Tutorial 6 - Computational Modelling

Ane López-González and Manel Vila-Vidal

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]. 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, 2]. 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 [3, 4, 5].

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 [6, 7], describes the transition from noisy to sustained oscillations oscillations [8], 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.

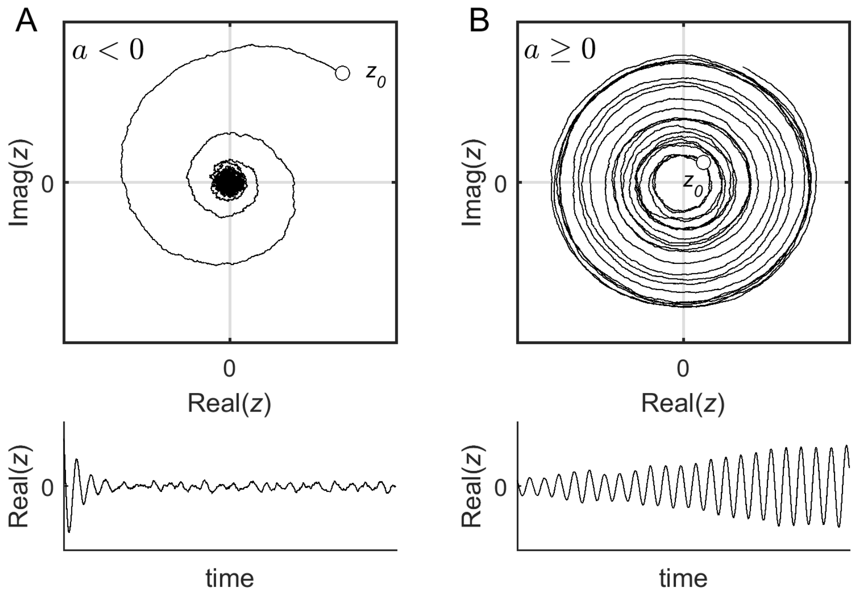

Figure 1: **Phase space for an example of a single Hopf oscillator. A)** Subcritical Hopf oscillator ($a < 0$). Top: In this regime, a stable spiral, or focus, exists at $\boldsymbol{z} = 0$. The system relaxes towards the focus with damped oscillations. In the presence of noise, however, the system 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 be understand the dynamics of the oscillators, the plotted signals should look similar to the following plots:

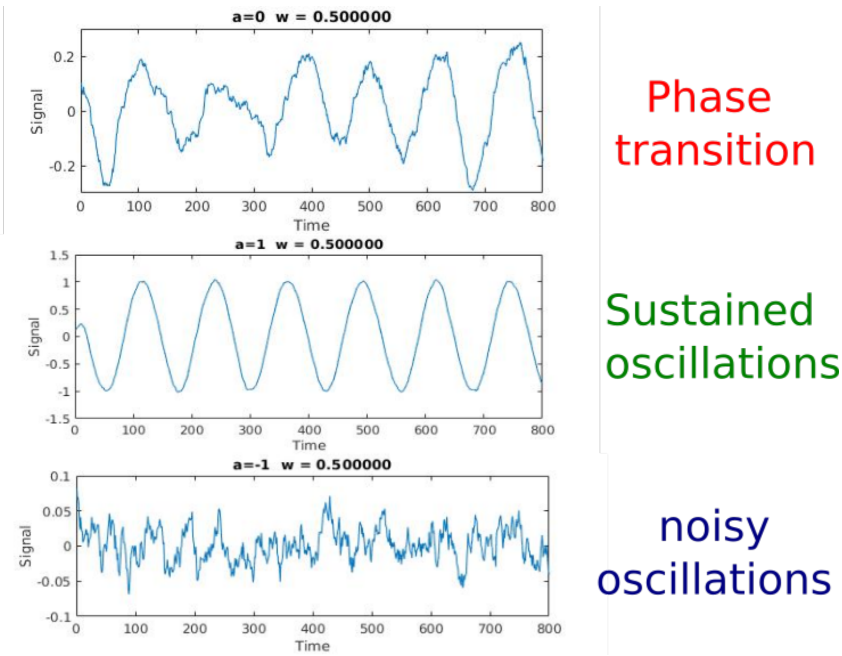

Figure 2: **Solution for exercise 1.** Subcritical Hopf oscillator ($a < 0$). Top: In this regime, a stable spiral, or focus, exists at $\boldsymbol{z} = 0$. The system relaxes towards the focus with damped oscillations. In the presence of noise, however, the system fluctuates around the focus, thus 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 $Real(z)$.

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:

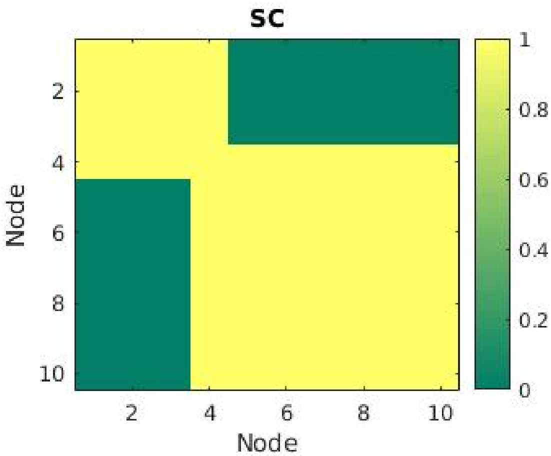

Figure 3: **Solution for exercise 1.** Structural connectivity matrix that fixes the interactions between nodes. This matrix contains two communities; the first one is composed by the first four nodes and the second one by the last six nodes. There is a hub which is connected to all the nodes of the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

– teoria, en general con N osciladores…

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.

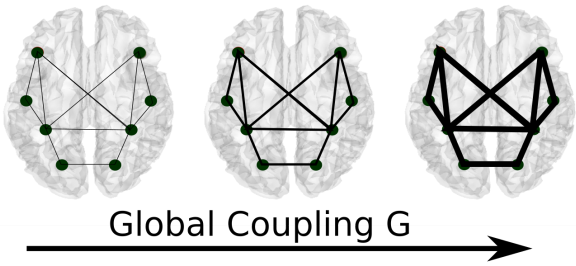

Figure 4: **Fitting of global coupling parameter in the whole-brain network model.** The global coupling model parameter g scales the weights of the SC matrix. Low and high values of g represent weakly and strongly coupled networks, respectively.

Exercise 2

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 ($a = 0$). 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

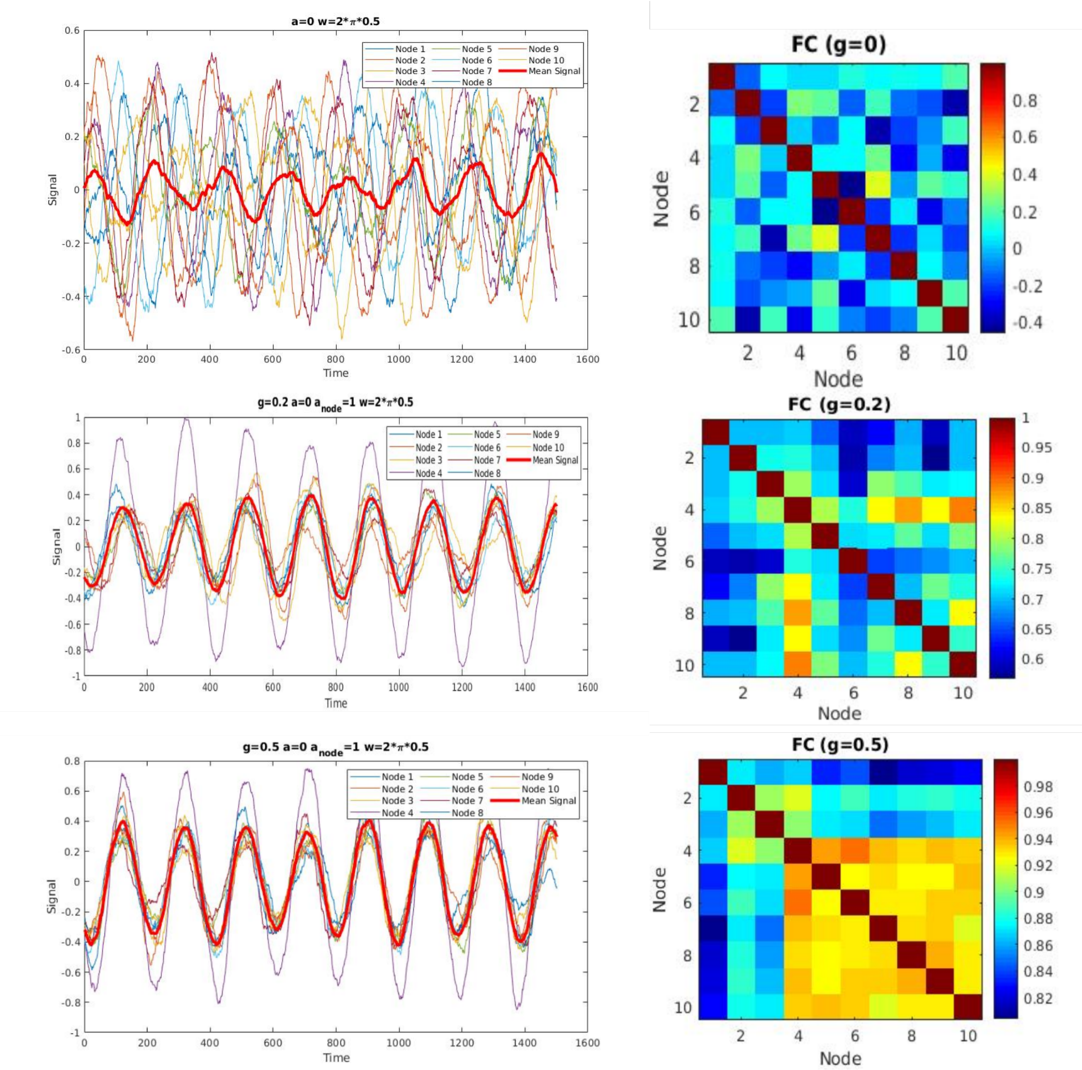

Figure 5: **Solution for exercise 2.** ***

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 was estimated from the peak of the power spectra estimated from their BOLD in the frequency band 0.04-0.07 Hz. Then, the N =?? brain regions were coupled through the connectivity matrix C_{jk}, which is given by the structural connectivity of healthy subjects. The matrix C_{jk} was scaled by a global coupling g.

This parameter is estimated by fitting the FCDs from the empirical data with the FCDs calculated from the simulated signals at various values of g [1, 3]. Specifically, empirical and simulated FCDs were compared using the Kolmogorov-Smirnov distance of their values (KS-distance).

Then, we will explain 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.

Exercise 3

Additional materials

- Examples of use of the described model
    - Loss of consciousness reduces the stability of brain hubs and the heterogeneity of brain dynamics (The MATLAB code of the whole-brain models are available on Github (`https://github.com/decolab/Hopf_consciousness`)).
- Other models used in whole-brain descriptions

Key Points

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] 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.

[3] 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.

[4] 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.

[5] 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.

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

[7] 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.

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