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# Stochastic Dynamics Out of Equilibrium

Institut Henri Poincaré, Paris, France,  
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# Preface

In statistical mechanics, it is common practice to use models of large interacting assemblies governed by stochastic dynamics. The trimester “Stochastic Dynamics Out of Equilibrium”, held at the Institut Henri Poincaré (IHP) in Paris from April to July 2017, focused on the “out-of-equilibrium” aspect. Indeed, non-reversible dynamics have features which cannot occur at equilibrium and for which novel methods have to be developed. The three domains relevant to this trimester were (i) transport in nonequilibrium statistical mechanics; (ii) the design of more efficient simulation methods; (iii) life sciences.

The trimester at IHP brought together physicists, mathematicians from many domains, computer scientists as well as researchers working at the interface between biology, physics and mathematics. Various events were scheduled during the trimester: a pre-school in Marseille-Luminy, three workshops and several series of courses and seminars; see the website of the trimester

<https://indico.math.cnrs.fr/e/stoneq17>

for complete information. Each chapter in this book corresponds to one of these events.

Part I gathers lecture notes from the pre-school at the Centre International de Recherche Mathématique (CIRM). This one-week event provided an introduction to the domains listed above. It was intended especially for a junior audience (PhD students and post-docs) but also for more senior researchers not familiar with some of these domains.

Part II includes lecture notes for two of the seven mini-courses which took place during the trimester. Each mini-course was a set of three sessions of one hour and a half, with a first lecture sufficiently introductory to be understood by all the participants of the trimester, and then more specialized sessions. A broad spectrum of scientific fields, topics and techniques was covered by the speakers. Indeed, with a balance depending on the speaker’s background, all lectures featured a mix of rigorous mathematical arguments and more physically motivated derivations; they

used, from the mathematical perspective, techniques from analysis, partial differential equations, probability theory and dynamical systems.

Part III corresponds to the workshop “Numerical aspects of nonequilibrium dynamics”. The scientific motivation for this event was that many successful approaches for the efficient simulation of equilibrium systems cannot be adapted as such to nonequilibrium dynamics. This is the case for instance for standard variance reduction techniques such as importance sampling or stratification. This three-day workshop (held from Tuesday, April 25 to Thursday, April 27) was focused on the developments of original numerical methods specifically dedicated to the simulation of nonequilibrium systems, as well as their certification in terms of error estimates.

Part IV corresponds to the workshop “Life sciences”. This three-day workshop (held from Tuesday, May 16 to Thursday, May 18) gathered researchers coming from different fields—mathematics, physics, life sciences—and working with different approaches and tools, ranging from researchers dealing directly with real data to scientists interested in the theoretical aspects of the models. The aim was on one hand to understand the impact that recent advances in nonequilibrium statistical mechanics and PDE analysis can have on life sciences and, on the other hand, to widen the spectrum of models and phenomenologies tackled by mathematicians and physicists.

Part V corresponds to the workshop “Stochastic dynamics out of equilibrium”. This one-week workshop (held from Monday, June 12 to Friday, June 16) was oriented towards general aspects of nonequilibrium stochastic dynamics, with a broad audience. The topics concerned interface dynamics and KPZ universality, nonequilibrium fluctuations, thermal conductivity and superconductivity in one dimension, connection to macroscopic thermodynamics and more.

Let us conclude by acknowledging the various institutions and persons who contributed to the success of the trimester we organized, and who helped us in producing this volume. Let us first thank the staff at the Centre Emile Borel of IHP who was in charge of the administrative aspects of the organization and handled them with a spectacular efficiency. The funding from CNRS (Centre National de la Recherche Scientifique), as well as from IHP and CIRM (through labex CARMIN) were crucial for hosting our visitors. We also benefited from additional fundings from various institutions in Paris (Fondation des Sciences Mathématiques de Paris, Institut des Hautes Etudes Scientifiques, Sorbonne Université, Université Paris Sud, Université Paris Dauphine, Université Paris Descartes, Université Paris Diderot, Inria Paris, etc.) and abroad (Technische Universität München, Italian–French agreement LYSM, Portugal–France agreement), as well as individual grants from French or European funding agencies (ANR COSMOS and LSD from Agence Nationale de la Recherche, projects HyLEF and MsMaths funded by the European

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November 2018

Giambattista Giacomini  
Stefano Olla  
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# **Mini-courses of the Pre-school at CIRM**



# Stochastic Mean-Field Dynamics and Applications to Life Sciences

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## 1 Introduction

Although we do not intend to give a general, formal definition, the stochastic mean-field dynamics we present in these notes can be conceived as the random evolution of a system comprised by  $N$  interacting components which is: (a) invariant in law for permutation of the components; (b) such that the contribution of each component to the evolution of any other is of order  $\frac{1}{N}$ . The permutation invariance clearly does not allow any freedom in the choice of the geometry of the interaction; however, this is exactly the feature that makes these models analytically treatable, and therefore attractive for a wide scientific community.

Originally designed as toy models in Statistical Mechanics, the emergence of applications in which the interaction is typically of very long range and not determined by fundamental laws, have renewed the interest in models of this sort. Applications include, in particular, *Life Sciences* and *Social Sciences*.

The goal of these lectures is to

- review some of the basic techniques allowing to derive the macroscopic limit of a mean-field model, and provide quantitative estimates on the rate of convergence;
- illustrate, without technical details, some applications relevant to life sciences, in particular for what concerns the study of the properties of the macroscopic limit.

## 2 Generalities

### 2.1 The Prototypical Model

Mainly inspired by [46], we introduce the topic by some heuristics on a simple class of models.

Consider a system of  $N$  interacting diffusions on  $\mathbb{R}^d$  solving the following system of SDE:

$$dX_t^{i,N} = \frac{1}{N} \sum_{j=1}^N b(X_t^{i,N}, X_t^{j,N}) dt + dW_t^i$$

where  $b : \mathbb{R}^d \times \mathbb{R}^d$  is a Lipschitz function,  $(W^i)_{i \geq 1}$  are independent standard Brownian motions, and we assume  $(X_0^{i,N})_{i=1}^N$  to be i.i.d square integrable random variables. In particular, the dynamical equation is well posed.

Note that, for  $t > 0$ , the random variables  $(X_t^{j,N})_{j=1}^N$  will be, by permutation invariance of the model, identically distributed, but the interaction will break the initial independence. The following heuristic is based on the assumption that a *Law of Large Numbers* for these random variables holds also for  $t > 0$ . Thus, if we consider the evolution of a single component  $X^{i,N}$ , and let  $N \rightarrow +\infty$ , it is natural to guess that  $X^{i,N}$  converges, as  $N \rightarrow +\infty$ , to a limit process  $\bar{X}^i$  solving

$$\begin{aligned} d\bar{X}_t^i &= \int b(\bar{X}_t^i, y) q_t(dy) dt + dW_t^i \\ \bar{X}_0^i &= X_0^i \end{aligned} \quad (2.1)$$

where  $q_t = \text{Law}(\bar{X}_t^i)$ . Once the nontrivial problem of well posedness of this last equation is settled, one aims at showing that, for any given  $T > 0$  and indicating by  $X_{[0,T]} \in \mathcal{C}([0,T])$  the whole trajectory up to time  $T$ , the following statement holds: for any  $m \geq 1$

$$(X_{[0,T]}^{1,N}, X_{[0,T]}^{2,N}, \dots, X_{[0,T]}^{m,N}) \rightarrow (\bar{X}_{[0,T]}^1, \bar{X}_{[0,T]}^2, \dots, \bar{X}_{[0,T]}^m)$$

in distribution as  $N \rightarrow +\infty$ . Note that the components of the process

$$(\bar{X}_{[0,T]}^1, \bar{X}_{[0,T]}^2, \dots, \bar{X}_{[0,T]}^m)$$

are independent. Thus, independence at time 0 propagates in time, at least in the macroscopic limit  $N \rightarrow +\infty$ . This property is referred to as *propagation of chaos*.

## 2.2 Propagation of Chaos and Law of Large Numbers

Propagation of chaos can be actually rephrased as a *Law of Large Numbers*. To this aim, given a generic vector  $\underline{x} = (x_1, x_2, \dots, x_N)$ , denote by  $\rho_N(\underline{x}; dy) := \frac{1}{N} \sum_{i=1}^N \delta_{x_i}(dy)$  the corresponding empirical measure. The propagation of chaos property stated above, is equivalent to the fact that the sequence of empirical measures  $\rho_N(\underline{X}_{[0,T]}^N)$  converges in distribution to  $Q \in \mathcal{P}(\mathcal{C}([0,T]))$ , where  $\mathcal{P}(\mathcal{C}([0,T]))$  denotes the set of probabilities on the space of continuous functions  $[0,T] \rightarrow \mathbb{R}^d$ , provided with the topology of weak convergence and  $Q$  is the law of the solution of (2.1). This is established in the following result (see also [46], Proposition 2.2).

**Proposition 1.** *Let  $(X^{i,N} : N \geq 1, 1 \leq i \leq N)$  be a triangular array of random variables taking values in a topological space  $E$ , such that for each  $N$  the law of  $(X^{i,N})_{1 \leq i \leq N}$  is symmetric (i.e. invariant by permutation of components). Moreover let  $(\bar{X}^i)_{i \geq 1}$  be a i.i.d. sequence of  $E$ -valued random variables. Then the following statements are equivalent:*

(a) for every  $m \geq 1$

$$(X^{1,N}, X^{2,N}, \dots, X^{m,N}) \rightarrow (\bar{X}^1, \bar{X}^2, \dots, \bar{X}^m)$$

in distribution as  $N \rightarrow +\infty$ ;

(b) the sequence of empirical measures  $\rho_N(\underline{X}^N)$  converges in distribution to  $Q := \text{Law}(\bar{X}^1)$  as  $N \rightarrow +\infty$ .

*Proof.* Denote by  $Q_N$  the joint law of  $(X^{1,N}, X^{2,N}, \dots, X^{N,N})$  in  $E^N$ , and by  $\Pi_m Q_N$  its projection on the first  $m$  components, i.e. the law of  $(X^{1,N}, X^{2,N}, \dots, X^{m,N})$ . The statements in (a) is equivalent to: for each  $m \geq 1$

$$\Pi_m Q_N \rightarrow Q^{\otimes m} \tag{2.2}$$

weakly, where  $Q^{\otimes m}$  is the  $m$ -fold product of  $Q$ .

(a)  $\Rightarrow$  (b).

To begin with, let  $F : E \rightarrow \mathbb{R}$  be bounded and continuous. Writing  $\langle F, \mu \rangle$  for  $\int F d\mu$  and denoting by  $\mathbb{E}^{Q_N}$  the expectation w.r.t.  $Q_N$ :

$$\begin{aligned} \mathbb{E}^{Q_N} (\langle F, \rho_N(\underline{x}) - Q \rangle^2) &= \frac{1}{N^2} \sum_{i,j=1}^N \mathbb{E}^{Q_N} [F(x_i)F(x_j)] \\ &\quad - \frac{2}{N} \langle F, Q \rangle \sum_{i=1}^N \mathbb{E}^{Q_N} [F(x_i)] + \langle F, Q \rangle^2 \\ &= \frac{1}{N} \mathbb{E}^{Q_N} [F^2(x_1)] + \frac{N-1}{N} \mathbb{E}^{Q_N} [F(x_1)F(x_2)] \\ &\quad - 2 \langle F, Q \rangle \mathbb{E}^{Q_N} [F(x_1)] + \langle F, Q \rangle^2, \end{aligned}$$

where we have used the symmetry of  $Q_N$ . By Assumption (a) this last expression goes to zero as  $N \rightarrow +\infty$ .

Now, let  $\Phi : \mathcal{P}(E) \rightarrow \mathbb{R}$  be continuous and bounded, where  $\mathcal{P}(E)$  is the space of probabilities on the Borel subsets of  $E$ , provided with the weak topology. By definition of weak topology, given  $\epsilon > 0$  one can find  $\delta > 0$  and  $F_1, \dots, F_k : E \rightarrow \mathbb{R}$  bounded and continuous such that if

$$U := \{P \in \mathcal{P}(E) : |\langle P - Q, F_j \rangle| < \delta \text{ for } j = 1, \dots, k\}$$

then  $P \in U$  implies  $|\Phi(P) - \Phi(Q)| < \epsilon$ . Thus

$$|\mathbb{E}^{Q_N} [\Phi(\rho_N(\underline{x}))] - \Phi(Q)| \leq \epsilon Q_N(\rho_N(\underline{x}) \in U) + \|\Phi\|_\infty Q_N(\rho_N(\underline{x}) \notin U).$$

Therefore, to show (b), i.e.  $|\mathbb{E}^{Q_N} [\Phi(\rho_N(\underline{x}))] - \Phi(Q)| \rightarrow 0$  for every  $\Phi$  bounded and continuous, it is enough to show that

$$\lim_{N \rightarrow +\infty} Q_N(\rho_N(\underline{x}) \notin U) = 0.$$

But, by what seen above and the Markov inequality,

$$\begin{aligned} Q_N(\rho_N(\underline{x}) \notin U) &\leq \sum_{j=1}^k Q_N(|\langle \rho_N(\underline{x}) - Q, F_j \rangle| \geq \delta) \\ &\leq \sum_{j=1}^k \frac{\mathbb{E}^{Q_N} (\langle F_j, \rho_N(\underline{x}) - Q \rangle^2)}{\delta^2} \rightarrow 0. \end{aligned}$$

(b)  $\Rightarrow$  (a).

It is enough to show that if  $F_1, F_2, \dots, F_m : E \rightarrow \mathbb{R}$  are bounded and continuous, then

$$\mathbb{E}^{Q_N} [F_1(x_1) \cdot F_2(x_2) \cdots F_m(x_m)] \rightarrow \prod_{j=1}^m \mathbb{E}^Q [F_j(x)] \quad (2.3)$$

Observe that

$$\begin{aligned} &\left| \mathbb{E}^{Q_N} [F_1(x_1) \cdot F_2(x_2) \cdots F_m(x_m)] - \prod_{j=1}^m \mathbb{E}^Q [F_j(x)] \right| \\ &\leq \left| \mathbb{E}^{Q_N} [F_1(x_1) \cdot F_2(x_2) \cdots F_m(x_m)] - \mathbb{E}^{Q_N} \left[ \prod_{j=1}^m \langle \rho_N(\underline{x}), F_j \rangle \right] \right| \\ &\quad + \left| \mathbb{E}^{Q_N} \left[ \prod_{j=1}^m \langle \rho_N(\underline{x}), F_j \rangle \right] - \prod_{j=1}^m \mathbb{E}^Q [F_j(x)] \right| \quad (2.4) \end{aligned}$$

By (b), the last summand converges to 0. Using symmetry

$$\begin{aligned} \mathbb{E}^{Q_N} \left[ \prod_{j=1}^m \langle \rho_N(\underline{x}), F_j \rangle \right] &= \frac{1}{N^m} \mathbb{E}^{Q_N} \left[ \sum_{\tau: \{1, \dots, m\} \rightarrow \{1, \dots, N\}} \prod_{j=1}^m F_j(x_{\tau(j)}) \right] \\ &= \frac{D_{N,m}}{N^m} \mathbb{E}^{Q_N} [F_1(x_1) \cdot F_2(x_2) \cdots F_m(x_m)] \\ &\quad + \frac{1}{N^m} \mathbb{E}^{Q_N} \left[ \sum_{\tau \text{ not injective}} \prod_{j=1}^m F_j(x_{\tau(j)}) \right], \end{aligned}$$

where  $D_{N,m} = \frac{N!}{(N-m)!}$  is the number of injective functions

$$\{1, \dots, m\} \rightarrow \{1, \dots, N\}.$$

Since  $\frac{D_{N,m}}{N^m} \rightarrow 1$ , we obtain

$$\mathbb{E}^{Q_N} \left[ \prod_{j=1}^m \langle \rho_N(\underline{x}), F_j \rangle \right] \rightarrow \mathbb{E}^{Q_N} [F_1(x_1) \cdot F_2(x_2) \cdots F_m(x_m)]$$

which, by (2.4), completes the proof.



Going back to the model in Sect. 2.1, once the propagation of chaos

$$(X_{[0,T]}^{1,N}, X_{[0,T]}^{2,N}, \dots, X_{[0,T]}^{m,N}) \rightarrow (\bar{X}_{[0,T]}^1, \bar{X}_{[0,T]}^2, \dots, \bar{X}_{[0,T]}^m)$$

is shown, Proposition 1 implies that the empirical measure at time  $t$ ,  $\rho_N(\underline{X}_t^N)$  converges in distribution to  $q_t = \text{Law}(\bar{X}_t^1)$ , for every  $t \geq 0$ . Moreover, being the law of the solution of (2.1),  $q_t$  solves the so-called *McKean-Vlasov equation*

$$\frac{\partial}{\partial t} q_t - \nabla \left[ q_t \int b(\cdot, y) q_t(dy) \right] + \frac{1}{2} \Delta q_t = 0.$$

### 2.3 Symmetry and Empirical Measures

Invariance by permutations of components is the main feature of mean-field dynamics. In practice, for most of the models considered in the literature, permutation invariance is obtained by assuming the characteristics of the dynamics, e.g. the drift for diffusions, to be a function of the empirical measure  $\rho_N$ . Next result provides sufficient conditions for a function which is invariant by permutation to be asymptotically a function of the empirical measure. The main assumption is that changing a single component produces variations of order  $\frac{1}{N}$  in the value of the function.

**Proposition 2.** *Let  $K \subseteq \mathbb{R}$  be a compact set, and, for  $N \geq 1$ ,  $f_N : K^N \rightarrow \mathbb{R}$ . Assume the following conditions hold:*

- (i) *the functions  $f_N$  are invariant by permutations of components;*
- (ii) *the functions  $f_N$  are uniformly bounded, i.e. there is  $C > 0$  such that  $|f_N(x)| \leq C$  for every  $N \geq 1$  and  $x \in \mathbb{R}^N$ ;*
- (iii) *there is a constant  $C > 0$  such that for every  $N \geq 1$ , if  $x, y \in \mathbb{R}^N$  and  $x_j = y_j$  for all  $j \neq i$ , then*

$$|f_N(x) - f_N(y)| \leq \frac{C}{N} |x_i - y_i|.$$

*Then there exists a continuous function  $U : \mathcal{P}(K) \rightarrow \mathbb{R}$  and an increasing sequence  $n_k$  such that*

$$\lim_{k \rightarrow +\infty} \sup_{x \in K^{n_k}} |f_{n_k}(x) - U(\rho_{n_k}(x))| = 0.$$

*Proof.* Consider the *Wasserstein metric* on  $\mathcal{P}(K)$

$$d(\nu, \nu') := \inf \left\{ \int |x - y| \Pi(dx, dy) : \Pi \text{ has marginals } \nu \text{ and } \nu' \right\}$$

which, by compactness of  $K$ , induces the weak topology.

We define the function  $U_N : \mathcal{P}(K) \rightarrow \mathbb{R}$  by

$$U_N(\mu) := \inf_{x \in K^N} [f_N(x) + Cd(\mu, \rho_N(x))],$$

where  $C$  is a constant for which assumption (iii) holds. We claim that, for each  $y \in K^N$

$$U_N(\rho_N(y)) = f_N(y). \quad (2.5)$$

If not, there would be  $x \in K^N$  with

$$f_N(x) + Cd(\rho_N(y), \rho_N(x)) < f_N(y),$$

in particular

$$|f_N(y) - f_N(x)| > Cd(\rho_N(y), \rho_N(x)). \quad (2.6)$$

However a basic result in optimal transport states that

$$d(\rho_N(y), \rho_N(x)) = \inf_{\sigma \in S_N} \frac{1}{N} \sum_{i=1}^N |x_i - y_{\sigma(i)}|,$$

where  $S_N$  denotes the set of permutations of  $\{1, 2, \dots, N\}$ . This, the permutation invariance of  $f_N$  and assumption (iii) imply

$$|f_N(y) - f_N(x)| \leq Cd(\rho_N(y), \rho_N(x)),$$

which contradicts (2.6), thus proving (2.5).

Now, let  $\mu, \nu \in \mathcal{P}(K)$ . By definition of  $U_N$ , given  $\epsilon > 0$  there is  $x \in K^N$  such that

$$U_N(\nu) \geq f_N(x) + Cd(\nu, \rho_N(x)) - \epsilon.$$

Thus

$$\begin{aligned} U_N(\mu) &\leq f_N(x) + Cd(\mu, \rho_N(x)) \leq U_N(\nu) + Cd(\mu, \rho_N(x)) - Cd(\nu, \rho_N(x)) + \epsilon \\ &\leq U_N(\nu) + Cd(\mu, \nu) + \epsilon. \end{aligned}$$

By symmetry this implies that

$$|U_N(\mu) - U_N(\nu)| \leq Cd(\mu, \nu).$$

Therefore, the sequence of functions  $(U_N)$  is *equicontinuous* and, clearly, bounded uniformly in  $N$ . By the Theorem of Ascoli-Arzelà there is a subsequence converging uniformly to a function  $U$ . This, together with Claim 1, completes the proof.

### 3 Propagation of Chaos for Interacting Systems

#### 3.1 The Microscopic Model

In this section we introduce a wide class of  $\mathbb{R}^d$ -valued interacting dynamics, which includes the prototypical model above. The main aim is to introduce *quenched disorder*, which accounts for inhomogeneities in the system, and jumps in the dynamics; this allows to include processes with discrete state space. The dynamics is determined by the following characteristics.

- “Local” parameters  $(h_i)_{i=1}^N$ , drawn independently from a distribution  $\mu$  on  $\mathbb{R}^{d'}$  with compact support.
- A drift  $b(x_i, h_i; \rho_N(\underline{x}, \underline{h}))$ , where

$$\rho_N(\underline{x}, \underline{h}) = \frac{1}{N} \sum_{i=1}^N \delta_{(x_i, h_i)},$$

and

$$b : \mathbb{R}^d \times \mathbb{R}^{d'} \times \mathcal{P}(\mathbb{R}^d \times \mathbb{R}^{d'}) \rightarrow \mathbb{R}^d.$$

- A diffusion coefficient  $\sigma(x_i, h_i; \rho_N(\underline{x}, \underline{h}))$

$$\sigma : \mathbb{R}^d \times \mathbb{R}^{d'} \times \mathcal{P}(\mathbb{R}^d \times \mathbb{R}^{d'}) \rightarrow \mathbb{R}^{d \times n},$$

where  $n$  is the dimension of the driving Brownian Motion.

- A jump rate  $\lambda(x_i, h_i; \rho_N(\underline{x}, \underline{h}))$  with

$$\lambda : \mathbb{R}^d \times \mathbb{R}^{d'} \times \mathcal{P}(\mathbb{R}^d \times \mathbb{R}^{d'}) \rightarrow [0, +\infty).$$

- A distribution for the jump  $f(x_i, h_i; \rho_N(\underline{x}, \underline{h}); v)\alpha(dv)$  with

$$f : \mathbb{R}^d \times \mathbb{R}^{d'} \times \mathcal{P}(\mathbb{R}^d \times \mathbb{R}^{d'}) \times [0, 1] \rightarrow \mathbb{R}^d$$

and  $\alpha(dv)$  is a probability on  $[0, 1]$ .

The dynamics could be introduced via generator and semigroup, but it will be convenient to use the language of Stochastic Differential Equations (SDE). So let  $(W^i)_{i \geq 1}$  be a i.i.d. sequence of  $n$ -dimensional Brownian motions; moreover let  $(N^i(dt, du, dv))_{i \geq 1}$  be i.i.d. Poisson random measures on  $[0, +\infty) \times [0, +\infty) \times [0, 1]$  with characteristic measure  $dt \otimes du \otimes \alpha(dv)$ . The microscopic model is given as solution of the SDE for every given realization of the local parameters  $(h_i)$ :

$$\begin{aligned} X_t^{i,N} &= X_0^i + \int_0^t b\left(X_s^{i,N}, h_i, \rho(\underline{X}_s^N, \underline{h})\right) ds + \int_0^t \sigma\left(X_s^{i,N}, h_i, \rho(\underline{X}_s^N, \underline{h})\right) dW_s^i \\ &+ \int_{[0,t] \times [0, +\infty) \times [0,1]} f\left(X_{s-}^{i,N}, h_i; \rho_N(\underline{X}_{s-}^N, \underline{h}); \alpha\right) \mathbf{1}_{[0,t](X_{s-}^{i,N}, h_i, \rho(\underline{X}_{s-}^N, \underline{h}))}(u) N^i(ds, du, dv) \end{aligned} \quad (3.1)$$

It will be assumed, without further notice, that the initial states  $X_0^i$  are i.i.d., square integrable, independent of both the local parameters  $(h_i)$  and of the driving noises  $(W^i, N^i)$ .

### 3.2 The Macroscopic Limit

At heuristic level it is not hard to identify the limit of a given component  $X^{i,N}$  of (3.1) subject to a local field  $h$ . We omit the apex  $i$  on the process and of the driving noises

$$\begin{aligned} \bar{X}_t(h) = & \bar{X}_0 + \int_0^t b(\bar{X}_s(h), h, r_s) ds + \int_0^t \sigma(\bar{X}_s(h), h, r_s) dW_s \\ & + \int_{[0,t] \times [0,+\infty) \times [0,1]} f(\bar{X}_{s-}(h), h; r_s; \alpha) \mathbf{1}_{[0,\lambda(\bar{X}_{s-}(h), h, r_s)]}(u) N(ds, du, dv) \end{aligned} \quad (3.2)$$

where  $r_s = Law(\bar{X}_s(h)) \otimes \mu(dh)$ . Choosing  $\bar{X}_0 = X_0^i$ , and driving noises  $W^i, N^i$ , we indicate by  $\bar{X}^i$  the corresponding solution (3.2).

### 3.3 Well Posedness of the Microscopic Model: Lipschitz Conditions

We now give conditions that guarantee well posedness of (3.1) and (3.2); they are far from being optimal, but allow a reasonable economy of notations. Weaker conditions can be found, for instance in [1]. It is useful to work with probability measures possessing mean value:

$$\mathcal{P}^1(\mathbb{R}^d) := \left\{ \nu \in \mathcal{P}(\mathbb{R}^d) : \int |x| \nu(dx) < +\infty \right\}$$

which is provided with the *Wasserstein metric*

$$d(\nu, \nu') := \inf \left\{ \int |x - y| \Pi(dx, dy) : \Pi \text{ has marginals } \nu \text{ and } \nu' \right\}.$$

- [L1] The function  $b(x, h, r)$  and  $\sigma(x, h, r)$ , defined in  $\mathbb{R}^d \times \mathbb{R}^{d'} \times \mathcal{P}^1(\mathbb{R}^d \times \mathbb{R}^{d'})$  are continuous, and globally Lipschitz in  $(x, r)$  uniformly in  $h$ .
- [L2] The Lipschitz condition of the jumps is slightly less obvious. We assume  $f : \mathbb{R}^d \times \mathbb{R}^{d'} \times \mathcal{P}^1(\mathbb{R}^d \times \mathbb{R}^{d'}) \times [0, 1] \rightarrow \mathbb{R}^d$  and  $\lambda : \mathbb{R}^d \times \mathbb{R}^{d'} \times \mathcal{P}(\mathbb{R}^d \times \mathbb{R}^{d'}) \rightarrow [0, +\infty)$  are continuous, and obey the following condition

$$\begin{aligned} \int |f(x, h, r, v) \mathbf{1}_{[0,\lambda(x,h,r)]}(u) - f(y, h, r', v) \mathbf{1}_{[0,\lambda(x,h,r)]}(u)| du \alpha(dv) \\ \leq L [|x - x'| + d(r, r')] \end{aligned} \quad (3.3)$$

for all  $x, y, r, r', h$ .

*Remark 1.* The above assumptions imply that when one replaces  $r$  by the empirical measure  $\rho_N(\underline{x}, \underline{h})$ , one recovers a Lipschitz condition in  $\underline{x}$ . For instance, the function  $b(x_i, h_i; \rho_N(\underline{x}, \underline{h}))$  is globally Lipschitz in  $\underline{x}$  uniformly in  $\underline{h}$ .

*Remark 2.* Continuity, global Lipschitzianity and compactness of the support of  $\mu$  imply the linear growth conditions

$$\begin{aligned} |b(x, h, r)| & \leq C \left[ 1 + |x| + \int |y| r(dy, dh) \right] \\ |\sigma(x, h, r)| & \leq C \left[ 1 + |x| + \int |y| r(dy, dh) \right] \\ \int |f(x, h, r, v)| \lambda(x, h, r) \alpha(dv) & \leq C \left[ 1 + |x| + \int |y| r(dy, dh) \right]. \end{aligned} \quad (3.4)$$

*Remark 3.* Condition **L2** is satisfied if both  $f$  and  $\lambda$  are continuous, bounded and globally Lipschitz in  $x, r$  uniformly of the other variables. In the case  $f$  does not depend on  $x, r$  but on  $h, v$  only, unbounded Lipschitz jump rate  $\lambda$  can be afforded.

Using Remark 1, together with standard methods in stochastic analysis, one obtains the following result. A detailed proof can be found e.g. in [30].

**Proposition 3.** *Under L1 and L2, the system (3.1) admits a unique strong solution.*

### 3.4 Well Posedness of the Macroscopic Limit

The proof of the convergence of one component of (3.1) toward a solution of (3.2) allows two alternative strategies. One consists in: (a) showing tightness of the sequence of microscopic processes; (b) showing that any limit point solves weakly (3.2); (c) showing that for (3.2) uniqueness in law holds true. We rather follow the following approach, which is somewhat simpler and allows for quantitative error estimates: (a) we show that (3.2) is well posed; (b) by a coupling argument we show  $L^1$ -convergence of one component of (3.1) to a solution of (3.2) driven by the *same noise*.

**Proposition 4.** *Under L1 and L2, the system (3.2) admits a unique strong solution.*

*Proof.* We sketch the proof of existence. We use a standard Picard iteration. Define  $X_t^{(0)}(h) \equiv \bar{X}_0$  and

$$\begin{aligned} X_t^{(k+1)}(h) &= \bar{X}_0 + \int_0^t b\left(X_s^{(k)}(h), h, r_s^{(k)}\right) ds + \int_0^t \sigma\left(X_s^{(k)}(h), h, r_s^{(k)}\right) dW_s \\ &+ \int_{[0,t] \times [0,+\infty) \times [0,1]} f\left(X_{s-}^{(k)}(h), h; r_s^{(k)}; \alpha\right) \mathbf{1}_{[0,\lambda(X_{s-}^{(k)}(h), h, r_s^{(k)})]}(u) N(ds, du, dv) \end{aligned} \quad (3.5)$$

where

$$r_s^{(k)} = \text{Law}\left(X_s^{(k)}(h)\right) \otimes \mu(dh).$$

We estimate

$$E_T^{(k)} := \int \mathbb{E} \left[ \sup_{t \in [0, T]} \left| X_t^{(k+1)}(h) - X_t^{(k)}(h) \right| \right] \mu(dh). \quad (3.6)$$

If we use (3.5) and subtract the equations for  $X^{(k+1)}$  and  $X^{(k)}$ , take the  $\sup_{t \in [0, T]}$  and use the triangular inequality, we obtain the sum of three terms.

(A) The first term comes from the drift.

$$\begin{aligned}
& \sup_{t \in [0, T]} \left| \int_0^t b \left( X_s^{(k)}(h), h, r_s^{(k)} \right) ds - \int_0^t b \left( X_s^{(k-1)}(h), h, r_s^{(k-1)} \right) ds \right| \\
& \leq \int_0^T \left| b \left( X_s^{(k)}(h), h, r_s^{(k)} \right) - b \left( X_s^{(k-1)}(h), h, r_s^{(k-1)} \right) \right| ds \\
& \leq L \int_0^T \left( \left| X_s^{(k)}(h) - X_s^{(k-1)}(h) \right| + d(r_s^{(k)}, r_s^{(k-1)}) \right) ds \\
& \leq L \int_0^T \left( \left| X_s^{(k)}(h) - X_s^{(k-1)}(h) \right| + \int \mathbb{E} \left| X_s^{(k)}(h') - X_s^{(k-1)}(h') \right| \mu(dh') \right) ds
\end{aligned}$$

where the inequality

$$d(r_s^{(k)}, r_s^{(k-1)}) \leq \int \mathbb{E} \left| X_s^{(k)}(h') - X_s^{(k-1)}(h') \right| \mu(dh') \quad (3.7)$$

comes directly from the definition of the metric  $d$ , and we have used **(L1)**. Averaging:

$$\begin{aligned}
& \int \mathbb{E} \left[ \sup_{t \in [0, T]} \left| \int_0^t b \left( X_s^{(k)}(h), h, r_s^{(k)} \right) ds - \int_0^t b \left( X_s^{(k-1)}(h), h, r_s^{(k-1)} \right) ds \right| \right] \mu(dh) \\
& \leq 2L \int_0^T \int \mathbb{E} \left| X_s^{(k)}(h) - X_s^{(k-1)}(h) \right| \mu(dh) \leq 2LT E_T^{(k-1)}.
\end{aligned}$$

(B) The second term comes from the diffusion coefficient.

$$\sup_{t \in [0, T]} \left| \int_0^t \sigma \left( X_s^{(k)}(h), h, r_s^{(k)} \right) dW_s - \int_0^t \sigma \left( X_s^{(k-1)}(h), h, r_s^{(k-1)} \right) dW_s \right|.$$

By the  $L^1$  Burkholder-Davis-Gundy inequality (see e.g. [42])

$$\begin{aligned}
& \mathbb{E} \left[ \sup_{t \in [0, T]} \left| \int_0^t \left[ \sigma \left( X_s^{(k)}(h), h, r_s^{(k)} \right) - \sigma \left( X_s^{(k-1)}(h), h, r_s^{(k-1)} \right) \right] dW_s \right| \right] \\
& \leq C \mathbb{E} \left[ \left( \int_0^T \left| \sigma \left( X_s^{(k)}(h), h, r_s^{(k)} \right) - \sigma \left( X_s^{(k-1)}(h), h, r_s^{(k-1)} \right) \right|^2 ds \right)^{\frac{1}{2}} \right] \\
& \leq CL \mathbb{E} \left[ \left( \int_0^T \left( \left| X_s^{(k)}(h) - X_s^{(k-1)}(h) \right| + d(r_s^{(k)}, r_s^{(k-1)}) \right)^2 ds \right)^{\frac{1}{2}} \right] \\
& \leq CL \sqrt{T} \mathbb{E} \left[ \sup_{s \in [0, T]} \left( \left| X_s^{(k)}(h) - X_s^{(k-1)}(h) \right| + d(r_s^{(k)}, r_s^{(k-1)}) \right) ds \right]
\end{aligned}$$

Averaging over  $h$  and using (3.7) as before, we obtain

$$\int \mathbb{E} \left[ \sup_{t \in [0, T]} \left| \int_0^t \left[ \sigma \left( X_s^{(k)}(h), h, r_s^{(k)} \right) - \sigma \left( X_s^{(k-1)}(h), h, r_s^{(k-1)} \right) \right] dW_s \right| \right] \mu(dh) \leq 2CL\sqrt{T}E_T^{(k-1)}.$$

(C) Finally, we have the term coming from the jumps.

$$\begin{aligned} & \sup_{t \in [0, T]} \left| \int_{[0, t] \times [0, +\infty) \times [0, 1]} f \left( X_{s-}^{(k)}(h), h; r_s^{(k)}; v \right) \mathbf{1}_{[0, \lambda(X_{s-}^{(k)}(h), h, r_s^{(k)})]}(u) N(ds, du, dv) \right. \\ & \left. - \int_{[0, t] \times [0, +\infty) \times [0, 1]} f \left( X_{s-}^{(k-1)}(h), h; r_s^{(k-1)}; v \right) \mathbf{1}_{[0, \lambda(X_{s-}^{(k-1)}(h), h, r_s^{(k-1)})]}(u) N(ds, du, dv) \right| \end{aligned} \quad (3.8)$$

Let

$$F_s^k := f \left( X_{s-}^{(k)}(h), h; r_s^{(k)}; v \right) \mathbf{1}_{[0, \lambda(X_{s-}^{(k)}(h), h, r_s^{(k)})]}(u).$$

Since  $N$  is a positive measure, (3.8) is bounded above by,

$$\begin{aligned} \int_0^T |F_s^k - F_s^{k-1}| N(ds, du, dv) &= \int_0^T |F_s^k - F_s^{k-1}| ds d\mu \alpha(dv) \\ &+ \int_0^T |F_s^k - F_s^{k-1}| \tilde{N}(ds, du, dv), \end{aligned} \quad (3.9)$$

where  $\int_0^T |F_s^k - F_s^{k-1}| \tilde{N}(ds, du, dv)$  has mean zero, since  $ds d\mu \alpha(dv)$  is the compensator of  $N(ds, du, dv)$ . Thus averaging, we are only left with the term  $\int_0^T |F_s^k - F_s^{k-1}| ds d\mu \alpha(dv)$ , which is dealt with using **(L2)**, and gives an upper bound similar of that of part **(A)**.

Summing up the contributions of **(A)**, **(B)** and **(C)**, we get, for a sufficiently large constant  $C$ ,

$$E_T^{(k)} \leq C(T + \sqrt{T})E_T^{(k-1)}.$$

We now observe that the processes  $X^{(k)}$ ,  $k \geq 0$ ,  $h \in \mathbb{R}^{d'}$  are progressively measurable for the filtration generated by the initial condition and the driving noise  $W, N$ , and satisfy

$$\int \mathbb{E} \left[ \sup_{t \in [0, T]} |X_t^{(k)}(h)| \right] \mu(dh) < +\infty.$$

This can be seen by induction on  $k$ , replicating the steps above but using, rather than the Lipschitz conditions, the linear growth conditions (3.4). If we denote by  $\mathcal{M}$  the space of progressively measurable, *cadlag*,  $\mathbb{R}^d$  valued processes such that

$$\|X\| := \mathbb{E} \left[ \sup_{t \in [0, T]} |X_t| \right] < +\infty,$$

and we take  $T$  sufficiently small, we have shown that

$$\sum_k \int \|X^{(k+1)}(h) - X^{(k)}(h)\| \mu(dh) < +\infty,$$

and therefore for all  $h$  in a set  $F$  of  $\mu$ -full measure

$$\sum_k \|X^{(k+1)}(h) - X^{(k)}(h)\| < +\infty.$$

The norm  $\|\cdot\|$  is not complete in  $\mathcal{M}$ , as the sup-norm is not complete in the space of *cadlag* functions. To get a complete metric, we replace the distance in sup-norm by the Skorohod distance  $d_S$  (see [5]), i.e.

$$D_S(X, Y) := \mathbb{E} [d_S(X, Y)].$$

Since the Skorohod distance is dominated by the distance in sup-norm, a Cauchy sequence for  $\|\cdot\|$  is also Cauchy for the metric  $D_S$ . Thus, the limit  $\bar{X}(h)$  of the sequence  $X^{(k)}(h)$  can be defined for all  $h \in F$ , where  $F$  is a set of measure one for  $\mu$ , and it is not hard to show (using also Proposition 1) that (3.2) holds for the limit.  $\bar{X}(h)$  can be then easily defined for  $h \notin F$  just by imposing that (3.2) holds.

This establishes existence of solution in  $\mathcal{M}$  for  $T$  small. Since the condition on  $T$  does not involve the initial condition, the argument can be iterated on adjacent time intervals, obtaining a solution on any time interval.

Establishing uniqueness would actually be easy by using similar arguments. For us it is not actually needed, as uniqueness will follow from the convergence result in next section (Theorem 1).

*Remark 4.* It is more customary to use  $L^2$  norms rather than  $L^1$  norms for constructing solutions to SDE. The main difference is in (C), where we estimate (3.8). When estimating the mean of the *square* of (3.9), the martingale contributes with

$$\int_0^T |F_s^k - F_s^{k-1}|^2 ds du \alpha(dv).$$

To complete the argument one needs a Lipschitz condition of the form

$$\begin{aligned} \int |f(x, h, r, v) \mathbf{1}_{[0, \lambda(x, h, r)]}(u) - f(y, h, r', v) \mathbf{1}_{[0, \lambda(y, h, r')]}(u)|^2 du \alpha(dv) \\ \leq L [|x - y|^2 + d_2^2(r, r')], \end{aligned} \quad (3.10)$$

where, in the whole argument, the distance

$$d_2(\nu, \nu') := \left( \inf \left\{ \int |x - y|^2 \Pi(dx, dy) : \Pi \text{ has marginals } \nu \text{ and } \nu' \right\} \right)^{\frac{1}{2}}$$



would be used. The Lipschitz condition (3.10) is harder to check than (3.3), for the simple reason that “squaring an indicator function does not produce any square”.

### 3.5 Propagation of Chaos

**Theorem 1.** *Suppose conditions **L1** and **L2** hold. For  $i \geq 1$  denote by  $\bar{X}^i(h)$  the solution of (3.2) with the local parameter  $h$  and the same initial condition  $X_0^i$  of (3.1). Then for each  $i$  and  $T > 0$*

$$\lim_{N \rightarrow +\infty} \int \mathbb{E} \left[ \sup_{t \in [0, T]} \left| X_t^{i, N} - \bar{X}_t^i(h_i) \right| \right] \mu^{\otimes N}(d\underline{h}) = 0$$

where  $\mu^{\otimes N}$  is the  $N$ -fold product of  $\mu$ .

*Proof.* As in the proof of Proposition 4 we subtract the two equations for  $X^{i, N}$  and  $\bar{X}^i$ . Using the triangular inequality, we estimate  $\sup_{t \in [0, T]} \left| X_t^{i, N} - \bar{X}_t^i(h_i) \right|$  as sum of three terms, corresponding respectively to drift, diffusion and jumps. In this proof we only show how to deal with the drift term. The other two terms, involving stochastic integrals, are reduced to terms with Lebesgue time integrals as in the proof of Proposition 4, and then are estimated as the drift term.

We therefore give estimates for

$$\begin{aligned} & \int \mathbb{E} \left[ \sup_{t \in [0, T]} \left| \int_0^t b \left( X_s^{i, N}, h_i, \rho(\underline{X}_s^N, \underline{h}) \right) ds - \int_0^t b \left( \bar{X}_s^i(h_i), h_i, r_s \right) ds \right| \right] \mu^{\otimes N}(d\underline{h}) \\ & \leq \int \mathbb{E} \left[ \int_0^T \left| b \left( X_s^{i, N}, h_i, \rho(\underline{X}_s^N, \underline{h}) \right) - b \left( \bar{X}_s^i(h_i), h_i, r_s \right) \right| \right] \mu^{\otimes N}(d\underline{h}) \end{aligned} \quad (3.11)$$

By **(L1)**

$$\begin{aligned} & \left| b \left( X_s^{i, N}, h_i, \rho(\underline{X}_s^N, \underline{h}) \right) - b \left( \bar{X}_s^i(h_i), h_i, r_s \right) \right| \\ & \leq L \left[ \left| X_s^{i, N} - \bar{X}_s^i(h_i) \right| + d \left( \rho(\underline{X}_s^N, \underline{h}), r_s \right) \right]. \end{aligned} \quad (3.12)$$

Now,

$$d \left( \rho(\underline{X}_s^N, \underline{h}), r_s \right) \leq d \left( \rho(\underline{X}_s^N, \underline{h}), \rho(\bar{\underline{X}}_s, \underline{h}) \right) + d \left( \rho(\bar{\underline{X}}_s, \underline{h}), r_s \right). \quad (3.13)$$

We consider the two summands in the r.h.s. of (3.13) separately. By definition of the metric  $d(\cdot, \cdot)$

$$d \left( \rho(\underline{X}_s^N, \underline{h}), \rho(\bar{\underline{X}}_s, \underline{h}) \right) \leq \frac{1}{N} \sum_{j=1}^N \left| X_s^{j, N} - \bar{X}_s^j \right|,$$

so, by symmetry,

$$\int \mathbb{E} [d(\rho(\underline{X}_s^N, \underline{h}), \rho(\overline{X}_s, \underline{h}))] \mu^{\otimes N}(d\underline{h}) \leq \int \mathbb{E} \left[ \left| X_s^{i,N} - \overline{X}_s^i(h_i) \right| \right] \mu^{\otimes N}(d\underline{h}). \quad (3.14)$$

For the second summand in (3.13) we observe that, under  $\mathbb{P} \otimes \mu^{\otimes \infty}$ , the random variables  $(\overline{X}_s^i(h_i), h_i)$  are i.i.d. with law  $r_s \in \mathcal{P}(\mathbb{R}^{d+d'})$ . By a recent version of the Law of Large Number ([27], Theorem 1), there exists a constant  $C > 0$ , only depending on  $d$  and  $d'$ , and  $\gamma > 0$  (any  $\gamma < \frac{1}{d+d'}$  does the job) such that

$$\int \mathbb{E} [d(\rho(\overline{X}_s, \underline{h}), r_s)] \mu^{\otimes N}(d\underline{h}) \leq \frac{C}{N^\gamma}. \quad (3.15)$$

Inserting what obtained in (3.12), (3.13) and (3.14) in (3.11) we get for some  $C > 0$ , which may also depend on  $T$ ,

$$\begin{aligned} \int \mathbb{E} \left[ \sup_{t \in [0, T]} \left| \int_0^t b(X_s^{i,N}, h_i, \rho(\underline{X}_s^N, \underline{h})) ds - \int_0^t b(\overline{X}_s^i(h_i), h_i, r_s) ds \right| \right] \mu^{\otimes N}(d\underline{h}) \\ \leq C \int \mathbb{E} \left[ \int_0^T \left| X_s^{i,N} - \overline{X}_s^i(h_i) \right| \right] \mu^{\otimes N}(d\underline{h}) + \frac{C}{N^\gamma}. \end{aligned}$$

Dealing similarly with all terms arising in  $\sup_{t \in [0, T]} \left| X_t^{i,N} - \overline{X}_t^i(h_i) \right|$ , if we set

$$E_t := \int \mathbb{E} \left[ \sup_{s \in [0, t]} \left| X_s^{i,N} - \overline{X}_s^i(h_i) \right| \right] \mu^{\otimes N}(d\underline{h})$$

we obtain

$$E_t \leq C \int_0^t E_s ds + \frac{C}{N^\gamma},$$

which, by Gromwall's Lemma and the fact that  $E_0 = 0$  yields

$$E_T \leq \frac{C_T}{N^\gamma}$$

for some  $T$ -dependent constant  $C_T$ , and this complete the proof.

## 4 Applications

In this section we review some classes of models that are relevant for life sciences. Some key results will be stated, but no proofs are given.

## 4.1 The Stochastic Kuramoto Model

Synchronization phenomena leading to macroscopic rhythms are ubiquitous in science. Most (ab)used examples include

- applauses;
- flashing fireflies;
- protein concentration within cells in a multicellular system (repressilators).

In these examples the systems are comprised by many units, each unit tending to behave periodically. Under circumstances depending on how units communicate, oscillation may *synchronize*, producing macroscopic pulsing. The (stochastic) Kuramoto model [33] is perhaps the most celebrated stylized model to capture this behavior.

In the Kuramoto model units are *rotators*, i.e. the state variable is an angle. Denoting by  $X^{i,N}$  the angular variable (*phase*) of the  $i$ -th rotator, with  $i = 1, 2, \dots, N$ , the evolution is given by

$$dX_t^{i,N} = h_i dt + \frac{\theta}{N} \sum_{j=1}^N \sin(X_t^{j,N} - X_t^{i,N}) dt + dW_t^i. \quad (4.1)$$

Here  $h_i$  is the characteristic angular velocity of the  $i$ -th rotator. The effect of the interaction term is to favor phases to stay close. We assume the  $h_i$ 's are i.i.d., drawn from a distribution  $\mu$  on  $\mathbb{R}$  with compact support. By possibly adding a constant speed rotation, there is no further loss of generality to assume that  $\mu$  has mean zero. We further assume  $\mu$  is symmetric, i.e. invariant by reflection around zero.

Clearly all results in Sect. 3 apply, and we get the following macroscopic limit:

$$d\bar{X}_t(h) = h dt + \theta \int \sin(y - \bar{X}_t) q_t(dy; h') \mu(dh') dt + dW_t, \quad (4.2)$$

where  $q_t(dy; h')$  is the law of  $\bar{X}_t(h')$ . The flow of measures  $q_t(\cdot, h)$  solves (indeed in the classical sense for the density w.r.t. the Lebesgue measure)

$$\frac{\partial}{\partial t} q_t(x; h) = \frac{1}{2} \frac{\partial^2}{\partial x^2} q_t(x; h) - \frac{\partial}{\partial x} [(h + \theta r_{q_t} \sin(\varphi_{q_t} - x)) q_t(x, h)] =: \mathcal{M}[q_t](h), \quad (4.3)$$

where

$$r_{q_t} e^{i\varphi_{q_t}} := \int e^{ix} q_t(dx; h) \mu(dh).$$

Equation (4.3) describes the collective behavior of the system of rotators.  $r_{q_t}$  captures the degree of synchronization of the system:  $r_{q_t} = 0$  indicates total lack of synchronization, while a perfectly synchronized systems has  $r_{q_t} = 1$ .

One is interested in the long time behavior of solutions of (4.3), in particular stable equilibria. Note that, since the model is rotation invariant, if  $q(x; h)$  solves  $\mathcal{M}[q] = 0$ , then also  $q(x + x_0; h)$  does; thus there is no loss of generality in looking for equilibria satisfying  $\varphi_q = 0$ .

The proof of the following statement can be found in [7].

**Theorem 2.**  $q^*$  is a solution of  $\mathcal{M}[q] = 0$  with  $\varphi_{q^*} = 0$  if and only if it is of the form

$$q^*(x; h) = (Z_*)^{-1} \cdot e^{2(hx + \theta r_* \cos x)} \left[ e^{4\pi h} \int_0^{2\pi} e^{-2(hx + \theta r_* \cos x)} dx + (1 - e^{4\pi h}) \int_0^x e^{-2(hy + \theta r_* \cos y)} dy \right], \quad (4.4)$$

where  $Z_*$  is a normalization factor and  $r_*$  satisfies the consistency relation

$$r_* = \int e^{ix} q_*(x, h) \mu(dh) dx. \quad (4.5)$$

$r_* = 0$  is a solution of (4.5), and it corresponds to the incoherent solution

$$q^*(x; h) \equiv \frac{1}{2\pi},$$

i.e. the phases of the rotators are uniformly distributed on the torus.

Linear stability of the incoherent solution depends in a highly nontrivial way on  $\theta$  and on the distribution  $\mu$  of the local parameters. It is rather well understood in some special cases [7, 8, 20].

**Theorem 3.** Denote by

$$\theta_c = \left[ \int \frac{\mu(dh)}{1 + 4h^2} \right]^{-1}. \quad (4.6)$$

- (a) Suppose  $\mu$  is unimodal, i.e. it has a (even) density decreasing on  $(0, +\infty)$ . Then the incoherent solution is linearly stable if and only if  $\theta < \theta_c$ . At  $\theta_c$  one (circle of) synchronized solution (i.e. with  $r_q > 0$ ) bifurcates for the incoherent solution.
- (b) Suppose  $\mu = \frac{1}{2}(\delta_{-h_0} + \delta_{h_0})$  for some  $h_0 > 0$ . Then the incoherent solution is linearly stable if and only if  $\theta < \theta_c \wedge 2$ . For  $\theta_c < 2$  at  $\theta = \theta_c$  one (circle of) synchronized solution (i.e. with  $r_q > 0$ ) bifurcates. For  $\theta_c > 2$  (which occurs for  $h_0$  sufficiently large), at  $\theta = 2$  the incoherent solution loses stability via a Hopf bifurcation: it is believed, but not rigorously proved, that stable time-periodic solutions emerge.

It is not true in general that when the incoherent solution is stable then it is unique. It is believed it is so in the unimodal case, but proved either for  $\theta$  small, or up to the critical point if  $\mu$  is sufficiently concentrated around zero [37]. In the binary case, for certain values of the parameters it is known that there are values of  $\theta$  smaller than the critical value for which *two distinct* circles of synchronized solutions exists [37].

In general, when the support of  $\mu$  is contained in a sufficiently small interval, then synchronized solutions exist if and only if  $\theta > \theta_c$ , are unique up to rotation, and are linearly stable [4, 28].

## 4.2 Interacting Fitzhugh-Nagumo Neurons

Designed as reduction of more realistic models (e.g. the Hodgkin-Huxley model), the Fitzhugh-Nagumo model describes the evolution of the membrane potential  $x_t$  of a neuron through the following differential equation

$$\begin{aligned}\dot{x}_t &= x_t - \frac{1}{3}x_t^3 + y_t + I_t^{ext} \\ \dot{y}_t &= \epsilon(a + bx_t - \gamma y_t)\end{aligned}\tag{4.7}$$

where

- $y_t$  is a *recovery variable* obtained by reduction of other variables;
- $I_t^{ext}$  is the input current, assumed to be random and stationary. Without loss of generality, choosing  $a$  properly, we can assume  $I_t^{ext}$  has mean zero.
- $b$  is the interaction strength between  $x$  and  $y$ ,  $\gamma \geq 0$  is a dissipation parameter, and  $a$  is a kinetic parameter related with input current and synaptic conductance.

The parameter  $\epsilon$  can be used to separate the time scales of the evolutions of the two variables. In what follows we assume  $dI_t^{ext} = \sigma dW_t$  for a Brownian motion  $W$ .

To begin with, consider the equation in absence of randomness in the input current ( $\sigma = 0$ ), and set  $b = -1$ ,  $\gamma = 0$  to make the analysis simpler. In this case (4.7) has a unique equilibrium in  $(a, -a + a^3/3)$ , which is globally stable for  $|a| < 1$ , is has a Hopf bifurcation at  $|a| = 1$  and a stable periodic orbit emerges for  $|a| > 1$ . Thus, the system can be excited by the input, producing, at least for appropriate choice of the parameters, rapid variations of the potential (*spikes*) which occur periodically.

There are various ways to make several neurons interact in a network, even within the mean-field scheme, depending of how we model synapsis (see [2]). The simplest, corresponding to electrical synapsis, leads to the following system. Here  $X^{i,N}$  denotes the membrane potential of the  $i$ -th neuron. The local parameter  $h_i$  may be interpreted as the *macroscopic location* of the neuron, or its *type*.

$$\begin{aligned}dX_t^{i,N} &= \left( X_t^{i,N} - \frac{1}{3}(X_t^{i,N})^3 + Y_t^{i,N} \right) dt \\ &\quad + \frac{1}{N} \sum_{j=1}^N J(h_i, h_j) \left( X_t^{i,N} - X_t^{j,N} \right) dt + \sigma dW_t^i \\ dY_t^{i,N} &= \epsilon(h_i) \left[ a(h_i) + b(h_i)X_t^{i,N} - \gamma(h_i)Y_t^{i,N} \right] dt,\end{aligned}\tag{4.8}$$

where the coupling parameters  $J(h_i, h_j)$  tune the interaction between pairs of neurons.

The model exhibits a richer behavior if one introduces a delay  $\tau$  in the transmission of informations between different neurons:

$$\begin{aligned} dX_t^{i,N} &= \left( X_t^{i,N} - \frac{1}{3}(X_t^{i,N})^3 + Y_t^{i,N} \right) dt \\ &\quad + \frac{1}{N} \sum_{j=1}^N J(h_i, h_j) \left( X_t^{i,N} - X_{t-\tau(h_i, h_j)}^{j,N} \right) dt + \sigma dW_t^i \\ dY_t^{i,N} &= \epsilon(h_i) \left[ a(h_i) + b(h_i)X_t^{i,N} - \gamma(h_i)Y_t^{i,N} \right] dt. \end{aligned} \quad (4.9)$$

Delay makes a bit more painful the well posedness analysis for both the model and its macroscopic limit, but for propagation of chaos the same proof carries through (see [48] for details), giving the following macroscopic limit

$$\begin{aligned} d\bar{X}_t(h) &= \left( \bar{X}_t(h) - \frac{1}{3}\bar{X}_t^3(h) + \bar{Y}_t(h) \right) dt \\ &\quad + \int J(h, h') (\bar{X}_t(h) - y) q_{t-\tau(h, h')}(dy; h') \mu(dh') dt + \sigma dW_t \\ d\bar{Y}_t(h) &= \epsilon(h) (a(h) + b(h)\bar{X}_t(h) - \gamma(h)\bar{Y}_t(h)) dt, \end{aligned} \quad (4.10)$$

where  $q_t(dx; h)$  denotes the law of  $\bar{X}_t(h)$ . Not much is known at this level of generality, so we consider the simplest, homogeneous case in which  $h$  is constant,  $\gamma = 0$ ,  $b = -1$  which gives

$$\begin{aligned} d\bar{X}_t &= \left[ \bar{X}_t - \frac{1}{3}\bar{X}_t^3 + \bar{Y}_t + J(\bar{X}_t - \mathbb{E}(\bar{X}_{t-\tau})) \right] dt + \sigma dW_t \\ d\bar{Y}_t &= \epsilon(a - \bar{X}_t) dt \end{aligned} \quad (4.11)$$

A further simplification consists in letting the noise go to zero, in both the diffusion and the initial condition. We obtain the deterministic system with delay

$$\begin{aligned} \dot{x}_t &= x_t - \frac{1}{3}x_t^3 + y_t + J(x_t - x_{t-\tau}) \\ \dot{y}_t &= \epsilon(a - x_t). \end{aligned} \quad (4.12)$$

This system has been extensively studied in [32]. Here we assume  $J \geq 0$

- The point  $(a, -a + a^3/3)$  is still the unique fixed point, and it is stable for  $|a| > \sqrt{1 + 2J}$  and unstable for  $|a| < 1$ , no matter what  $\tau$  is.
- For  $1 < |a| < \sqrt{1 + 2J}$  loss of stability via a Hopf bifurcation can be obtained by increasing  $\tau$ : *interaction and transmission delay may produce oscillations even if single neurons are in the stability region.*

*Does noise play any role in exciting the neuronal network?*