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 oscillations [9], and is given, in the complex plane, by the following differential equations:

$$\frac{d\mathbf{z}}{dt} = (\mathbf{a} + i\boldsymbol{\omega}) \odot \mathbf{z} - (\mathbf{z} \odot \bar{\mathbf{z}})\mathbf{z} + \beta\boldsymbol{\mu}(t), \tag{0.1}$$

where $\odot$ is the Hadamard element-wise product, $\boldsymbol{z} = [z_1, ..., z_N]$ are the complex-valued state variables of each node, $\bar{\boldsymbol{z}}$ is the complex conjugate of $\boldsymbol{z}$, $\mathbf{a} = [a_1, ..., a_N]$ and $\boldsymbol{\omega} = [\omega_1, ..., \omega_N]$ are the vectors containing the bifurcation parameters and intrinsic frequencies of each node in the range of 0.04-0.07 Hz band, respectively, and $\boldsymbol{\mu} = [\mu_1, ..., \mu_N]$ is a Gaussian noise vector with standard deviation $\beta = 0.02$.

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

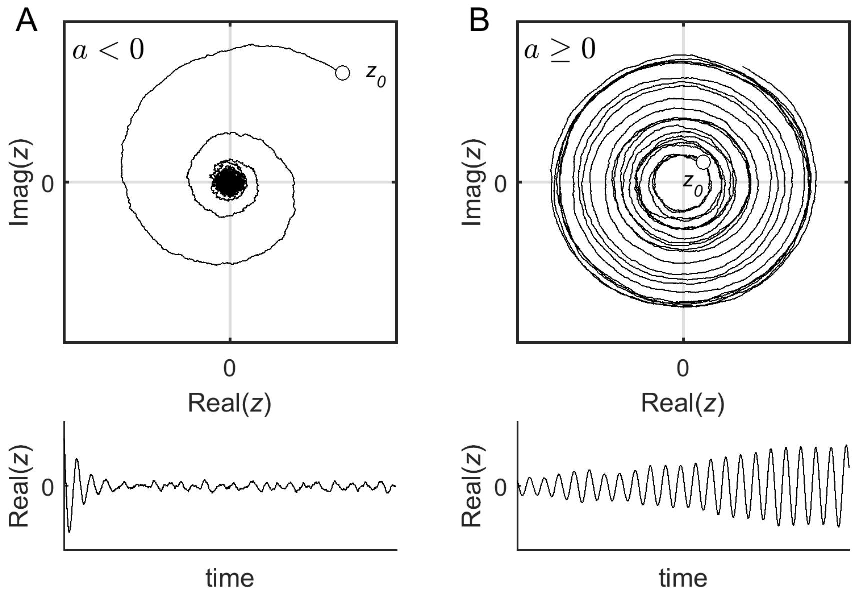

Figure 1: **Phase space for an example of a single Hopf oscillator. A)** Subcritical Hopf oscillator ($a < 0$). Top: In this regime, a stable spiral, or focus, exists at $\boldsymbol{z} = 0$. The system relaxes towards the focus with damped oscillations. In the presence of noise, however, the system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

1. Open the script 'exercise1.m' in the VM with MATLAB.
2. Print an overview of the dynamics of a hopf oscillator when a=0 (deafult value). The script will plot the signal of the oscillator in the case that 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. You should change the value of a=1 and plot the signal of the simulated dynamics to obtain sustained oscillations over time.
4. Modify the value of the bifurcation parameter of the oscillator to simulate noisy oscillations, i.e. a>0. You should change the value of a=-1 and plot the signal of the simulated dynamics to obtain noisy signals

Solution of the exercise 1

To understand the dynamics of the oscillators, the plotted signals should look similar to the following plots:

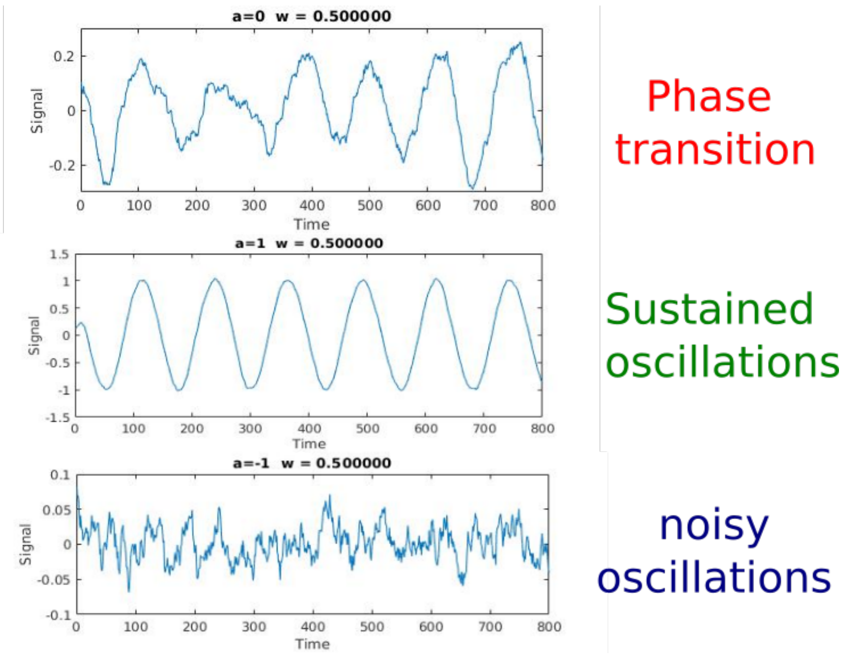

Figure 2: **Solution for exercise 1.** Depending on the bifurcation parameter of the oscillator, the signals show dynamics representing different dynamical regimes. Top: oscillators in the phase transition show signals that combine noise and oscillations. Middle: the signals shows self-sustained oscillations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

EXTRA EXERCISE: study the stability of the oscillators in the different regime in the phase plane. For that, the goal is to study the imaginary and real part of the signal and plot the two variables one against the other to 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 modelled by hopf oscillators that are coupled between them (i.e. they are interacting through their connections). We will consider a network containing 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 the described network:

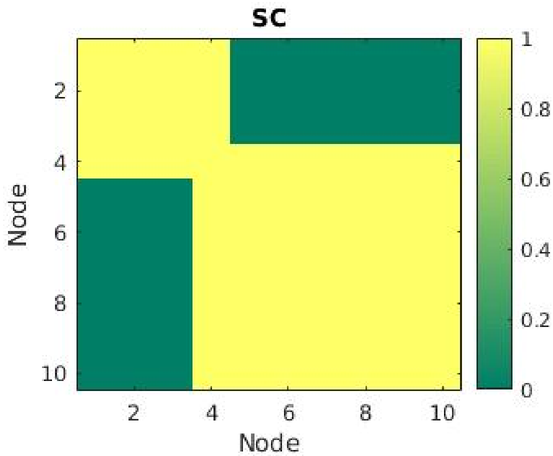

Figure 3: **Solution for exercise 1.** Structural connectivity matrix that fixes the interactions between nodes. This matrix contains two communities; the first one is composed by the first four nodes and the second one by the last six nodes. There is a hub which is connected to all the nodes of the network.

Furthermore, we will set the ω (i.e. the dynamics) of all the nodes. Once we have the description of the network, we will understand the model parameters and interpret their changes. At this level of description the network dynamics depended on two ingredients: the global strength of connections (g) and the local parameters for each node (a_j).

The whole-brain dynamics were obtained by coupling the local dynamics through the C_{ij} matrix:

$$\frac{dz_j}{dt} = z_j[(a_j + i\omega_j) - |z_j|^2] + g \sum_{k=1}^{N} C_{jk}(z_k - z_j) + \beta\mu_j(t), \tag{1.1}$$

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.

- First, we will study how a low or high value of the global coupling parameter, g, alters the dynamics described by the model. The global coupling g is a scaling parameter that controls for the conductivity of the fibers given by the SC. At low g the network interactions are mainly restricted to ROIs directly connected by high strength links. Thus, 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.

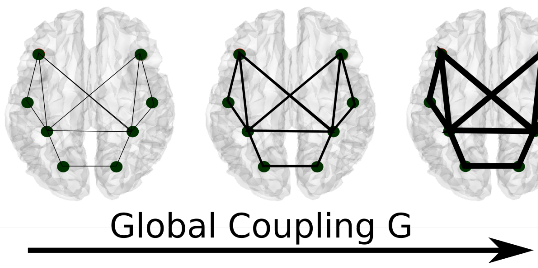

Figure 4: **Fitting of global coupling parameter in the whole-brain network model.** The global coupling model parameter g scales the weights of the SC matrix. Low and high values of g represent weakly and strongly coupled networks, respectively.

Exercise 2

The goal of this exercise is to understand the role of the global coupling parameter in the model and how alterations in the value of the coupling of the interactions echo the simulated signals and their correlations:

1. Open the script named ‘exercise2.mat’ in the VM.
2. First, you will run the part where the simulated network is defined (*Define the network*). At the end of this section, you will plot the matrix in Figure 3, where the interactions between the nodes are fixed.
3. Then, in the first case, you will simulate the dynamics when there is no global coupling in the model (g=0), i.e. there is not conductivity and thus, no interactions between nodes. Furthermore, all the nodes working in the same regime ($a = 0$), except the hub that will work in the oscillatory regime ($a = 1$). This choice was 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]. You will plot the signals of the nodes and the Functional Connectivity.
4. In the second case, there will be a global coupling (g=0.5), i.e. the nodes are coupled and interacting between them. To study the difference that the coupling can exert over the whole network, all the nodes will be working in the same ragime (a=0) and the hub will work in the oscillatory regime (a=1).
5. Change the g (low value (g=0.2) and high value (g=0.5)) and plot the signals and the FC.

Solution of the exercise 2

In this exercise, we have changed the value of the global coupling parameter in a simulated network containing two modules and one hub. The dynamics of all the nodes have been fixed to $a = 0$, except the hub which $a = 1$, and we have only changed the value of the local dynamics of the hub.

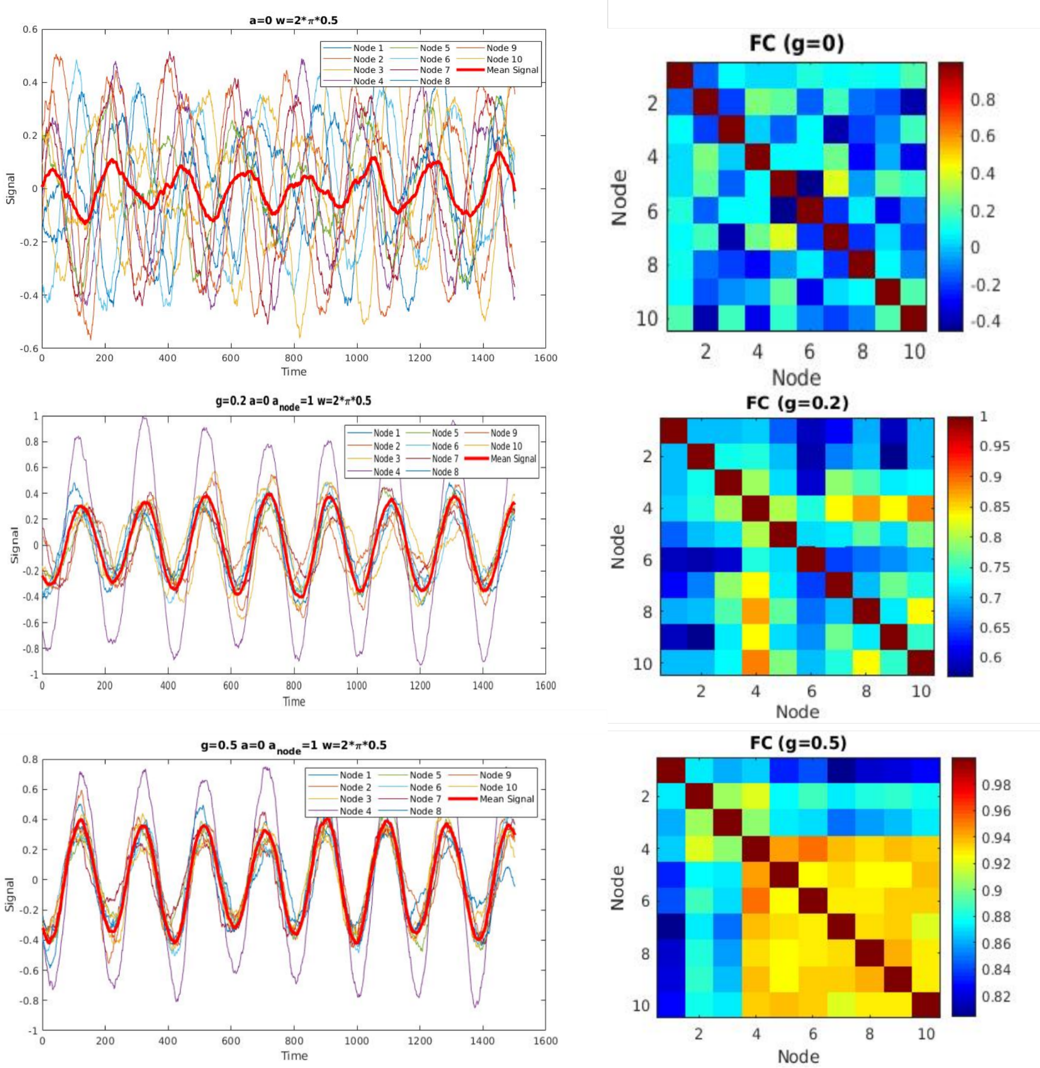

Figure 5: **Solution for exercise 2.** Different outputs obtained changing the global coupling parameter. Top: the case where there is no coupling, i.e. $g = 0$ shows that the signals of the nodes composing the networks show very different timecourses over time. This variability is reflected in the FC where the matrix show a sparse distribution of values, with maximum values of 0.5 (without considering the diagonal). Middle: when increasing the global coupling parameter, the signals starts to synchronize with the hub and the effect of the interactions increases the correlation between the signals. Bottom: A high value of the g favours the propagation of recurrent activity within the network allowing for correlations to emerge, reflected in the very high values of correlations in the FC. Furthermore, the hub, working in the oscillatory regime, brings all the nodes to show sustained oscillations.

Part 3: Fitting and modelling resting-state data

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

First, we studied the network dynamics for the homogeneous case, in which we set $a_j = 0$ for all nodes. This choice was 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 were determined by a single free parameter: the global coupling strength g. This parameter was estimated by fitting the FCDs from the empirical data with the FCDs calculated from the simulated signals at various values of g [1, 2, 4], see Figure 6. Specifically, empirical and simulated FCDs were 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 evidenced a closer similarity between the empirical and the simulated FCDs. We considered the g where KS distance is minimised as the optimal working point of the model.

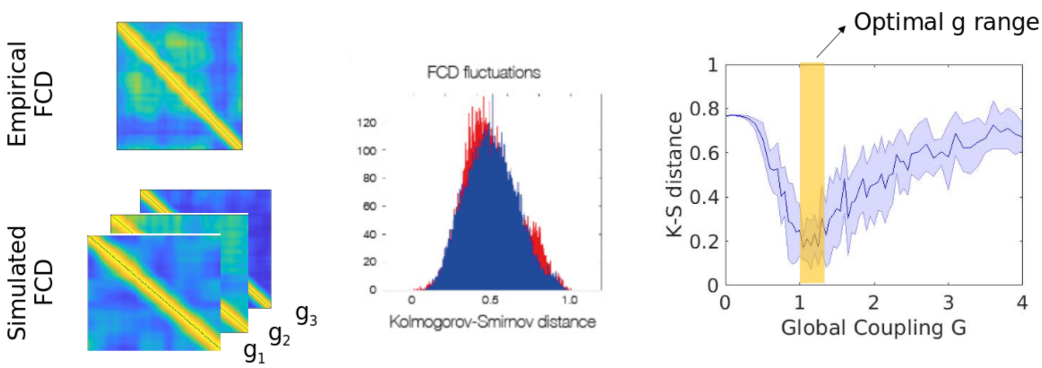

Figure 6: **Fitting of global coupling parameter in the whole-brain network model.** To estimate this global parameter, we sought for the model that best reproduced the distribution of FCD values (fixing all other model parameters). For that, first, the FCDs calculated for the simulated signals using different values of g. Then, empirical and simulated FCDs were compared using the Kolmogorov-Smirnov distance (KS distance) of their values. The KS-distance show minimal values for specific range of g values, considered the optimal global coupling g.

The optimal global coupling g shows distinct values for different brain states characterize 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 obtain information and simulate the dynamics of the whole-brain dynamics (without considering the local heterogeneity).

Additional information can be extracted by relaxing the homogeneity constraint on the local bifurcation parameters. In this case, the global coupling parameters g were fixed to the ones estimated previously, but the local parameters a_j were 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. For that, considering the previous exercises, you are going to run the model for different values of the global coupling g and determine the optimal global coupling.

1. Open the script named 'exercise3.mat' in the VM.
2. First, you will load the structural connectivity and BOLD timeserie of one subject. After fixing all the model parameters, you will run the pre-modelling where you will calculate the FC, power spectrum, omega and other variables that will be used in the model simulation. Specially the ω values will be obtained from the power spectra properties of the BOLD and the phases matrices are extracted for later use them in the calculation of the FCD.
3. Then, you will start a loop where you will simulate the dynamics of a network of 83 nodes and the ω given by the power spectra of the BOLD signals, but using different values of g. In each loop, the fitting between the FCD matrices will be also computed.
4. Plot the values of the fitting and interpret their values. You can also plot the empirical and simulated FCDs to interpret the values of the K-S distance.
5. Load the 'ksP.mat' vector which contains the values of the fitting for a lower resolution of the g, i.e. the fitting has been calculated for all the range of g and interpret the results.

Solution of the exercise 3

In this exercise, we have simulated the dynamics of a real case, considering the structural connectivity extracted from DTI and the resting-state activity of BOLD-fMRI. We have extracted from the empirical data the basic model parameters values and then, calculate the fitting using the empirical and simulated FCD.

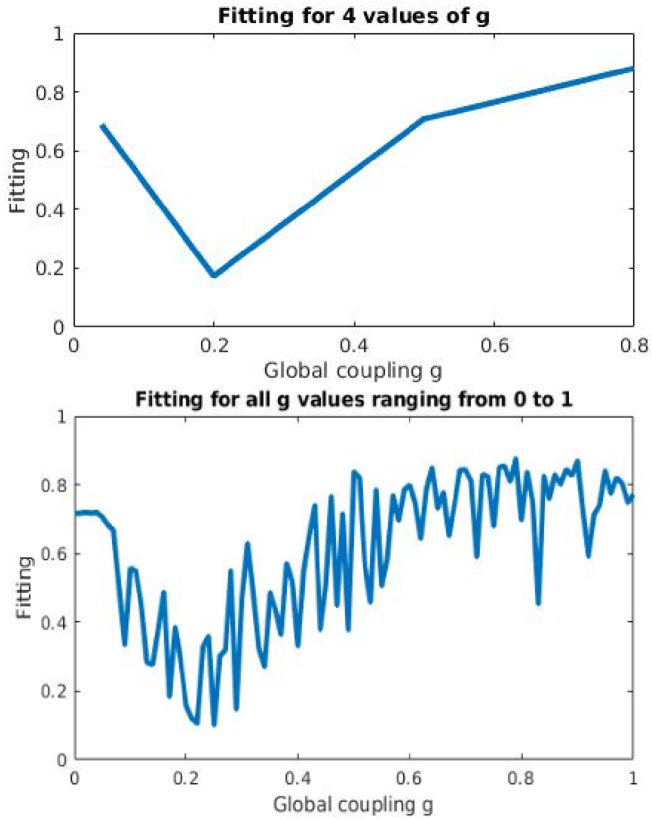

Figure 7: **Solution for exercise 3.** KS-distance between the empirical and the model FCD distributions, as a function of g, for one participant. For low and high values of g, large KS distance indicates differences between the mean values of the FCD distributions. In the intermediate range of g shorter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

EXTRA EXERCISE:
You can also use the optimization algorithm for extracting 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 humanneuroimaging 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=slCBN7-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.

References

[1] Gustavo Deco, Morten L. Kringelbach, Viktor K. Jirsa, and Petra Ritter. The dynamics of resting fluctuations in the brain: Metastability and its dynamical cortical core. *Scientific Reports*, 7(1):1–14, 12 2017.

[2] Ane López-González, Rajanikant Panda, Adrián Ponce-Alvarez, Gorka Zamora-López, Anira Escrichs, Charlotte Martial, Aurore Thibaut, Olivia Gosseries, Morten L. Kringelbach, Jitka Annen, Steven Laureys, and Gustavo Deco. Loss of consciousness reduces the stability of brain hubs and the heterogeneity of brain dynamics. *Communications Biology*, 4(1):1037, 12 2021.

[3] Victor M. Saenger, Adrián Ponce-Alvarez, Mohit Adhikari, Patric Hagmann, Gustavo Deco, and Maurizio Corbetta. Linking entropy at rest with the underlying structural connectivity in the healthy and lesioned brain. *Cerebral Cortex*, 28(8):2948–2958, 8 2018.

[4] Victor M Saenger, Joshua Kahan, Tom Foltynie, Karl Friston, Tipu Z Aziz, Alexander L Green, Tim J van Hartevelt, Joana Cabral, Angus B A Stevner, Henrique M Fernandes, Laura Mancini, John Thornton, Tarek Yousry, Patricia Limousin, Ludvic Zrinzo, Marwan Hariz, Paulo Marques, Nuno Sousa, Morten L Kringelbach, and Gustavo Deco. Uncovering the underlying mechanisms and whole-brain dynamics of deep brain stimulation for Parkinson's disease. *Scientific reports*, 7(1):9882, 12 2017.

[5] Beatrice M. Jobst, Rikkert Hindriks, Helmut Laufs, Enzo Tagliazucchi, Gerald Hahn, Adrián Ponce-Alvarez, Angus B. A. Stevner, Morten L. Kringelbach, and Gustavo Deco. Increased Stability and Breakdown of Brain Effective Connectivity During Slow-Wave Sleep: Mechanistic Insights from Whole-Brain Computational Modelling. *Scientific Reports*, 7(1):4634, 12 2017.

[6] Mario Senden, Niels Reuter, Martijn P. van den Heuvel, Rainer Goebel, and Gustavo Deco. Cortical rich club regions can organize state-dependent functional network formation by engaging in oscillatory behavior. *NeuroImage*, 146:561–574, 2 2017.

[7] LANDAU and L. D. On the problem of turbulence. *Dokl. Akad. Nauk USSR*, 44:311, 1944.

[8] J. T. Stuart. On the non-linear mechanics of wave disturbances in stable and unstable parallel flows Part 1. The basic behaviour in plane Poiseuille flow. *Journal of Fluid Mechanics*, 9(3):353–370, 1960.

[9] Yuri A. Kuznetsov. *Elements of Applied Bifurcation Theory*, volume 112 of *Applied Mathematical Sciences*. Springer New York, New York, NY, 2004.

[10] Gustavo Deco, Josephine Cruzat, Joana Cabral, Enzo Tagliazucchi, Helmut Laufs, Nikos K Logothetis, and Morten L Kringelbach. Awakening: Predicting external stimulation to force transitions between different brain states. *Proceedings of the National Academy of Sciences of the United States of America*, 116(36):18088–18097, 9 2019.

[11] Gustavo Deco and Morten L. Kringelbach. Turbulent-like Dynamics in the Human Brain. *Cell Reports*, 33(10):108471, 12 2020.