Entrainment of Coupled Noisy Oscillators: Simulation Results

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Abstract

Concentrating on the noisy Van Der Pol (VDP) oscillators, we first reproduce some of their properties in the uncoupled case. Using numerical simulations, we find that there is indeed phase diffusion as well as (and as a consequence) a broadening of the entrainment region at the population level.

In the coupled case, using two simple linear coupling functions, we find that coupling significantly reduces the entrainment region at the population level. This effect is proportional to the coupling strength. Further, the entrainment behavior at the individual level is not influenced.

Future goals are mentioned. The general mapping problem between coupling functions and desired entrainment responses will be of interest. Another question is the relation between population entropy (maximized when uncoupled) and entrainment response (in terms of Arnold Tongue area). first steps can be directed towards achieving digital amplitude modulation at the population level, using specific dependencies. The noise filtering problem is also addressed.

1 Introduction

This document serves three purposes:

1. Reproducing some results in [1] with new matlab code.
2. Presenting preliminary results about a population of coupled Van Der Pol oscillators using numerical simulations.
3. Stating future goals in the continuation of [1].

Code, outputs and graphs can be found on the khammash group file server, in the folder *Yoann/Entrainment/MatlabCode*.

Numerical analysis has been restricted to the Van Der Pol Oscillator as a first step in the study of coupled non-linear oscillators. Parameters have been set to the ones found in the supplementary material of [1]. We reproduce below the drift term for the SDE model:

$$\mu_i(x,t) = \begin{pmatrix} x_{i,2} \\ u(t) + c(x) + (d - Bx_{i,1})x_{i,2} - x_{i,1} \end{pmatrix}$$

with x an $m \times 2$ matrix representing a number m of two dimensional stochastic processes. $u(t)$ represents the forcing term, a sinusoidal with amplitude and frequency as input for Arnold Tongue sampling. An additive coupling term c is also added. The diffusion term is written as

$$\sigma_i\left(x_i,t\right) = \begin{pmatrix} \sqrt{|x_{i,2}|} & 0 & 0 & 0 \\ 0 & \sqrt{|Bx_{i,1}^2 x_{i,2}|} & \sqrt{|u\left(t\right) + d \cdot x_{i,2}|} & \sqrt{|x_{i,1}|} \end{pmatrix}.$$

We may now frame the object of our study as the collection of stochastic differential equations

$$dx_{i,\cdot} = \mu_i(x,t)dt + \sigma_i(x,t)dW_i \tag{1}$$

with the above drift and diffusion terms.

2 Simulation Results

Simulations are done using the *Euler-Maruyama* scheme with the same parameters as in [1]. Further, Entrainment Scores have been computed using the same method as in [1].

2.1 Uncoupled Case

Putting the coupling term c to zero, we reproduce some results, namely the phase diffusion, the difference between the individual and averaged behavior, and finally the Arnold Tongue extension.

2.1.1 Phase Diffusion

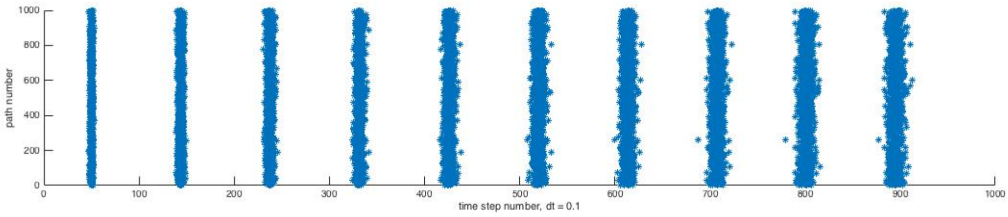

Figure 1: The first 10 maximum peaks of 1000 paths, within the first 100 simulated seconds. No forcing applied.

One can observe the phase diffusion by looking at the first 10 peaks in Figure 1. A broadening of the peaks can be noticed, indicating an increase in variance. Further, after 9000 simulated seconds, figure 2 shows a distribution of the local maximas which resembles a uniform distribution.

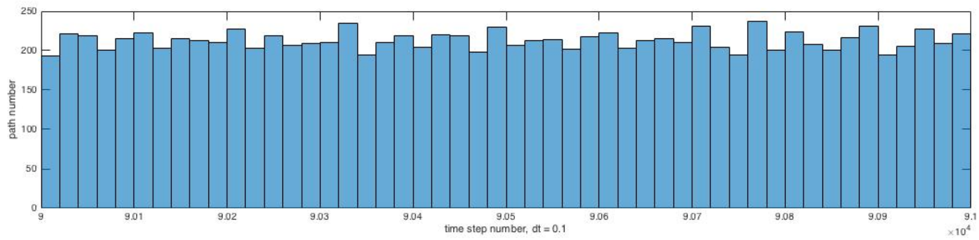

Figure 2: Maximum peaks for 1000 paths, after 9000 simulated seconds. Distribution over 100 seconds. No forcing applied.

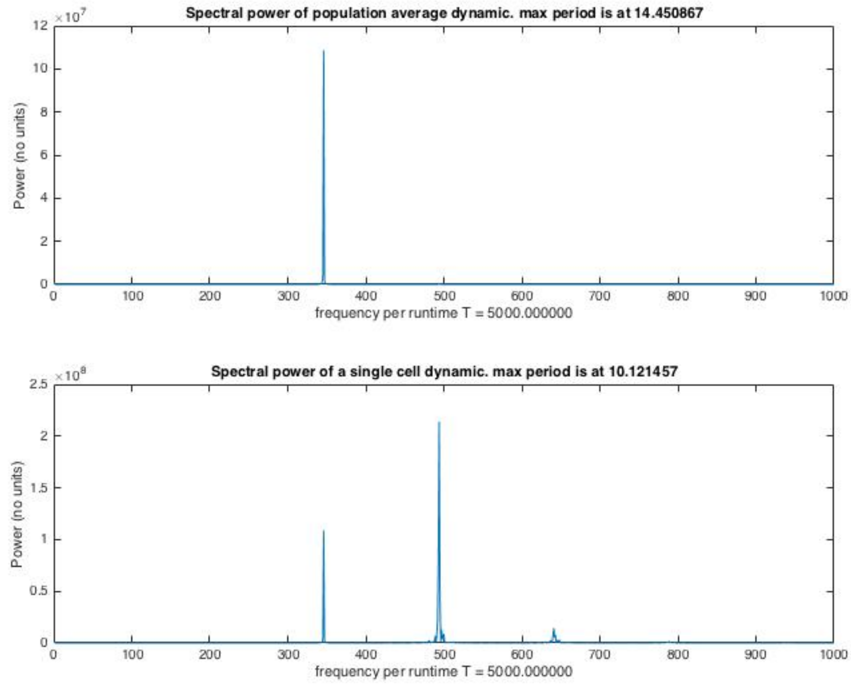

Figure 3: Power Spectral Density for single cell and population average dynamics. Forcing Amplitude is 0.25 and Forcing Period is 14.5 seconds.

2.1.2 Distinct Behavior

For a subset of the Arnold Tongue region, one can observe a dual behavior where the dominant frequency changes when one looks at the individual or at the population level (Figure 3).

2.1.3 Arnold Tongues

The distinct behavior becomes even more apparent when looking at the Arnold Tongue in Figure 4. The bright yellow color indicates entrainment, and one easily notices the broadening of the Arnold Tongue when looking at the population level. The deterministic case for the population level resembles the stochastic case at the individual level (Figure 8).

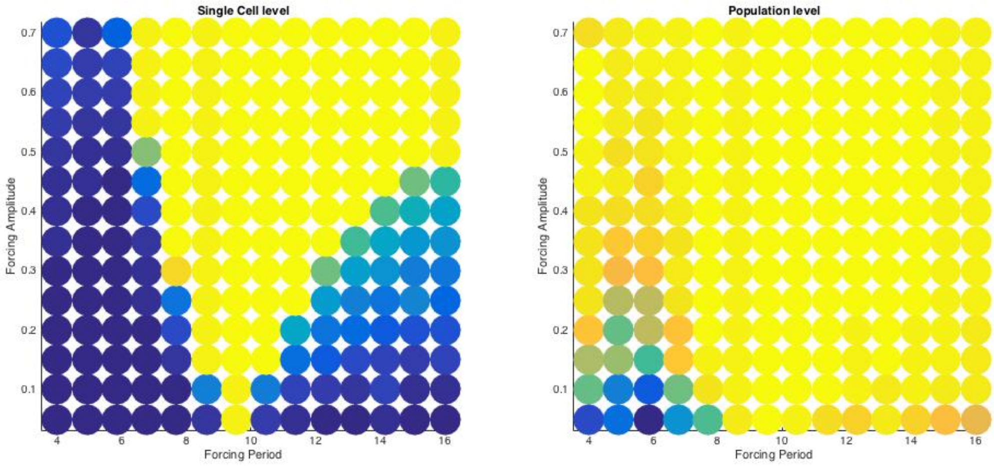

Figure 4: Entrainment Regions for Uncoupled Van Der Pol, lighter colors means better entrainment.

2.2 Coupled Case

Two global linear coupling functions are tested. The first one is denoted *Mean Field* while the second is named *Osmotic*. The name *Osmotic* is motivated by the additional subtraction term. Similarly to the osmose phenomenon, only the relative difference in concentration affects the dynamic. Both are subject to an amplitude parameter $C > 0$ which controls the coupling strength.

Mean Field

$$\begin{aligned} c : \mathbb{R}^{m\times 2} &\to \mathbb{R}^2 \\ x &\mapsto C \begin{pmatrix} 0 \\ \frac{1}{m}\sum_{i=1}^{m} x_{i2} \end{pmatrix}. \end{aligned}$$

Osmotic

$$\begin{aligned} c_j : \mathbb{R}^{m\times 2} &\to \mathbb{R}^2 \\ x &\mapsto C \begin{pmatrix} 0 \\ \frac{1}{m}\sum_{i=1}^{m} x_{i2} - x_{j2} \end{pmatrix}. \end{aligned}$$

Two things can be noticed in Figure 5. Firstly, the entrainment region at the population level decreases when the coupling strength increases. Secondly, the entrainment region at the individual level is not affected by the coupling. This happens for both coupling functions. In the deterministic case, red and blue values (population and individual scores) are equal.

Additionally, for bigger values of C, the entrainment region shrinks.

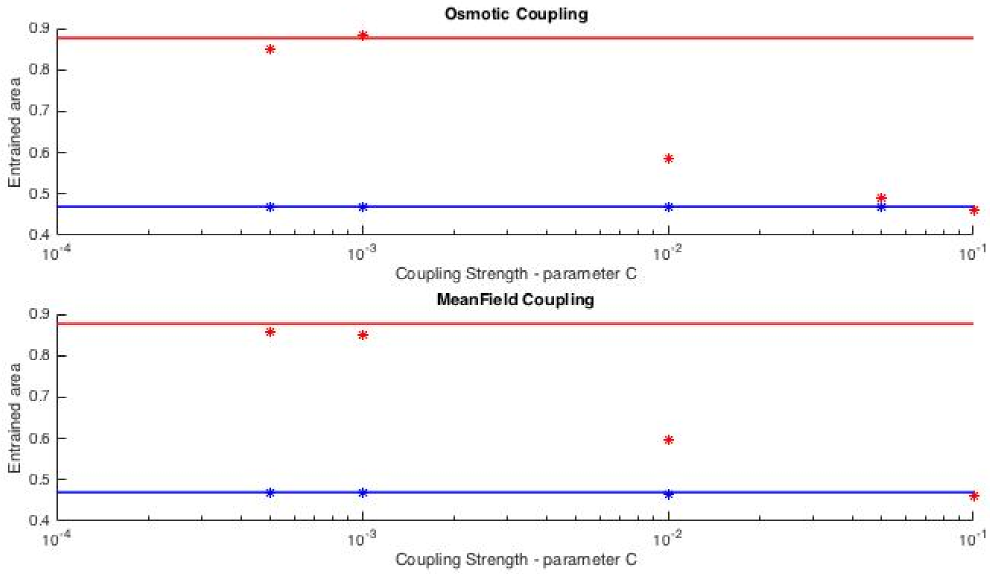

Figure 5: For different values of the coupling strength C on a logarithmic scale, the proportion of the Arnold Tongue region which is entrained (at the 0.9 level) is returned. This proportion is the number of entrained results, divided by the number of trials, over the forcing parameters. Trial positions can be seen for example on Figure 4. Blue color indicates single cell entrainment, red indicates population entrainment. Reference lines are given for the uncoupled case.

3 Discussion & Future Goals

Looking at a population of i.i.d oscillators through the mean, allows one to average out the independent character of individual uncoupled oscillators. As a result, entrainment at the population level was improved.

This result raises a few questions. We have seen that as $t \to \infty$, individuals are distributed uniformly on the limit cycle. As a consequence, the distribution of the average tends towards maximal entropy. This is made rigorous by saying that on the phase space $[0, 2\pi]$, the population average X has a uniform distribution. It is then well known that it maximizes the entropy measure

$$H(X) := -\int_{-\infty}^{\infty} p(x)log(p(x))dx$$

where p is the continuous probability density of X.

1. In general, can we relate entrainment response at the population level and $H(X)$? If so, is the uncoupled case optimal (in the sense of area maximization for Arnold Tongue region)?

We then have considered simple linear coupling functions which decreased $H(X)$, as can be seen on Figure 6. We have seen that the entrainment region at the population level decreased as well (see also Figure 9), further motivating our first question. However, it did not influence the entrainment at the individual level.

2. Can we design a coupling mechanism which has *initially* a low impact on H(X), but allows better entrainment at the single cell level? Should this mechanism be non-linear and/or introduce delay? How could such a mechanism be implemented biologically?

Broadly speaking, coupling mechanisms between noisy oscillators allows one to implement special statistical dependencies. A general goal is then to understand how these dependencies will affect the system response to external input. Ideally, one would like to better understand the mapping between desired entrainment response and implementable coupling functions. We can already point towards two naive control problems to drive the first steps:

3. It has been shown that common noisy input ([2], [3], [4]) may also lead to entrainment. When entrainment is desirable only at specific times, can we design a coupling mechanism which filters out common noise input?

4. It has also been shown in [5] that the NF-κB dynamic leads to analog information processing at the population level. This is also the case for our

population of VDP oscillators (Figure 7). However, notice that to achieve digital amplitude modulation, the coupling should not affect the population average for weak (and vanishing) entrainment signals. This motivates looking for mechanisms which have low impact on $H(X)$.

To answer these questions, it is proposed to continue experimenting using numerical simulations (*in silico* experiments), to gain intuition and understanding on these complex dynamics. In a second step, numerical results will be mathematically proved using stochastic calculus and other appropriate tools. Finally, obtained models should be tested *in vivo* so as to biologically validate, or further refine them.

References

[1] B. Hepp, A. Gupta, M. Khammash; Supplementary Material for "Intrinsic noise induces entrainment of biological oscillators"; In review, 2015.

[2] R. V. Jensen, "Synchronization of driven nonlinear oscillators", American Journal of Physics, vol. 70, no. 6, p. 607, 2002.

[3] J.-n. Teramae and D. Tanaka, Robustness of the Noise-Induced Phase Synchronization in a General Class of Limit Cycle Oscillators, Physical Review Letters, vol. 93, p. 204103, Nov. 2004.

[4] N. C. Butzin, P. Hochendoner, C. T. Ogle, P. Hill, and W. H. Mather, Marching along to an offbeat drum: Entrainment of synthetic gene oscillators by a noisy stimulus, ACS Synthetic Biology, 2015. PMID: 26524465.

[5] S. Tay, JJ. Hughey, TK. Lee, T. Lipniacki, SR. Quake, MW. Covert; Single-cell NF-κB dynamics reveal digital activation and analog information processing in cells; Nature; 2010;466(7303):267-271.

4 Additional Plots

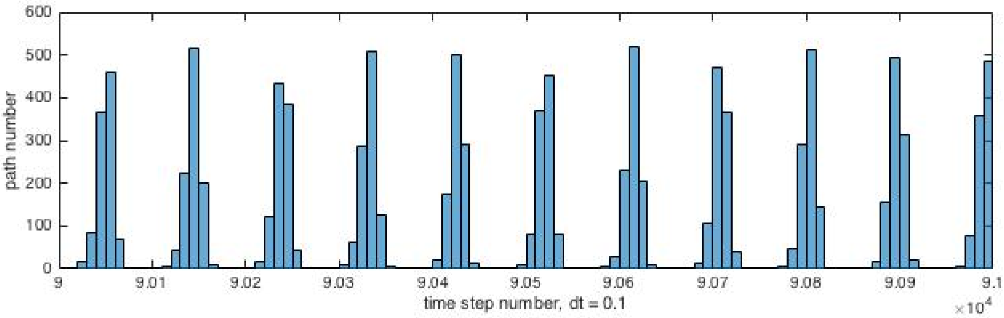

Figure 6: Phase diffusion with coupling (C = 0.01). Maximum peaks for 1000 paths after 9000 simulated seconds. Distribution over 100 seconds. No forcing applied.

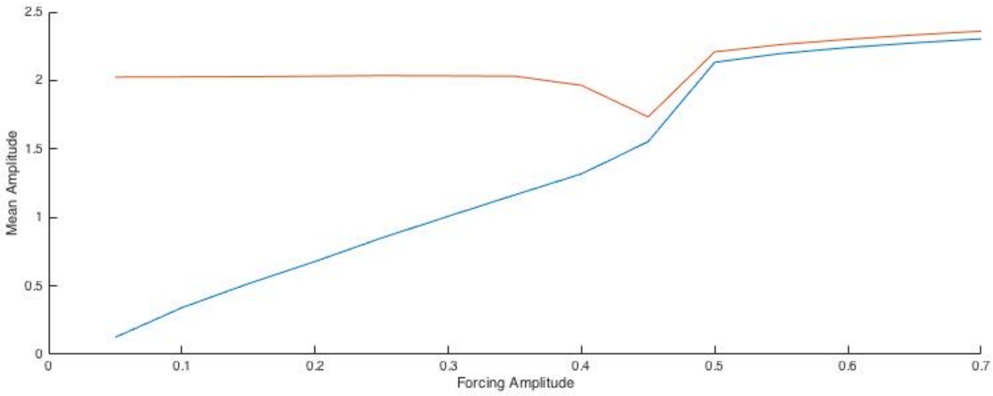

Figure 7: Mean Amplitude of population average, as a function of forcing amplitude. Blue line is the uncoupled case, red line is the coupled ($C = 0.1$) case.

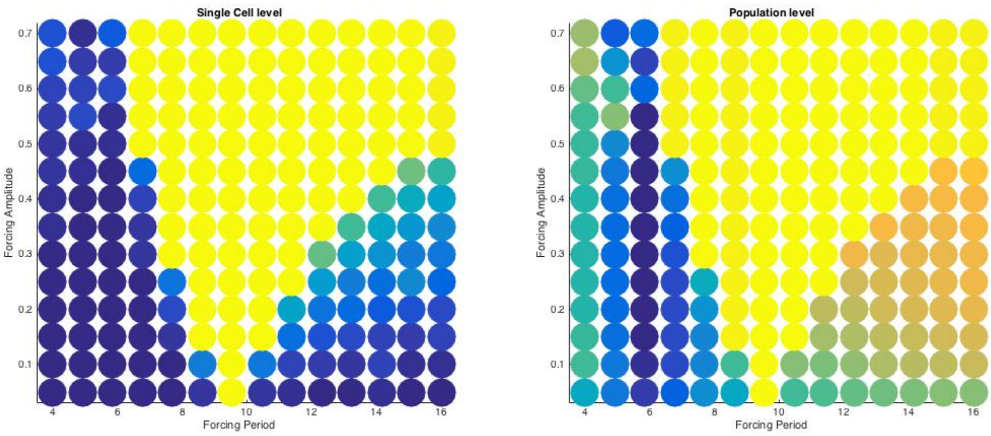

Figure 8: Entrainment regions for uncoupled deterministic Van Der Pol, lighter colors means better entrainment.

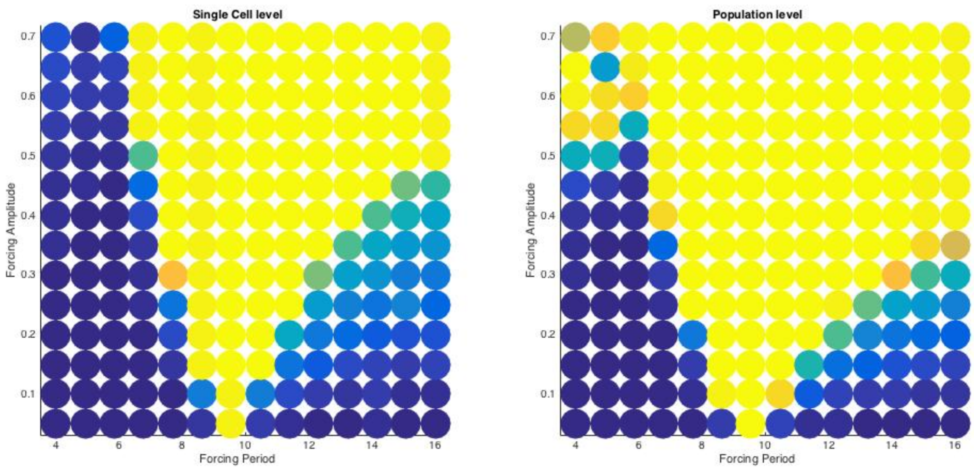

Figure 9: Entrainment regions for coupled ($C = 0.01$, Mean Field) noisy Van Der Pol, lighter colors means better entrainment.

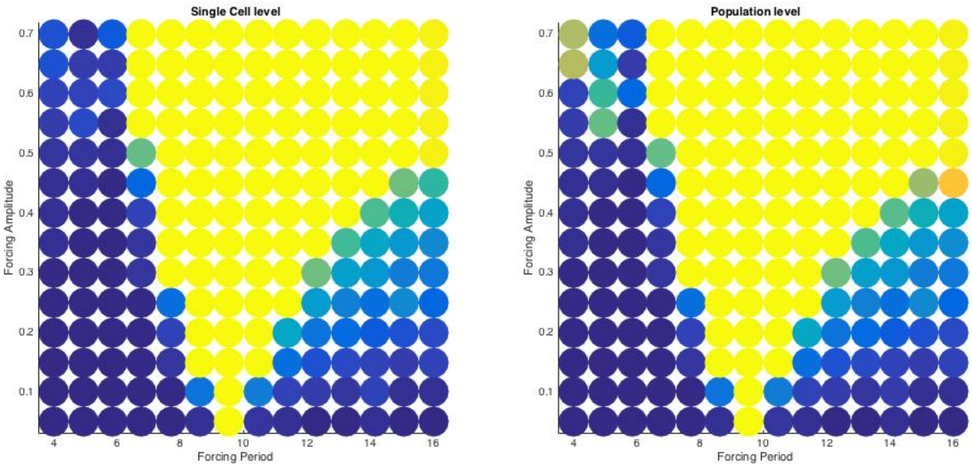

Figure 10: Entrainment regions for coupled ($C = 0.01$, Mean Field) deterministic Van Der Pol, lighter colors means better entrainment.