

Tutorial 6 - Computational Modelling

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Questions

- What is a Stuart-Landau oscillator (Hopf oscillator)?
- How can a model based on coupled oscillators simulate the dynamics of a simple network?
- How can such a model be used to characterize certain dynamical aspects of brain activity?

Objectives

1. Generating local dynamics: single-node oscillator
 - Visualize and describe the dynamics of a single-node oscillating system near a Hopf bifurcation.
 - Change the regime (bifurcation parameter) of the oscillator to generate different local dynamics.
2. From local to global: network of coupled oscillators
 - Understand how different oscillators can be linked to obtain a network of coupled oscillators and simulate data.
 - Characterize changes in certain aspects of network dynamics as a function of different model parameters (coupling parameter, connectome).
3. Using a model of coupled oscillators to characterize brain dynamics
 - Understand the role of the model parameters to constrain the model with real data.
 - Fit the model with empirical resting-state human fMRI data and characterize certain aspects of brain activity.
 - Understand the use, applicability and limitations of whole-brain models.

Introduction

Computational brain network models have emerged as a powerful tool to investigate the dynamics of the human brain. In a broad sense, modelling refers to idealizing (or simplifying while keeping the essential ingredients) the processes that generate the observed phenomena in a real system. Theoretical models are often applied to study complex non-linear systems, such as the brain, in order to investigate the interplay between known dynamical and structural features, e.g. combining SC with local dynamics to generate resting-state FC. For this, it is required to explain the relevant observable features and to ensure a robust interpretation of the models' parameters to link them back to biological variables. Thus, theoretical models need to achieve a trade-off between simplicity and richness to explain the mechanisms underlying complex biological systems.

In this tutorial, a relatively simple whole-brain model will be introduced based on a set of coupled oscillators near a Hopf bifurcation [1, 2]. This model is a deterministic model with a bottom-up approach that has been used to describe the brain's rsfMRI network activity in different experimental contexts. The model assumes that the brain's resting-state activity emerges from the interaction between brain regions in an interconnected neuroanatomical network. Furthermore, the local dynamics are modelled by Stuart-Landau oscillators, which allow us to study the phase and amplitude interactions in large networks. This whole-brain model has been successfully applied to simulate the network non-linear dynamics occurring at the ultra-slow scale of resting-state BOLD signals [1, 3]. Furthermore, the model global and regional parameters obtained from the model can discriminate between brain states, thereby improving our understanding of brain network and local alterations in different brain states [2, 4, 5, 6].

Overline

1. We will focus on understanding the key properties of a Hopf oscillator. In particular, we will investigate the role of its bifurcation parameter, which describes if the system presents oscillatory or noisy activity.
2. We will study the behaviour of a network of coupled Hopf oscillators in a simple simulated network. The complexity of the network structure and dynamics will be altered by changing the underlying connectivity matrix and the global coupling parameter.
3. Finally, the previously introduced whole-brain model will be used to fit empirical data of resting state fMRI brain activity. The model parameters will be used to interpret certain aspects of the underlying dynamics.

Part 1: Understanding a Hopf oscillator

First, we will introduce the Hopf oscillator. The normal form of a supercritical Hopf bifurcation, i.e. Stuart-Landau oscillator [7, 8], describes the transition from noisy to sustained oscillations [9], and is given, in the complex plane, by the following differential equation:

$$\frac{dz}{dt} = (a - |z|^2 + i\omega)z + \beta\mu(t), \quad (1)$$

where z is the complex-valued state variables \bar{z} is the complex conjugate of z , a and ω are the bifurcation parameter and the intrinsic frequencies of the system in the range of 0.04-0.07 Hz, respectively, and μ is a Gaussian noise vector with standard deviation $\beta = 0.02$.

For $a < 0$, the local dynamics present a stable spiral point, producing damped or noisy oscillations in absence or presence of noise, respectively. For $a > 0$, the spiral becomes unstable and a stable limit cycle oscillation appears, producing autonomous oscillations with frequency $2\pi f = \omega$. At the transition, when $a \sim 0$, the dynamics display flexible noisy oscillations of low amplitude.

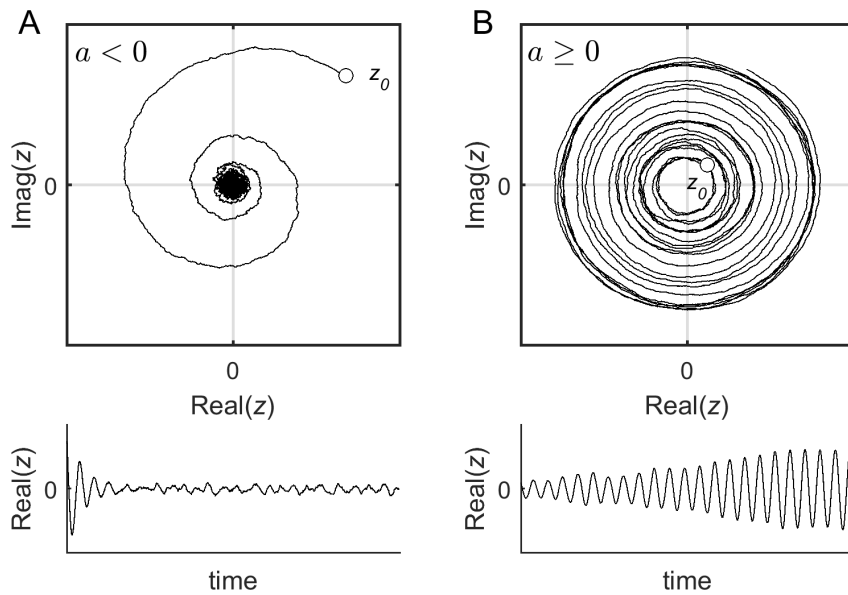


Figure 1: Phase space for an example of a single Hopf oscillator. A) Subcritical Hopf oscillator ($a < 0$). Top: In this regime, a stable spiral, or focus, exists at $z = 0$. The system relaxes towards the focus with damped oscillations. In the presence of noise, however, the system fluctuates around the focus, thus producing noise-induced oscillations. $z_0 = z(t = 0)$ indicates the initial condition. Bottom: temporal evolution of $Real(z)$. **B)** Supercritical Hopf bifurcation ($a \geq 0$). Top: In this regime, the focus at $z = 0$ becomes unstable and a stable limit-cycle appears, thus producing autonomous or self-sustained oscillations. Bottom: temporal evolution of $Real(z)$.

Exercise 1

In this exercise, you will work with a Hopf oscillator. In particular, you will simulate the dynamics of the oscillator for different regimes (changing the local bifurcation parameter). Please follow the next steps:

1. Open the script 'exercise1.m' in the VM with MATLAB.
2. Plot an overview of the dynamics of a Hopf oscillator when $a = 0$ (default value), i.e., when the oscillator is working in the phase transition.
3. Modify the value of the bifurcation parameter of the oscillator to simulate sustained oscillations, i.e. $a > 0$. Try with different values of a and observe the oscillations that you obtain.
4. Modify the value of the bifurcation parameter of the oscillator to simulate noisy oscillations, i.e., $a < 0$. Try with different values of a and observe the oscillations that you obtain.

Solution of exercise 1

You should obtain plots similar to the following ones:

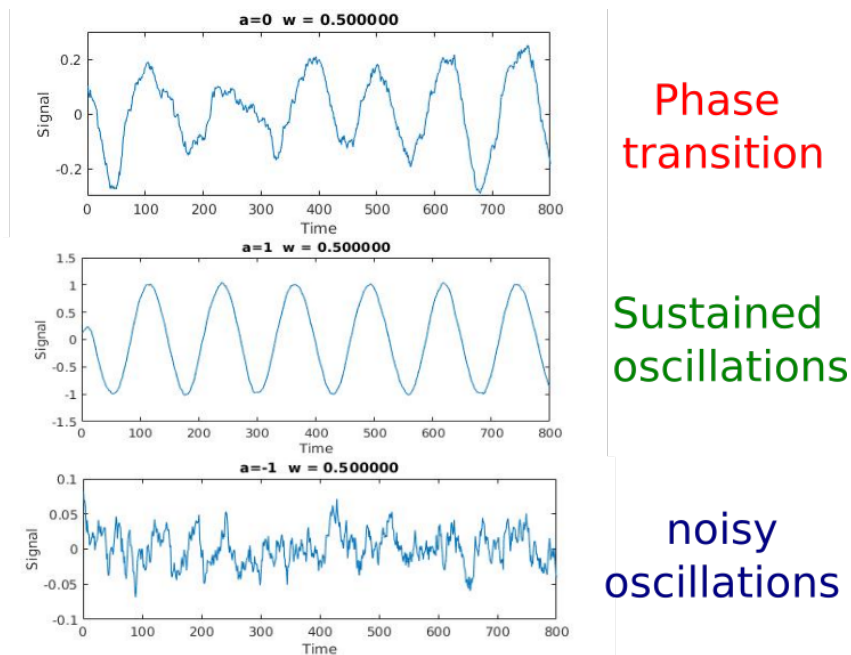


Figure 2: **Solution for exercise 1.** Depending on the bifurcation parameter of the oscillator, the signals show dynamics representing different dynamical regimes. Top: oscillators in the phase transition show signals that combine noise and oscillations. Middle: the signal shows self-sustained oscillations for $a > 0$. Bottom: the system produces noise-induced oscillations for $a < 0$.

EXTRA EXERCISE: study the stability of the oscillators in the different regimes displaying the dynamics in the phase plane. You should plot the imaginary and real parts of the signal in the complex plane and obtain the plots showed in Figure 1.

Part 2: Simulating coupled dynamics in a network of oscillators

In this second part of the tutorial, we will study the dynamics of a network of coupled Hopf oscillators. The network consists of different oscillators that influence each other's activity. We will consider a network containing $N = 10$ nodes that are separated in two communities and with a hubs connecting both communities. The following matrix describes the interaction between the nodes in such a network:

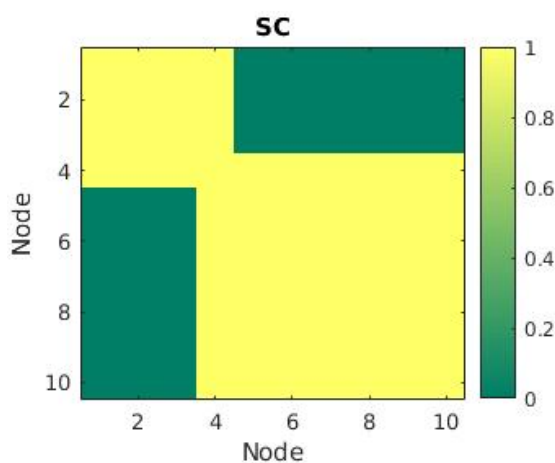


Figure 3: **Network connectivity.** Structural connectivity matrix describing the interaction strength between nodes. This matrix contains two communities: the first one is composed by the first four nodes and the second one by the last six nodes. There is a hub interconnecting all network nodes.

The network dynamics can be described by coupling the different oscillators with a strength proportional to the coefficients of the matrix C , i.e., C_{ij} :

$$\frac{dz_j}{dt} = (a_j + -|z_j|^2 + i\omega_j)z_j + g \sum_{k=1}^N C_{jk}(z_k - z_j) + \beta\mu_j(t), \quad (2)$$

where g represents a global coupling scaling the structural connectivity C_{ij} . The matrix C_{ij} is scaled to a maximum value of 0.2 to prevent full synchronization of the model. If we set the values of each ω_i , the network dynamics depend on two ingredients: the global coupling coefficient (g) and the local parameters for each node (a_j).

If we think of each node's signal as describing the activity of a different brain ROI and the matrix C as the structural brain connectivity (SC), the model can be used to describe whole-brain dynamics. The global coupling, g , is a scaling parameter that controls for the conductivity of the fibers given by the SC. For low values of g the functional network interactions are mainly restricted to nodes directly connected by high strength links in C . Increasing the global coupling favours the propagation of recurrent activity within the network, allowing

for correlations to emerge between nodes that are not directly connected with each other via structural connections.

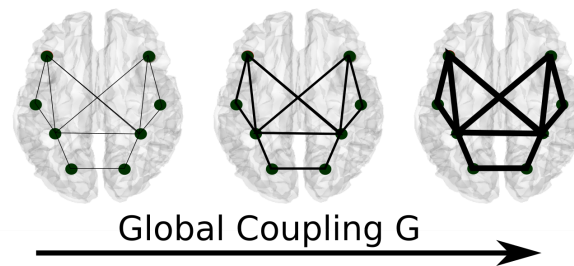


Figure 4: **Global coupling parameter in the whole-brain network model.** The global coupling model parameter g scales the weights of the SC matrix. Low and high values of g represent weakly and strongly coupled networks, respectively.

Exercise 2

The goal of this exercise is to understand the role of the global coupling parameter in the model and how its value may influence the functional correlation patterns.

1. Open the script named 'exercise2.mat' in the VM.
2. Run the part where the network is defined (*Define the network*). At the end of this section, you should be able to plot the matrix in Figure 3, where the interactions between the nodes are defined.
3. Simulate the network dynamics in the case where there is no global coupling ($g = 0$), i.e., there is no coupling between nodes. For the purpose of this exercise, we suggest to set all nodes to be working at $a = 0$, except the hub, that should be working in the oscillatory regime ($a = 1$). This choice is based on previous studies which suggest that the best fit to empirical data arises at the brink of the Hopf bifurcation where $a \sim 0$ [1]. Plot the nodes' signals and the functional connectivity matrix.
4. Simulate the network dynamics in the case where there is global coupling ($g > 0$), i.e., the nodes interact with one another. To study the difference that the coupling parameter can exert over the whole network, you can keep all nodes in the same regime as before (all nodes at $a=0$, except for the hub, which works at $1=1$). Plot the nodes' signals and the functional connectivity matrix for $g = 0.5$.
5. Change the g to a lower value ($g = 0.2$) and plot the nodes' signals and the functional connectivity matrix again.

Solution of the exercise 2

In this exercise, we have changed the value of the global coupling parameter, while keeping local properties fixed. We have used a simulated network containing two modules and one hub. All nodes' have been set to $a = 0$, except for the hub, for which we have used $a = 1$.

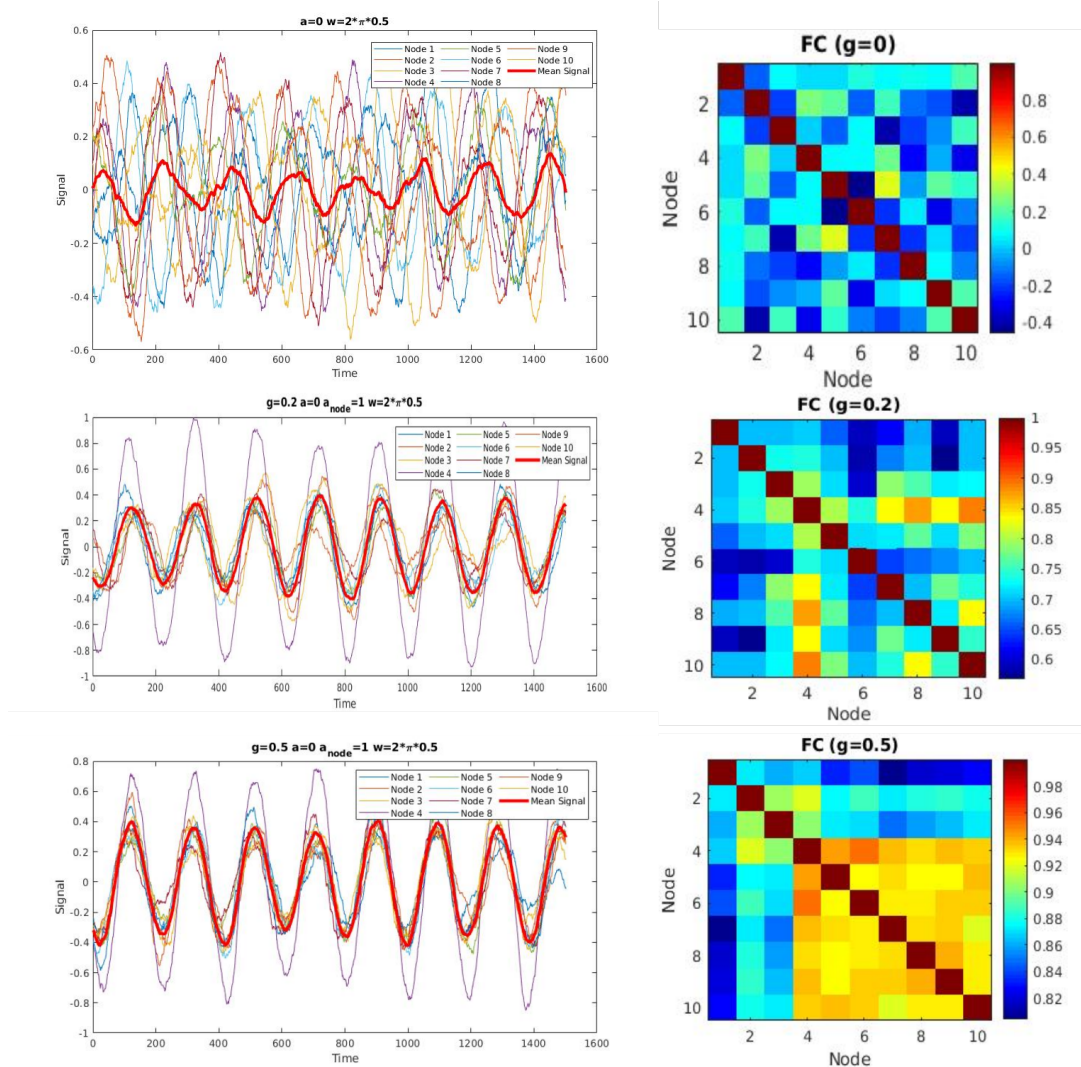


Figure 5: Solution for exercise 2. Different outputs obtained changing the global coupling parameter. Top: the case where there is no coupling, i.e., $g = 0$, shows that the nodes' signals display asynchronous activity. This variability is reflected in the FC where the matrix shows a sparse distribution of values, with maximum values of 0.5 (without considering the diagonal). Middle: when increasing the global coupling parameter, all nodes start to synchronize with the hub. The effect of the interactions translates into an increased correlation between signals. Bottom: A high value of g favours the propagation of recurrent activity within the network, allowing for correlations to emerge between nodes that are not structurally connected. Notice the high correlation values in the FC. Furthermore, the hub, working in the oscillatory regime, orchestrates the network dynamics and keeps all nodes in an oscillatory regime.

Part 3: Fitting and modelling resting-state data

Finally, we will use the network model to understand some mechanisms of brain dynamics in healthy subjects during resting-state. In this part, we will fit the dynamics of the oscillators and the model parameters to reproduce empirical data (fMRI BOLD and DTI- SC). The natural frequency of oscillations for each ROI is estimated from the peak of the power spectra obtained from their BOLD signals in the frequency band 0.04-0.07 Hz. Then, the $N = 83$ brain regions are coupled through the connectivity matrix C_{jk} , which is given by the structural connectivity of healthy subjects. The matrix C_{jk} is scaled by the global coupling parameter g .

First, we can study the network dynamics for the homogeneous case, in which we set $a_j = 0$ for all nodes. This choice is based on previous studies which suggest that the best fit to the empirical data arises at the brink of the Hopf bifurcation where $a \sim 0$ [1]. In this case, the network dynamics are determined by a single free parameter: the global coupling strength g . This parameter is estimated by maximizing the fit between the functional connectivity dynamics (FCD) obtained using the empirical data and the simulated signals at various values of g [1, 2, 4]. See Fig. 6. Specifically, empirical and simulated FCDs are compared using the Kolmogorov-Smirnov distance of their values (KS-distance). For low and high values of g , large KS distance indicates differences between the mean values of the FCD distributions. In the intermediate range of g , shorter KS distance evidences a closer similarity between the empirical and the simulated FCDs. We choose the g where the KS distance is minimized as the optimal working point of the model.

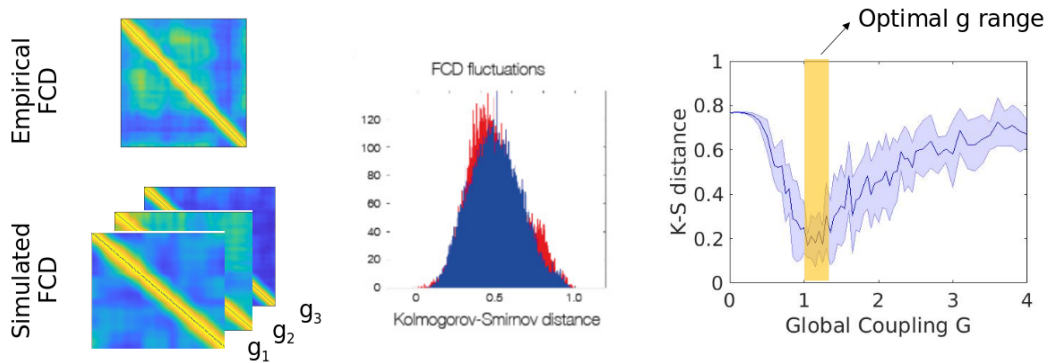


Figure 6: Fitting of global coupling parameter in the whole-brain network model. To estimate the global parameter, we look for the model that best reproduces the distribution of FCD values (fixing all other model parameters). We first obtain a single FCD matrix for the empirical signals and an FCD matrix using the simulated signals for each value of g . Then, empirical and simulated FCDs are compared (for each value of g) using the Kolmogorov-Smirnov distance (KS distance) of their values. The KS-distance shows minimal values for a specific range of g values, which is considered to be the optimal global coupling g .

The optimal global coupling g shows distinct values for different brain states characterized by different dynamics [5, 2], suggesting that this value contains information about the global dynamics of the empirical data. Furthermore, by fixing this value, we can simulate whole-brain dynamics under certain conditions of interest. Additional information can be extracted by relaxing the homogeneity constraint on the local bifurcation parameters. To do so, the global coupling parameters g can be fixed to the ones estimated previously, and the local parameters a_j are allowed to vary, thus introducing heterogeneity in the working point of the ROIs (see extra exercise).

Exercise 3

The goal of this exercise is to simulate the dynamics of resting-state activity in a healthy subject. To do so, you are going to run the model for different values of the global coupling g and compare the simulated signals with empirical ones. Keep in mind that the final goal is to determine the optimal value of g to reproduce the empirical observations.

1. Open the script named 'exercise3.mat' in the VM.
2. Load the structural connectivity and the BOLD time series of one subject. After fixing all model parameters, run the pre-modelling part of the script. In this initial part, you calculate the FC, the power spectrum, the omega and other variables that will be used in the model simulation. In particular, the ω values are obtained from the power spectra of the BOLD signals and the signal phases are stored for later use during the calculation of the FCD.
3. Start a loop simulating the dynamics of a network with $N = 83$ nodes for different values of g . In each loop, the fit between the FCD matrices is also computed.
4. Plot the values of the fitting and interpret their values. You can also plot the empirical and simulated FCDs to better understand the values of the K-S distance.
5. Load the 'ksP.mat' vector which contains the values of the fitting for a higher resolution of the g (i.e., the fitting has been calculated for smaller steps of g within the same range) and interpret the results.

Solution of the exercise 3

In this exercise, we have fitted the model to describe the dynamics of a real case, considering the structural connectivity extracted from DTI and the resting-state activity of BOLD-fMRI. First, we have extracted some basic model parameters from the empirical data. Then, we have performed a model fitting using the empirical and simulated FCD matrices.

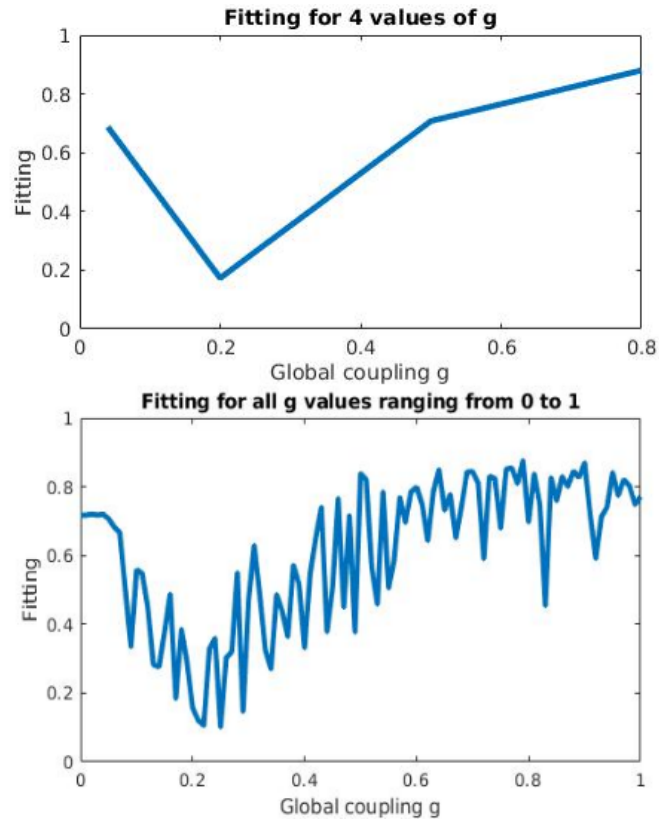


Figure 7: **Solution for exercise 3.** KS-distance between the empirical and the model FCD distributions, as a function of g , for one subject. For low and high values of g , large KS distance indicates differences between the mean values of the FCD distributions. In the intermediate range of g , shorter KS distance evidenced a closer similarity between the empirical and the simulated FCDs. We considered the g where KS distance is minimized as the optimal working point of the model. Top: the fitting for 4 values of g . Bottom: the fitting for a finer resolution of the g values.

EXTRA EXERCISE:

You can also use the optimization algorithm to extract the optimal values of the local bifurcation parameters. In this case, the global coupling parameters g is fixed, but the local parameters a_j are allowed to vary, thus introducing heterogeneity in the working point of the nodes. The individual a_j are estimated from the data using a gradient descent method. You can find the code and details in (https://github.com/decolab/Hopf_consciousness).

Additional materials

- Examples of use of the described model:
 - *Loss of consciousness reduces the stability of brain hubs and the heterogeneity of brain dynamics* by Lopez-Gonzalez et al. (The MATLAB code of the whole-brain models are available on Github (https://github.com/decolab/Hopf_consciousness)) [2].
 - A Hopf oscillator-based method for estimating effective connectivity. Groups of effective connectivity estimates may be compared using the network-based statistic. <https://github.com/decolab/Effective-Connectivity--Hopf> [10]. See also <https://www.youtube.com/watch?v=y6Hv-Jo8Etk>.
 - Turbulent-like dynamics in empirical human neuroimaging data, by using a whole-brain model for discovering the underlying mechanistic principles (<https://github.com/decolab/cr-turbulence>)[11]. See also <https://www.youtube.com/watch?v=s1CBN7-oIOI>.

Key Points

- Whole-brain modelling study complex non-linear systems, such as the brain, in order to investigate the interplay between known dynamical and structural features.
- The model based on Hopf oscillators has been successfully applied to simulate and explain the mechanism underlying the network non-linear dynamics occurring at the ultra-slow scale of resting-state BOLD signals.

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