Extensive clustering in populations of degrade-and-fire oscillators

Bastien Fernandez[1] & Lev Tsimring[2]

[1] Centre de Physique Théorique, UMR 7332 CNRS - Aix-Marseille Université, Campus de Luminy, 13288 Marseille CEDEX 9
[2] BioCircuits Institute, University of California, San Diego, La Jolla, CA, 92093-0328
fernandez@cpt.univ-mrs.fr

Résumé. Dans cet article, nous présentons des résultats analytiques rigoureux pour un modèle d'oscillateurs couplés inspiré d'expériences récentes sur des colonies de circuits géniques en interaction. Tout en ayant une phénoménologie propre, le modèle partage certaines caractéristiques des modèles classiques d'oscillateurs couplés, tels qu'employés en Neuroscience. Dans un article précédent, nous avons prouvé l'existence d'une transition nette avec le paramètre de couplage, entre un régime où toutes les distributions d'agrégats peuvent être atteintes dans le temps, à une phase où seules les distributions comportant un groupe de taille extensive, proportionnelle à la taille de la population, persistent. Cependant, le nombre maximal d'agrégats asymptotiques reste extensif dans tous les cas. Or les simulations numériques révèlent que dans le régime fortement couplé, les trajectoires issues de conditions initiales aléatoires convergent typiquement vers des distributions à faible nombre d'agrégats. Ici, nous présentons une série de résultats sur ces trajectoires, notamment une probabilité positive d'obtenir un nombre d'agrégats intensif à la limite thermodynamique, pourvu que le couplage soit suffisamment fort.

Abstract. In this paper, we present mathematical results on a piecewise affine model of coupled oscillators inspired by recent experiments on synchronization in colonies of bacteria-embedded genetic circuits. The model phenomenology is similar to that of systems of pulse-coupled oscillators with global inhibitory interaction. In [5], we proved the existence of a phase transition with the coupling strength, from a regime of arbitrary asymptotic cluster sizes, to a strongly clustered regime where every asymptotic distribution contains an extensive cluster. We also analytically computed the maximal number $K_{\max}$ of asymptotic clusters and showed that, while it decreases in the strong coupling regime, this number stays extensive for every coupling parameter. Here, we report on manifestations of this phase transition in the dynamics of uniformly drawn random initial conditions. The most significant feature is that, when the coupling strength is sufficiently large, with positive probability, the number of clusters remains intensive in the thermodynamic limit.

1 Introduction

Understanding changes in behavior of interacting oscillatory systems as their parameters vary is pivotal for the comprehension of population dynamics in Biology and Ecology. An archetypical example is the collective synchronization that progressively takes place in the (heterogeneous) Kuramoto model as the coupling strength increases beyond a positive threshold [1,10]. This mechanism has been repeatedly invoked to elucidate observed behaviors in a variety of concrete systems, including the flashing of fireflies populations and the functioning of pacemaker cell networks in the heart and in the brain [8,11].

Beside the Kuramoto model, proofs of synchrony (at any coupling strength), have been given for assemblies of pulse-coupled oscillators with excitatory couplings [2,7], not only in the case of homogeneous systems where all individual characteristics are identical, but also for certain heterogeneous models with variable individual frequency, threshold and/or coupling parameters [9]. For inhibitory couplings, the phenomenology is richer and a multi-stable clustering is commonly observed [4]. However, the analysis is more involved in this case and proofs are scarce, especially when the population size N exceeds 2 units.

Recently, we introduced a discontinuous piecewise affine model of coupled oscillators with repressive interactions [5] inspired by experiments on synchronization in colonies of bacteria-embedded genetic circuits [3]. This simple model mimics the degrade-and-fire (DF) behaviors generated by the associated nonlinear delay-differential equations [6]. Up to a change of repressor concentration $x \mapsto 1-x$, it is similar to the well-known integrate-and-fire (IF) model in Neuroscience. Its oscillations are of sawtooth type with a slow degradation phase followed by a fast production phase (firing) and resetting to a normalized value. Assuming no delay for a simpler analysis, the main difference with IF models is that firing is triggered by a repressor field (that involves the entire population state), rather than only by the local concentration.

The model (detailed at the beginning of section 2 below) exhibits a similar phenomenology as in systems of pulse-coupled oscillators with inhibitory interaction (excepted that for $N=2$, it has a unique globally stable periodic trajectory with positive phase shift) and is amenable to rigorous analytical study for populations of any size $N \in \mathbb{N}$. In [5], we proved the existence of critical coupling strength ϵ_c up to which all cluster distributions can be reached asymptotically. Beyond that threshold, another regime takes place where only distributions containing at least one group of extensive size $\sim \rho N$ perdure. Moreover, we analytically computed the maximal number $K_{\max}$ of asymptotic groups, a number that turned out to be extensive for every coupling intensity. Despite that extensive maximal number of clusters, numerical simulations of large populations indicate that, starting from totally unclustered initial configurations (such that $x_i \neq x_j$ when $i \neq j$), the number of asymptotic clusters is typically much smaller than $K_{\max}$ when $\epsilon > 2$ (while it appears that $K_{\max} = N$ when $\epsilon < 2$), see Figure 1.

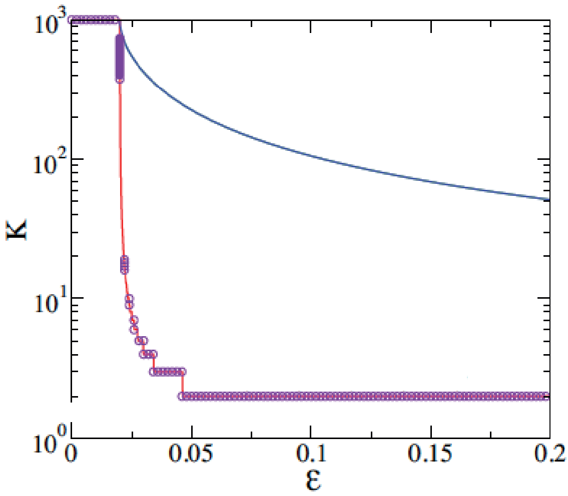

Figure 1. Number of clusters in the asymptotic regime for 1000 coupled oscillators with $\eta = 0.01$ and 1000 different random initial conditions for each $\epsilon\eta$. The solid blue line represents the maximal number $K_{\max}$ analytically computed in ref. [5]. It illustrates that $K_{\max} = N$ for $\epsilon\eta < 2\eta$ and $K_{\max}$ decreases beyond this threshold. The solid red line represents the number of clusters obtained for totally unclustered initial conditions. Clearly, this number is much smaller than $K_{\max}$ when $\epsilon\eta$ increases beyond 2η.

This paper presents mathematically results that confirm these evidences. We address the dynamics of uniformly drawn random initial conditions across the coupling range. In brief terms, our results show that, as ϵ crosses 2, immediate extensive clustering takes place almost surely in the thermodynamic limit, a drastic change from a regime where the first firing(s) typically occurred without clustering. Furthermore, when the coupling is increased further, the clusters formed during the first firing become so large that the total number of clusters becomes intensive with, again, positive probability in the limit of large populations.

2 Dynamics of degrade-and-fire oscillators

The model assumes that the time-dependent repressor protein concentration $x_i(t) \in [0,1]$ of the ith DF oscillator, $i \in \{1, \cdots, N\}$, linearly degrades with unit rate in time, *i.e.* $\dot{x}_i = -1$, or remains constant if it has reached 0. When the locally averaged concentration $\chi_i(t)$ defined by

$$\chi_i(t) = (1-\epsilon\eta)x_i(t) + \frac{\epsilon\eta}{N}\sum_{j=1}^{N} x_j(t),$$

(where $0 < \epsilon < 1/\eta$ is the **coupling strength parameter**) reaches the (small) threshold $\eta > 0$, the ith oscillator fires, and its concentration is reset to 1, *i.e.* $x_i(t+) = 1$.

According to these evolution rules, in every trajectory $\{x_i(t)\}_{i=1}^N$, all oscillators must fire indefinitely for any initial configuration ($x_i(0) = x_i$ for $i = 1, \cdots, N$) such that $\chi_i(0) > \eta$ for $i = 1, \cdots, N$, all concentrations decay towards 0 with time (those that have reached 0 remain at zero) and so do all $\chi_i(t)$. Thus the oscillator with the lowest $x_i(t)$ (possibly, more than one if several oscillators have identical concentrations $x_i(t)$) eventually fires when the corresponding $\chi_i(t)$ reaches η. After that, the oscillator j with new lowest x_j has to fire when its $\chi_j(t)$ reaches η, and so on. It is also clear that if any two oscillators in a population are in sync at certain time t_*, i.e. $x_i(t_*) = x_j(t_*)$, they will remain in sync for all $t > t_*$. What is not obvious however, is under which conditions oscillators that are initially out of sync will synchronize in the course of the dynamics, and what the number of asymptotic clusters is.

To answer these questions, we need some technical considerations. By grouping oscillators with identical value of $x_i(t)$ into one cluster, the population configuration can be depicted via

$$\{(n_k, x_k)(t)\}_{k=1}^K$$

where $n_k(t) \in \{1, \cdots, N\}$ denotes the size of group k and

$$\sum_{k=1}^{K} n_k(t) = N \ (K \leq N \text{ is the total number of groups}),$$

and $x_k(t)$ is the corresponding repressor concentration. In this viewpoint, cluster sizes n_k remain unaffected in time unless two clusters k and k' fire together.

The dynamics can be described by the discrete time map acting on configuration vectors after firings. Notice that any ordering in $\{(n_k, x_k)\}$ is irrelevant here thanks to the permutation symmetry. Accordingly, we choose to consider ordered values of x_k when defining the firing map.
Thus we assume that

$$0 < x_1 < x_2 < \cdots < x_{K-1} < x_K = 1$$

for the initial configuration and we include cyclic permutations of indices in the action of the firing map. For instance, in absence of clustering, the map writes

$$\{(n_k, x_k)(0)\}_{k=1}^K \mapsto \{(n_k, x_k)(t_f+)\}_{k=1}^K$$

where t_f is the firing time and the updated configuration reads

$$(n_k, x_k)(t_f+) = \begin{cases} (n_{k+1}(0), x_{k+1}(0) - t_f) & \text{if } k = 1, \cdots, K-1 \\ (n_1, 1) & \text{if } k = K\,, \end{cases}$$

which is also suitably ordered, *i.e.* we have

$$0 < x_1(t_f+) < x_2(t_f+) < \cdots < x_{K-1}(t_f+) < x_K(t_f+) = 1\,.$$

Our aim is to analyze the fate of trajectories issued from random, totally unclustered, initial distributions (such that $n_k = 1$ for $k = 1, \cdots, N$). In this case, it suffices to specify the initial concentrations x_k (bearing in mind that $x_N = 1$). For simplicity, we assume that the ordered **configuration** $x = \{x_k\}_{k=1}^{N-1}$ (which is identified with $\{(1, x_k)\}_{k=1}^N$) is **randomly chosen with uniform probability distribution** in

$$\mathcal{T}_N := \{x := (x_1, \cdots, x_{N-1}) \ : \ 0 < x_1 < x_2 < \cdots < x_{N-1} < 1 \ (= x_N)\}\,.$$

More precisely, there exists a normalizing constant $\alpha_N > 0$ such that the probability measure $\text{Prob}(A) = \alpha_N \text{Leb}_{N-1}(A)$ for every measurable subset $A \subset \mathcal{T}_N$, where Leb_{N-1} is the $(N-1)$-dimensional Lebesgue measure of A. A simple reasoning shows that α_N must be must equal to $(N-1)!$. In other words, we consider the random process defined in $\mathcal{T}_N$ that consists in iterating the firing map for random initial configurations.

With these technical considerations provided, we can describe (no-)clustering properties at successive firings. Given an initial condition in $\mathcal{T}_N$, let n_ℓ be the size of the ℓth firing cluster ($\ell \in \mathbb{N}$). Lemma 1 in [5] implies that no clustering occurs (*viz.* $\mathrm{n}_\ell = 1$ for all ℓ) for ϵ up to 1.
To some extent, this threshold $\epsilon = 1$ appears to be sharp because [5] also showed that, when $\epsilon > 1$ and N is sufficiently large, there exists an open set of $x \in \mathcal{T}_N$ for which $\mathrm{n}_1 > 1$. Notwithstanding this evidence, for the random process here, firing before clustering (*i.e.* $\mathrm{n}_1 = 1$) persists almost surely in the thermodynamic limit, while ϵ remains smaller than 2. This is formally claimed in Proposition 1 below. Furthermore, the statistical behavior remarkably changes past $\epsilon = 2$, as extensive clustering emerges, again with probability 1 in the limit of large N. Throughout the paper, $\mathbb{P}$ denotes the probability distribution of a random variable.

Proposition 1 *(i)* $\lim\limits_{N\to\infty} \mathbb{P}(\mathrm{n}_1 = 1) = 1$ *for every* $\epsilon < 2$.
(ii) For every $\epsilon > 2$*, there exist* $\rho_1 \in (0,1)$ *such that* $\lim\limits_{N\to\infty} \mathbb{P}(\mathrm{n}_1 \geq \lceil \rho_1 N \rceil) = 1$ *where* $\lceil\cdot\rceil$ *stands for the ceiling function. There also exists* $\rho_2 \in (0,1)$ *such that* $\lim\limits_{N\to\infty} \mathbb{P}(\mathrm{n}_2 \geq \lceil \rho_2 N \rceil) = 1$.

Of note, no statement here depends on the threshold parameter η. We only need to choose η small enough in order to ensure that the inequality $\epsilon > 1/\eta$ holds in every statement; for instance $\eta \leq 1/20$ suffices.
For $\epsilon > 2$, the maximum number of clusters $K_{\max}$ is realized by an (asymptotically) stable configuration with a single group of extensive size $N - K_{\max} + 1$ (and all other groups having a single individual, $n_k = 1$) [5]. Proposition 1 implies that the associated basin of attraction in $\mathcal{T}_N$ has vanishing measure in the thermodynamic limit.

The critical value $\epsilon = 2$ is the maximum coupling strength up to which the firing map has an asymptotically stable fixed point $x_{(N)} \in \mathcal{T}_N$ for all $N > 2$. When $\epsilon < 2$, $x_{(N)}$ attracts the orbit of every configuration in $\mathcal{T}_N$ that never clusters (*i.e.* such that $K_\ell = N$ for all ℓ) and these vectors constitute a set of positive measure Prob for every N [5]. We do not know if this measure remains positive in the thermodynamics limit. Nonetheless, any number of firings without clustering can be realized with positive probability, namely

Proposition 2 *For every* $\epsilon < 2$ *and every* $L \in \mathbb{N}$*, there exists* $p_L \in (0,1)$ *such that*

$$\liminf_{N\to\infty} \mathbb{P}(\mathrm{n}_\ell = 1 \text{ for } \ell = 1, \cdots, L) > p_L.$$

For $\epsilon > 2$, extensive clustering at firings does not only apply to the first two firings. It extends to any firing as the next statement claims and completes statement *(ii)* of Proposition 1.

Proposition 3 *For every* $\epsilon > 2$ *and* $L \in \mathbb{N}$*, there exists* $\rho_\ell > 0$ *such that*

$$\lim_{N\to\infty} \text{Prob}\left\{ \text{either } \exists L' \leq L \ : \ \sum_{\ell=1}^{L'} \mathrm{n}_\ell = N \text{ or } \mathrm{n}_L \geq \lceil \rho_L N \rceil \right\} = 1.$$

In other terms, with large probability, extensive clustering occurs for an arbitrary number of successive firings unless an intensive number of cluster results. This suggests that the asymptotic number of clusters should typically be much smaller than $K_{\max}$, as is observed in the numerics.

Finally, for sufficiently large coupling, one can make sure that the first alternative in Proposition 3 occurs with positive probability, that is positive probability of an intensive asymptotic number of clusters.

Proposition 4 *There exists* $\epsilon_c > 2$*, such that for every* $\epsilon > \epsilon_c$ *we have*

$$\lim_{N\to\infty} \mathbb{P}(\mathrm{n}_1 + \mathrm{n}_2 = N) > 0.$$

We do not know if intensive asymptotic number of clusters happens almost surely in $\mathcal{T}_N$ and/or for every $\epsilon > 2$. In this regime, trajectories from initial configurations in a sufficiently small neighborhood of the equi-distributed configuration $x_k = k/N$ do asymptotically lead to intensive number of clusters. However, this set has vanishing measure in the thermodynamic limit.

Références

1. J. A. Acebron, L. L. Bonilla, C. J. Perez-Vicente, F. Ritort & R. Spigler, The Kuramoto model : A simple paradigm for synchronization phenomena, *Review of Modern Physics*, **77**, 137–185 (2005)
2. S. Bottani, Pulse-coupled relaxation oscillators : From biological synchronization to self-organized criticality, *Physical Review Letters*, **74**, 4189 (1995)
3. T. Danino, O. Mondragon-Palomino, L. S. Tsimring & J. Hasty, A synchronized quorum of genetic clocks, Nature **463**, 326–330 (2010)
4. U. Ernst, K. Pawelzik & T. Geisel, Synchronization induced by temporal delays in pulse-coupled oscillators, *Physical Review Letters*, **74**, 1570 (1995)
5. B. Fernandez and L. S. Tsimring, Corepressive interaction and clustering of degrade-and-fire oscillators, *Physical Review E*, **84**, 051916 (2011)
6. W. Mather, M. R. Bennet, J. Hasty & L. S. Tsimring, Delay-induced degrade-and-fire oscillations in small genetic circuits, *Physical Review Letters*, **102**, 068105 (2009)
7. R. E. Mirollo & S. H. Strogatz, Synchronization of pulse-coupled biological oscillators, *SIAM Journal of Applied Mathematics*, **50**, 1645–1662 (1990)
8. C. S. Peskin, *Mathematical aspects of heart physiology*, Courant Institute of Mathematical Science Publication, New York (1975)
9. W. Senn & R. Urbanczik, Similar nonleaky integrate-and-fire neurons with instantaneous couplings always synchronize, *SIAM Journal of Applied Mathematics*, **61**, 1143–1155 (2000)
10. S. H. Strogatz, From Kuramoto to Crawford : exploring the onset of synchronization in populations of coupled oscillators, *Physica D*, **143**, 1–20 (2000)
11. P. A. Tass, *Phase resetting in medicine and biology*, Springer, Berlin (1999)