Published in final edited form as:

J Math Biol. 2014 June ; 68(7): 1627–1652. doi:10.1007/s00285-013-0680-8.

Typical trajectories of coupled degrade-and-fire oscillators: from dispersed populations to massive clustering

Bastien Fernandez and

Centre de Physique Théorique, UMR 7332 CNRS, Aix-Marseille Université, Campus de Luminy,
13288 Marseille Cedex 9, France

Lev S. Tsimring

BioCircuits Institute, University of California, La Jolla, San Diego, CA 92093-0328, USA

Abstract

We consider the dynamics of a piecewise affine system of degrade-and-fire oscillators with global repressive interaction, inspired by experiments on synchronization in colonies of bacteria-embedded genetic circuits. Due to global coupling, if any two oscillators happen to be in the same state at some time, they remain in sync at all subsequent times; thus clusters of synchronized oscillators cannot shrink as a result of the dynamics. Assuming that the system is initiated from random initial configurations of fully dispersed populations (no clusters), we estimate asymptotic cluster sizes as a function of the coupling strength. A sharp transition is proved to exist that separates a weak coupling regime of unclustered populations from a strong coupling phase where clusters of extensive size are formed. Each phenomena occurs with full probability in the thermodynamics limit. Moreover, the maximum number of asymptotic clusters is known to diverge linearly in this limit. In contrast, we show that with positive probability, the number of asymptotic clusters remains bounded, provided that the coupling strength is sufficiently large.

Keywords

Coupled oscillators; Extensive clustering; Random initial conditions

1 Introduction

Simple models of interacting oscillators are important for understanding synchronization phenomena in many branches of physics and biology. An archetypical example is the Kuramoto model of globally-coupled oscillators with distributed frequencies, in which synchronization takes place when the coupling strength increases beyond a positive threshold (Acebron et al. 2005; Strogatz 2000). This mechanism has been repeatedly invoked to elucidate observed behaviors in a variety of concrete systems, including the collective dynamics of Josephson junctions (Wiesenfeld and Swift 1995), fireflies (Buck

1988), pacemaker cells in the heart (Peskin 1975), and neural networks in the brain (Tass 1999), among others.

Beyond the Kuramoto model, proofs of synchrony have been given for assemblies of pulse-coupled oscillators with excitatory couplings (Bottani 1995; Mirollo and Strogatz 1990), at any coupling strength, not only in the case of homogeneous systems where all individual characteristics are identical, but also for certain heterogeneous models with distributed individual frequencies, thresholds and/or coupling parameters (Seen and Urbanczik 2000). For inhibitory couplings, the phenomenology is richer and populations commonly break into distinct clusters. However, in this case the analysis is more involved, and proofs are scarce, especially when the population size N exceeds two units (Ernst et al. 1995).

Recently, we introduced a discontinuous piecewise affine model of coupled oscillators with repressive interactions (Fernandez and Tsimring 2011) inspired by experiments on synchronization in colonies of bacteria-embedded synthetics gene oscillators (Danino et al. 2010). This simple model mimics the basic phenomenology of the degrade-and-fire (DF) regime of oscillations described by the associated nonlinear delay-differential equations (Mather et al. 2009). The DF oscillations are of saw-tooth type with a slow linear degradation phase of a repressor protein followed by a short production phase (firing) and resetting to a normalized value. The oscillators are coupled via a global repressor field. Before each firing, a group of oscillators may accumulate at the zero level until the global repression is sufficiently reduced, and then fire together. If that is the case, the clustered elements subsequently evolve in sync. This model is qualitatively similar to the well-known integrate-and-fire (IF) model in Neuroscience (Burkitt 2006). The main difference is that here firing is triggered by a global repressor field (that involves the entire population state), rather than only by the local membrane potential.

Our model first introduced in Fernandez and Tsimring (2011) assumes that the time-dependent repressor protein concentration $x_i(t) \in [0, 1]$ ($t \in \mathbb{R}^+$) of the i th DF oscillator ($i \in \{1, \dots, N\}$) linearly degrades with unit rate in time, or remains constant (until further notice) if it has reached 0 i.e.

$$\dot{x}_i = \begin{cases} -1 & \text{if } x_i > 0 \\ 0 & \text{if } x_i = 0 \end{cases}$$

Moreover, 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 $\eta > 0$ (i.e. $\chi_i(t) = \eta$), the i th oscillator **fires** and its concentration is reset to 1, i.e. $x_i(t+) = 1$. This model exhibits a phenomenology similar to systems of pulse-coupled oscillators with inhibitory interaction (except for the population size $N = 2$ it has a unique globally stable

periodic trajectory with positive phase shift), and its global properties are amenable to rigorous analytical study for populations of any size $N \in \mathbb{N}$.

The analysis in Fernandez and Tsimring (2011) showed that every trajectory must be asymptotically periodic and every periodic orbit is entirely determined by its cluster distribution (i.e. the distribution of oscillators into groups of synchronized elements).

Moreover, there exists a critical coupling strength $\epsilon^*(N) = \frac{2N}{N-2}$ up to which every cluster distribution (or more correctly, every possible periodic orbit) can be reached, depending on the initial condition. The threshold $\epsilon^*(N)$ converges to $\epsilon^* = 2$ in the thermodynamic limit $N \rightarrow \infty$. Beyond $\epsilon^*(N)$, another regime takes place where only distributions containing at least one group of extensive size (i.e. proportional to N) perdure.

In Fernandez and Tsimring (2011), we also analytically computed the maximal number $K_{\max}$ of asymptotic clusters. While this number is equal to N for $\epsilon \leq \epsilon^*(N)$, it is approximatively given by $N \left(1 - \sqrt{1 - \epsilon^*(N)/\epsilon}\right)$ in the strongly coupled phase $\epsilon > \epsilon^*(N)$ (and remains extensive for every coupling intensity).

In this paper, we investigate related properties for the trajectories initiated from random, fully dispersed initial conditions (i.e. such that $x_i \neq x_j$ when $i \neq j$). According to numerical simulations, for $\epsilon \lesssim \epsilon^*$, their dynamical behavior is similar to as before and the asymptotic number of clusters appears to be equal (or close) to N . Yet, a striking difference appears at large coupling as the number of aggregated clusters typically shrinks to a small intensive quantity (i.e. bounded above by a integer that is independent of N), see Fig. 1.

Based on these observations, we have developed a rigorous mathematical analysis of the coupling-dependent dynamics of populations of arbitrary size N . Our study mostly consists in estimating the size of aggregating clusters before consecutive firings. The main tools are the Central Limit Theorem (whose main consequence here is given in Appendix A), the approximation of continuous increasing functions by finitely many strictly increasing ones (Appendix B), and some explicit computations of probability estimates.

2 Dynamics of degrade-and-fire oscillators: main results

According to evolution rules stipulated by the model, the trajectory $t \mapsto \{x_i(t)\}_{i=1}^N$ is globally well-defined for every initial condition such that $\chi_i(0) > \eta$ for all $i = 1, \dots, N$. Moreover, the dynamics has the following basic properties.

- In every trajectory, each oscillator must fire indefinitely.
- If $x_i(t^*) = x_j(t^*)$ for some $t^* \geq 0$, then $x_i(t) = x_j(t)$ for all $t > t^*$ (cluster invariance).
- If $x_i(0) > x_j(0)$ and $x_i(t^*) = x_j(t^*) = 0$ for some $t^* \geq 0$ while $\chi_i(t^*) > \eta$ and $\chi_j(t^*) > \eta$, then $x_i(t) = x_j(t)$ for all $t > t^*$ (cluster formation).

The latter mechanism is the only way two initially distinct oscillator concentrations can merge together. In particular, if $i_{\min}$ denotes the oscillator with lowest initial concentration

and if $\{x_i\}_{i=1}^N$ denotes the initial configuration at $t = 0$, the property that $x_i \in [0, 1]$ for all i implies the following inequality

$$\chi_{i_{\min}}(x_{i_{\min}}) = \frac{\epsilon\eta}{N} \sum_{j=1}^N (x_j - x_{i_{\min}}) \leq \epsilon\eta.$$

Therefore we have $\chi_{i_{\min}}(x_{i_{\min}}) \geq \eta$ when $\epsilon \leq 1$, which means that oscillator $i_{\min}$ fires before any other oscillator can merge with it. In other words, no clustering occurs for $\epsilon \leq 1$.

On the other hand, massive merging of oscillators is expected when ϵ is close to $1/\eta$, because all local averages χ_i are close to each other. Nonetheless, no simple global estimate can be obtained in this domain because the size of the aggregating clusters actually depend on the initial configuration. More generally, the conditions under which, oscillators that are initially dispersed, will (or will not) gather in the course of the dynamics, require elaborated considerations; so does any evaluation on the number of asymptotic clusters.

To address these issues, we need some technical preliminaries. By grouping together oscillators with identical concentrations, the population configuration at time t can be depicted by the vector $\{(n_k, x_k)(t)\}_{k=1}^K$ where

- $K \leq N$ is the total number of clusters
- $n_k(t) \in \{1, \dots, N\}$ denotes the size of cluster k (a cluster of size 1 means an isolated oscillator; $\sum_{k=1}^K n_k(t) = N$)
- $x_k(t)$ is the corresponding concentration.

The vector $\{n_k\}$ itself is called the **cluster distribution**. In this viewpoint, group sizes $n_k(t)$ remain unaffected in time unless two groups k and k' merge together before a firing event.

The dynamics can be described by using the so-called firing map acting on configurations after firings. Thanks to the permutation symmetry, any ordering in the vector $\{(n_k, x_k)\}$ is irrelevant here. When defining the firing map, we choose to consider monotonically ordered values of x_k .

Thus we assume that $x_1 < x_2 < \dots < x_{K-1} < x_K = 1$ for the initial configuration (with arbitrary cluster distribution $\{n_k\}_{k=1}^K$). In order to maintain this ordering in time, we include cyclic permutations of indices in the action of the firing map.

Letting t_f be the first firing time and K_f be the number of clusters that merge together before this event. The **firing map** writes $\{(n_k, x_k)\}_{k=1}^K \mapsto \{(n_k, x_k)(t_f+)\}_{k=1}^{K-K_f+1}$ where the updated configuration reads

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

(which is also suitably ordered, i.e. $x_1(t_f+) < x_2(t_f+) < \dots < x_{K-K_f}(t_f+) < x_{K-K_f+1}(t_f+) = 1$).

Our aim is to analyze the fate of trajectories initiated from random initial configurations with fully dispersed cluster distribution (i.e. $n_k = 1$ for $k = 1, \dots, N$). In this case, there is only 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

$$\mathcal{T}_N := \left\{ x = \{x_k\}_{k=1}^{N-1} : \eta < x_1 < x_2 < \dots < x_{N-1} < 1 \right\}.$$

More precisely, we consider the (Borel) probability measure μ on $\mathcal{T}_N$ such that, for every measurable subset $A \subset \mathcal{T}_N$, we have

$$\mu(A) = \alpha_N \text{Leb}_{N-1}(A),$$

where Leb_{N-1} is the $(N-1)$ -dimensional Lebesgue measure of A and $\alpha_N > 0$ is a normalizing constant. A reasoning in the end of Appendix A shows that the equality

$$\mu(\mathcal{T}_N) = 1 \text{ imposes } \alpha_N = \frac{(N-1)!}{(1-\eta)^{N-1}}.$$

With these technical considerations provided, we can proceed to the analysis of clustering properties at successive firings. (Clearly, for every initial configuration in $\mathcal{T}_N$, the corresponding trajectory is globally well-defined.) Given $\ell \in \mathbb{N}$, let K_ℓ be the **size of the firing cluster at the ℓ th firing event**. More precisely, K_1 (resp. t_1) is the quantity K_f (resp. t_f) defined above when computed for a configuration $x \in \mathcal{T}_N$; K_2 is nothing but K_f when evaluated for the configuration $\{(n_k, x_k)(t_1+)\}_{k=1}^{K-K_1+1}$ after the 1st firing, and so on.

Lemma 1 in Fernandez and Tsimring (2011) implies that absolutely no clustering occurs

(viz. $K_\ell = 1$ for all $\ell \in \mathbb{N}$) when $\epsilon \leq \frac{N}{N-2}$. (In view of the property mentioned above about the dynamics in the domain $\epsilon < 1$, notice that $\frac{N}{N-2}$ is (slightly) larger than 1; hence the property here is an improvement of the previous one.)

To some extent, this threshold $\epsilon = \frac{N}{N-2}$ appears to be sharp because Fernandez and

Tsimring (2011) also showed that, when $\epsilon > \frac{N}{N-2}$ and N is sufficiently large, there exists an open subset of $\mathcal{T}_N$ for which $K_1 > 1$. Notwithstanding this evidence, for the random process

here, firings without clustering persist almost surely in the thermodynamic limit, while ϵ remains smaller than $\frac{2}{1+\eta}$. This property is formally stated in the next statement. (Throughout the paper, $\mathbb{P}$ denotes the **probability distribution of a random variable**.)

Proposition 2.1

For every $\epsilon < \frac{2}{1+\eta}$ and $\ell \in \mathbb{N}$, we have $\lim_{N \rightarrow \infty} \mathbb{P}(K_i = 1 \text{ for } i=1, \dots, \ell) = 1$.

For completeness, we mention that, for every $N > 2$ and $\epsilon < \epsilon^*(N) = \frac{2N}{N-2} \gtrsim 2$, the firing map has a stable fixed point in $\mathcal{T}_N$ (Fernandez and Tsimring 2011). Every trajectory in $\mathcal{T}_N$ that never clusters (i.e. such that $K_\ell = 1$ for all $\ell \in \mathbb{N}$) converges to this fixed point. In particular, this is the case for all trajectories initiated from initial conditions in a set of positive measure μ (viz. the fixed point has positive basin of attraction). We do not know if the basin measure remains positive in the thermodynamic limit $N \rightarrow +\infty$.

All proofs are given in the sections below. Of note, there is no restriction on the threshold parameter η here other than to make sure that the inequality $\epsilon < 1/\eta$ holds in every statement. This is indeed the case when η is sufficiently small; for instance $\eta < 1/20$ suffices.

The statistical behavior remarkably changes past $\epsilon = \frac{2}{1+\eta}$, as extensive merging of clusters appears, again with probability 1 in the limit of large N . Let $\lfloor \cdot \rfloor$ stands for the floor function.

Proposition 2.2

(i) For every $\epsilon > \frac{2}{1+\eta}$, there exist $0 < \underline{\rho}_1 < \bar{\rho}_1 < 1$ such that

$$\lim_{N \rightarrow \infty} \mathbb{P}(\lfloor \underline{\rho}_1 N \rfloor \leq K_1 \leq \lfloor \bar{\rho}_1 N \rfloor) = 1.$$

(ii) There also exists $\rho_2 < 0$ such that $\lim_{N \rightarrow \infty} \mathbb{P}(K_2 \geq \lfloor \rho_2 N \rfloor) = 1$.

When $\epsilon > \frac{2N}{N-2}$, the maximum number $K_{\max}$ of clusters in the limit of large times mentioned in the introduction, is realized by the periodic orbit associated with the cluster distribution holding a single group of extensive size $n_1 = N - K_{\max} + 1$ (and all other groups having a single individual, i.e. $n_k = 1$ for $k = 2, \dots, K_{\max}$) (Fernandez and Tsimring 2011). Statement (ii) in Proposition 2.2 implies that the basin of attraction of this orbit in $\mathcal{T}_N$ must have vanishing measure as $N \rightarrow +\infty$. Therefore, this periodic configuration with $K_{\max}$ clusters can hardly be observed in large populations.

Extensive merging of clusters may become so important that the first two firings can absorb the entire population and the resulting distribution can consist of only two clusters. Our last

result states that this phenomenon occurs with positive probability, provided that the coupling is sufficiently large.

Proposition 2.3

There exists $\epsilon_c > \frac{2}{1+\eta}$ such that for every $\epsilon > \epsilon_c$, we have

$$\lim_{N \rightarrow \infty} \inf \mathbb{P}(K_1 + K_2 = N) > 0.$$

To be more concrete, the proof below actually shows that when ϵ exceeds 20, we have $\mathbb{P}(K_1 + K_2 = N) \geq 1/2$ for N sufficiently large. Notice that full synchrony (i.e. all clusters merging into a single group) can not be expected in this system because no collapse onto a unique cluster can ever occur (see comment in Sect. 3.1 below).

In the case where $K_1 + K_2 < N$, the size K_3 of the cluster firing at the third event must also be extensive, with larger fraction K_3/N when $(K_1 + K_2)/N$ is smaller, and this property applies to subsequent firings (see Lemma 5.2 in Sect. 5.2 below). Of note, any probabilistic statement providing some extensive estimate on K_3 (and on subsequent cluster sizes) requires control of the measure of the configuration set for which $(K_1 + K_2)/N$ is uniformly bounded from above. This lies beyond the scope of this paper.

On the other hand, as suggested by Fig. 1, we believe in the existence of a strictly sequence $\{\epsilon_\ell\}_{\ell \in \mathbb{N}}$ such that for every $\epsilon > 1$ and every $\epsilon > \epsilon_\ell$ we have $N_\ell = N$ with positive (full) probability, where $N_\ell = \sum_{i=1}^{\ell} K_i$ denotes the **accumulated reset population size at the**

firing. This conjecture is also motivated by the fact that, for every $\epsilon > \frac{2}{1-\eta}$, the asymptotic number of clusters becomes intensive for the trajectory started from the initially equidistant

configuration $x_i = \eta + (1 - \eta) \frac{i-1}{N-1}$ for $i = 1, \dots, N$. (see Appendix C).

3 Analytic expressions for the size of merging cluster at successive firings

As mentioned in the introduction, our strategy of proof consists in estimating the size of merging clusters before successive firings, depending on the initial configuration and on the coupling strength. In this section, we first establish a general formula that holds for an arbitrary configuration $\{(n_k, x_k)\}_{k=1}^K$. Then we apply the resulting expression to fully dispersed initial conditions $\{(1, x_k)\}_{k=1}^N$ and their iterates under the firing map.

3.1 Size of the first firing cluster for an arbitrary initial configuration

Let $\{(n_k, x_k)\}_{k=1}^K$ be an ordered initial configuration with arbitrary $n_k \in \{1, \dots, N\}$ such that $\sum_{k=1}^K n_k = N$. We claim that the size of the first firing group is given by $\sum_{k=1}^{K_f} n_k$ where

$$K_f = \max \left\{ j \in \{1, \dots, K\} : \frac{\epsilon}{N} \sum_{k=j+1}^K n_k (x_k - x_j) \geq 1 \right\} \quad (1)$$

is the number of merging clusters. In addition, the following comments apply.

- We have $K_f \leq K - 1$ because the sum in expression (1) vanishes for $j = K$. This implies that no cluster distribution (with $K \geq 2$) can ever shrink to a single component vector ($K = 1$).
- The quantity $\frac{\epsilon}{N} \sum_{k=j+1}^K n_k (x_k - x_j)$ decreases as j increases between 1 and $K-1$.
- In the case where $\frac{\epsilon}{N} \sum_{k=2}^K n_k (x_k - x_1) < 1$ (i.e. when all quantities in the expression of K_f in Eq. (1) are < 1), we set $K_f = 1$ because the first firing occurs before x_1 reaches 0 as already observed. In that way, the number K_f is well-defined in all cases.

Proof of expression (1) of K_f . According to the previous comment, we can assume that

$\frac{\epsilon}{N} \sum_{k=2}^K n_k (x_k - x_1) \geq 1$, i.e. x_1 reaches 0 before oscillator 1 fires. If, for some $j \geq 2$, the coordinate x_j also reaches 0 before oscillator 1 fires, then by monotonicity all lower coordinates for $i = 1, \dots, j-1$ must also vanish. During the time interval defined by $x_j = 0 < x_{j+1}$, we have

$$\chi_i(t) = \chi_1(t) = \frac{\epsilon \eta}{N} \sum_{k=j+1}^K n_k (x_k - t) \quad \text{for } i=1, \dots, j.$$

This expression holds until these quantities reach η or x_{j+1} reaches 0, whichever occurs first. In the first case, a firing takes place at time t_j given by $\chi_j(t_j) = \eta$ viz.

$$t_j = \frac{\sum_{k=j+1}^K n_k x_k - N/\epsilon}{\sum_{k=j+1}^K n_k} \quad (2)$$

and this happens iff $t_j < x_{j+1}$. If otherwise $t_j \geq x_{j+1}$, then we need to check the inequality $t_{j+1} < x_{j+2}$, and possibly repeat the process until the inequality $t_i < x_{i+1}$ holds for some $i \in \{1, \dots, K-1\}$. This must eventually happen because $t_{K-1} < 1$. Accordingly, the first firing time of the trajectory initiated with the (arbitrary) configuration $\{(n_k, x_k)\}_{k=1}^K$ is given by $t_f = t_{K_f}$ where the quantity in relation (2) is to be computed with index

$$K_f := \max \{ j \in \{1, \dots, K\} : t_{j-1} \geq x_j \}.$$

A direct calculation shows that the expression of K_f here is equivalent to the one in relation

(1). The size of the firing cluster is evidently $\sum_{k=1}^{K_f} n_k$. Of note, we have shown that the

inequality $\frac{\epsilon}{N} \sum_{k=2}^K n_k (x_k - x_1) \geq 1$ —which necessarily holds when $K_f > 1$ —implies $t_f < x_{K_f+1}$ and

$$t_f \geq x_{K_f}. \quad (3)$$

We shall often rely on this inequality in the proofs below.

3.2 Cluster sizes at successive firings for initial configurations in $\mathcal{T}_N$

Cluster sizes at successive firings can now simply be computed by applying the expression (1) to successive population configurations under iterations of the firing map. Here, we implement this procedure for trajectories started on totally dispersed initial configurations

$\{(1, x_k)\}_{k=1}^N$ (which, again, are identified with $x = \{x_k\}_{k=1}^{N-1} \in \mathcal{T}_N$). In this case, the quantity $K_1 = K_f(\{(1, x_k)\}_{k=1}^N)$ is the size of the cluster that fires first. Its explicit expression is

$$K_1 = \max \left\{ j \in \{1, \dots, N\} : \frac{\epsilon}{N} \sum_{k=j+1}^N (x_k - x_j) \geq 1 \right\},$$

let also $t_1 := t_{K_1}$ (i.e. $t_1 = t_j$ with $j = K_1$ in expression (2)) be the first firing time. The population configuration immediately after this first event writes $\{(n_k, x_k)(t_1+)\}_{k=1}^{N-K_1+1}$ where

$$(n_k, x_k)(t_1+) = \begin{cases} (1, x_{K_1+k} - t_1) & \text{if } k=1, \dots, N-K_1 \\ (K_1, 1) & \text{if } k=N-K_1+1 \end{cases}$$

Similarly, let $K_2 = K_f(\{(n_k, x_k)(t_1+)\}_{k=1}^{N-K_1+1})$. Direct calculations show that K_2 is given by (notice that we must have $K_2 \leq N-K_1$)

$$K_2 = \max \left\{ j \in \{1, \dots, N-K_1\} : \frac{1}{N} \sum_{k=K_1+j+1}^N x_k - \left(1 - \frac{j}{N}\right) x_{K_1+j} + \frac{K_1}{N} (1+t_1) \geq 1/\epsilon \right\}.$$

Let $t_2 = t_{K_2}$ be the time interval between the first and second firings. The second iterated of the firing map is given by $\{(n_k, x_k)(t_1+t_2+)\}_{k=1}^{N-K_1-K_2+2}$ where

$$(n_k, x_k)(t_1+t_2+) = \begin{cases} (1, x_{K_1+K_2+k} - t_1 - t_2) & \text{if } k=1, \dots, N-K_1-K_2 \\ (K_1, 1-t_2) & \text{if } k=N-K_1-K_2+1 \\ (K_2, 1) & \text{if } k=N-K_1-K_2+2 \end{cases}$$

(Obviously, the first line here does not exist when $N_2(=K_1+K_2)=N$.)

For subsequent firings, we proceed by induction. Let $\ell \in \mathbb{N}$ and suppose that the sizes $\{K_i\}_{i=1}^\ell$ have already been computed. For our purpose, it is sufficient to follow the induction only while $N_\ell = \sum_{i=1}^\ell K_i < N$; this condition ensures that merging only involve individual oscillators (and not groups of oscillators that have already fired). In this case, letting $T_\ell = \sum_{i=1}^\ell t_i$ be the time of the ℓ th firing event, the population configuration immediately after that event writes $\{(n_k, x_k)(T_\ell+)\}_{k=1}^{N-N_\ell+\ell}$ where

$$(n_k, x_k)(T_\ell+) = \begin{cases} (1, x_{N_\ell+k} - T_\ell) & \text{if } k=1, \dots, N - N_\ell \\ (K_i, 1 - T_\ell + T_i) & \text{if } k=N - N_\ell + i, i=1, \dots, \ell \end{cases} \quad (4)$$

(One can check that this expression is well-defined and the coordinates $x_k(T_\ell+)$ are monotonically ordered.) Then, the size $K_{\ell+1}$ at the next firing is given by

$$K_{\ell+1} = \max \left\{ j \in \{1, \dots, N - N_\ell\} : \frac{1}{N} \sum_{k=N_\ell+j+1}^N x_k - \left(1 - \frac{j}{N}\right) x_{N_\ell+j} + \sum_{i=1}^\ell \frac{K_i}{N} (1 + T_i) \geq 1/\epsilon \right\}. \quad (5)$$

One can check that if $N_{\ell+1} < N$, then the next iterated $\{(n_k, x_k)(T_{\ell+1}+)\}_{k=1}^{N-N_{\ell+1}+\ell+1}$ is given by the analogue of expression (4) where ℓ is replaced by $\ell + 1$. The induction then follows while the number N_ℓ of oscillators that have fired remains smaller than N .

4 Dispersed populations at small coupling: proof of Proposition 2.1

In this section, we assume that $\epsilon < \frac{2}{1+\eta}$ and $N > 2$. The proof of Proposition 2.1 separates the analysis of the first firing event to that of the subsequent ones. Given $\delta > 0$, let

$$\mathcal{T}_{N,\delta} = \left\{ x \in \mathcal{T}_N : \left| \frac{1}{N} \sum_{k=1}^N x_k - \frac{1+\eta}{2} \right| < \delta \right\}. \quad (6)$$

The size of the first firing cluster for a dispersed initial configuration $x \in \mathcal{T}_N$ is given by $K_1 = K_f(x)$. We are going to show that $K_1 = 1$ for every $x \in \mathcal{T}_{N, \frac{2-\epsilon(1+\eta)}{2\epsilon}}$. Lemma 7.1 in

Appendix A implies that the measure $\mu\left(\mathcal{T}_{N, \frac{2-\epsilon(1+\eta)}{2\epsilon}}\right)$ converges to 1 in the thermodynamics limit $N \rightarrow \infty$. The conclusion of Proposition 2.1 will follow for $\ell = 1$.

The assumption $x_1 > \eta > 0$ implies the inequality

$$\frac{1}{N} \sum_{k=2}^N (x_k - x_1) = \frac{1}{N} \sum_{k=1}^N (x_k - x_1) < \frac{1}{N} \sum_{k=1}^N x_k. \text{ Moreover, the condition } x \in \mathcal{T}_{N, \frac{2-\epsilon(1+\eta)}{2\epsilon}} \text{ yields}$$

$$\frac{1}{N} \sum_{k=1}^N x_k < \frac{1+\eta}{2} + \frac{2-\epsilon(1+\eta)}{2\epsilon} = 1/\epsilon.$$

It follows that $\frac{1}{N} \sum_{k=2}^N (x_k - x_1) < 1/\epsilon$ from which the equality $K_1 = 1$ (and the inequality $x_1 > t_1$) result, as commented in Sect. 3.1.

Consider now an arbitrary number $\ell \geq 2$ of firings and let accordingly $N > \ell$. We are going to show by induction that $K_i = 1$ for $i = 1, \dots, \ell$ for the successive cluster sizes, for every

$x \in \mathcal{J}_{N, \frac{2-\epsilon(1+\eta)}{2\epsilon}}$ such that $x_k > \frac{k-1}{N}$ for $k = 2, \dots, \ell$. When the inequality $N \geq \lceil \ell \eta \rceil$ holds (where $\lceil \cdot \rceil$ stands for the ceiling function), the latter condition holds for every

$x \in \mathcal{J}_{N, \frac{2-\epsilon(1+\eta)}{2\epsilon}}$ because the smallest coordinate satisfies $x_1 > \eta \ell N$. As said before, the

measure $\mu \left(\mathcal{J}_{N, \frac{2-\epsilon(1+\eta)}{2\epsilon}} \right)$ converges to 1 in the thermodynamic limit. Hence, the conclusion of Proposition 2.1 will be granted for every $\ell \in \mathbb{N}$ and the proof will be complete.

The induction actually proves that $K_i = 1$ and x_i fires prior reaching 0 (i.e. $x_i > T_i$) for $i = 1, \dots, \ell$. For $\ell = 1$, the properties $K_1 = 1$ and $x_1 > T_1 = t_1$ have been proved above. Assume now that the property holds up to some $\ell - 1$. Then, we have $N_{\ell} = \ell$ and the definition (5) of $K_{\ell+1}$ shows that a sufficient condition for $K_{\ell+1} = 1$ and $x_{\ell+1} > T_{\ell+1}$ is

$$\frac{1}{N} \sum_{k=\ell+2}^N x_k - \left(1 - \frac{1}{N}\right) x_{\ell+1} + \sum_{i=1}^{\ell} \frac{1}{N} (1 + T_i) < 1/\epsilon$$

Using that $\frac{1}{N} \sum_{k=\ell+2}^N x_k = \frac{1}{N} \sum_{k=1}^N x_k - \frac{1}{N} \sum_{k=1}^{\ell+1} x_k$ and $\frac{1}{N} \sum_{k=1}^N x_k < 1/\epsilon$ for every $x \in \mathcal{J}_{N, \frac{2-\epsilon(1+\eta)}{2\epsilon}}$ (see above), it suffices to check the inequality

$$-\frac{1}{N} \sum_{k=1}^{\ell+1} x_k - \left(1 - \frac{1}{N}\right) x_{\ell+1} + \sum_{i=1}^{\ell} \frac{1}{N} (1 + T_i) < 0.$$

The inequalities $T_i < x_i$ for $i = 1, \dots, \ell$ imply in turn that it is sufficient to impose

$$-x_{\ell+1} + \frac{\ell}{N} < 0, \text{ which is exactly the constraint required above.}$$

5 Massive clustering at strong coupling

In this section, we take $\epsilon > \frac{2}{1+\eta}$ and we prove separately statement (i) and (ii) of Proposition 2.2, and Proposition 2.3.

5.1 Extensive clustering at first firing: proof of Proposition 2.2, statement (i)

Let $\delta_\epsilon = \min \left\{ \frac{1}{\epsilon}, \frac{\epsilon(1+\eta) - 2}{4\epsilon} \right\} > 0$. We are going to prove the existence of $\rho_1 < \bar{\rho}_1 \in (0, 1)$ and $M_\epsilon \in \mathbb{N}$ such that, for every $N > M_\epsilon$, we have

$$\lceil \rho_1 N \rceil \leq K_1 \leq \lfloor \bar{\rho}_1 N \rfloor,$$

for every $x \in \mathcal{T}_{N, \delta_\epsilon/3}$ (recall the definition of $\mathcal{T}_{N, \delta}$ in relation (6) above). As before, Lemma

7.1 implies that the measure $\mu \left(\mathcal{T}_{N, \delta_\epsilon/3} \right)$ approaches 1 in the thermodynamic limit and Proposition 2.2, statement (i) will follow (also using the inequality $\lfloor \cdot \rfloor \geq \lceil \cdot \rceil - 1$). By Proposition

8.1 in Appendix B, there exists a finite collection $\left\{ x_{(i, \delta_\epsilon/3)} \right\}_{i=1}^{i_{\delta_\epsilon/3}}$ of continuous strictly increasing functions that $\delta_\epsilon/3$ -approximates piecewise affine continuous increasing functions from $[0, 1]$ into itself. For each i , let the function $Y_{i, \epsilon}$ be defined by

$$Y_{i, \epsilon}(\omega) = \int_{\omega}^1 \left(X_{(i, \delta_\epsilon/3)}(\theta) - X_{(i, \delta_\epsilon/3)}(\omega) \right) d\theta, \quad \forall \omega \in [0, 1].$$

Each function $\omega \mapsto Y_{i, \epsilon}(\omega)$ is strictly decreasing. Indeed,

- as the integral of a summable function, the derivative of $\omega \mapsto \int_{\omega}^1 x_{(i, \delta_\epsilon/3)}(\theta) d\theta = -x_{(i, \delta_\epsilon/3)}(\omega)$ exists for almost every $\omega \in [0, 1]$, see e.g. Kolmogorov and Fomin (1999).
- Moreover, as an increasing function, the derivative of $\omega \mapsto -(1 - \omega) x_{(i, \delta_\epsilon/3)}(\omega) = -(1 - \omega) x'_{(i, \delta_\epsilon/3)}(\omega) + x_{(i, \delta_\epsilon/3)}(\omega)$ also exists for almost every $\omega \in [0, 1]$, see again Kolmogorov and Fomin (1999).

Therefore, there exists a subset $A \subset [0, 1]$ with full Lebesgue measure such that for every $\omega \in A$, the derivative of $\omega \mapsto Y_{i, \epsilon}(\omega) = -(1 - \omega) x'_{(i, \delta_\epsilon/3)}(\omega) < 0$ exists, hence strict monotonicity of $\omega \mapsto Y_{i, \epsilon}(\omega)$.

By compactness of $[0, 1]$, each function $Y_{i, \epsilon}$ is uniformly continuous. Accordingly, there exists $\nu_\epsilon > 0$ such that

$$|\rho - \rho'| < \nu_\epsilon \Rightarrow |Y_{i, \epsilon}(\rho) - Y_{i, \epsilon}(\rho')| < \delta_\epsilon/3, \forall i \in \{1, \dots, i_{\delta_\epsilon/3}\}.$$

Now, let $M_\epsilon = \max \left\{ \left\lceil \frac{1}{\nu_\epsilon} \right\rceil, \left\lfloor \frac{3}{2\delta_\epsilon} \right\rfloor \right\}$, let $N > M_\epsilon$ and let $x \in \mathcal{T}_{N, \delta_\epsilon/3}$ be given. Let x_{lin} be the linear interpolation of x , viz. x_{lin} is the piecewise affine continuous function from $[0, 1]$ into itself defined by

$$x_{\text{lin}}(0) = 0, x_{\text{lin}}(k/N) = x_k \text{ and } x_{\text{lin}} \text{ is affine in the interval } [(k-1)/N, k/N] \text{ for each } k \in \{1, \dots, N\}.$$

Proposition 8.1 states that the family $\left\{x_{(i, \delta_\epsilon/3)}\right\}_{i=1}^{i_{\delta_\epsilon/3}}$ constitutes a $\delta_\epsilon/3$ -net of the linear interpolations x_{lin} . Accordingly, there exists $i_x \in \{1, \dots, i_{\delta_\epsilon/3}\}$ such that the supremum norm $\|x_{lin} - x_{(i_x, \delta_\epsilon/3)}\|_\infty < \delta_\epsilon/3$.

Lemma 5.1—We have

$$\left| \frac{1}{N} \sum_{k=\lceil \rho N \rceil + 1}^N (x_k - x_{\lceil \rho N \rceil}) - Y_{i_x, \epsilon}(\rho) \right| < \delta_\epsilon, \quad \forall \rho \in (0, 1).$$

Proof of the Lemma: Let $j \in \{1, \dots, N-1\}$ be fixed. The sum $\frac{1}{N} \sum_{k=j+1}^N x_k$ can be regarded as the integral $\int_{j/N}^1 x_{sup}(\theta) d\theta$ (Riemann sum) where $x_{sup}(\theta)$ is the step function defined by

$$x_{sup}(\omega) = x_k, \quad \forall \omega \in ((k-1)/N, k/N], k \in \{1, \dots, N\}.$$

On the other hand, on each interval $[(k-1)/N, k/N]$, the function x_{lin} is affine between x_{k-1} (resp. 0 if $k=0$) and x_k . Hence, the integral $\int_{(k-1)/N}^{k/N} (x_{sup}(\theta) - x_{lin}(\theta)) d\theta$ represents the area of the triangle between x_{lin} and x_{sup} in this interval. Accordingly, we have

$$\int_{(k-1)/N}^{k/N} (x_{sup}(\theta) - x_{lin}(\theta)) d\theta = \frac{x_k - x_{k-1}}{2N}$$

and by summing over $k \in \{j+1, \dots, N\}$, this implies the inequalities

$$\int_{j/N}^1 x_{lin}(\theta) d\theta \leq \frac{1}{N} \sum_{k=j+1}^N x_k \leq \int_{j/N}^1 x_{sup}(\theta) d\theta + \frac{1}{2N}. \quad (7)$$

Together with the estimate $\|x_{lin} - x_{(i_x, \delta_\epsilon/3)}\|_\infty < \delta_\epsilon/3$, the left inequality here yields

$$\frac{1}{N} \sum_{k=j+1}^N (x_k - x_j) > Y_{i_x, \epsilon}\left(\frac{j}{N}\right) - 2\delta_\epsilon/3. \quad (8)$$

Now, the definition of M_ϵ and the condition $N > M_\epsilon$ imply $\left| \frac{\lceil \rho N \rceil}{N} - \rho \right| < 1/N < \nu_\epsilon$ for all $\rho \in (0, 1)$. By definition of ν_ϵ , it results that

$$Y_{i_x, \epsilon}\left(\frac{\lceil \rho N \rceil}{N}\right) > Y_{i_x, \epsilon}(\rho) - \delta_\epsilon/3, \quad \forall \rho \in (0, 1).$$

Letting $j = \lceil \rho N \rceil$ in the inequality (8), one of the two inequalities in the statement follows, namely

$$\frac{1}{N} \sum_{k=\lceil \rho N \rceil+1}^N (x_k - x_{\lceil \rho N \rceil}) > Y_{i_x, \epsilon}(\rho) - \delta_\epsilon.$$

On the other hand, the right inequality in (7) together with $\|x_{lin} - x_{(i_x, \delta_\epsilon/3)}\|_\infty < \delta_\epsilon/3$ implies

$$\frac{1}{N} \sum_{k=j+1}^N (x_k - x_j) < Y_{i_x, \epsilon}\left(\frac{j}{N}\right) + \delta_\epsilon,$$

from which the second inequality of the Lemma immediately follows by taking again $j = \lceil \rho N \rceil$ and by using strict monotonicity of $\omega \mapsto Y_{i_x, \epsilon}(\omega)$.

Independently of Lemma 5.1, the right inequality in relation (7) above (more precisely, its extension to $j = 0$) and the inequality $\frac{1}{2N} < \frac{\delta_\epsilon}{3}$ (which holds for every $N > M_\epsilon$) imply

$$\int_0^{x_{lin}}(\theta) > \frac{1+\eta}{2} - 2\delta_\epsilon/3, \quad \forall x \in \mathcal{T}_{N, \delta_\epsilon/3}.$$

The inequality $\|x_{lin} - x_{(i_x, \delta_\epsilon/3)}\|_\infty < \delta_\epsilon/3$ and the definition of δ_ϵ then yield

$$Y_{i_x, \epsilon}(0) - \delta_\epsilon > \frac{1+\eta}{2} - 2\delta_\epsilon = 1/\epsilon.$$

By continuity of $\omega \mapsto Y_{i_x, \epsilon}(\omega)$, we are sure that the quantity $\underline{\rho}_{i_x}$ defined by

$$\underline{\rho}_{i_x} = \max \{ \omega \in [0, 1] : Y_{i_x, \epsilon}(\omega) - \delta_\epsilon \geq 1/\epsilon \},$$

is positive. By Lemma 5.1, for every $x \in \mathcal{T}_{N, \delta_\epsilon/3}$, we conclude that

$$\frac{\epsilon}{N} \sum_{k=\lceil \underline{\rho}_{i_x} N \rceil+1}^N (x_k - x_{\lceil \underline{\rho}_{i_x} N \rceil}) \geq 1,$$

i.e. $K_1 \geq \lceil \underline{\rho}_{i_x} N \rceil$. Consequently, the inequality $K_1 \geq \lceil \underline{\rho}_1 N \rceil$ holds with $\underline{\rho}_1 = \min \underline{\rho}_{i_x} > 0$ where the minimum is taken over all $x_{(i_x, \delta_\epsilon/3)}$ that lie at distance less than $\delta_\epsilon/3$ of the linear interpolation of some configuration $x \in \mathcal{T}_{N, \delta_\epsilon/3}$. (Positivity of $\underline{\rho}_1$ is granted by the fact that there are finitely many $\underline{\rho}_{i_x} > 0$.)

On another hand, we have $Y_{i_x, \epsilon}(1) = 0$ and $\delta_\epsilon < 1/\epsilon$; hence the quantity $\bar{\rho}_{i_x}$ defined by

$$\bar{\rho}_{i_x} = \max \{ \omega \in [0, 1] : Y_{i_x, \epsilon}(\omega) + \delta_\epsilon \geq 1/\epsilon \},$$

is certainly smaller than 1. By Lemma 5.1 and strict monotonicity of the function $Y_{i_x, \epsilon}$, we get

$$\frac{\epsilon}{N} \sum_{k=\lceil \rho N \rceil + 1}^N (x_k - x_{\lceil \rho N \rceil}) < 1, \quad \forall \rho > \bar{\rho}_{i_x}.$$

i.e. $K_1 < \lceil \rho N \rceil$ for all $\rho > \bar{\rho}_{i_x}$. By taking the right limit $\rho \rightarrow \bar{\rho}_{i_x}^+$, we conclude that $K_1 \geq \lfloor \bar{\rho}_1 N \rfloor$ where $\bar{\rho}_1 = \max \bar{\rho}_{i_x} < 1$. The proof is complete.

5.2 Extensive clustering at subsequent firings: proof of Proposition 2.2, statement (ii)

This section focuses on establishing the following extensive clustering property at any firing.

Lemma 5.2—For every $\rho, \omega \in (0, 1)$, there exists $\rho^* > 0$ and $N_* \in \mathbb{N}$ such that, for any $N > N_*$, $\ell < N$ and $x \in \mathcal{T}_N$ so that

- $K_1 \geq \lceil \rho N \rceil$,
- $K_i > 1$ for $i = 2, \dots, \ell$,
- $N_\ell \geq \lfloor \omega N \rfloor$,

we have $K_{\ell+1} \geq \lfloor \rho^* N \rfloor$.

Clearly, by statement (i) of Proposition 2.2, statement (ii) immediately follows from applying Lemma 5.2 with $\rho = \rho_1$ and $\omega = \bar{\rho}_1$.

Proof of Lemma 5.2: The first step is to obtain a simple lower estimate for the size $K_{\ell+1}$. This step relies on the inequality $T_\ell \leq x_{N_\ell}$ which is granted by the assumption $K_i > 1$ for $i = 1, \dots, \ell$. Indeed, the inequality $T_1 = t_1 \leq x_{K_1} = x_{N_1}$ is nothing but the inequality (3) at the end of Sect. 3.1 applied to the first firing here, and the latter is ensured by assumption $K_1 > 1$. For subsequent firings $i = 2, \dots, \ell$, the constraints $K_i > 1$ for $i = 2, \dots, \ell$ similarly yield $t_i \leq x_{N_{i-1} + K_i} - T_{i-1}$ from where the desired inequality follows for $i = \ell$.

Using the definition of K_ℓ the ordering $x_k \leq x_{k+1}$ and the inequality $T_\ell \leq x_{N_\ell}$ the quantity involved in the definition (5) of $K_{\ell+1}$ can be bounded as follows

$$\begin{aligned} \frac{1}{N} \sum_{k=N_\ell+j+1}^N x_k - \left(1 - \frac{j}{N}\right) x_{N_\ell+j} + \sum_{i=1}^{\ell} \frac{K_i}{N} (1 + T_i) \\ \geq 1/\epsilon - \frac{1}{N} \sum_{k=N_\ell+1}^{N_\ell+j} x_k + \left(1 - \frac{K_\ell}{N}\right) x_{N_\ell} - \left(1 - \frac{j}{N}\right) x_{N_\ell+j} + \frac{K_\ell}{N} (1 + T_\ell) \\ > 1/\epsilon + x_{N_\ell} - x_{N_\ell+j} + \frac{K_\ell}{N} \end{aligned}$$

It results that

$$K_{\ell+1} \geq \max \left\{ j \in \{1, \dots, N - N_\ell\} : x_{N_\ell+j} \leq x_{N_\ell} + \frac{K_\ell}{N} \right\}. \quad (9)$$

Now, the assumption $N_\ell \leq \lfloor \omega N \rfloor$ necessarily implies $N_i \leq \lfloor \omega N \rfloor$ for $i = 1, \dots, \ell$ and, if we assume by induction that the conclusion already holds for $i = 1, \dots, \ell-1$, we get the existence of $\rho'(\rho, \omega)$ such that

$$\min_{i=1, \dots, \ell} K_i \geq \left\lfloor \rho'(\rho, \omega) N \right\rfloor.$$

In particular, we can ascertain that $\frac{K_\ell}{N} > 0.9\rho'(\rho, \omega)$ provided that N is sufficiently large, say $N > N^*$.

Let $\delta < 0.9\rho'(\rho, \omega)$ and consider the collection $\left\{ x_{(i, \delta/2)} \right\}_{i=1}^{i_{\delta/2}}$ given by Proposition 8.1. By uniform continuity, there exists $\rho_* > 0$ such that

$$x_{(i, \delta/2)}(\alpha + \rho_*) \leq x_{(i, \delta/2)}(\alpha) + 0.9\rho'(\rho, \omega) - \delta, \quad \forall \alpha \leq \omega \wedge (1 - \rho_*), i \in \{1, \dots, i_{\delta/2}\}.$$

Let i_x be such that $\|x_{\text{lin}} - x_{(i_x, \delta/2)}\|_\infty < \delta/2$ where x_{lin} is the linear interpolation of x (see previous section). The definition of i_x implies $x_{(i_x, \delta/2)}\left(\frac{N_\ell}{N}\right) - \delta/2 < x_{N_\ell}$. Using monotonicity, we also have

$$x_{N_\ell + \lfloor \rho_* N \rfloor} = x_{\text{lin}}\left(\frac{N_\ell + \lfloor \rho_* N \rfloor}{N}\right) < x_{(i_x, \delta/2)}\left(\frac{N_\ell}{N} + \rho_*\right) + \delta/2.$$

The definition of ρ_* and the assumption $N_\ell \leq \lfloor \omega N \rfloor$ then yield

$$x_{N_\ell + \lfloor \rho_* N \rfloor} < x_{(i_x, \delta/2)}\left(\frac{N_\ell}{N}\right) - \delta/2 + 0.9\rho'(\rho, \omega) \leq x_{N_\ell} + \frac{K_\ell}{N}$$

from where the estimate (9) immediately implies the desired conclusion.

5.3 Intensive asymptotic number of clusters: proof of Proposition 2.3

We begin by establishing a sufficient condition for intensive asymptotic number of clusters. Given $x \in \mathcal{T}_N$, the ordering $x_k < x_{k+1}$ implies that the quantity involved in the definition (5) of $K_{\ell+1}$ is strictly decreasing with j . Accordingly, the relation $N_{\ell+1} = N$ holds if, when computed with $j = N - N_\ell$ this quantity is not smaller than $1/\epsilon$, viz.

$$\sum_{i=1}^{\ell} \frac{K_i}{N} T_i \geq 1/\epsilon,$$

Assuming the inequalities $T_i \geq x_{K_i}$ (which hold under the condition of Lemma 5.2), it

follows that one only has to check that $\sum_{i=1}^{\ell} \frac{K_i}{N} x_{K_i} \geq 1/\epsilon$.

Focusing now on the proof of Proposition 2.3, we assume $\ell = 1$. Thanks to the inequality (3)

at the end of Sect. 3.1, the property $K_1 \geq \lfloor \rho_1 N \rfloor$ in statement (i) of Proposition 2.2 implies

that $\lim_{N \rightarrow \infty} \mathbb{P}(T_1 \geq x_{K_1}) = 1$ for every $\epsilon > \frac{2}{1+\eta}$. Therefore, in order to prove Proposition 2.3

(that is to say $\lim_{N \rightarrow \infty} \inf \mathbb{P}(N_2 = N) > 0$) it suffices to show that

$$\liminf_{N \rightarrow \infty} \mathbb{P}\left(\frac{K_1}{N} x_{K_1} \geq 1/\epsilon\right) > 0.$$

provided that ϵ is sufficiently large. As we shall see below, a sufficient condition is $\epsilon \alpha_{\epsilon}^2 > 1$

where $\alpha_{\epsilon} = \frac{\epsilon(1+\eta) - 2}{4\epsilon}$. This condition holds when

$$\epsilon > \epsilon_c := \frac{2(5+\eta) + 4\sqrt{6+2\eta}}{(1+\eta)^2}$$

and $\epsilon_c < 1/\eta$ provided that η is small enough. Explicit calculations show that $\eta < 1/20$ works and this explains the inequality $\eta < 1/20$ in the comments after Proposition 2.1 in Sect. 2.

For a configuration $x \in \mathcal{T}_N$, the ordering $x_k < x_{k+1}$ implies that the quantity involved in the definition of K_1 in Sect. 3.2 can be bounded from below as follows

$$\frac{1}{N} \sum_{k=j+1}^N (x_k - x_j) = \frac{1}{N} \sum_{k=1}^N x_k - \frac{1}{N} \sum_{k=1}^j x_k - \left(1 - \frac{j}{N}\right) x_j \geq \frac{1}{N} \sum_{k=1}^N x_k - x_j$$

It results that $K_1 \geq \max \left\{ j \in \{1, \dots, N\} : x_j \leq \frac{1}{N} \sum_{k=1}^N x_k - 1/\epsilon \right\}$. In particular, for a

configuration $x \in \mathcal{T}_{N, \alpha_{\epsilon}}$, the relation $\frac{1+\eta}{2} - 1/\epsilon - \alpha_{\epsilon} = \alpha_{\epsilon}$ proffers the following estimate

$$K_1 \geq \max \{ j \in \{1, \dots, N\} : x_j \leq \alpha_{\epsilon} \}.$$

By using this inequality, we aim to estimate the probability of $\frac{K_1}{N} x_{K_1} \geq 1/\epsilon$ in the thermodynamic limit.

Let $x \in \mathcal{T}_{N,\alpha_\epsilon}$ be such that $x_m - \alpha_\epsilon < x_{m+1}$ for some $m \in \{0, \dots, N-1\}$. For such configuration, we obviously have $K_1 \leq m$. If in addition, we can ensure that $x_m \geq \frac{N}{\epsilon m}$, then we would have $\frac{K_1}{N} x_{K_1} \geq 1/\epsilon$ as desired. Therefore, all we have to do is to estimate the probability that

$$\frac{N}{\epsilon m} \leq x_m \leq \alpha_\epsilon < x_{m+1}.$$

for those values of $m \in \{0, \dots, N-1\}$ such that $m > \frac{N}{\epsilon \alpha_\epsilon}$. The condition $\epsilon \alpha_\epsilon^2 > 1$ guarantees that the latter holds for every $m \in \{\lfloor \alpha_\epsilon N \rfloor + 1, \dots, N-1\}$ (provided that N is large enough). Moreover, the inequality $\frac{N}{\epsilon m} > \eta$ holds for every such m (and thus we have $\eta < \alpha_\epsilon$) thanks to the assumption $\epsilon < 1/\eta$. Hence, we aim to estimate the quantity

$$\mu \left(\bigcup_{m=\lfloor \alpha_\epsilon N \rfloor + 1}^{N-1} \left\{ x \in \mathcal{T}_{N,\alpha_\epsilon} : \frac{N}{\epsilon m} \leq x_m \leq \alpha_\epsilon < x_{m+1} \right\} \right)$$

Thanks to Lemma 7.1, assuming that $x \in \mathcal{T}_N$ instead of $x \in \mathcal{T}_{N,\alpha_\epsilon}$ in this probability does not affect its asymptotic value in the thermodynamic limit $N \rightarrow \infty$. By the definition of the measure μ and the fact that the sets in the union are pair-wise disjoint, we finally have to compute

$$\frac{(N-1)!}{(1-\eta)^{N-1}} \sum_{m=\lfloor \alpha_\epsilon N \rfloor + 1}^{N-1} \text{Leb}_{N-1} \left\{ x \in \mathcal{T}_N : \frac{N}{\epsilon m} \leq x_m \leq \alpha_\epsilon < x_{m+1} \right\} \quad (10)$$

Since Leb_{N-1} is a product measure, each element in this sum writes as the product $I_m \bar{I}_m$ where

$$\begin{aligned} I_m &= \int_{\frac{N}{\epsilon m}}^{\alpha_\epsilon} \left(\int_{\eta}^{x_m} \left(\int_{\eta}^{x_{m-1}} \left(\dots \left(\int_{\eta}^{x_3} \left(\int_{\eta}^{x_2} dx_1 \right) dx_2 \right) \dots \right) dx_{m-2} \right) dx_{m-1} \right) dx_m \\ &= \int_{\frac{N}{\epsilon}}^{\alpha_\epsilon} \frac{(x_m - \eta)^{m-1}}{(m-1)!} dx_m = \frac{(\alpha_\epsilon - \eta)^m - \left(\frac{N}{\epsilon m} - \eta\right)^m}{m!} \end{aligned}$$

and

$$\begin{aligned} \bar{I}_m &= \int_{\alpha_\epsilon}^1 \left(\int_{x_{m+1}}^1 \left(\dots \left(\int_{x_{N-3}}^1 \left(\int_{x_{N-2}}^1 dx_{N-1} \right) dx_{N-2} \right) \dots \right) dx_{m+2} \right) dx_{m+1} \\ &= \frac{(1-\alpha)^{N-m-1}}{(N-m-1)!} \end{aligned}$$

where we used the change of variables $y_i = 1 - x_i$ for $i = m+1, \dots, N-1$ in the last computation. Expression (10) then becomes

$$\sum_{m=\lfloor \alpha_\epsilon N \rfloor + 1}^{N-1} \binom{N-1}{m} \left(\frac{\alpha_\epsilon - \eta}{1 - \eta} \right)^m \left(1 - \frac{\alpha_\epsilon - \eta}{1 - \eta} \right)^{N-m-1} \left(1 - \left(\frac{\frac{N}{\epsilon m} - \eta}{\alpha_\epsilon - \eta} \right)^m \right)$$

We have

$$\left(\frac{\frac{N}{\epsilon m} - \eta}{\alpha_\epsilon - \eta} \right)^m < \left(\frac{\frac{1}{\epsilon \alpha_\epsilon} - \eta}{\alpha_\epsilon - \eta} \right)^{\alpha_\epsilon N}, \forall m \geq \lfloor \alpha_\epsilon N \rfloor + 1.$$

The inequality $\epsilon \alpha_\epsilon^2 > 1$ implies that, for every $\beta \in (0, 1)$, there exists $N_\beta \in \mathbb{N}$ such that

$$1 - \left(\frac{\frac{1}{\epsilon \alpha_\epsilon} - \eta}{\alpha_\epsilon - \eta} \right)^{\alpha_\epsilon N} \geq 1 - \beta, \quad \forall N \geq N_\beta.$$

Accordingly, for $N \geq N_\beta$, we have

$$\begin{aligned} & \frac{(N-1)!}{(1-\eta)^{N-1}} \sum_{m=\lfloor \alpha_\epsilon N \rfloor + 1}^{N-1} \text{Leb}_{N-1} \left\{ x \in \mathcal{T}_N : \frac{N}{\epsilon m} \leq x_m \leq \alpha_\epsilon < x_{m+1} \right\} \\ & \geq (1 - \beta) \sum_{m=\lfloor \alpha_\epsilon N \rfloor + 1}^{N-1} \binom{N-1}{m} \left(\frac{\alpha_\epsilon - \eta}{1 - \eta} \right)^m \left(1 - \frac{\alpha_\epsilon - \eta}{1 - \eta} \right)^{N-m-1} \\ & \geq (1 - \beta) \sum_{m=\lfloor \left(\frac{\alpha_\epsilon - \eta}{1 - \eta} \right) N \rfloor + 1}^{N-1} \binom{N-1}{m} \left(\frac{\alpha_\epsilon - \eta}{1 - \eta} \right)^m \left(1 - \frac{\alpha_\epsilon - \eta}{1 - \eta} \right)^{N-m-1} \end{aligned}$$

where the last inequality follows from the fact that $\alpha_\epsilon < 1$. This number is actually smaller than $1/4$; hence the last sum is certainly not smaller than the similar sum that starts from

$m = \left\lfloor \frac{N-3}{2} \right\rfloor$. However, for every $\alpha \in (0, 1)$, the binomial coefficient symmetry $m \leftrightarrow N-1-m$ implies that

$$\sum_{m=\lfloor \frac{N-3}{2} \rfloor}^{N-1} \binom{N-1}{m} \alpha^m (1-\alpha)^{N-m-1} \geq \frac{1}{2} \sum_{m=0}^{N-1} \binom{N-1}{m} \alpha^m (1-\alpha)^{N-m-1} = \frac{1}{2}$$

It results that the measure (10) must be at least $1/2$ when $N < N_\beta$ and the Proposition follows.

6 Conclusion

Clustering and synchronization dynamics of coupled biological oscillators is a well-known phenomenon observed in a variety of contexts from neuronal assemblies to heart tissues and populations of fireflies (Golomb et al. 1992; Pikovsky et al. 2003). Recently, the dynamics of coupled gene oscillators emerged as a subject of active research (Danino et al. 2010; Gonze et al. 2005). These oscillators periodically vary levels of proteins in individual cells,

however they can be sensitive to extracellular biochemical regulators and thus synchronize their behavior. Furthermore, recent advances in synthetic biology made it possible to engineer specific mechanisms of (co-operative) coupling among gene oscillators that can lead to synchronization across large populations (Danino et al. 2010; Prindle et al. 2012; Yamaguchi et al. 2003). In most cases, coupling is provided by global activators, such as the well-known bacterial quorum-sensing agent AHL (Acyl-Homoserine Lactone) (Danino et al. 2010) or through direct synaptic coupling among neuronal cells (Yamaguchi et al. 2003).

On the other hand, co-repressive interactions received comparatively less attention (Brunel and Hakim 1999; Ernst et al. 1995; Tsimring et al. 2005; Van Vreeswijk et al. 1994), although they provide an effective mechanism of controlling the behavior of gene oscillators and can be used in synthetic biology (Prindle et al. 2012). In this paper, we obtained mathematically rigorous results on the clustering dynamics of large co-repressively coupled populations of degrade-and-fire oscillators.

In the limit of fast production (“firing”) and slow degradation of the repressor proteins, the behavior of an individual DF oscillator can be modeled by discontinuous dynamics where the protein concentration decays linearly and jumps back to the initial state when it reaches a certain threshold. The co-repressive coupling is achieved when the threshold value depends on the global level of the repressor protein. When this dependence is weak, the oscillators remain in a dispersed regime where each keeps its own distinct phase. However, increasing coupling strength leads to increased tendency for oscillators to fire simultaneously and form synchronized clusters.

We proved the existence of a sharp transition of the clustering properties of almost every trajectory in the thermodynamic limit, that reflects the abrupt change in the global dynamics of all trajectories. At the transition, the dynamics switches from a regime where the populations remain dispersed after an arbitrary large number of firings, to a strongly coupled phase where clusters of extensive size are formed immediately. For even stronger couplings, with finite probability as $N \rightarrow \infty$, clustering is extremely intense and the asymptotic population is shown to consist of a few giant clusters.

In summary, our results show that the dynamics of random orbits in populations of globally coupled DF oscillators is amenable to an extensive mathematical analysis across the coupling parameter range, for populations of arbitrary size (see Lee DeVille et al. 2010 for a similar global analysis of a random cellular automaton with global coupling). Altogether, they confirm the numerical observations and show that the coupling-induced phase transition that globally affects the dynamics in phase space, can be identified in the dynamics of typical trajectories of large populations. Based on our theoretical predictions, we anticipate that by tuning of the coupling strength (for example by varying cell density) various clustering regimes could be observed in experiments with repressively coupled synthetic gene oscillators. This behavior contrasts with the more typical phenomenology in the case of a co-operative interaction, where instead of clustering, global synchronization usually occurs.

Acknowledgments

BF acknowledges stimulating discussions with Jean-Marc Gambaudo and Lai-Sang Young. He is also grateful to Neil Dobbs for pointing out a gap in the original arguments and to the BioCircuits Institute for hospitality during his stay at UCSD. The work of BF was supported by EU Marie Curie fellowship PIOF-GA-2009-235741 and by CNRS PEPS *Physique Théorique et ses interfaces* and the work of LT was supported by the National Institutes of Health and General Medicine (Grant R01-GM69811) and the San Diego Center for Systems Biology (Grant P50-GM085764).

Appendix A: Mean estimates for configurations in TN

Throughout the proofs, we use the following estimate on the mean $\frac{1}{N} \sum_{k=1}^N x_k$ for a subset of configurations $\{x_k\}_{k=1}^{N-1} \in \mathcal{T}_N$ that has arbitrarily large probability measure. The estimate is a straightforward consequence of the Central Limit Theorem. It can be stated as follows. Recall that the symbol $\mathbb{P}$ denotes the law of a random variable.

Lemma 7.1

For every $\delta \in (0, 1)$, we have $\lim_{N \rightarrow \infty} \mathbb{P} \left(\left| \frac{1}{N} \sum_{k=1}^N x_k - \frac{1+\eta}{2} \right| < \delta \right) = 1$.

Proof

Let $N \in \mathbb{N}$, $N > 1$ be fixed and for every configuration $x = \{x_k\}_{k=1}^{N-1}$, let

$S_{N-1}(x) = \frac{1}{N-1} \sum_{k=1}^{N-1} x_k$. The quantity S_{N-1} is regarded as a random variable with law $\mathbb{P}$.

Consider now the random process in the hypercube $[\eta, 1]^{N-1}$ endowed with the uniform measure $(1 - \eta)^{-(N-1)} \text{Leb}_{N-1}$. For this process, the law of S_{N-1} is simply

$(1 - \eta)^{-(N-1)} \text{Leb}_{N-1} \circ S_{N-1}^{-1}$. A standard argument (presented at the end of this proof below) shows that we have $\mathbb{P} = (1 - \eta)^{-(N-1)} \text{Leb}_{N-1} \circ S_{N-1}^{-1}$.

For the process in the hypercube, the quantity S_{N-1} appears to be the normalized sum of i.i.d. random variables x_i with Lebesgue distribution in $[\eta, 1]$. The corresponding mean value is

$\frac{1+\eta}{2}$ and the variance is finite. By the Central Limit Theorem, we conclude that for every $p \in (0, 1)$ there exists $c_p > 0$ and $N_p \in \mathbb{N}$ such that

$$\mathbb{P} \left(\left| S_{N-1} - \frac{1+\eta}{2} \right| \leq c_p / \sqrt{N-1} \right) = (1 - \eta)^{-(N-1)} \text{Leb}_{N-1} \left(\left| S_{N-1} - \frac{1+\eta}{2} \right| \leq c_p / \sqrt{N-1} \right) > p, \quad \forall N > N_p.$$

In particular, for every $\delta \in (0, 1)$, we can ensure that $|S_{N-1} - \frac{1+\eta}{2}| < \delta/2$ holds with probability larger than p , provided that $N > \max\{N_p, (2c_p/\delta)^2 + 1\}$ (so that we also have $c_p/\sqrt{N-1} < \delta/2$). Furthermore, the normalization $x_N = 1$ yields the following inequality

$$\left| \frac{1}{N} \sum_{k=1}^N x_k - \frac{1+\eta}{2} \right| \leq \left| S_{N-1}(x) - \frac{1+\eta}{2} \right| \frac{1}{N} (1 - S_{N-1}(x)), \quad \forall x \in \mathcal{T}_N.$$

By taking $N > \max\{N_p, (2c_p/\delta)^2 + 1, 2/\delta\}$ (so that we also have $1/N < \delta/2$), we can be sure

that $\left| \frac{1}{N} \sum_{k=1}^N x_k - \frac{1+\eta}{2} \right| < \delta$ whenever $\left| S_{N-1} - \frac{1+\eta}{2} \right| < \delta/2$. The Lemma then immediately follows.

It remains to show the equality of laws $\mathbb{P} = (1-\eta)^{-(N-1)} \text{Leb}_{N-1} \circ S_{N-1}^{-1}$. First, notice that we have

$$\begin{aligned} \text{Leb}_{N-1} \circ S_{N-1}^{-1} &= \text{Leb}_{N-1} \circ (S_{N-1}|_{C_{N-1}})^{-1} \quad \text{where } C_{N-1} \\ &= \left\{ x \in [0, 1]^{N-1} : i \neq j \Rightarrow x_i \neq x_j \right\}. \end{aligned}$$

Indeed, any subset of $[\eta, 1]^{N-1} \setminus C_{N-1}$ has vanishing Leb_{N-1} measure. Moreover, we have $S_{N-1} \circ \sigma = S_{N-1}$ for every permutation of coordinates σ . Consequently, the following decomposition holds for every $\omega \in [\eta, 1]$

$$(S_{N-1}|_{C_{N-1}})^{-1}(\omega) = \bigcup_{\sigma \in \Pi_{N-1}} \sigma \circ (S_{N-1}|_{\mathcal{T}_N})^{-1}(\omega)$$

where Π_{N-1} is the set of all permutations. By construction, the sets $\sigma \circ (S_{N-1}|_{\mathcal{T}_N})^{-1}(\omega)$ are pairwise disjoint. In addition, they all have the same Leb_{N-1} measure because permuting coordinates does not affect the volume. Since there are $(N-1)!$ permutations, it results that for every $\omega \in [\eta, 1]$, we have

$$\text{Leb}_{N-1} \circ S_{N-1}^{-1}(\omega) = (N-1)! \text{Leb}_{N-1} \circ (S_{N-1}|_{\mathcal{T}_N})^{-1}(\omega) = \frac{(N-1)!}{\alpha N} \mathbb{P}(S_{N-1} = \omega),$$

where the last equality follows from the definition of the uniform distribution in Sect. 2. By

integrating over $[\eta, 1]$, normalization then implies $\frac{(N-1)!}{\alpha_N(1-\eta)^{N-1}} = 1$, viz.

$$(1-\eta)^{-(N-1)} \text{Leb}_{N-1} \circ S_{N-1}^{-1} = \mathbb{P} \text{ as desired.}$$

Appendix B: Compactness of the set of increasing functions

Throughout the proofs, we also often need to approximate the piecewise affine interpolation x_{lin} of a configuration $x \in \mathcal{T}_N$ by a continuous and strictly increasing function chosen in a finite collection. Such approximation relies on the following statement. Let $\|\cdot\|_\infty$ denote the uniform norm of a function defined on $[0, 1]$.

Proposition 8.1

For every $\delta < 0$, there exists a finite collection $\{x_{(i,\delta)}\}_{i=1}^{i_\delta}$ of continuous and strictly increasing functions such that, for every piecewise affine continuous increasing function x , there exists $i \in \{1, \dots, i_\delta\}$ such that $\|x - x_{(i,\delta)}\|_\infty < \delta$.

This statement is a consequence of a similar property in the weaker L^1 -norm, which we denote by $\|\cdot\|_1$.

Lemma 8.2

For every $\delta > 0$, there exists a finite collection $\{\tilde{x}_{(i,\delta)}\}_{i=1}^{i_\delta}$ of continuous strictly increasing functions such that, for every piecewise affine continuous increasing function x , there exists $i \in \{1, \dots, i_\delta\}$ such that $\|x - \tilde{x}_{(i,\delta)}\|_1 < \delta$.

Proof of Lemma

By Helly Selection Theorem (Kolmogorov and Fomin 1999), the set of (right continuous) increasing functions from $[0, 1]$ into itself is compact for the L_1 -topology. Hence, for every

$\delta > 0$, there exists a finite collection $\{\tilde{x}_{(i,\delta)}\}_{i=1}^{i_\delta}$ of (right continuous) increasing functions such that, for every piecewise affine continuous increasing function x , there exists $i \in \{1, \dots, i_\delta\}$ such that $\|x - \tilde{x}_{(i,\delta)}\|_1 < \delta/2$.

Let h be a strictly increasing continuous function from $[-1, 1]$ onto $[0, 1]$. Then for each extended function $\tilde{x}_{(i,\delta)}$ on $[-1, 1]$ (where $\tilde{x}_{(i,\delta)}(\omega) = 0$ for $\omega < 0$), consider the function $x_{(i,\delta)}$ defined by the normalized convolution

$$x_{(i,\delta)}(\omega) = \frac{(\tilde{x}_{(i,\delta)} * h)(\omega)}{(\tilde{x}_{(i,\delta)} * h)(1)} \quad \forall \omega \in [0, 1]$$

where $(u * h)(\omega) = \int_{\omega-1}^{\omega} u(\omega - \theta) dh(\theta)$ (Lebesgue–Stieltjes integral). Each function $x_{(i,\delta)}$ is continuous and strictly increasing from $[0, 1]$ onto itself. Moreover, by taking h sufficiently close to the Heaviside function H , one can ensure that $\|x_{(i,\delta)} - \tilde{x}_{(i,\delta)}\|_1 < \delta/2$ for every $i \in \{1, \dots, i_\delta\}$ and the Lemma follows.

Indeed, if the sequence $\{h_n\}_{n \in \mathbb{N}}$ pointwise converges to H on $[-1, 1]$, Helly Convergence Theorem (Kolmogorov and Fomin 1999) implies that the sequence $\{(u * h_n)(\omega)\}_{n \in \mathbb{N}}$ converges to $(u * H)(\omega) = u(\omega)$ for every $\omega \in [0, 1]$. Lebesgue dominated convergence then yields

$$\lim_{n \rightarrow \infty} \int_0^1 \frac{(u * h_n)(\omega)}{(u * h_n)(1)} d\omega = \int_0^1 u$$

from which the desired L^1 -bound on the difference $x_{(i,\delta)} - \tilde{x}_{(i,\delta)}$ easily follows.

Proof of Proposition 8.1

According to the Lemma, it suffices to show that if $\{x_n\}_{n \in \mathbb{N}}$ is a sequence of (strictly) increasing functions such that $\lim_{n \rightarrow \infty} \|x - x_n\|_1 = 0$ where x is continuous, then $\lim_{n \rightarrow \infty} \|x - x_n\|_\infty = 0$. The proof is similar to that of Lemma B.3 in Coutinho and Fernandez (2004).

By contradiction, assume there exist $\delta > 0$ and a subsequence $\{x_{n_i}\}_{i \in \mathbb{N}}$ (with $\lim_{i \rightarrow \infty} n_i = \infty$) such that

$$\|x - x_{n_i}\|_\infty \geq \delta, \quad \forall i \in \mathbb{N}.$$

Accordingly, there exists $\omega_i \in [0, 1]$ for every i such that

$$\text{either } x(\omega_i) \geq x_{n_i}(\omega_i) + \delta \quad \text{or } x(\omega_i) \leq x_{n_i}(\omega_i) - \delta.$$

By taking a subsequence if necessary, we can assume to have either $x(\omega_i) \geq x_{n_i}(\omega_i) + \delta$ for all $i \in \mathbb{N}$ or $x(\omega_i) \leq x_{n_i}(\omega_i) - \delta$ for all $i \in \mathbb{N}$.

Assume to be in the first case. The second case can be treated similarly. Since $\omega_i \in [0, 1]$ for all i , there exists a convergent subsequence. W.l.o.g. assume that we have $\lim_{i \rightarrow \infty} \omega_i = \omega_\infty$.

By compactness, the function x is uniformly continuous. Let then $\gamma > 0$ be small enough so that we have

$$|x(\omega) - x(\omega + \gamma)| < \delta/2, \quad \forall \omega \in [0, 1 - \gamma].$$

Let now $\tilde{\omega} \in (\omega_\infty - \delta/2, \omega_\infty)$ be such that $\lim_{i \rightarrow \infty} x_{n_i}(\tilde{\omega}) = x(\tilde{\omega})$. (The existence of $\tilde{\omega}$ is a consequence of L^1 -convergence.) Convergence to ω_∞ and the choice of $\tilde{\omega}$ imply that we simultaneously have $|\omega_i - \omega_\infty| < \gamma/2$ and $\tilde{\omega} < \omega_i$, and hence $|\tilde{\omega} - \omega_i| < \gamma$,

$$|\omega_i - \omega_\infty| < \gamma/2 \text{ and } \tilde{\omega} < \omega_i, \quad \text{and hence } |\tilde{\omega} - \omega_i| < \gamma,$$

provided that i is sufficiently large. The last inequality implies that $x(\tilde{\omega}) - \delta/2 \geq x(\omega_i) - \delta$ and thus $x(\tilde{\omega}) - \delta/2 \geq x_{n_i}(\omega_i)$ by the initial assumption. Monotonicity of the x_{n_i} and the middle inequality above then yield $x(\tilde{\omega}) - \delta/2 \geq x_{n_i}(\tilde{\omega})$. By taking the limit $i \rightarrow \infty$, we obtain from the convergence at $\tilde{\omega}$ that $-\delta/2 \leq 0$, which is impossible.

Appendix C: Intensive number of clusters for trajectories starting on equidistant configurations

In this section, we examine the fate at strong coupling, of trajectories initiated from equidistant configurations (or initial conditions close to equidistant configurations) and prove that their asymptotic number of clusters must be intensive. This property is an immediate consequence of the following technical statement.

Lemma 9.1

Let $\epsilon > \frac{2}{1-\eta}$ and consider the trajectory started from $x_i = \eta + (1-\eta) \frac{i-1}{N-1}$ ($i=1, \dots, N$).

(i) For every $\ell \in \mathbb{N}$ and there exist $\rho_\ell \in (0, 1)$ and $M_\ell \in \mathbb{N}$ such that for every $N > M_\ell$ the cluster size K_ℓ at ℓ th firing satisfies $K_\ell \geq \lceil \rho_\ell N \rceil$, unless the accumulated reset size $K_1 + \dots + K_{L_\epsilon} = N$.

(ii) We have $\rho_{\ell+1} > \rho_\ell$ for every ℓ

Naturally, property (ii) implies the existence of L_ϵ such that $\sum_{\ell=1}^{L_\epsilon} \rho_\ell \geq 1$. Property (i) then forces $K_1 + \dots + K_{L_\epsilon} = N$ for every $N > M_{L_\epsilon}$. Thus, for every $N \in \mathbb{N}$, when starting from the equidistant configuration, the asymptotic number of clusters cannot exceed $\max\{L_\epsilon, M_\epsilon\}$.

With a bit of additional effort, one can show that a similar upper bound applies to every trajectory started from configurations in some ℓ^∞ -neighborhood of the equidistant configuration. (However, this neighborhood has vanishing measure μ in the thermodynamics

limit.) Therefore, our result indicates that for every $\epsilon > \frac{2}{1-\eta}$ (a threshold that is larger but close to $\frac{2}{1-\eta}$), for every population size, there is positive probability μ to obtain an intensive number of clusters in the long time limit.

Proof

We begin by showing the extensive bound on the size K_1 of the first firing cluster. Explicit calculations show that the quantity involved in the definition of K_1 in Sect. 3.2 is given by

$$\frac{1}{N} \sum_{k=j+1}^N (x_k - x_j) = \frac{1-\eta}{2} \left(1 - \frac{j}{N}\right) \left(1 - \frac{j-2}{N-1}\right).$$

Using $\frac{j-2}{N-1} < \frac{j}{N}$ yields $K_1 \geq \max \left\{ j \in \{1, \dots, N\} : \left(1 - \frac{j}{N}\right)^2 \geq (1 - \rho_1)^2 \right\}$ where $\rho_1 \in (0, 1)$ is such that $(1 - \rho_1)^2 = \frac{2}{(1-\eta)\epsilon}$. This quantity ρ_1 exists for every $\epsilon > \frac{2}{1-\eta}$. It follows that $K_1 \geq \lceil \rho_1 N \rceil$ for all $N \in \mathbb{N}$ as desired.

For $\ell > 1$, we proceed by induction. Assume that we have already proved that for $i = 1, \dots, \ell$ we have $K_i \geq \lceil \rho_i N \rceil$ with $\rho_i \in (0, 1)$ provided that N is sufficiently large. Then, the reasoning at the beginning of the proof of Lemma 5.2 applies here; hence Eq. (9) is a lower bound for K_{L+1} . Using the expression of the equidistant configuration, it easily follows that

$$K_{\ell+1} \geq \left\lfloor \frac{\rho_\ell}{1-\eta} (N-1) \right\rfloor \text{ (provided that } K_1 + \dots + K_\ell + \left\lfloor \frac{\rho_\ell}{1-\eta} (N-1) \right\rfloor \leq N \text{)}.$$

Let then $M_{\ell+1}$ be sufficiently large so that $\left\lfloor \frac{\rho_\ell}{1-\eta} (N-1) \right\rfloor \geq \lceil \frac{\rho_\ell}{1-1.1\eta} N \rceil$ for all $N > M_{\ell+1}$.

Then, we clearly have $K_{L+1} \geq \lceil \rho_{\ell+1} N \rceil$ for all $N > M_{\ell+1}$, where $\rho_{\ell+1} = \frac{\rho_\ell}{1-1.1\eta} > \rho_\ell$. The induction follows.

References

- Acebron JA, Bonilla LL, Perez-Vicente CJ, Ritort F, Spigler R. The Kuramoto model: a simple paradigm for synchronization phenomena. *Rev Mod Phys.* 2005; 77:137–185.
- Bottani S. Pulse-coupled relaxation oscillators: from biological synchronization to self-organized criticality. *Phys Rev Lett.* 1995; 74:4189. [PubMed: 10058438]
- Brunel N, Hakim V. Fast global oscillations in networks of integrate-and-fire neurons with low firing rates. *Neural Comput.* 1999; 11:1621–1671. [PubMed: 10490941]
- Buck J. Synchronous rhythmic flashing of fireflies. II. *Q Rev Biol.* 1988; 63:265–289. [PubMed: 3059390]
- Burkitt AN. A review of the integrate-and-fire neuron model: I. homogeneous synaptic input. *Biol Cybern.* 2006; 95:1–19. [PubMed: 16622699]
- Coutinho R, Fernandez B. Fronts in extended systems of bistable maps coupled via convolutions. *Nonlinearity.* 2004; 17:23–47.
- Danino T, Mondragon-Palomino O, Tsimring LS, Hasty J. A synchronized quorum of genetic clocks. *Nature.* 2010; 463:326–330. [PubMed: 20090747]
- Ernst U, Pawelzik K, Geisel T. Synchronization induced by temporal delays in pulse-coupled oscillators. *Phys Rev Lett.* 1995; 74:1570. [PubMed: 10059062]
- Fernandez B, Tsimring LS. Corepressive interaction and clustering of degrade-and-fire oscillators. *Phys Rev E.* 2011; 84:051916.
- Gonze D, Bernard S, Waltermann C, Kramer A, Herzel H. Spontaneous synchronization of coupled circadian oscillators. *Biophys J.* 2005; 89:120–129. [PubMed: 15849258]
- Golomb D, Hansel D, Shraiman B, Sompolsky H. Clustering in globally coupled phase oscillators. *Phys Rev A.* 1992; 45:3516–3530.
- Kolmogorov, AN.; Fomin, SV. Elements of the theory of functions and functional analysis. Dover Publications; Mineola: 1999.
- Lee DeVille RE, Peskin CS, Spencer JH. Dynamics of stochastic neuronal networks and the connections to random graph theory. *Math Mod Nat Phenom.* 2010; 5:26–66.
- Mather W, Bennet MR, Hasty J, Tsimring LS. Delay-induced degrade-and-fire oscillations in small genetic circuits. *Phys Rev Lett.* 2009; 102:068105. [PubMed: 19257639]
- Mirollo RE, Strogatz SH. Synchronization of pulse-coupled biological oscillators. *SIAM J Appl Math.* 1990; 50:1645–1662.
- Peskin, CS. Mathematical aspects of heart physiology. Courant Institute of Mathematical Science Publication; New York: 1975.
- Pikovsky, A.; Rosenblum, M.; Kurths, J. Synchronization: a universal concept in nonlinear sciences. Cambridge University Press; Cambridge: 2003.
- Prindle A, Samayoa P, Razinkov I, Danino T, Tsimring LS, Hasty J. A sensing array of radically coupled genetic ‘biopixels’. *Nature.* 2012; 481:39–44. [PubMed: 22178928]

- Seen W, Urbanczik R. Similar nonleaky integrate-and-fire neurons with instantaneous couplings always synchronize. *SIAM J Appl Math.* 2000; 61:1143–1155.
- Strogatz SH. From Kuramoto to Crawford: exploring the onset of synchronization in populations of coupled oscillators. *Physica D.* 2000; 143:1–20.
- Tass, PA. Phase resetting in medicine and biology. Springer; Berlin: 1999.
- Tsimring LS, Rulkov NF, Larsen ML, Gabbay M. Repulsive synchronization in an array of phase oscillators. *Phys Rev Lett.* 2005; 95:14101.
- Van Vreeswijk C, Abbott LF, Ermentrout GB. When inhibition not excitation synchronizes neural firing. *J Comput Neurosci.* 1994; 1:313–321. [PubMed: 8792237]
- Wiesenfeld K, Swift JW. Averaged equations for Josephson junction series arrays. *Phys Rev E.* 1995; 51:1020–1025.
- Yamaguchi S, Isejima H, Matsuo T, Okura K, Yagita R, Kobayashi M, Okamura H. Synchronization of cellular clocks in the suprachiasmatic nucleus. *Science's STKE.* 2003; 302(5649):1408.

Fig. 1.

Number of clusters in the asymptotic regime as a function of ϵ for $\eta = 0.01$ and three different population sizes $N = 10^2, 10^3, 10^4$: *point symbols* indicate simulation results for 1,000 different sets of random initial conditions $\{x_i\}_{i=1}^N$ drawn from the uniform distribution in the hypercube $[\eta, 1]^N$; *dashed lines* show the mean number of clusters obtained by averaging over 1,000 simulations, and the *solid lines* the number of clusters obtained for the trajectory initiated from the configuration with equi-distributed concentrations

$x_i = \eta + (1 - \eta) \frac{i - 1}{N - 1}, i = 1, \dots, N$. *Lines with circles* show the upper bound (maximum possible number of clusters $\sim N \left(1 - \sqrt{1 - \epsilon^*(N)/\epsilon}\right)$, see text). The right panel shows the zoomed region near the transition point $\epsilon^* = 2$