The economy of anatomy: Discovering the turbulent homogeneous isotropic functional core organisation of the human brain

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Abstract

Using large-scale neuroimaging data from 1003 healthy participants, we demonstrate empirically and theoretically that human brain dynamics is organised around a *homogeneous isotropic functional core*. More importantly, this homogeneous isotropic functional core follows a *turbulent-like power scaling law* for functional correlations in a broad spatial range suggestive of a *cascade* of information processing. The underlying anatomy of the brain is expensive in terms of material and metabolic costs and it has been suggested that the trade-offs between wiring cost and topological value change over many timescales but exactly how is not known (*1*). Here, we demonstrate how the economy of anatomy has evolved a *homogeneous isotropic functional core* by using whole-brain modelling with the *exponential Markov-Kennedy distance rule* of anatomical connections as the cost-of-wiring principle demonstrated in the massive retrograde tract tracing studies in non-human primates by Markov, Kennedy and colleagues (*2*). Overall, our results reveal a novel way of analysing and modelling whole-brain dynamics that establishes a fundamental basic principle of brain organisation.

Introduction

Over the last decades, a tremendous amount of research has demonstrated that the core of the functional organisation of the human brain is highly structured in the low dimensional manifold of the so-called resting state networks (*3*). These networks emerge and are shaped by the underlying anatomy (*4*). Recent detailed and exhaustive anatomical research in non-human primates has shown that the anatomical structural core appears to be radically simple, following a homogeneous isotropic rule, namely the exponential Markov-Kennedy distance rule (*2*). This raises the crucial question addressed here, namely whether the functional core of the human brain is also homogeneous isotropic at the appropriate spatial scale, and thus radically more simple than resting state networks. We were inspired by the phenomenological theory of turbulence of Andrey Kolmogorov (*5*) who introduced the concept of *structure functions*, essentially built on the spatial correlations of any two points. He was able to demonstrate the fundamental power scaling law which reveals the underlying key mechanisms of fluid dynamics, namely the energy cascades that balance kinetics and viscous dissipation. This spatial power scaling law is a hallmark of turbulence and appears at an intermediate spatial range called the "inertial subrange" where essentially kinetic energy is not dissipated, and just merely transferred to smaller scales following Richardson's concept of *cascaded eddies* (*6*). In that inertial subrange, the *structure functions* show a universal scaling $r^{2/3}$ and an energy scaling $k^{-5/3}$, being *r* the spatial scale and *k* the associated wave number of the spectral scale *(see **Figure 1A and 1B**)*. Furthermore, Kolmogorov demonstrated that at small scales turbulence is homogeneous isotropic and universal.

This approach was very successful in overcoming the severe limitations of inferring macroscopic laws from a pure constructivist approach based on studying fluid dynamics at the microscopic level described by the Navier-Stokes equations. Similarly, in neuroscience the microscopic Hodgkin-Huxley equations are inappropriate for explaining whole-brain brain dynamics. Instead, in the following we draw inspiration from the phenomenological approach of Kolmogorov to uncover fundamental principles of brain dynamics at the macroscopic level. In order to discover if human brain dynamics are organised around a *homogeneous isotropic functional core*, we use Kolmogorov's concept of *structure functions* of a variable *u* (in turbulence usually a transversal or longitudinal velocity), defined by:

$$S(\mathrm{r}) = \langle (u(\bar{x}+r) - u(\bar{x}))^2 \rangle = 2[B(0) - B(\mathrm{r})] \qquad (1)$$

where the basic spatial correlations of two points separated by an Euclidean distance *r*, are given by:

$$B(r) = \langle u(\bar{x}+r)u(\bar{x}) \rangle \qquad (2)$$

Here, the variable *u* denotes the spatiotemporal fMRI BOLD signals from our analysis of the whole-brain dynamics of the resting state conditions of 1003 healthy human participants of the Human Connectome Project (HCP) database. The symbol $\langle \; \rangle$ refers to the average across node locations $\bar{x}$ of the nodes, i.e. over time and space. Note that many pairs across the brain has the same Euclidean distance *r* and thus they are averaged in the $\langle \; \rangle$. $B(r)$ characterises the functional correlation between two points as a function of the distance between those nodes (averaged across nodes and time) *(see **Figure 1C**)*.

Following this empirical analysis to find traces of a potential *homogeneous isotropic functional core* and if there are *turbulent-like power scaling law* for functional correlations in a broad spatial range, we then rigorously demonstrate these fundamental principles using a whole-brain model using the ERD Markov-Kennedy anatomy.

Results: Empirical

The empirical data is minimally pre-processed according to the HCP protocol and subsequently filtered in the narrow relevant band between 0.008 and 0.08 Hz, detrended and z-scored. We use the Schaefer parcellation with 500 nodes in each cortical hemisphere (*7*). For each node we compute its physical location in MNI space and the Euclidean distances *r* between two node locations. Average across participants, **Figure 1D** shows the structure function *S(r)* and **Figure 1E** shows the correlation function *B(r)* as a function of *log(r)*. **Figure 1F** plots the correlation function *B(r)* as a function of the distance r, but instead showing the dispersion across participants. In these Figures, we observe clearly what we call the *inertial subrange* inspired by fluid dynamics (but in an abuse of semantics), where there is a power scaling law (exponent is approximately -1/2) in the range between *r*=8.13 and *r*=33.82 (shaded area in all three figures). In order to study the homogeneity of the *B(r)* correlation as a function of the node location $\bar{x}$, we perform for each participant and for each node location $\bar{x}$ the fitting of the power scaling law in the same inertial subrange, i.e. $\log\left(B(r)\right) = a\ log(r) + h$. Here, the parameters a (slope) and h (bias) describe the power scaling law for each participant and each location. **Figure 1G** shows the density distribution (across participants and node locations) of the slope parameter a, while **Figure 1H** shows this for the bias parameter h. Both distributions are unimodal, which is suggestive of a core of homogeneity of the correlation function *B(r)* across node location. Furthermore, **Figure 1I** shows the density distribution (across participants and node locations) of the mean (across *r* in the intertial subrange) of the standard deviation of *B(r)*. This distribution reflects also a unimodal distribution suggestive of isotropy, given that the variability across directions (standard deviation of *B(r)*) is consistent with an isotropic peak.

Results: Modelling

Nevertheless, the empirical findings are not conclusive of a homogeneous isotropic functional core, which observes spatial power scaling behaviour in the inertial subrange given the dispersion and correlative nature of the structure function. Proving that human neuroimaging data observes this fundamental law requires a rigorous causal demonstration with a model of the empirical data.

Here we use a whole-brain model constructed using coupled Hopf oscillators at each node location for emulating the local dynamics (*see Supplementary Methods*). Conventionally, the coupling is determined by the underlying anatomical connectivity, typically created from tractography of diffusion MRI. Here, we test the strong hypothesis that the human brain contains a functional homogenous isotropic core following a turbulent-like spatial power law for a given inertial subrange, derived from the exponential Markov-Kennedy distance rule

$$C_{np} = Ge^{-\lambda(r(n,p))} \qquad (3)$$

where C_{np} is the anatomical coupling between node *n* and *p*, G is the strength of the coupling and λ is the exponential decay of the connectivity as a function of the distance, i.e. $r(n,p)$, which is simply the Euclidean distance between nodes.

With this model, we were able to test the hypothesis by studying the root squared error between the empirical and simulated *B(r)* in the inertial subrange as a function of the two free parameters *G* and λ**. Figure 1J** confirms that the hypothesis as can be seen from the perfect fit with *G=0.825* and $\lambda=0.24\ mm^{-1}$, which is used to plot the remarkable fit in **Figure 1K** between empirical and simulated *B(r)* for the inertial subrange. On the other hand, as shown in **Figure 1L**, the traditional correlations between empirical and simulated functional connectivity matrices is not informative for constraining the model.

This causally demonstrates that the human brain contains a homogeneous isotropic functional core, which observes spatial power scaling behaviour in the inertial subrange, generated by the exponential Markov-Kennedy distance rule. Furthermore, this result fits well with the empirical $\lambda = 0.18\ mm^{-1}$ observed in non-human primates (*2*).

This novel discovery of the fundamental functional organisation of the human brain is even more profound given that **Figure 1M** shows that at the optimal working point there is optimal balance between integration (**Figure 1N**) and segregation (**Figure 1O**). The balance is simply computed as the product of the segregation and integration (*see Supplementary Methods*). It has been proposed that segregation and integration hold the keys to optimal brain function (*8*).

Discussion

In their landmark anatomical studies, Kennedy and colleagues have remarked that the most relevant connectivity for implementing cognition and higher brain function can be found in the *exceptions* to the exponential Markov-Kennedy distance rule, i.e. long-range connections. This is perhaps understating the importance of the anatomical core.

In contrast, here we propose that the functional core is essential for brain function and reflect the underlying economy of anatomy that keeps the human brain cost effective. Beyond the functional core, higher brain function is achieved through the breaking of the homogeneity and isotropy of the functional core organisation.

The Hopf whole-brain model uses the simple exponential Markov-Kennedy distance rule to generate the spatial power scaling law in the inertial subrange of the empirical neuroimaging data. This clearly demonstrates that the human brain works through a cascade of information transfer processing. Perhaps we will soon be a position to substitute the turbulent cascades of fluids with turbulent information cascades, or to paraphrase the poetic words of Richardson, a pioneer of turbulence (who was himself rephrasing Jonathan Swift):

Big whirls have little whirls that inform their activity
And little whirls have lesser whirls and ad recursivity

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Figure

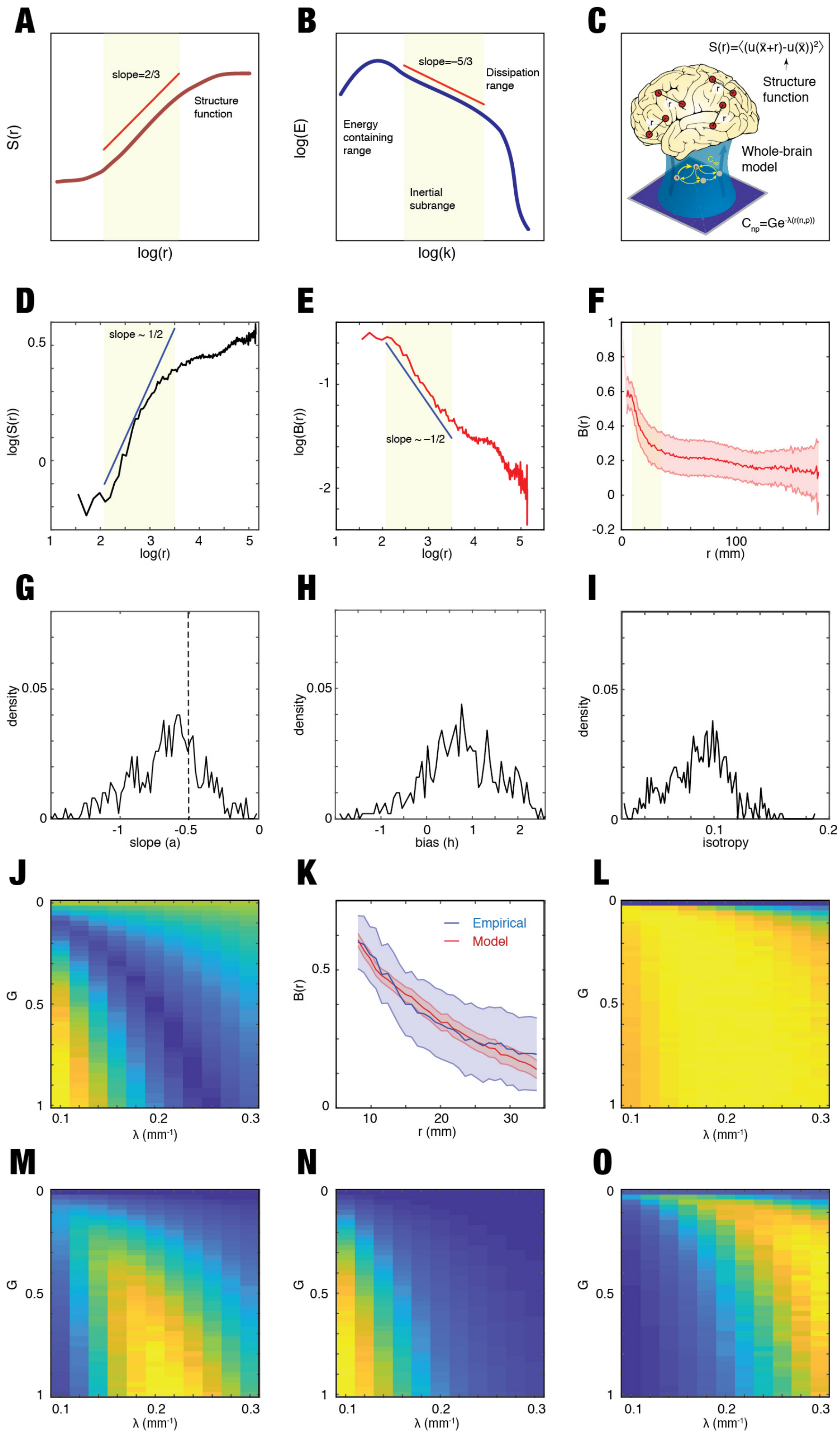

Figure 1. Discovering the turbulent homogeneous isotropic core functional organisation. A) *Kolmogorov's structure function law showing universal spatial scaling in the inertial subrange for turbulence.* ***B)*** *Same but energy scaling associated with the wave number of the Fourier of the spatial scale.* ***C)*** *Cartoon of our whole-brain modelling framework that links the anatomical*

exponential Markov-Kennedy distance rule with the turbulent-like correlation functions in the human brain for demonstrating turbulent-like homogeneous isotropic functional core and spatial power scaling. ***D)*** *Spatial power scaling law of the structure function S(r) as a function of log(r) in human neuroimaging data for the correlation function.* ***E)*** *Same spatial power scaling law for the correlation B(r) as a function of log(r).* ***F)*** *The correlation function B(r) as a function of the distance r, but with the dispersion across participants.* ***G)*** *The unimodal density distribution (across participants and node locations) of the slope parameter* α*.* ***H)*** *Similar unimodal density distribution of the bias parameter* h*.* ***I)*** *Unimodal density distribution of the mean (across r in the intertial subrange) of the standard deviation of B(r). These distributions strongly suggest a core of homogeneous isotropic function.* ***J)*** *The results of modelling provide causal support for our hypothesis that the human brain contains a functional homogenous isotropic core following a turbulent-like spatial power law for a given inertial subrange. We show the root squared error between the empirical and simulated B(r) in the inertial subrange as a function of the two free parameters G and* **λ***. This finds a perfect fit with G=0.825 and* λ*=0.24* mm^{-1}. ***K)*** *For these optimal parameters, we plot the remarkable fit between empirical and simulated B(r) for the inertial subrange.* ***L)*** *In contrast, traditional correlations between empirical and simulated functional connectivity matrices are not informative for constraining the model.* ***M)*** *At the optimal point, we show the optimal balance between integration and segregation, computed as their product.* ***N)*** *The figure shows the integration, and* ***O)*** *the segregation, demonstrating their complementary nature.*