c) Differences of spectral proportions between small (HV below mean-1SD) and large (HV over mean+1SD) brains of the database. Student testing for mean differences. HV: hemispheric volume, NS: non significant.

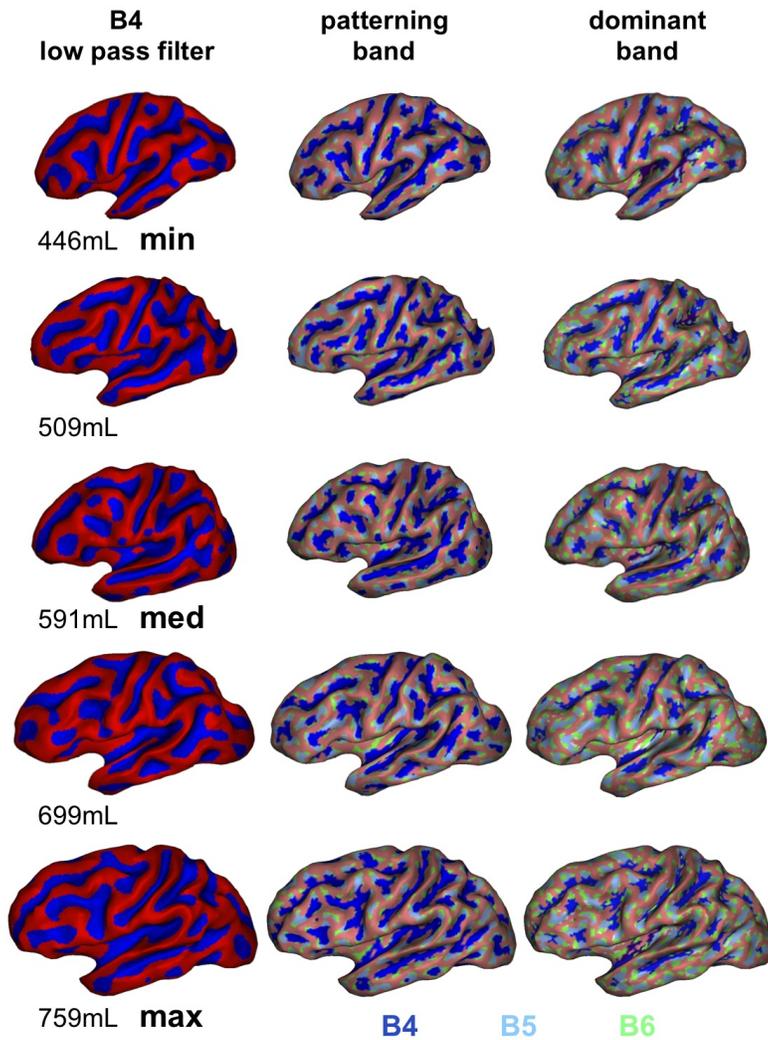


Fig 7: Spectral segmentation of CFP along dataset.

Brains of increasing size, measured by their hemispheric volume. 1st column: regular pattern of B4 low-pass filtered CFP. 2nd column: segmentation according to patterning band showing increase of B6 tagged ramifications with size. 3rd column: segmentation according to dominant band showing extension of B5 and B6 tagged surface. CFP segmentation is presented on a smoothed anatomy with a gyral mask (salmon red).

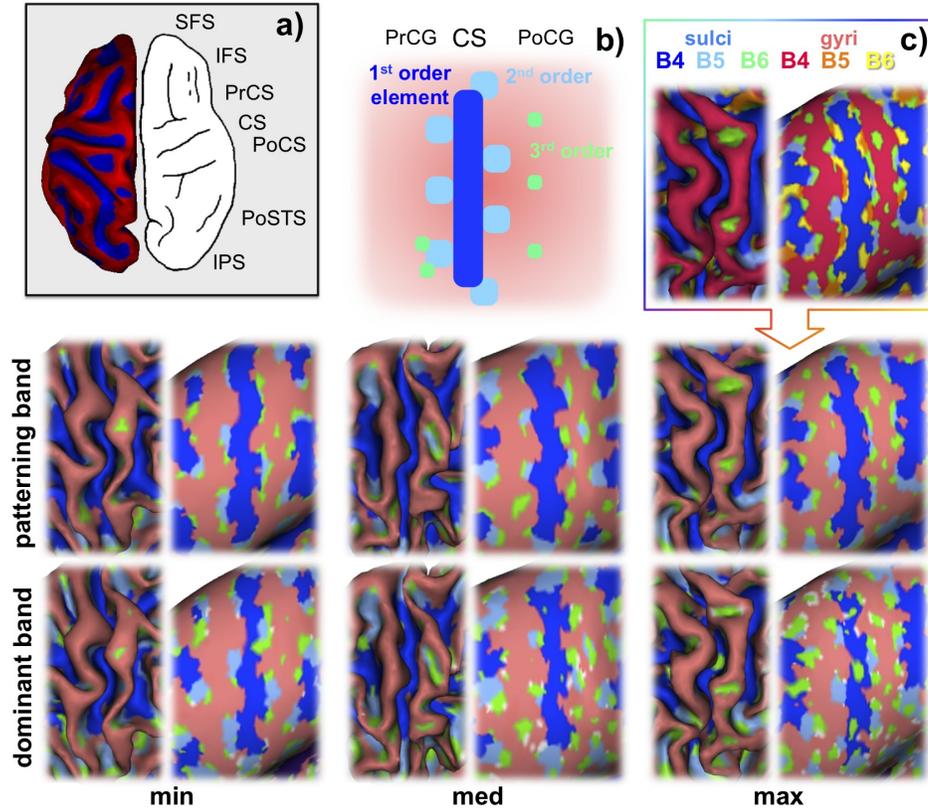


Fig 8: Anatomical- spectral correlations.

a) Primary folding fields corresponding to B4 low-pass filtered CFP. Comparison between regular pattern of B4 low-pass filtered CFP and primary folds described by (Chi et al., 1977) for left hemisphere. Primary folds appears before 32weeks of gestation. The schematic left hemisphere is adapted from (Chi et al., 1977) and switched to the right side. SFS: superior frontal sulcus, IFS: inferior frontal sulcus, PrCS: pre-central sulcus, CS: central sulcus, PoCS: post-central sulcus, PoSTS: posterior branch of the superior temporal sulcus, IPS: intra-parietal sulcus. b) Spectral segmentations of the central region: 1st 2nd and 3rd order elements of CFP.

Schematic interpretation of the segmentations is given in the 1st row. The number of 3rd order elements is arbitrary since it increases with brain size. For each brain, the segmentation is presented on the native (left) and totally smoothed (right) anatomy with a gyral mask (salmon red). min, med, max: brain of minimum, median and maximum size of the database.

c) Spectral segmentations of the central region for the whole CFP (without gyral masking).

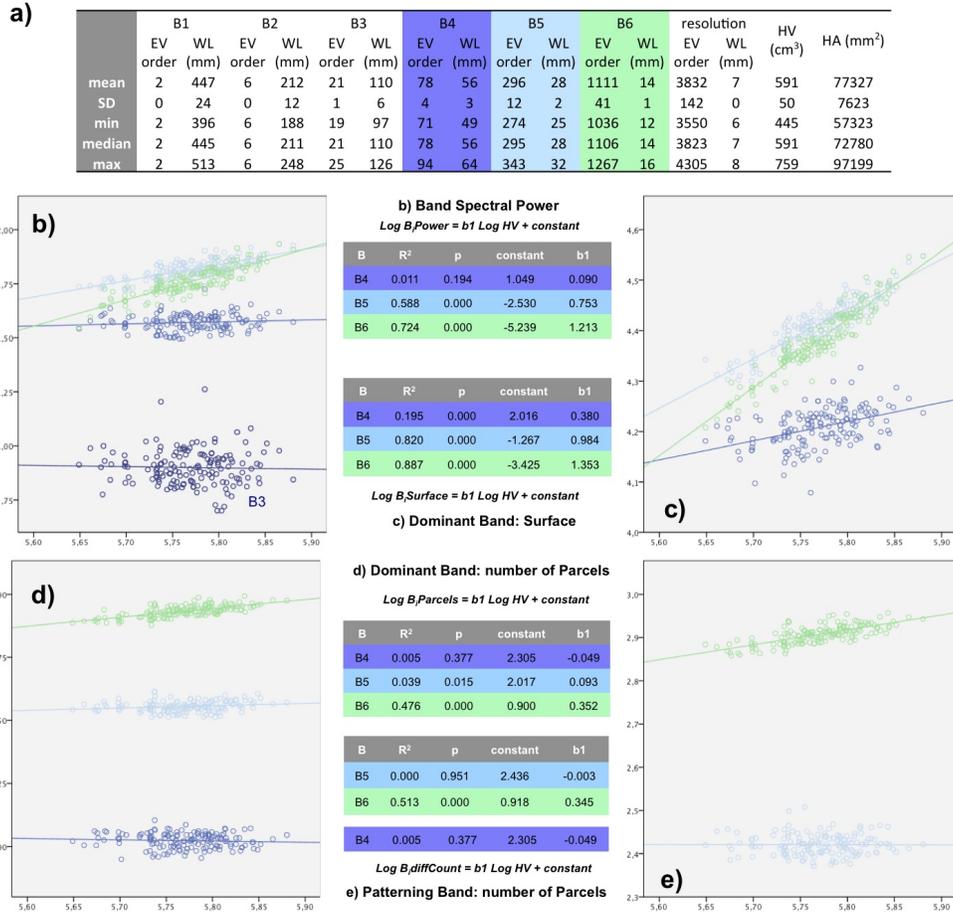


Fig 9: Allometric scaling for CFP extension.

- a) Spectral sizing: bandwidth, resolution and brain size WL: wavelength, EV: eigenvalue/eigenfunction.
- b) Band spectral power scaling. Isometry for B4, following global positive allometry for B5 (same scaling exponent than total folding power = 0.753), accentuated positive allometry for B6 (1.213).
- c) Scaling of the surface of dominance for each band. Same behavior than band spectral power.
- d) Scaling of the number of parcels of dominance for each band. The number is independent of size for B4 and B5 but increases for B6.
- e) Scaling of the number of patterned parcels for each band. Same behavior than number of parcels of dominance.