



Hierarchical and Modular organization of Corticocortical Networks supports Functional Integration and Segregation in the Mammalian Brain

Gorka Zamora-López^{1,2,6,*}, Changsong Zhou^{3,4} and Jürgen Kurths^{5,6}

¹ Interdisciplinary Center for Dynamics of Complex Dynamical Systems, University of Potsdam, Germany

² Bernstein Center for Computational Neuroscience, Berlin, Germany

³ Department of Physics, Center for Nonlinear Studies, Hong Kong Baptist University, Hong Kong, China

⁴ The Beijing-Hong Kong-Singapore Joint Centre for Nonlinear and Complex Systems,
Hong Kong Baptist University, Hong Kong, China

⁵ Potsdam Institute for Climate Impact Research, Potsdam, Germany

⁶ Department of Physics, Humboldt University, Berlin, Germany

*Email: gorka@agnld.uni-potsdam.de

Abstract—There is increasing evidence that the architecture of corticocortical networks support the capacity of the brain to simultaneously segregate and integrate information. Here, we confront the concept of integration, which is rarely addressed in the literature of information theory, to cross-validate the functional implications assigned to such networks. We propose a novel framework to quantify the segregative and integrative properties of cortical networks by defining a minimal set of conditions their nodes need to obey from a functional perspective. Application of these conditions shows that a particular set of cortical areas are highly responsible for the integration of multisensory information. This set coincides with the areas predicted from the purely topological analysis to perform such a function. Our findings are in agreement with modern models which propose that high-level brain functions emerge from interactive and overlapping networks of neurons which transcend any of the traditional subdivisions of the cortex by structural (cytoarchitecture) and functional criteria.

1. Introduction

Sensory neurones encode environmental information into electrical signals which propagate in a “bottom-up” manner through different processing stages of the nervous system [1, 6]. Information of the same modality (e.g. visual, auditory, somatosensory, etc.) traverses the body together, typically separated from the processing paths of other modalities. This permits that particular regions of the cortex specialise in detecting features of the sensory stimuli, e.g. orientation, velocity and colour of the visual input; or frequency and pitch of the auditory stimuli. However, in order to generate a coherent perception of the reality, the brain needs to combine (integrate) this multisensory information at some place [8] and during some time [2, 3, 11]. For that, the paths of information need to converge.

There is increasing evidence that the functional capacity of the nervous system to balance between segregation (spe-

cialisation) and integration might be facilitated by its structural organisation. Analysis of the connectivity between regions of the cerebral cortex in macaque monkeys and cats has revealed their modular organisation [10, 9, 4, 5]. Two areas are more likely connected if both are specialised in the processing of the same modal information (e.g. visual or auditory information). Additionally, the network contains several interconnected hubs, conforming a modular organisation with centralised hierarchy [13] that might be an optimal natural solution to keep different information separated, but permitting at the same time a controlled integration of all the information.

In this paper we challenge the functional properties of this modular and hierarchical structure by means of dynamical and information theoretical measures. We propose minimal conditions that lead to integration of multisensory information and we test them in the corticocortical network of the cat. In order to objectively detect the set of hubs that optimise integration, we perform a statistical analysis of these properties in a wider ensemble of possible hub combinations. We find that only simultaneous lesion of particular hubs leads to a dynamical segregation of the sensory modules (visual, auditory, somatosensory-motor and frontolimbic), and only the same hubs form a dynamical cluster after simultaneous excitation of primary sensory areas, a clear sign of their integrative capacities.

2. Data

After an extensive collation of literature reporting anatomical tract-tracing experiments, Scannell and Young [10, 9] published a dataset containing the corticocortical and cortico-thalamic projections between regions of one brain hemisphere in cats. The connections were weighted according to the axonal density of the projections. Connections originally reported as *weak* or *sparse* were classified with 1 and, the connections originally reported as *strong* or *dense* with 3. The connections reported as *intermediate* strength, as well as those connections for

which no strength information was available, were classified with 2. Here we make use of a version of the network consisting of $N = 53$ cortical areas interconnected by $L = 826$ directed corticocortical projections.

3. Functional Capacity of Integration

While information theory has largely dealt with describing and quantifying channel capacity, coding and decoding of signals, etc., it has not faced the problem of integration. Many natural and artificial systems, such as the nervous system, need to deal with information arising from different sources. In this sense, we aim for a definition of integration which characterises *the capacity of a system to receive and process information of different character and to combine it generating new useful information*. Certainly, this definition involves crucial theoretical problems, e.g. what the *character* of information is, or what are the rules under which information is *combined*. Nevertheless, within a networked system, the nodes with a capacity to integrate information should obey certain measurable conditions. We propose the following:

1) Accessibility to information: A node can perform an integrative function only if it has general access to the information contained within the system.

2) Sharing of information: Two or more nodes can perform integrative function in a collaborative manner only if they are sufficiently connected with each other.

As a corollary of these two conditions, we should include the following, third condition:

3) Segregation after selective damage: If a node has an integrative function, its removal should lead to a decrease of the integrative capabilities of the whole system.

In order to test these conditions on the central hubs of the corticocortical network of the cat, we perform two numerical experiments: (i) after excitation of primary sensory areas, we quantify the dynamical interdependence between the hubs, see Figure 1a, and (ii) we measure the decrease in integration capacity of the network after the hubs have been removed, Figure 1b. Aiming for a statistical description that objectively highlights the more relevant hubs for integration, we relax the definition of hub and perform both experiments for each of the 524,097 possible sets of cortical hubs, of sizes $N_S = 1$ to $N_S = 19$, formed by the following set of areas:

$S_{hubs} = \{20a, 7, AES, EPP, 6l, 6m, 5Am, 5Al, 5Bm, 5Bl, SSSAi, SSAo, PFCL, Ia, Ig, CGa, CGp, 35, 36\}$.

The *steady-state* of a linear system whose N subsystems $\mathbf{x} = (x_1, x_2, \dots, x_N)$ are driven by a Gaussian noise $\xi = (\xi_1, \xi_2, \dots, \xi_N)$, is described by $x_i = g \sum_j \hat{A}_{ij}^t x_j + \xi_i$, where g is the coupling strength and \hat{A}^t is the normalised transpose of the adjacency matrix. Otherwise the dynamics of x_i would be characterised by its own outputs, not by the inputs it receives. The adjacency matrix is normalised by its largest eigenvalue such that the coupling strength g

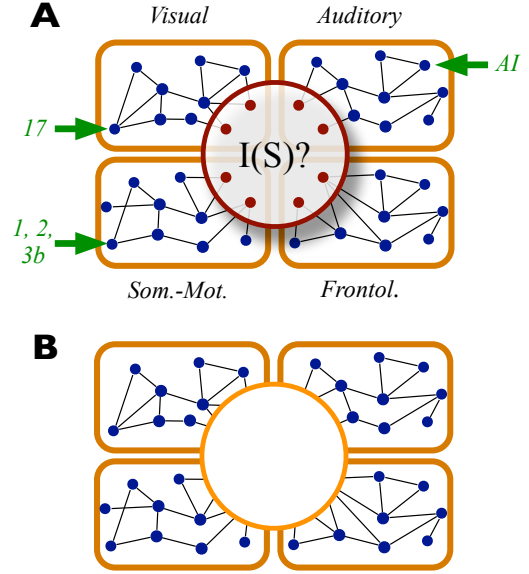


Figure 1: Schematic representation of the numerical experiments. (A) The network is stimulated by increasing the noise level of the primary sensory areas. The consequent integration $I(S)$ between a group of hubs is measured. (B) After simultaneous removal of a set of hubs, the integration capacity $I(X - S)$ of the remaining network is measured.

is equivalent for networks of different size and topology. Written in matrix form:

$$\mathbf{x} = g \hat{A}^t \mathbf{x} + \xi. \quad (1)$$

The entropy of such a multivariate Gaussian system can be analytically calculated as $H(X) = \frac{1}{2} \log [(2\pi e)^N |\text{COV}(X)|]$, where $|\cdot|$ stands for the determinant [7, 12]. The entropy of an individual Gaussian process is $H(x_i) = \frac{1}{2} \log(2\pi e v_i)$, where v_i is the variance of x_i , say, the i^{th} diagonal element of the $\text{COV}(X)$ matrix. The covariance matrix can be analytically computed by solving the system such that $\mathbf{x} = \frac{1}{1-g\hat{A}^t} \cdot \xi = Q \cdot \xi$, and averaging over the states produced by successive values of ξ one finds: $\text{COV}(X) = \langle \mathbf{x} \cdot \mathbf{x}^t \rangle = \langle (Q \cdot \xi) \cdot (\xi^t \cdot Q^t) \rangle = Q \cdot Q^t$.

Following Tononi and Sporns [12] we define the integration of the system X as the extension of the mutual information for X composed of more than two subsystems:

$$I(X) = \sum_{i=1}^N H(x_i) - H(X) \quad (2)$$

where $H(x_i)$ is the entropy of one subsystem and $H(X) = H(x_1, x_2, \dots, x_n)$ is the joint entropy of the system considered as a whole. $I(X) = 0$ only if all $x_i \in X$ are statistically independent of each other, and positive otherwise. $I(X)$ measures the internal level of statistical dependence among all the subsystems $x_i \in X$. Replacing $H(X)$ and $H(x_i)$ of the linear system into Equation (2) and applying basic algebra,

we reduce the integration of such a multivariate Gaussian system as:

$$I(X) = \frac{1}{2} \log \left[\frac{\prod_{i=1}^N v_i}{|\text{COV}(X)|} \right]. \quad (3)$$

4. Results

In the following, we perform the two numerical experiments considering, unless otherwise stated, coupling strength $g = 0.5$ for all the links and a noise level of $\xi_i = 1.0$ is added to all the areas. These parameters lead to similar covariance matrices as those obtained from more realistic models [14, 15, 16].

4.1. Dynamical integration after sensory stimulation

We simulate external stimulation by an increase in the noise level of primary sensory areas: primary visual cortex (area *17*), primary auditory cortex (area *AI*) and primary somatosensory cortex (areas *1*, *2* and *3b*). According to [9] the cortical areas *1*, *2* and *3b* are subregions of the primary somatosensory area, named by some authors as *SI*. We simultaneously excite all the primary sensory areas $\{17, AI, 1, 2 \text{ and } 3b\}$ by assigning them a larger noise level $\xi_j = 10.0$ and we measure the local integration among the areas in a subsets S of hubs out of S_{hubs} . Because of the excited condition, the integration of the subsets is denoted as $I^e(S)$. The integration $I(S)$ of a subset of nodes S is computed as in Equation 3 by extracting $\text{COV}(S)$ as a submatrix of $\text{COV}(X)$ formed by the nodes in the set S , and by considering the variance v_i of the nodes in the set.

The results depicted in Figure 2A show that $I^e(S)$ can largely differ. For example, among all the subsets of size $N_s = 10$, the integration of some of them is very small, $I^e(S) \sim 0.1$, while the integration of others becomes much larger, $I^e(S) \sim 0.5$. These differences permit us to identify those cortical hubs which, grouped together, become more dynamically dependent among them as a consequence of the multisensory stimulation. Considering only those subsets whose $I^e(S)$ lies within the largest 10% (red crosses in Figure 2A) a *co-participation matrix* \mathbf{C} is constructed such that C_{ij} is the number of times (given in frequency) that two cortical hubs participate together in one of the maximal sets, Figure 2B. It is observed that areas $\{7, AES; EPP; 6m; Ia, Ig, CGp, 35, 36\}$ participate together in over 75% of all the maximal sets. Visual area *20a* and the somatosensory-motor area *6l* participate only in 50% of the occasions with those areas in the core. The remaining areas, $\{5Am, 5AI, 5Bm, 5Bl, SSSAi, SSSAo \text{ and } PFCL\}$, can be discarded as members of the dynamical core.

4.2. Dynamical segregation after multiple lesions

For all the possible subsets S composed of hubs in S_{hubs} , we perform a lesion to the network by simultaneously removing the nodes $x_i \in S$ and characterise the consequent

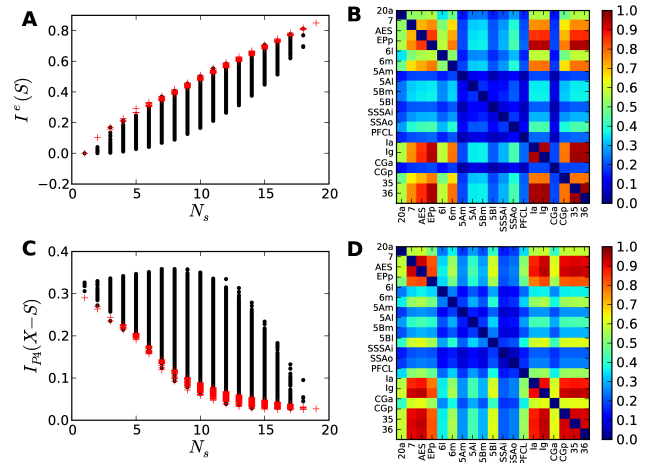


Figure 2: Functional segregation and integration. (A) *Local integration* $I^e(S)$ of cortical hubs after stimulation of the primary sensory areas. (B) Co-participation matrix of cortical hubs within the subsets leading to large $I^e(S)$ (red dots). (C) *Modular integration* I_{P_4} of the sensory modules V, A, SM and FL after simultaneous lesion of cortical hubs. N_s is the number of hubs removed. (D) Co-participation matrix of the hubs within the subsets S which lead to a larger decrease in the dynamical dependence ($I_{P_4}(S)$) of the sensory modules (marked by red dots).

functional segregation of the network as the change in statistical dependence between the four modules (V, A, SM and FL). Lesion of areas critical for the integration capacities of the system should lead to a dynamical segregation of the modules, i.e. a decrease in their statistical dependence.

As defined in Equation (3), $I(X)$ represents the limit case in which the statistical dependence among all the elements x_i in the system X is quantified. To cover different scales of organisation we propose to characterise the statistical dependence between groups of elements. Imagine a partition $\mathcal{P} = \{S_1, S_2 \dots S_n\}$ into n groups (modules) of the elements x_i such that $X = S_1 \cup S_2 \cup \dots \cup S_n$. Then, we define the *modular integration* of the partition \mathcal{P} as:

$$I_{\mathcal{P}}(X) = \sum_{j=1}^n H(S_j) - H(X). \quad (4)$$

Note that when $n = N$, then $I_{\mathcal{P}}(X) = I(X)$.

Considering the partition $\mathcal{P}_4 = \{V, A, SM, FL\}$ and the corticocortical network of the cat, then $I_{P_4}(\mathcal{G}_{cat}) = 0.292$. The modular integration of each lesioned network \mathcal{G}_S is computed for the partition \mathcal{P}_4 . Notice that *a*) the nodes are also removed from the partition and *b*) every \mathcal{G}_S is adequately normalised by its largest eigenvalue such that the measured observables are comparable across realisations. The results in Figure 2C permit us again to discriminate between subsets of hubs whose simultaneous removal lead to a large segregation of the network, while removal of other subsets has barely no effect.

Selecting only those subsets whose lesion leads to a larger segregation of the modules, i.e. $I_{\mathcal{P}_4}(\mathcal{G}_S)$ lies among 10% of the minimal modular integration for each size N_S (red dots in Figure 2A), a co-participation matrix \mathbf{C} is constructed, Figure 2D. The entries C_{ij} are the number of times (given in frequency) that two areas participate together in one of the minimal subsets. A core of cortical areas is found which participate together in over 70% of these cases: $\{7, AES; EPP; Ia, Ig, CGp, 35, 36\}$. Somatosensory-motor areas $6m, 5Al$ and $5Bl$ join them in over 50% of the cases.

5. Conclusions

In summary, we have analysed the modular and hierarchical organisation of the corticocortical network of the cat and its relationship to the intrinsic necessities of the brain to simultaneously segregate and integrate multisensory information. By means of dynamical and information theoretical measures, we have corroborated its capacity to integrate multisensory information, i.e. after simultaneous excitation of visual, auditory and somatosensory primary areas, a particular set of hubs becomes dynamically dependent forming a cluster. Additionally, the simultaneous lesion of these hubs leads to a largest decrease in the integrative capacities of the network. Both numerical experiments indicate that visual areas 7 and AES , auditory area EPP and frontolimbic areas $Ia, Ig, CGp, 35$ and 36 are the most likely candidates to form the top hierarchical module. The participation of somatosensory-motor areas is less clear, although area $6m$ is the strongest candidate of them. Visual area $20a$ and somatosensory-motor areas $5Al$ and $5Bl$ are also potential candidates. This set largely coincides with the top hierarchical level found by the graph analysis [13], corroborating the integrative function assigned to the hubs by intuitive interpretation of their topological characteristics.

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