

Modelling high-order synchronisation epochs and transitions in the cardiovascular system

David García-Álvarez *, Alireza Bahraminasab,
Aneta Stefanovska, and Peter V.E. McClintock

*Department of Physics, Lancaster University,
Lancaster LA1 4YB, United Kingdom*

* `d.garcia-alvarez@lancaster.ac.uk`

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Abstract

We study a system consisting of two coupled phase oscillators in the presence of noise. This system is used as a model for the cardiorespiratory interaction in wakefulness and anaesthesia. We show that long-range correlated noise produces transitions between epochs with different $n:m$ synchronisation ratios, as observed in the cardiovascular system. Also, we see that, the smaller the noise (specially the one acting on the slower oscillator), the bigger the synchronisation time, exactly as happens in anaesthesia compared with wakefulness. The dependence of the synchronisation time on the couplings, in the presence of noise, is studied; such dependence is softened by low-frequency noise. We show that the coupling from the slow oscillator to the fast one (respiration to heart) plays a more important role in synchronisation. Finally, we see that the isolines with same synchronisation time seem to be a linear combination of the two couplings.

1 Introduction

1.1 Oscillators and synchronisation

There are innumerable examples in nature of self-sustained oscillators. Such systems exhibit an oscillatory behaviour by themselves, i.e., even without any external action ¹. When two or more oscillatory processes are coupled, there exists the possibility of their becoming synchronised. Synchronisation entails an adjustment of rhythms of oscillating objects due to their interaction [1].

For instance, if we isolate a plant, an animal or a human volunteer and keep them at constant conditions of light and temperature, they still exhibit a rhythm with a period of *approximately* 24 hours. Therefore, this biological clock is definitely self-sustained, because it exhibits an oscillatory nature without any other interactions. In normal life, however, we are exposed to the variations in light, temperature, etc., as the day goes. That is how our biological clock synchronises with the day's rhythm and, as a result, our internal rhythm repeats every 24 hours.

Synchronisation happens everywhere in nature. This entrainment can be either “intended” or “mechanical”. The former occurs when intelligent individuals adjust their rhythms in order to achieve a goal, e.g., workers in an assembly line, or musicians playing in an orchestra. We call here “mechanical” synchronisation when it happens in non-intelligent systems, e.g., two pendulum clocks placed on a common support. This “mechanical” synchronisation is perfectly described by Strogatz: “Sync does not depend on intelligence, or life, or natural selection. It springs from the deepest source of all: the laws of mathematics and physics” [2]. One might also think of an intermediate stage, synchronisation in intelligent individuals arising spontaneously. One example

¹As dissipation almost always occurs, oscillators must have an internal source of energy that maintains their rhythm.

of this are the occasions when people inside a completely silent room unwittingly end up breathing exactly at once. Another example is the claps by an audience: after a few seconds a main rhythm is heard, generated by spectators clapping synchronously, and also some “noise”, generated by the not-so-synchronised spectators². The borderline between “intended” and “mechanical” synchronisation may not be well-defined, as some “mechanical” couplings might play a role in order for the system to achieve a common goal (in the previous example of the musicians, a violinist with tendency to slow down will *unwittingly* speed up as hearing his/her neighbour colleagues).

The example of the spectators’ claps above is an everyday example of high-order synchronisation. Although most (of the synchronised) spectators applaud at the same rhythm, there are some enthusiasts who applaud at higher rate, and some people more lazy (or dissatisfied with the performance) that clap more slowly. But, still, they are synchronised with the main group: the enthusiasts clap, for example, twice when the bigger group claps once, and the lazies clap, say, once every four claps of the big group. That is why this high-order synchronisation is also called $n:m$ synchronisation. High-order synchronisation happens when the oscillatory processes operate in different timescales.

1.2 Synchronisation in the cardiorespiratory interaction

One case of two oscillatory processes operating in different timescales is the cardiorespiratory interaction. The heart beats at rest at approximately once per second, and one respiratory cycle at rest may take around four seconds (both values depend on the individual). For this individual, the preferred synchronisation ratio, if any, would be 4:1. In fact, episodes of synchronisation in the cardiorespiratory system are inferred from the data obtained from non-invasive measurements [3], and the probability of such synchronisation happening by chance is extremely small [4]. Moreover, cardiorespiratory synchronisation may have some outstanding applications in medical assessment and monitoring. For example, athletes are observed to synchronise for periods up to 10 times longer than non-athletes [5]. Also, in measurements on anaesthetised rats [6, 7], lengthy synchronisation epochs, and transitions from one synchronisation ratio to another, are observed. Such transitions may be useful in monitoring depth of anaesthesia.

Whether cardiorespiratory synchronisation is just “mechanical” or it also has an “intelligence component” – we might speculate if the brain could smartly give orders to heart and respiration to synchronise to some extent, in case it would be more efficient for the body – is not clear. But the existence of couplings between heart and respiration is known, some signs of that are the following:

- Heart rate is slightly higher in inspiration than in expiration, phenomenon known as “respiratory sinus arrhythmia” [8].
- The respiratory function can modify the amplitude of cardiac oscillations (stroke volume) [9].
- Traube in 1865 and Hering in 1869 independently observed waves in systemic blood pressure associated [10] with respiration.

Therefore, and for the sake of simplicity, we can model cardiorespiratory interaction as two coupled oscillators (the heart and the respiration). As these oscillators operate in different timescales, we can expect episodes of high-order synchronisation, which is in accordance with what is observed [3]. It is known that the coupling from respiration to heart is stronger than vice versa [11].

The existence of transitions between different $n:m$ synchronisation ratios, and also to and from non-synchronised epochs, exhibits that the system is *non-autonomous*, i.e., it has an explicit time dependence. From the Physics viewpoint, explicit time dependence means that there is something from outside acting on the system. In the case of the cardiorespiratory system, this action comes (at least) from the low-frequency oscillatory processes in the cardiovascular system, known to be metabolic, neurogenic and myogenic [12].

² Cf. http://www.audionetworkplc.com/sfx/sfx_list.asp?subcat_id=8961, that we found via google. On that webpage we can listen to several demos for free, and purchase the tracks in full quality. On track with number S_402410 we hear a perfectly synchronised clapping audience, phenomenon found in some countries of Eastern Europe. On the other hand, on track with number S_377155, for example, we hear a main rhythm plus some “noise”.

1.3 Anaesthesia versus awareness

Usually in anaesthesia, the coupling from respiration to heart decreases, and the coupling from heart to respiration increases, compared with awareness. However, the former interaction usually remains stronger than the latter. Nevertheless, in some moments of anaesthesia, the direction may either reverse, or the cardiorespiratory interaction may become insignificant [7].

Both heart rate variability (HRV) and respiration rate variability (RRV) dramatically decrease in anaesthesia compared to awareness. Also, wavelet analysis reveals that low frequency components in blood flow are dramatically lower in anaesthesia than in wakefulness. On the other hand, the ratio of synchronisation time over total time is much bigger in anaesthesia.

In fact, analysis of experimental data [13] also reveals that synchronisation and modulation are competing effects: in short, the stronger the modulation, the lower the ratio of synchronisation time. In principle, intuition says that this is consistent, because the bigger the system is disturbed, the more difficult it is for it to “settle” (synchronise); but a deeper analysis on how time variability interferes with synchronisation is still lacking.

In this paper, we use a simple model for the cardiorespiratory interaction. We obtain numerically several synchronisation epochs and the transitions. We also analyse the effect of the noise – white and coloured –, that acts on each oscillator, on the total synchronisation time; and the same with the values of the couplings from one oscillator to the other. We will see that the results arising from the model reproduce the properties, inferred from the experimental observations, that we have stated.

2 Model and analytical tools

2.1 The model

Assuming that the values of the couplings are small, we can make phase dynamics [14]. We use then two phase oscillators, modelling respiration and heart. For simplicity, we consider the same function for the interaction on both equations, although this function is multiplied by different values (the couplings) on each equation. A noise term is added to the equations of both oscillators,

$$\begin{aligned}\dot{\theta} &= \omega_1 + \varepsilon_1 f(\theta, \phi) + \eta_1(t) \\ \dot{\phi} &= \omega_2 - \varepsilon_2 f(\theta, \phi) + \eta_2(t)\end{aligned}\tag{1}$$

Here ϕ is the slow oscillator, modelling the respiration, and θ the fast oscillator, modelling the heart. The ω 's are the autonomous frequencies, the ε 's are the couplings, the function f is the interaction, and the η 's are the noise terms.

The function f must be 2π -periodic in both arguments. For this work, we chose a very simple function, consisting of a limited number of harmonics with the same weight:

$$f(\theta, \phi) = \sum_{j=1}^2 \sum_{i=1}^{10} \sin(j\theta - i\phi)\tag{2}$$

2.2 High-order synchronisation

We describe briefly how interaction can induce synchronisation. Let us consider equations (1) without the noise terms. In the zero approximation (neglecting the interaction) the phases rotate with their autonomous frequencies:

$$\theta = \omega_1 t, \quad \phi = \omega_2 t$$

When “plugging in” the interaction, all the terms in f correspond to fast rotations except for those satisfying the resonance condition [1]:

$$j\omega_1 - i\omega_2 \approx 0\tag{3}$$

In the case that the two autonomous frequencies are nearly in resonance

$$\frac{\omega_1}{\omega_2} \approx \frac{n}{m}, \quad n, m \in \mathbb{N},\tag{4}$$

all the harmonics in f with $j = mk$, $i = nk$, k being an integer, are resonant and contribute to the equations averaged in time. That is how the interaction produces $n:m$ synchronisation when ω_1/ω_2 does not differ too much from n/m . The maximum allowed *detuning* $m\omega_1 - n\omega_2$ for which synchronisation is still induced is bigger for higher values of the couplings (Cf. [1, 14] for details).

2.3 Coloured noise

Sequences of long-range correlated values $\eta_i(t)$ are produced by the Fourier filtering method in [15]. This method is based on a transformation of the Fourier components $\{u(k)\}$ of a random number sequence $\{u(t)\}$ which are uncorrelated random numbers following a Gaussian distribution. A sequence of $\eta_i(k)$ is generated for a given α using the formula:

$$\eta_i(k) = k^{-(2\alpha-1)/2} u(k) = k^{-\beta/2} u(k).$$

Inverse Fourier transformation of the sequence $\eta_i(k)$ leads to the sequence of interest $\eta_i(t)$. The resulting sequence of random variables are spatially correlated with spectral density

$$S_k \propto k^{-(2\alpha-1)} = k^{-\beta},$$

and they have Gaussian distribution. The parameter α is called the correlation exponent, and quantifies the degree of correlations imposed in the sequence. The case $\alpha = 0.5$ (or $\beta = 0$) corresponds to uncorrelated disorder (white noise), while the case $\alpha > 0.5$ ($\beta > 0$) indicates positive correlations. The mean value of the sequences produced by this method is set to zero.

2.4 Synchronisation index

To characterise the strength of synchronisation we need a quantitative measure. We will use an index based on conditional probability introduced in [16]. First we must choose the $n:m$ ratio in which we are interested.

The phase of the faster oscillator is observed at fixed values of the slower oscillator. In a situation of perfect $n:m$ synchronisation, always that $(\phi \bmod 2\pi m)$ has a given fixed value, $(\theta \bmod 2\pi n)$ has always the same value as well. In noisy systems, of course, instead of saying “the same value” for the latter, we must say “the same value up to some tolerance”.

First of all, the interval to which $(\phi \bmod 2\pi m)$ belongs, $[0, 2\pi m)$, is divided into N bins. As we are calculating the synchronisation index as a function of time, we use a time window, centred at t_k , in which we analyse the distribution of the phases. Let us think of the bin number l of the interval $[0, 2\pi m)$, and let us call t_j , with $j = 1, \dots, M_l$, the values of the time, inside the timewindow, for which $(\phi \bmod 2\pi m)$ falls into the l^{th} bin³. We have, then, M_l values $\{\theta(t_j) \bmod 2\pi n\}$. If there is no synchronisation at all, then a uniform distribution of $\{\theta(t_j) \bmod 2\pi n\}$ can be expected in the interval $[0, 2\pi n)$. In the case of $n:m$ synchronisation, these numbers cluster around a certain value. The strength of such clustering is quantified as

$$r_l(t_k) = \frac{1}{M_l} \sum_{j=1}^{M_l(t_k)} \exp\left(i \frac{\theta(t_j)}{n}\right) \quad (5)$$

When the phases are completely locked, or completely unlocked, we get $|r_l(t_k)| = 1$ or $|r_l(t_k)| = 0$ respectively. To improve reliability we also calculate the average over all bins and obtain the index of synchronisation as

$$\lambda_{nm}(t_k) = \frac{1}{N} \sum_{l=1}^N |r_l(t_k)| \quad (6)$$

We consider, then, that the system is $n:m$ synchronised at time t_k when $\lambda_{nm}(t_k)$ is bigger than a given threshold. In practice we usually find, by trial and error, values for the threshold that may be regarded, at first sight, as too stringent. In this work, we set the threshold to 0.98.

We must test the synchronisation index for different values of n and m . According with what was explained in Subsection 2.2, we test the numbers over which the summation in (2) runs.

³We are working, of course, with *discrete* values of time, because we are dealing with either experimental or numerical data. That is why M_l makes sense (i.e., “it is not infinite”).

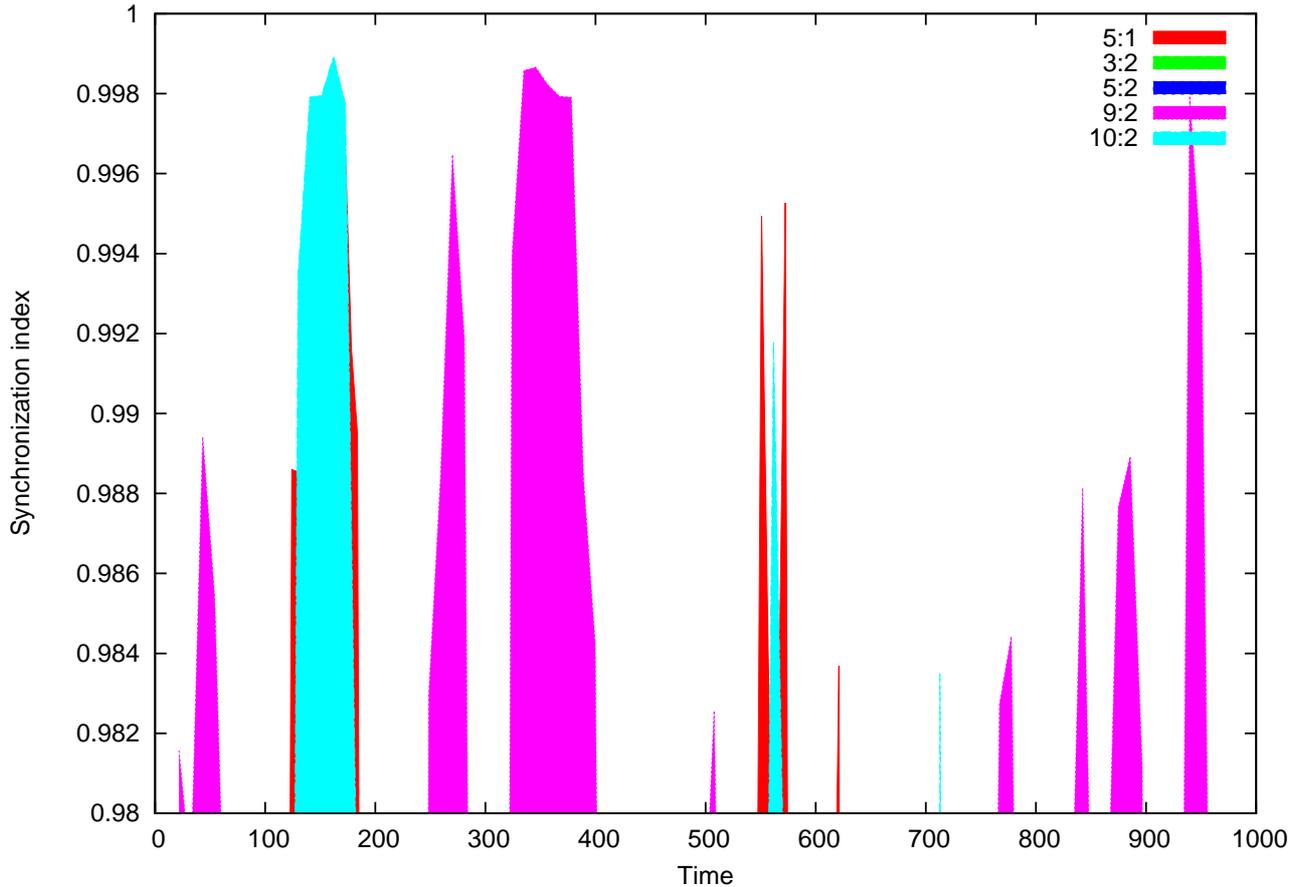


Figure 1: Synchronisation epochs and transitions

3 Simulations

3.1 Synchronisation epochs and transitions

We simulated equations (1) with parameters $\nu_1 = 1.07$, $\nu_2 = 0.23$ ⁴, $\varepsilon_1 = 0.2$, $\varepsilon_2 = 0.05$. The intensity of the noise is given by its variance σ^2 , that we will call D . Here we use $D_1=5 \text{ e-}4$, $D_2=5 \text{ e-}5$.

Figure 1 shows the different synchronisation epochs. Transitions between different $n:m$ synchronisation ratios are observed as well (strictly speaking: transitions from a synchronisation epoch to a non-synchronised epoch, and then a transition from a non-synchronised epoch to a different synchronisation ratio). Note that the transitions are “continuous”, i.e., from a synchronisation ratio to another ratio similar to the former.

Long-range correlated noise produces transitions between epochs with different $n:m$ synchronisation ratios, which is consistent with the observations of the cardiovascular system (remember the low frequency components mentioned in Subsection 1.2). On the other hand, with white noise, there are very few transitions between synchronisation indices [17].

Basically, the trick is that we might absorb the noise term into the autonomous frequency:

$$\omega + \eta(t) \equiv \tilde{\omega}(t),$$

⁴Of course, $\nu = \omega/2\pi$. Strictly speaking, dimensionless units are used throughout this paper. Nevertheless, if we consider the time to be in seconds, these frequencies are chosen as two possible realistic values for the frequencies of heart and respiration.

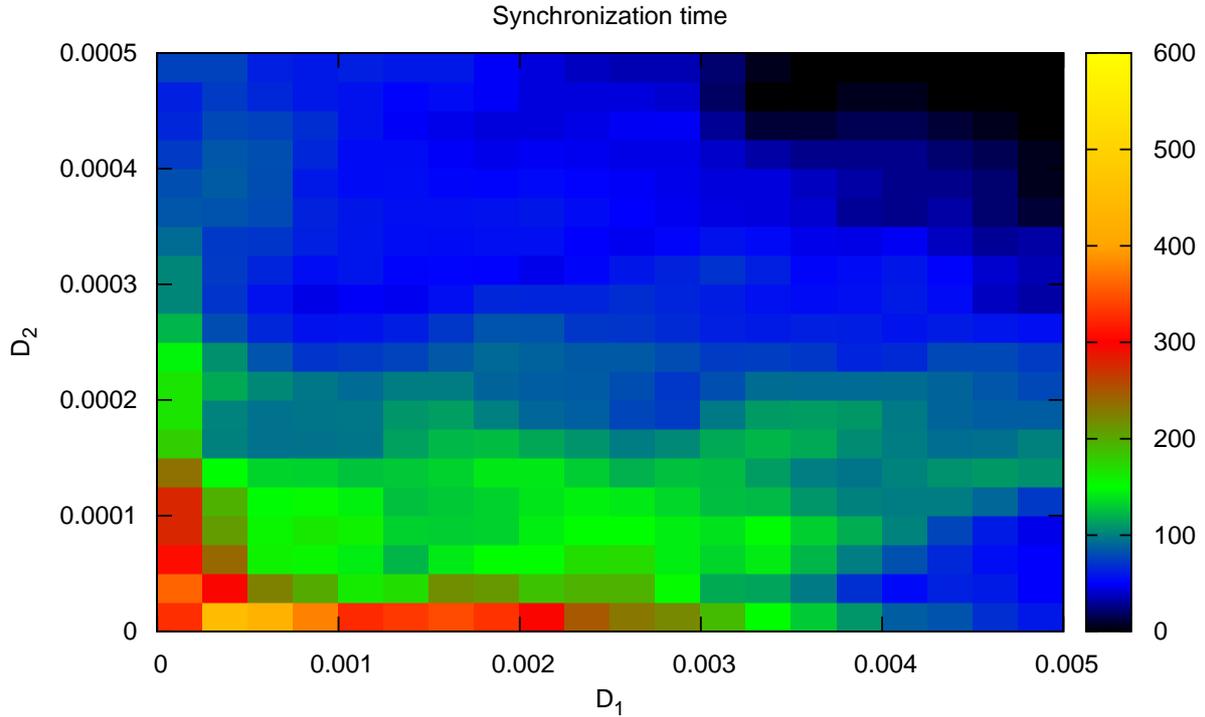


Figure 2: Synchronisation time as a function of the intensities of the two noises. The total simulation time is 1,000

thereby considering, in the case of long-range correlated noise, as though the ω 's had a slow trend in time. As a result, the integers of the RHS of (4) change in time, and so does the synchronisation ratio. In the case of white noise, however, the “time-dependent frequencies” do not have any trend.

3.2 Noise and synchronisation

Now we analyse how the intensity of the noise influences the synchronisation time. We chose the parameters $\nu_1 = 1.07$, $\nu_2 = 0.23$, $\varepsilon_1 = 0.1$, $\varepsilon_2 = 0.01$, and varied the parameters D_1 and D_2 (the range of variation of D_1 and D_2 is not the same because η_1 and η_2 are summed to ω_1 and ω_2 respectively, and the frequencies are considerably different).

Figure 2 shows the total synchronisation time as a function of the intensities of the two noises. This figure clearly shows that the bigger the noise, the smaller the synchronisation time. This result reproduces the experimental result that, in anaesthesia, the low-frequency components are dramatically suppressed compared to wakefulness, and the synchronisation time is considerably bigger.

If we move vertically in Figure 2, the synchronisation time changes much more than moving horizontally. It means that the noise in the slower oscillator (the respiration) hinders synchronisation much more strongly than the noise in the faster oscillator.

3.3 Couplings and synchronisation

Finally, we analyse how the values of the two couplings influence the synchronisation time, in the scenarios of coloured and white noise, and with different intensities of such noise. The couplings ε_1 and ε_2 are varied (again, the range of variation is not the same because ω_1 and ω_2 are considerably different). The results are plotted in Figure 3.

From this figure, we can obtain several conclusions. The first one is that low-frequency noise “softens” the dependence of the synchronisation time on the couplings: when the synchronisation time is big, it lowers in the presence of coloured noise; when the synchronisation time is small, it rises in the presence of coloured noise.

Secondly, as expected, the synchronisation time is bigger for bigger values of the couplings. Furthermore, visual inspection of Figure 3 reveals that the equations of the isolines, in the ε_1 – ε_2 plane, with same synchronisation time, seem to be a linear combination of the couplings ε_1 and ε_2 .

Finally, we observe that ε_1 , the coupling from the slow oscillator to the fast one (respiration to heart) plays a more important role in synchronisation than ε_2 (for example, if we go to the right border in Figure 3, i.e., make ε_1 big, the synchronisation time hardly varies with ε_2).

For the white noise scenario, the results are plotted in Figure 4. Note that the intensity of the noise here is much bigger than in Figure 3, and unrealistic for most physical situations. The reason for making the intensity so big was to obtain some noticeable differences in the three plots in Figure 4.

The conclusions here are the same as in the former scenario with coloured noise, except that, although white noise also “softens” the dependence of the synchronisation time on the couplings, the effect is dramatically lower than in the case of coloured noise (the intensities of the noise in Figure 4 are much bigger than in Figure 3 and, still, the former is much less “softened” than the latter).

4 Conclusions

We have shown that long-range correlated noise produces transitions between epochs with different $n:m$ synchronisation ratios, which is consistent with observations in the cardiovascular system.

Also, we have seen that, the bigger the noise, the smaller the synchronisation time. Furthermore, the noise in the slower oscillator (the respiration) hinders synchronisation much more strongly than the noise in the faster oscillator. These results also reproduce the observed result that, in anaesthesia, the synchronisation time is bigger than in wakefulness.

Regarding the dependence of the synchronisation time on the couplings, such dependence is softened by low-frequency noise. White noise also softens the dependence, but much less than coloured noise.

The synchronisation time increases as any of the two couplings increases. Nevertheless, the coupling from the slow oscillator to the fast one (respiration to heart) plays a more important role in synchronisation.

The isolines, in the plane ε_1 – ε_2 of the values of the couplings, with same synchronisation time, seem to be a linear combination of the couplings ε_1 and ε_2 . So if, in anaesthesia, ε_1 (respiration to heart) lowers *but* ε_2 (heart to respiration) rises, *and* noise drops, the synchronisation time is definitely bigger than in awareness, despite the drop in ε_1 .

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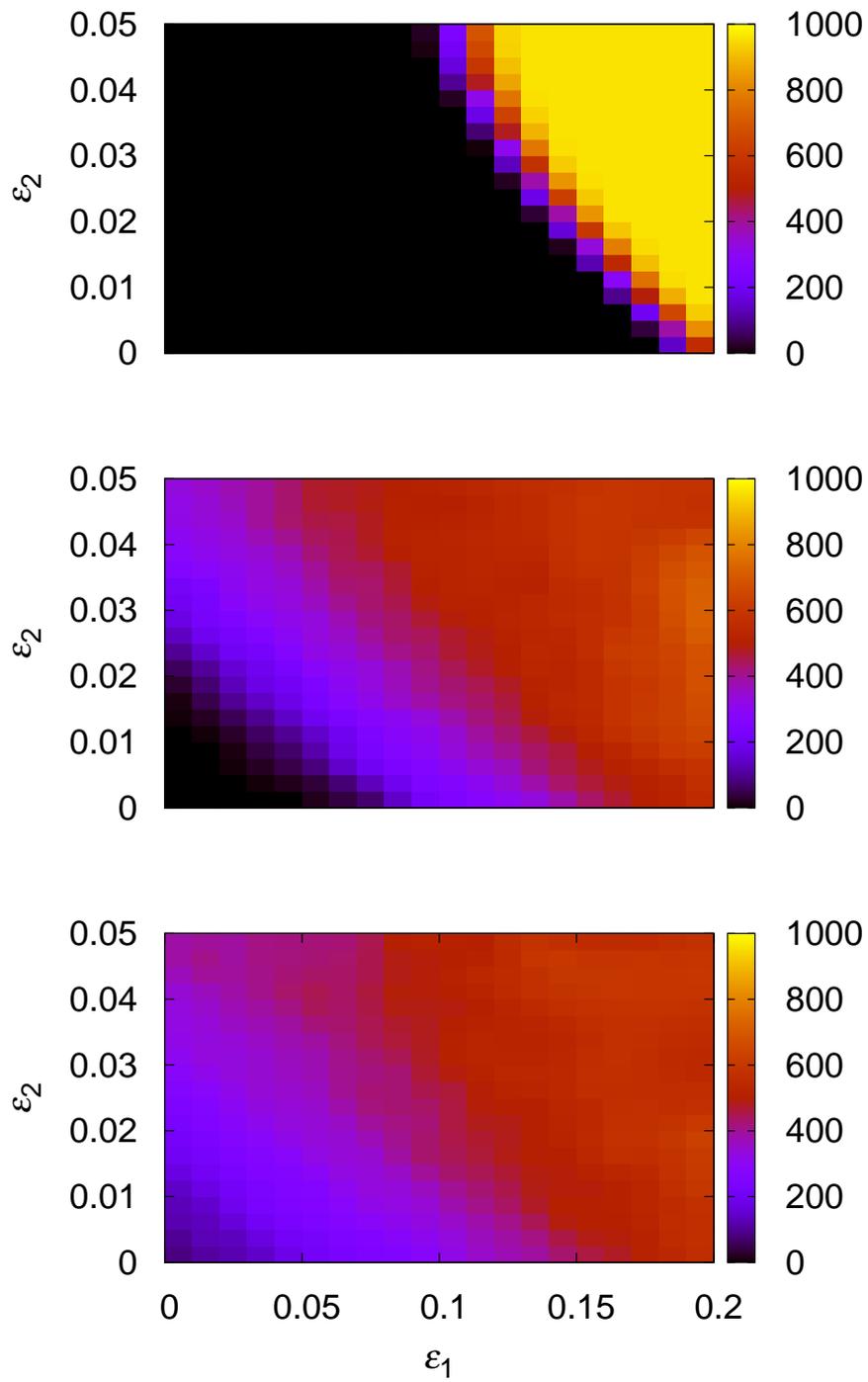


Figure 3: Synchronisation time as a function of the two couplings, with coloured noise. At the top, without any noise. In the middle, with $D_1 = 1 \text{ e-}5$, $D_2 = 1 \text{ e-}6$. At the bottom, with $D_1 = 2 \text{ e-}5$, $D_2 = 2 \text{ e-}6$. The total simulation time is 1,000

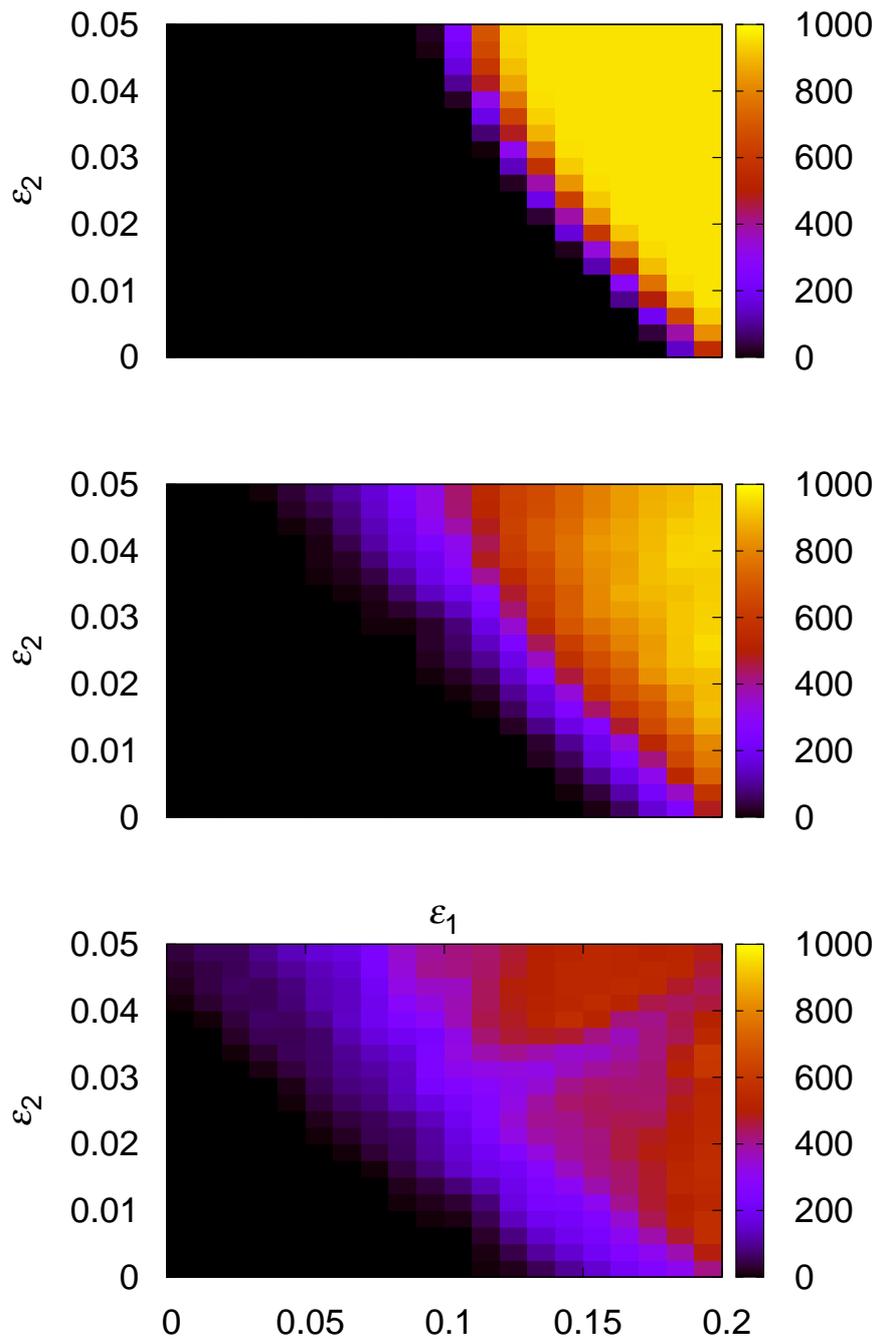


Figure 4: Synchronisation time as a function of the two couplings, with white noise. At the top, without any noise. In the middle, with $D_1 = 2 \times 10^{-4}$, $D_2 = 2 \times 10^{-5}$. At the bottom, with $D_1 = 2 \times 10^{-3}$, $D_2 = 2 \times 10^{-4}$. The total simulation time is 1,000

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