

How the flow and processing of information shapes the cerebrum

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Abstract

The cerebrum of mammals spans a vast range of sizes and yet has a very regular structure. The amount of folding of the cortical surface and the proportion of white matter gradually increase with size, but the underlying mechanisms remain elusive. Here, two laws are derived to fully explain these cerebral scaling relations. The two general laws are derived from the notion that total processing power of the cortex is determined by the total cortical surface (i.e., the number of neurons), whereas the most efficient over-all flow of information is governed by the size of local networks (cortical columns). Since information is transferred by axonal connections which have a definite volume, a trade-off can be formulated from theoretical considerations between local, inter-gyrus information transfer and long-range information transfer. It can be shown that this trade-off is governed by a single parameter describing the size of local networks, t_{local} . Despite having just one free parameter, the first law fits the mammalian cerebrum better than any existing function, both across species and within humans. According to the second law, the scaling of white matter volume is also determined by the information principles. It follows that large cerebrums have much local processing and little global information flow. Moreover, paradoxically, a further increase in long-range connections would decrease the efficiency of information flow. These theoretical scaling principles help to compare the cerebrums across mammals regardless their size.

Keywords: Scaling law, Power relation, Evolution, Brain, Volume surface ratio

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1. Introduction

One of the most successful classical concepts of motor control is the speed-accuracy trade-off. It was introduced in the 1950s by Paul Fitts who could explain his results quantitatively from the hypothesis that the trade-off between speed and accuracy of any movement is governed by the maximal rate of information that can flow to control the movement (Fitts, 1954, Fitts and Petterson, 1964). The rate of information is expressed in bits per second (bit/s), so that Fitts proposed that any movement can be expressed with an index of difficulty (bit).

If information flow is a crucial factor in shaping motor control, it is likely to be a central factor too in the evolution of the shape of the central nervous system. Even if this notion may seem trivial, I am not aware it has ever been formulated explicitly. The goal of this work therefore is to test this idea. A most suitable structure to test seems to be the mammalian cerebrum, because its anatomy and function have been extremely well studied, whereas the laws that govern its macroscopic structure are unknown.

The mammalian cerebrum is a highly regular structure, having a cortex of grey matter on its surface which is wrapped around a core of white matter. The cortex is built up of regular layers, which have specific afferent or efferent long-distance connections (Shipp, 2005). The white matter contains long-range axonal connections. The white color comes from myelination of these axons.

Despite this regular structure, the mammalian cerebrums span a tremendous size range from 11 mm^3 ($11 \mu\text{l}$, pigmy shrew) to $2.5 \cdot 10^6 \text{ mm}^3$ (2.5 l, elephant) (Zhang and Sejnowski, 2000), with the brain of the sperm whale being even 60% larger (Marino, 1998). Given these extreme size differences, measures of the cerebrum are usually plotted on a double-logarithmic graph.

There exists a vast literature on interspecific scaling relationships of any thinkable measure of the vertebrate body. What becomes clear on a glance is that such relationships usually show a large variance, whereas narrow distributions are rare. The reason for this is obvious: most scaling relationships are governed by many factors and parameters and thus lead to a trend with much scatter (typically in the order of magnitudes). On the other hand, if one does find a narrow distribution, the chances are good that its singular cause is a simple mechanism.

Interestingly, a number of such narrow distributions with little variability around the general trend are known for the mammalian cerebrum (Harrison et al., 2002). These are usually described by a power relation

(i.e., a linear relation on a double-logarithmic scale). However, not every
40 relation that is well described by a linear regression on a double logarithmic
scale underlies a power-relation, as pointed out, for example, by [Zhang
and Sejnowski \(2000\)](#). These authors investigated the power-relationships
between the volume of the cortex, the white matter and the grey matter.
Each of the three relationships between these parameters followed a simple
45 power over the entire size range and with remarkably little deviation.
These volumetric measures, but also the outer surface and the total cortical
surface (including the inward folded surfaces) show power-relations to the
brain volume, and the latter also to the cortical volume ([Hofman, 1989](#)).
However, as the sum of two different powers (e.g., $x^1 + x^{1.5}$ or $x + 1$) is never
50 a power relation, at least some of the above relations do not truly reflect a
power law ([Zhang and Sejnowski, 2000](#)). Similar relations with little variability
from the trend have been reported for the number of neurons in the
cerebrum, the cerebellum and the rest of the brain ([Barton and Venditti,
2013](#), [Gabi et al., 2010](#), [Herculano-Houzel, 2011](#), [Herculano-Houzel et al.,
2010](#)).

Two most prominent neuro-anatomic properties of the mammalian cerebrum
is the division in grey and white matter and the convoluted (folded)
surface, which increases gradually with brain size. Whereas the smallest
mammalian brains possess a lissencephalic (smooth) cerebral surface, larger
60 cerebrums have ridges (gyri) and folds (sulci). The number and depth of the
sulci increase monotonically with brain size. Thus, since the outer shape
changes with size, the mammalian cerebrums do not scale isometrically.
According to [Gross \(1999, p. 90\)](#), already Franz Joseph Gall (1758-1828)
asked why the cerebral cortex is convoluted and proposed that the folds
65 conserve space. Many studies and a number of theories has been proposed
since the early approaches ([Changizi, 2001](#), [Le Gros Clark, 1945](#), [Mota and
Herculano-Houzel, 2012](#), [Prothero and Sundsten, 1984](#), [Van Essen, 1997](#),
[Zhang and Sejnowski, 2000](#)). Unfortunately these theories make no or extremely
vague quantitative predictions, are circular, or contain serious errors
70 so the problem remains unsolved (see [Supplement 1](#)).

The goal of the present work is to derive scaling laws for the cerebral
surface-volume relation and for the white-grey matter volume relation. The
laws are derived on the basis of a simple hypothesis, i.e., that the two central
functions of the cerebrum, processing and transmission of information, are
75 the forces that shape the cerebrum. In the following it is shown that the
volume-outer surface of the cerebrum scales isometrically. Subsequently,

theoretical relations for the cerebral cortical surface (including the typical convolutions in large brains) to volume relation as well as for the volume of the white matter are derived.

80 2. Methods and theoretical background

2.1. Datasets

With the advent of neuroanatomy in the second half of the 19th century, methods have been developed to estimate the surface area of the cortex (Zilles et al., 2013). According to (Jerison, 1982) the first systematic
85 approach was made already by Baillarger (1845), who did measurements of the cortical surface of a number of mammals and proposed a relation between total surface area and intelligence. To my knowledge, the first systematic and accurate measurements of a wide range of mammals have been developed and published by Brodmann and Henneberg (Brodmann, 1913,
90 Henneberg-Neubabelsberg, 1910). A statistical approach for estimating the surface area was developed in the 1960-1970s, whereas modern methods are usually based on neuroimaging techniques.

The latter kind of measurements are likely to be the most accurate, because they are based on fresh, in-vivo measurements and can employ
95 computerized triangulation methods. Probably the best database for the human cortex is by Toro et al. (2008). Unfortunately, similar databases for a range of mammals measured only the ratio of outer to total surface (“gyrification index”) without retaining the true surface or volume of the cortex and are thus useless here. Thus, the older measurements had to be
100 used here. The selection criteria for studies were as follows: 1. Systematic usage of a validated method; 2. Reporting of a range of mammals (not just humans); 3. Reporting of at least the cerebral surface area and the cerebral volume and/or the cerebral outer surface area from the same specimen. Seven studies applied to these criteria: (Brodmann, 1913, Elias and
105 Schwartz, 1971, Haug, 1970, Mayhew et al., 1996, Schlenska, 1969, 1974). Finally, the measurements of reported total/outer surface ratio of 1.0 were added from Hofman (1985).

Exclusion criteria were applied as follows: 1. Malformed or diseased brains (Brodmann, 1913); 2. excessively deformed brains (Brodmann suspected excessive shrinkage of two brains of Ganese origin); 3. Estimates (e.g., of cerebral volume) that were based on other specimens or taken from
110 the literature; 4. Measures of cerebral volume that do not fit into a sphere

of the reported total cortical surface¹; in the case of a large enough sample of a single species, the statistical outliers were excluded.

115 The dataset thus 141 samples from 56 species (incl. 29 humans) and 17 orders of mammals. The cerebral volume was available in 97 samples and the outer surface of 104 samples. For the fitting (Section 3.1) a single average per species was calculated: 45 species for the A_c - V_c fit and 51 species for the A_c - A_{out} fit. In either case, the A_c of a species was calculated over the
120 samples that were available for the second parameter, so that the mean A_c for a given species could differ depending on the fit. The complete dataset as well as a commented listing of the excluded measurements is provided for downloading (see Supplement 3; de Lussanet, 2013).

The dataset of human data by Toro et al. (2008) was fitted individually.
125 Furthermore, a dataset by Zhang and Sejnowski (2000) was used for fitting the grey and white matter volume.

2.2. Volume-surface relations and sphericity

The relation between the surface area and the volume of a sphere can be calculated from the standard formula:

$$\begin{aligned} V_{\text{sphere}} &= \frac{3}{4}\pi r^3 \\ S_{\text{sphere}} &= 4\pi r^2 \\ V_{\text{sphere}} &= \sigma A_{\text{sphere}}^{3/2} \end{aligned} \quad (1)$$

where

$$\begin{aligned} \sigma &= \frac{V_{\text{sphere}}}{S_{\text{sphere}}^{3/2}} = \frac{\frac{4}{3}\pi}{(4\pi)^{3/2}} = \frac{1}{6\sqrt{\pi}} \approx 0.094 \\ \hat{\sigma} &= \frac{S_{\text{sphere}}}{V_{\text{sphere}}^{2/3}} = \sqrt[3]{36\pi} \approx 4.84. \end{aligned} \quad (2)$$

130 The cerebral hemispheres deviate from a perfect sphere, so we can express the cerebral volume V_c as a function of the outer cerebral surface area, S_c :

¹This is a typical problem in the studies that made use of statistical approaches, which most probably led to underestimation of the surface measurements. In order to keep as many measurements as possible, I assumed that the ratio of inner and outer surface area is retained in these measurements.

$$V_c = \sigma s S_c^{3/2}, \quad (3)$$

where the sphericity factor s expresses how much the outer cerebral surface area differs from that of a sphere. Since the hemispheres are not exactly spherical, $s < 1$. It can be computed directly from the outer cerebral surface, S_c , which is reported for part of the dataset:

$$s = \frac{V_c}{\sigma S_c^{3/2}} = 0.56 \pm 0.09 \text{ (mean } \pm \text{ standard deviation)}$$

$$\hat{s} = \frac{S_c}{\hat{\sigma} V_c^{2/3}} = 1.51 \pm 0.16 \text{ (mean } \pm \text{ standard deviation)}$$

with $N = 49$ species. However, the mean can only be used if S_c and V_c scale isometrically. To test this, a linear regression on the log-transformed data was performed, which gives $V_c = -1.32 S_c^{1.52}$ ($R^2 = 0.998$). Since the power is very close to the $\frac{3}{2}$ power predicted for isometric scaling, and not significantly different ($P = 0.16$), the sphericity factor s is indeed scale-invariant (the same is true for \hat{s}).

2.3. The concept of equivalent thickness

A central observation of the gross anatomy of the cerebrum is that the thickness of the grey-matter cortex tends to saturate with cerebral size. This has typically been quantified by simply dividing the grey matter volume by the cortical surface area (Harman, 1947, Hofman, 1988). This measure is not the average thickness, because it neglects that the cerebrum is convex so that the surface area of the grey-white matter border is smaller than the outer surface (i.e., the equivalent thickness is smaller than the geometric thickness).

The equivalent thickness is a measure of the dimensionality of the cortical surface. For a sphere, the equivalent thickness is proportional to the radius. For a basket filled with laundry, the total surface of the laundry is proportional to the volume of the basket, because the [equivalent] thickness of the laundry is independent of the volume of the basket. Thus, the observation that the thickness of the grey matter seems to saturate with brain size, is an indication that the cortical surface tends to scale proportionally to the cerebral volume for large cerebrums.

This can be expressed formally as:

$$V_c = T_c A_c. \quad (4)$$

where T_c is the equivalent cerebral thickness (i.e., the sum of grey and white matter), and A_c the total cortical surface area (i.e., including the cortical area that is located inside the sulci). In this relation, $T_c = V_c/A_c$ indeed saturates for large cerebrums. (see Fig. S1 of Supplement 1).

165 Similarly, the equivalent thickness in terms of the outer surface S_c is:

$$T_s = \frac{V_c}{S_c} = \frac{V_c}{\hat{\sigma} \hat{s} V_c^{2/3}} = \frac{\sqrt[3]{V_c}}{\hat{\sigma} \hat{s}}. \quad (5)$$

2.4. Neurons in the cortex

The total cerebral surface is composed of the cortex of grey matter. The cortex is the region where the vast majority of cerebral neurons are located. Since the computational power of the cortex will depend largely on the number of neurons, the distribution of neurons is highly relevant for scaling relations of the cerebrum.

170 The number of neurons per unit cerebral cortical surface is constant, 10^5 neurons/mm². This was first estimated by Bok (1929), and confirmed using cell counts (Carlo and Stevens, 2013, Rockel et al., 1980). In both latter studies, cell counts (neurons and glia cells) were performed for five regions on the cerebral cortex that differ strongly in thickness and composition of the layers. Moreover, these samples were taken from four mammals of very different brain size (mouse, rat, cat, monkey). Both studies found not only the same number of 10^5 neurons per mm² for the different samples of each species, but also for each of the four species tested. The average cortical surface per neuron is thus $k = 10^{-5}$ mm², irrespective of the cerebral size and the location of the cortical surface.

2.5. Information conduction and axonal diameter

185 The diameter of axons in the white matter increases with cerebral size (Harrison et al., 2002). It is known that both, the average spike rate and the transmission velocity increase linearly with axonal diameter (Perge et al., 2009, 2012). Based on theoretical considerations, an increase of the signal band width will not increase the information rate in a proportional manner (Balasubramanian et al., 2001, Shannon, 1948). Measurements on the optic tract have indicated that the higher spiking rate in wide axons also leads to a stronger correlation of subsequent spikes (Koch et al., 2006). The latter

study estimated that the information rate per axon is independent of its diameter. Thus, increasing the diameter leads to a quadratic increase of its cross-sectional area, but only a linear increase in its transduction velocity.

195 Assuming that the axonal diameter is scaled such transmission time is approximately size-independent, means that the information rate in a processing loop will decrease quadratically with the length of the connection.

3. Results

200 On the basis of the above background, a law can be derived to predict the scaling of the cerebrum using just a single free parameter. The relations address the surface-volume relation with respect information flow and local processing. A second part addresses the grey and white matter volume.

3.1. Scaling law for the cortical surface

205 The two central functions of the cerebrum are computational power and information transfer. Assuming that the number of neurons in the cortex determines computational power, and given that the number of neurons per cortical surface area is constant, the scaling parameter for the cerebral volume V_c is cortical surface area, A_c .

210 There are two components to the information transfer in a neuron: long-range afferent axonal connections and efferent dendritic trees. The length of axonal connections in the cerebrum has a typical, gamma-like distribution, and increases with the size of the cerebrum (Jones and Wise, 1977, Kaiser et al., 2009). Dendritic trees on the other hand, have a finite size. That this is indeed so, is reflected by the fact that the number of neurons per cortical surface area is constant (cf. section 2.4), and the established concept of the cortical column (Mountcastle, 1997, Roerig and Chen, 2002). These two properties have been described as long-range scale-free connectedness (Eguíluz et al., 2005, Markov et al., 2013) and small-scale, small-world properties (Stoop et al., 2013, Watts and Strogatz, 1998). In other words, the network of the cerebrum has two different scales: the small scale is manifested on the level the cortical columns and the limited size of dendritic trees, whereas the large scale is manifested in the long-range axonal connections.

225 The volume to a given cortical surface area is thus determined by the flow information processed by the neurons, and the transfer of this information on the local- and global-scale. This can easiest be expressed in terms of *information resistance*: how the flow of information [bit/s] divides

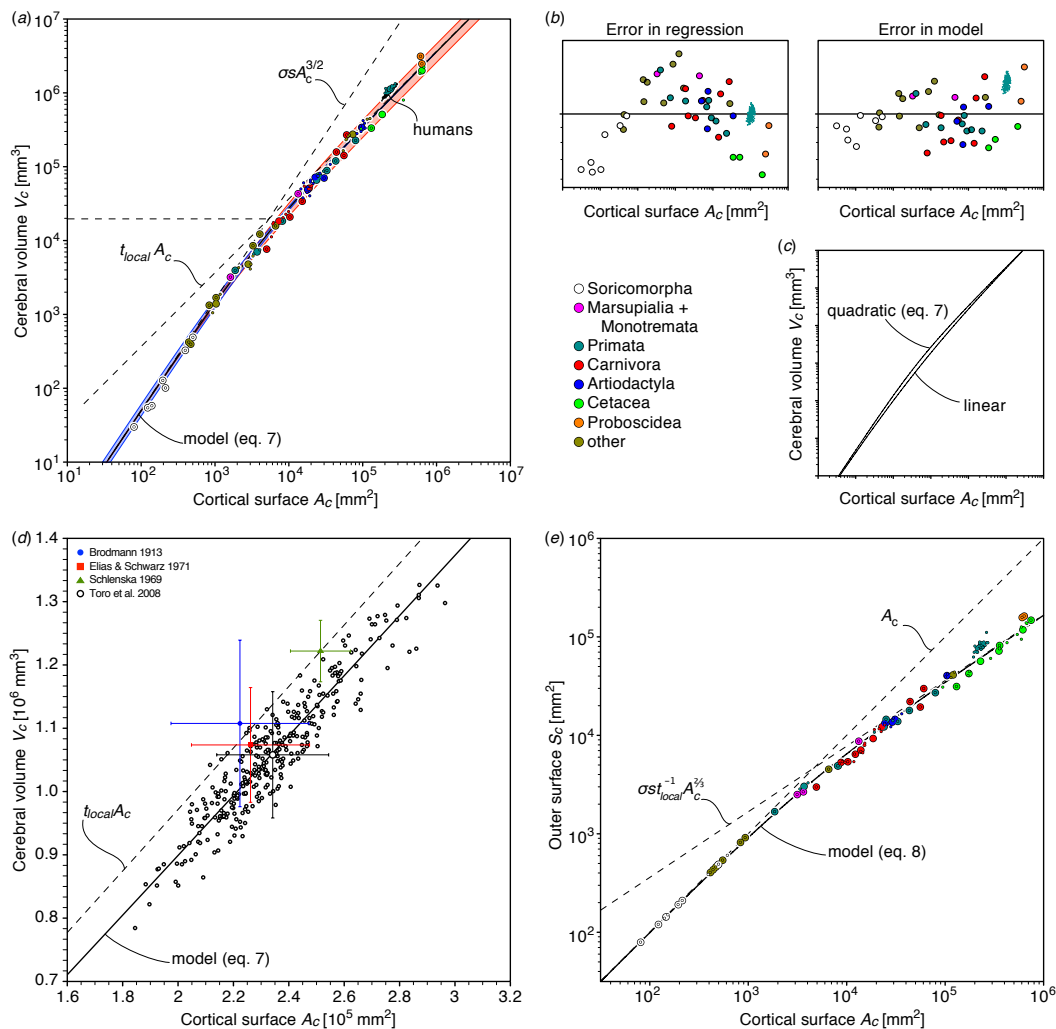


Figure 1: (a) The model fit of t_{local} (eq. (7)) on the mean values per species. Continuous line: the model fit; dashed lines: the asymptotic relations with power slopes of 1 (cf. eq. (4)) and 1.5 (cf. eq. (3)). Large dots: species means; small dots: single measurements. Blue-shaded range: the limits of $s \pm 1$ standard deviation (SD); red-shaded range: $t_{local} \pm 1$ mm. (b) Comparison of the distribution of errors for the single-parameter fit of panel a (right) and a conventional two-parameter regression fit (left). The vertical scale measures ± 0.25 order of magnitude. (c) Comparison of the model, equation (7), and a model based on a linear relation between information resistance and channel length. (d) The model fit of t_{local} on the human data of Toro et al. (2008) (also indicated as black dots in panel a). (e) Model fit of t_{local} on the mean values per species, using the outer surface values (eq. (8)).

among local and global networks depends on how well each route trans-
fers information. Information resistance is directly related to the inverse
230 of the *channel capacity* which expresses the rate of information that can
be reliably transmitted by a channel (Balasubramanian et al., 2001, Shan-
non, 1948). Assuming that the resistance to information increases with the
squared length of the connection (Section 2.5), it becomes clear that the
relative contribution of the small-scale and large-scale connections depends
235 directly on the size of the cerebrum (T_s : eq. (5)). Thus, expressing informa-
tion resistance in terms of equivalent connection length, and subsequently
substituting equation (5) we get:

$$\begin{aligned} \frac{1}{R_{I,total}} &= \frac{1}{R_{I,global}} + \frac{1}{R_{I,local}} \\ \frac{1}{T_c^2} &= \frac{1}{T_s^2} + \frac{1}{t_{local}^2} \\ &= \left(\frac{\hat{\sigma}\hat{s}}{\sqrt[3]{V_c}} \right)^2 + \frac{1}{t_{local}^2}, \end{aligned} \quad (6)$$

where the constant t_{local} expresses the scale-invariant information resistance
of the local networks [m]. By substitution of the equivalent thickness (T_c ,
240 equation (4)), the volume to cortical surface is obtained as:

$$A_c^2 = (\hat{\sigma}\hat{s}V_c^{2/3})^2 + \left(\frac{1}{t_{local}}V_c \right)^2. \quad (7)$$

A remarkable property of this surface-volume relation is that it has just
a single free parameter: t_{local} .

The fit of equation (7) on the log-transformed data (Section 2.1) resulted
in $t_{local} = 3.6$ mm (N = 45 species, $R^2 = 0.995$). This result is presented
245 in Figure 1a. Even though the model has just a single free parameter, it
describes the data much better than a conventional linear regression on the
log-transformed data (which yields: $\log(V_c) = 0.67 + 1.24 \log(A_c)$, with an
 $R^2 = 0.98$).

Another manner to analyze the quality of the model is by the trend in
250 the errors. These are illustrated in Figure 1b. Whereas the linear regression
shows a clear trend in the form of an inverted U, the model does not show
any trend in the errors.

For part of the dataset, the volume data are not present or not reliable (see Section 2.1), but the outer surface is given in these data. Given that the sphericity parameter is invariant (Section 2.2), we can rewrite the model (eqn. (7)) as a function of the outer surface S_c , by substitution of equation (3):

$$A_c^2 = S_c^2 + \left(\frac{\sigma s}{t_{local}} \right)^2 S_c^3 \quad (8)$$

(given that $(\hat{\sigma}\hat{s})^3 = (\sigma s)^{-2}$).

The fit of relation is as good as the first ($t_{local} = 3.4$ mm, $R^2 = 0.996$, $N = 51$ species). This is shown in Figure 1d.

The second fit involves 7 species of cetaceans (rather than just three species in the first fit). A fit of the 15 samples collected from these 7 species of cetaceans resulted in $t_{local} = 3.1$ mm, $R^2 = 0.92$, which was thus close to the ensemble-fitting result.

Since the wide availability of neuroimaging facilities, it has become possible to measure the gross anatomy of large samples of cerebrums with standardized and automatized procedures. Such a data set of human subjects (Pausova et al., 2007) was analyzed by Toro et al. (2008). These data (314 subjects, 164 females and 150 males of 12-20 years old) are presented in Figure 1c. The fit resulted in $t_{local} = 4.8$ mm ($R^2 = 0.96$), which was slightly better than the linear regression on the log-transformed data (which resulted in a power slope of 1.0, intercept 0.54 and $R^2 = 0.94$). Thus, the model not only describes the inter- but also the intraspecific variation with high accuracy.

To test for phylogenetic trends, t-tests were performed on the fitting errors, using $t_{local} = 3.6$ mm (i.e., the result of the fit on all species). Orders for which more than 5 species (and species with more than 10 samples) were available were included, i.e., Carnivora ($N=8$), Primata without humans ($N = 8$), Soricomorpha ($N=7$), and humans ($N=315$). The test only gave a significant result for the human data ($t(314) = 133$, $P < 0.001$, Bonferroni-corrected). To test for systematic differences between the five literature sources of the database (Brodmann, Haug, Hofman, Mayhew et al., Schlenkska) t-tests were performed on the non-averaged data (again with $t_{local} = 3.6$ mm). This test gave no significant results (Bonferroni-corrected).

3.1.1. Sensitivity

As shown in Figure 1b, the fit of the scaling law (eq. (7)) has no systematic errors. Two main causes can underly the variable errors: measurement

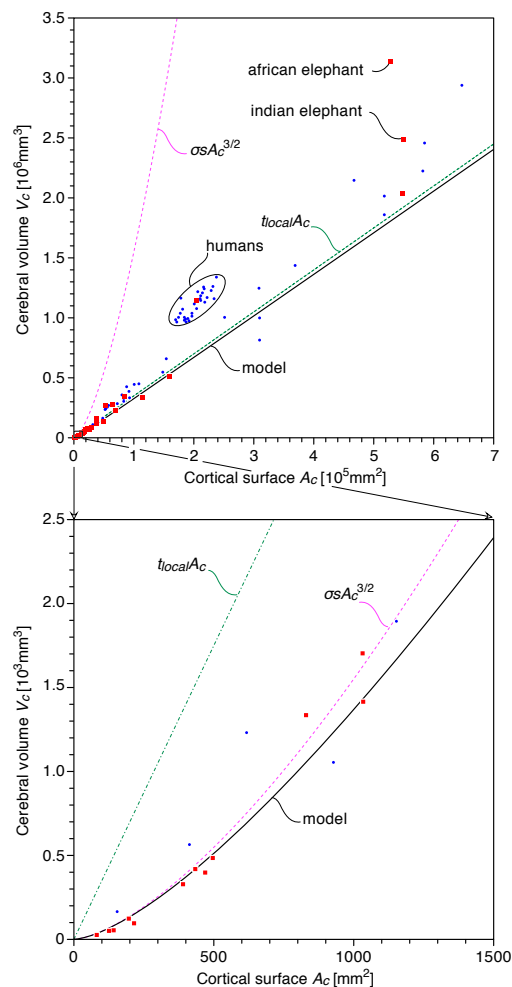


Figure 2: The data of Figure 1a on a linear scale. Top panel shows the entire data range, whereas the bottom panel shows the lissencephalic range on a much enlarged scale.

errors and true variations of the model parameters. The measurement errors are difficult to estimate due to the generally low number of samples measured per species. Judging from the human data (Fig. 1d) and taking the data of (Toro et al., 2008) as a reference, it seems that systematic errors may be considerable, depending on the author.

The sphericity parameter, s had a standard deviation (SD) of 0.09. The variations in the sphericity parameter mainly affect the model predictions for the small range of the cerebrums (Fig. 1a). Variations in t_{local} , on the other hand affect the model predictions in the range of large cerebrums (Fig.

1a).

The model was based on a quadratic relation between brain size and information resistance for long-range axonal connections (see section 2.5), but there are no reliable data to tell whether this really is the correct relation. The effect of assuming a linear relation is show in Figure 1c. The linear assumption gives a slightly less good description of the data, but the effect is small. A fit of the linear model resulted in $t_{local} = 6.1$ mm ($R^2 = 0.995$).

Even if double logarithmic plots have huge merits, they can be misleading. Therefore, the data are plotted on linear scales as well (Fig. 2). The figures confirm that the fits are good over most of the range. On the linear scale it is much more clear that the human data are systematically off the Cortical surface–cerebral volume model (eqn. (8)). Also, the indian and african elephants may fit better with a larger t_{local} , but more measurements would be needed to confirm this.

3.2. Relation of grey and white matter

In 2000, Zhang and Sejnowski discovered that there is a remarkably regular relationship between the volumes of grey and white matter in the mammalian cerebrum, as reproduced in Figure 3. They found that the relation between the grey (G) and white (W) volume almost perfectly describes a straight line on a double-logarithmic scale, over a range of more than five magnitudes of cerebral volume. A straight line on a double-logarithmic scale can always be described by a simple power of the form

$$y = ax^b$$

with constants a and b .

Interestingly, the same was true for the relations between the total volume (V_c) with the grey volume, but also with the white volume. As Zhang and Sejnowski acknowledged, it is not possible that all three relations really are simple power relations, because $W + G = V_c$. Zhang and Sejnowski tried to derive a power law for the empirical relation, but their equations were circular (see Supplement 1). Moreover, the empirical power of 1.23 was significantly lower than the expected natural scaling power of 4/3. Thus, the relation between white and grey matter volume is not explained by a simple power law. Moreover, a large family of relations are approximately linear on double logarithmic scale.

Again the information transfer can be used as a starting point for deriving a general scaling theory. Above has become clear that two scales play

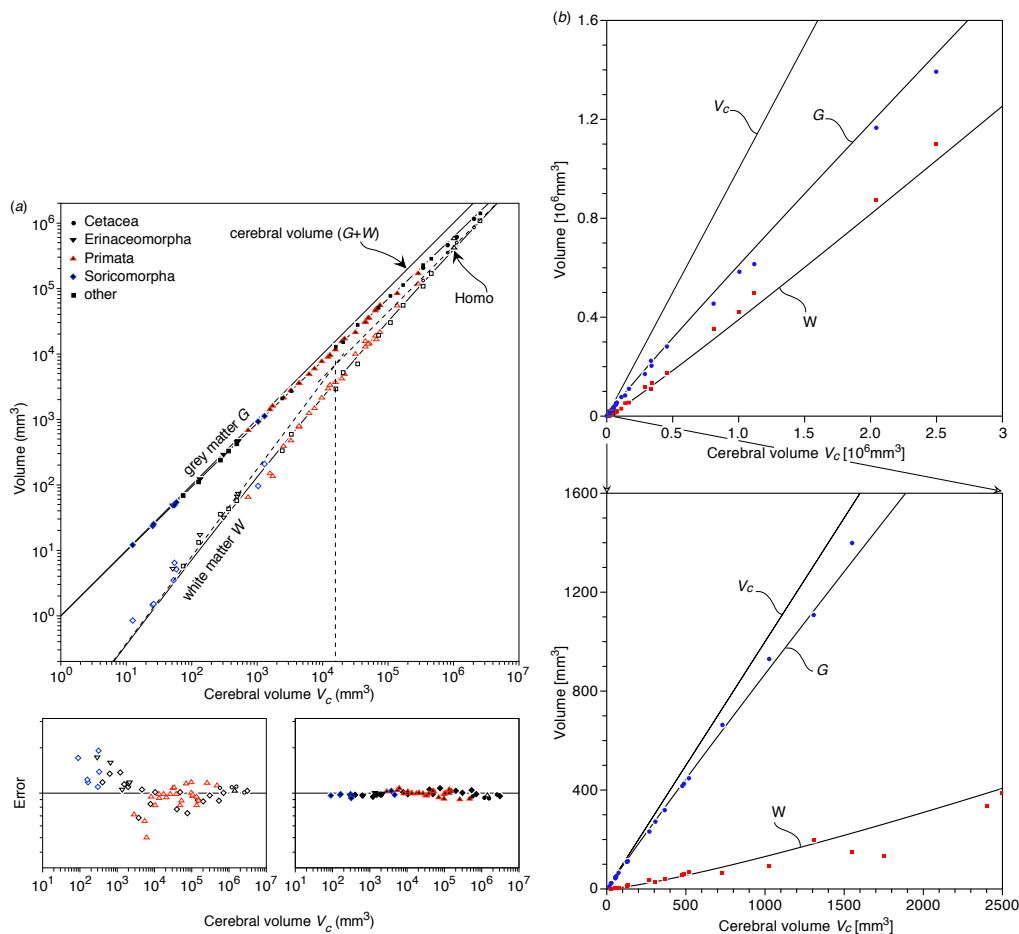


Figure 3: (a) White and grey mater volumes from Zhang and Sejnowski (2000). The white matter volumes (open symbols) and the model fit (eqn. (9)). (b) The same data on a linear scale. Top panel shows the entire data range, whereas the bottom panel shows the lissencephalic range on a much enlarged scale.

a role in the scaling: the local, intra-gyral and the global, extra-gyral scale. On the local, intra-gyral scale the information transfer is scale-invariant, so the white matter volume, W , should scale proportionally to the total volume, V_c .

335

On the global scale the W should also scale with V_c . However, in addition the distances scale with cerebral size, so that W should also scale with the radius. Since the scaling due to information transfer is governed by the *information resistance* according to equation (6), the scaling of the white

340 matter volume should also be governed by the inverse sum of the local and
global scales. Thus we obtain the following equation:

$$\frac{1}{W} = \frac{1}{arV_c} + \frac{1}{bV_c} \quad (9)$$

with r as given by equation (1). Fitting yields $a = 0.0025 \text{ mm}^{-1}$ and
 $b = 0.50$ ($R_W^2 = 0.995$ and $R_G^2 = 0.9998$ for the white and grey matter
volume respectively). The fit is shown in Figure 3. This fit is as good as the
345 one by Zhang and Sejnowski (who obtained an $R^2 = 0.996$ for their model).

Both, the volume-surface model (eq. (7)) and the grey-white matter
volume model (eq. (9)) are limit relations, indicated by dashed lines in
Figures 1a and 3a. A measure for the transition between the limit relations
is the point of intersection between them. As expected if the models are
350 both driven by the same mechanism, the points of intersection are almost
the same (at $1.9 \cdot 10^4$ and $1.6 \cdot 10^4 \text{ mm}^3$ respectively).

4. Discussion

Compared to other scaling relations known for animals over a wide size
range, the here treated scaling relations of the mammalian brain are re-
355 markably regular, and seemingly linear, on a double-logarithmic scale. This
has been known for a long time but the reasons have remained elusive, be-
cause the power relations that are obtained by such linear regressions on
log-transformed data are incompatible with isometric scaling laws. Here,
for the first time, a theory is developed that fully explains these narrow
360 scaling relations. Moreover it predicts these relations with parameters that
are physiologically meaningful, determined by the central functions of the
cerebrum –processing and transmitting information– and that can in part
be derived from independent measurements.

The obvious advantage of the current theory driven approach over mere
365 regression fitting, is that it opens the possibility to analyze exceptions to
the scaling. The first thing that can be noted here is that such exceptions
are remarkably scarce. On the basis of the available data, there are no phy-
logenetic trends, either for the grey and white matter volumes nor for the
volume-surface relations. This is remarkable, given recent claims for such
370 effects, e.g., between Glires and Primates (Herculano-Houzel, 2011). In this
sense the discussion remains similar to that of a century ago when Brod-
mann proposed that the six-layered structure of the mammalian neocortex
is a universal feature (Brodmann, 1909).

375 There are, however also clear indications of a divergence in the volume-
surface relations for the largest cerebrums. The human data set is the
most reliable, in having a t_{local} of almost a mm more than the general fit.
The elephants appear to have a similar t_{local} to humans. Interestingly, the
cetaceans align very well with the data of smaller mammals, although it is
380 usually thought that cetacean cerebrums are deviant, i.e., have a unusually
large cerebral surface. This latter conviction is an artifact of fitting the
logarithmic data with a linear regression.

The scale-invariant sphericity s is assumed to be constant, though, as
indicated by the standard deviation, it does shows considerable variation.
The effect of such variations mainly affects the predictions for small cere-
385 brums, as shown by the sensitivity analysis (cf. Fig. 1a). Overall, the vol-
ume of lissencephalic cerebrums is slightly underestimated by the model,
which is due to the very small (statistically not significant) size dependency
indicating that Ss increases slightly with brain size (cf. Section 2.2).

The only free parameter of the volume-surface model, $t_{local} \approx 3.6$ mm,
390 expresses the information resistance on the local scale, but is also a length
measure for the local networks. The measure expresses equivalent length
(cf. Section 2.3). This is in the order of the size of the gyral lobes of
convoluted brains. The largest cerebrums closely approximate the limit
relation t_{local} . That means, such large cerebrums effectively function more
395 like a communicating cluster of local processing centers than as a global
processor. The model is only a first order approximation in so far, that
axonal lengths show a wide distribution within a cerebrum (Jones and Wise,
1977, Kaiser et al., 2009). Further the regional properties are likely to vary
(Shipp, 2005). The deviation of humans and elephants indicates a change
400 in the local network properties, so that the local processing is increased.
As a result, the current result indicates that the large number of cortical
areas in the human brain is a true and remarkable property (Felleman and
Van Essen, 1991). It remains to be tested whether this is a property of
specific regions of the human cerebrum, such as the prefrontal cortex.

405 It was estimated that the information resistance increases quadratically
with connective distance, but this may not be entirely accurate. As a com-
parison, the scaling law was also estimated with a linear scaling of informa-
tion resistance with connective distance (Fig. 1c). As shown by the figure,
the predicted surface-volume relation is rather insensitive to such a seem-
410 ingly grave difference. The theoretical, quadratic scaling of information
resistance with distance describes the available data better than the linear

example, which is still better than a linear regression.

415 Lastly, the principle of information processing can even be applied to the
grey and white matter volumes. This last law is the best that is currently
available, but it is less strong than the surface-volume model, because its two
420 parameters (a and b) so-far do not have direct physiological meaning. The
model confirms that local processing networks are very prominent in large
cerebrums. The model seems to systematically underestimate the white
matter volume in the very small cerebrums (cf. Fig. 3a). This may in part
425 be due to systematic measurement errors in these very small cerebrums. In
part it may be due to the deviation in sphericity parameter s indicating
that small cerebrums and therefore have relatively longer connections than
assumed by the model.

Several earlier studies have developed a theoretical approach to explain
430 the empirical scaling relations (Changizi, 2001, Mota and Herculano-Houzel,
2012, Prothero and Sundsten, 1984, Toro and Burnod, 2005, Zhang and
Sejnowski, 2000, see also Supplement 1). Different to these studies, the
present approach started from the notion that the computational power
and information transfer are the most likely candidates as basic parameters
435 in shaping the cortex. Since computational power depends directly on the
number of neurons, which is again constant per cortical surface, it follows
that cortical surface is to be taken as the independent parameter.

Still, the relations are mainly based on relatively scarce data from het-
erogenous sources. It would therefore be highly valuable to improve the
440 measurements, and with modern imaging techniques it is feasible to mea-
sure much larger samples within species in a much more automated manner
(Manger et al., 2012, Pillay and Manger, 2007, Toro et al., 2008). Such
databases with larger samples should also enable to test more specific pat-
terns such as developmental and gender patterns (Paus and Toro, 2009) as
well as local differences between regions of the cerebrum.

The result suggests that the structure of our cerebrum has landed us in
a local optimum, because the wrinkled surface structure makes that many
distances are longer than necessary (think of the two flanking sides of a
sulcus). In a nuclear structure such as the birds' cerebrum this problem does
445 probably not exist (The Avian Brain Nomenclature Consortium, 2005).

In conclusion, the general basis for scaling of the cerebrum are the corti-
cal surface area, A_c , and the size of the local networks, as expressed by the
 t_{local} parameter. These local networks may well differ between regions of
the cortex, because the expression of layers differs substantially, for exam-

450 ple between granular and non-granular cortex. Moreover, the scaling of the
cortex is only sensitive to variations in t_{local} for large cerebrums (Section
3.1.1).

On the basis of the dataset used, there is no evidence for phylogenetic
trends in contrast to earlier claims for systematic phylogenetic differences.
455 With respect to the t_{local} with one exception: Humans and elephants appear
to have a significantly larger t_{local} parameter than all other mammals (ex-
cept, possibly elephants), indicating that information flow within regional
networks may play a larger role than in other mammals.

Third, the amount of white matter in the cerebrum scales according to the
460 current information approach.

Fourth, the relation between cortical surface and cortical volume could
be fitted using just a single parameter, $t_{local} = 3.6$ mm. The underlying
theory is based on efficient information processing and transmission. The
 t_{local} of 3.6 mm is consistent with an average gyral width of about 10 mm,
465 and a maximal lissencephalic radius of 10 mm ($\approx 2 \cdot 10^2$ mm³ volume).

The theoretical foundation of the scaling laws suggests that the functions
of the cerebrum, i.e., processing and transmission of information also are
central in defining its macroscopic shape. This in turn suggests that the
local structures in the cerebrum are also strongly related to their function,
470 which is consistent with the fact that primary sulci tend to be located at
the primary sensory and motor regions, and that the borders of functional
regions in the cerebrum usually follow the gyral folds.

Thus, the volume to surface relation does seem to be optimal. The
optimization criterion is derived directly from the central function of the
475 cerebrum: the processing and transfer of information. This result also has
a direct and important consequence for the way the brain works, because
it means that small cerebrums work fundamentally differently than large
cerebrums, in the regionalization of information processing.

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Supplement 1

Earlier theories

The theory of brain scaling has a long history. It is outside the scope
620 to give a complete listing and I am not even sure to know all theories. A
few are worth treating in more detail though because they are cited and
mentioned frequently.

Surface-volume relations

The theories for the convoluted surface area of the cerebrum seem to have
625 to longest history [Baillarger \(1845\)](#), [Gross \(1999\)](#). For a review, see ([Hof-
man, 1989](#)). For a long time it has been thought that the folding is a result
of a large cortical area being fitted inside a comparably small space inside
the skull. This model apparently dates back to [Le Gros Clark \(1945\)](#), and
has been modeled numerically in a slightly modified form ([Toro & Burnod,
630 2005](#), [Toro, 2012](#)). However, for this model to work, one has to assume that
the grey matter is incompressible, rubber-like in the dimensions parallel to
the surface, and that the white matter is viscous. These are highly unlikely
properties making the model as a whole questionable. Moreover, the model
does not make any predictions as to the scaling relations of the cortical
635 surface area.

A popular theory was developed by [Prothero & Sundsten \(1984\)](#) in a
number of works. According to this model, the gyral width and height are
governed by the white matter of the long-range axonal connections. The
strongest prediction of the model is that there exists an upper limit to the
640 size of the cerebral cortex. The strongest weakness of the model is that it
approximates the cerebrum with a cubical core of white matter which has a
surface of equally-shaped gyral ridges, separated by sulci of equal depth. In
such a design, the gyri of a large cerebrum cannot contain any white matter.
However, in a true cerebrum, the depth of neighboring sulci shows strong
645 differences, so in practice this is unlikely to present a real design problem
to the cerebrum.

According to one intuition the space required by the site matter is a
shaping factor for the gyri ([Prothero & Sundsten, 1984](#)). According to a
second notion, the anisotropic material properties of the grey and white
650 matter are essential shaping factors. For example, according to an early
proposal, the cortex behaves like a thick, lubricated rubber sheet that is
packed inside a skull that is too small for its surface ([Le Gros Clark, 1945](#)).
It will fold (as Le Gros Clark demonstrated experimentally) because the

655 sheet is hardly compressible in the tangential directions. This proposal has also been modeled numerically in a slightly modified form (Toro & Burnod, 2005). In this model, the cortical sheet did not grow against a skull, but against a compliant centripetal force.

660 A very interesting mechanism for the development of folding has been made by Van Essen (1997). According to Van Essen, the mechanical stiffness of axons make that the cerebral white matter is a highly anisotropic material (Peter & Mofrad, 2012). It seems plausible that the mechanism of Van Essen accounts for the development of the relationship between cerebral volume and cortical surface.

A general law for white and grey volume?

665 Zhang & Sejnowski (2000) also derived what they called “a general law” to predict the relation between the grey and white matter volume. Unfortunately, there was a circularity in their equations as I demonstrate here. To avoid confusion, I will use symbols that are consistent with the present work.

670 Zhang and Sejnowski started with two assumptions. (1) That there is a direct linear relation between the cortical surface area (A_c) and the physiological cross-sectional area (PCSA) of the axons. (2) That the global geometry minimizes the average length of the axonal fibers (L_{ax}). This latter assumption is somehow incomplete, because the shortest possible average length would obviously be zero.

The grey matter volume V_g is the surface A_c times the equivalent cortical thickness T_g (cf. eq. (4)):

$$V_g = T_g A_c. \quad (\text{s1})$$

Given assumption no. 1, the white matter volume V_w is:

$$V_w = c_1 A_c L_{ax} \quad (\text{s2})$$

680 the constant $0.5 < c_1 < 1$ was introduced by Zhang and Sejnowski to acknowledge that axons have a start and an end, so that cortico-cortical connections would be counted double.

685 The crucial step is to obtain the relation between G and W . Zhang and Sejnowski postulated that the total grey matter volume V_g depends on the average axon length L_{ax} . To match the dimensions they assumed that $V_g = c_2 L^3$. They tested this postulate against a family of alternative postulates in which L^3 is replaced by $L^{3-n} X^n$ with $n < 2$ and X another length measure such as the cortical thickness T or average gyrus length, etc.

They then showed that L_{ax} is smallest for the original postulate, assuming that all alternative parameters $X < L$. Combining this postulate with equations (s1) and (s2) yields the “universal scaling law”:

$$V_w = \frac{c_3}{T_g} G^{4/3}. \quad (\text{s3})$$

This formulation is misleading because according to equation (s1) V_g equals $T_g A_c$ so “the law” really states:

$$V_w = c_3 T_g^{1/3} A_c^{4/3} \quad (\text{s4})$$

so, in fact, the equation does not directly link W and G at all. If we replace V_w again with equation (s2) we obtain again the postulation, so we have not learned anything. The circularity in the derivation of their law occurred in their equation [13], where they substituted the axonal length from their equation [2] (eq. (s2)), which already been substituted in their equation [5] (i.e., the “universal scaling law”, eq. (s3)).

Other relations

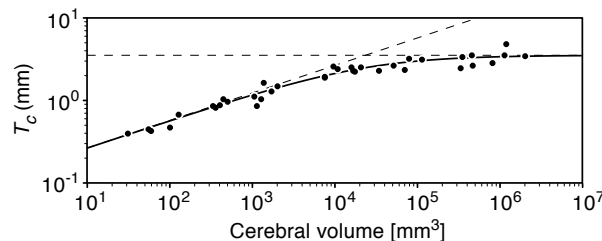


Figure S1: Equivalent cerebral thickness ($T_c = V_c/A_c$). Computed from the data of (Hofman, 1989). Dashed lines have a power slope of 1/3 and 1; the curve is equation (6).

A popular measure of the property of the cortex is the equivalent thickness (see Section 2.3). The model also predicts the equivalent cerebral thickness T_c , in equation (6). This relation is presented in Figure S1. It shows again the very good fit of the model to the data.

The theoretical approach by Changizi (2001) is interesting for its attempt to explain a whole set of scaling relations of the mammalian cerebrum at once, and thus aiming at a general theory, instead of focussing on just one relation at the time. A weakness of his approach is that it is

based on the power fitted from double-logarithmic relations of a long, heterogeneous list of studies, without any reference to the quality of these fits. For example, he lists a power of 0.08-0.197 for the relation between cortical thickness and grey matter volume although this relation deviates strongly from a power relation (cf. Fig. S1). His model consists of two parts. The first part predicts that the number of synapses per volume of dendritic tree is a scale-invariant constant. However he fails to mention the implicit assumption that the branching rate must be independent of dendritic length. The second part builds upon this, and a number of far-reaching assumptions. For example, it is assumed that each region of the brain connects to a limited, fixed fraction of other regions, independent of the number of regions in the cerebrum. Not only is the fraction of connected regions assumed constant, also the fraction of neurons connected to in each connected area is assumed constant.

A recent modeling approach has been presented by Mota & Herculano-Houzel (2012), to develop a computational framework for the data on cell counts in the cerebrum and other brain regions in a large range of mammals by Susana Herculano-Houzel et al. (Gabi *et al.*, 2010, Herculano-Houzel, 2009, Herculano-Houzel *et al.*, 2010, Herculano-Houzel, 2011, 2012). This model treats the cerebral volume as the sum of grey and white matter. It has neurons, axons and glia as major parameters, and is explorative in nature, meaning that it is an attempt to list and identify probable parameters that underly the empirical scaling laws. The main result is that it is a complex matter.

Supplement 3

Dataset

The data used for validating the scaling laws are attached as a tab-separated ascii table. At first the included measurements are printed, followed by the excluded ones including the reason for exclusion, and finally the species' mean values used for fitting.

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