Fluctuations in interacting-particle systems: a theoretical study

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Fluctuations in interacting-particle systems: a theoretical study

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Resumen del contenido de la tesis

La presente tesis doctoral, se centra en el desarrollo de métodos matemáticos para el estudio de procesos estocásticos de interés en física y otras ciencias.

En la primera parte de la tesis se realiza un breve análisis sobre el modo en el que la aleatoriedad entra en la descripción científica de la realidad. A continuación se exponen algunos elementos básicos de la teoría de la probabilidad y los procesos estocásticos, introduciendo la notación y algunos de los resultados que se usarán más adelante en la tesis.

El segundo capítulo consiste en el estudio de un método aproximado general, la aproximación gausiana, habitualmente utilizado en el contexto de procesos estocásticos debido a su simplicidad y amplio rango de aplicabilidad.
Los procesos estocásticos rara vez pueden ser resueltos de forma exacta, especialmente cuando hay no-linealidades e interacciones presentes. Por este motivo es de gran importancia el desarrollo y análisis de métodos aproximados. En el trabajo se derivan cotas máximas del error introducido al usar la aproximación gausiana y se muestra que este error es de hecho menor que el introducido con otros métodos más elaborados. De este modo se resalta la utilidad de la aproximación gausiana.

El tercer capítulo está centrado en el desarrollo de métodos matemáticos para el análisis de procesos estocásticos que incluyen términos con retraso, en el contexto de sistemas de partículas en interacción y dinámica de poblaciones.
Términos con retraso aparecen de forma genérica debido a los tiempos finitos de propagación de la información y respuesta, así como cuando se realiza una

descripción efectiva en términos de unas pocas variables de sistemas más complicados. Aleatoriedad y retraso aparecen juntos en muchas situaciones de interés, como regulación genética, procesos fisiológicos o control postural. Sin embargo, el efecto combinado de la aleatoriedad y el retraso no ha sido entendido completamente. Desde el punto de vista matemático, los procesos estocásticos que incluyen retraso son difíciles de analizar debido a su carácter no markoviano, ya que la mayoría de los resultados derivados en el campo de procesos estocásticos sólo son válidos para procesos markovianos.
El trabajo en este punto consiste en el desarrollo de varios métodos matemáticos apropiados para el estudio de este tipo de sistemas, centrándonos en procesos de tipo nacimiento-muerte. El rango de aplicabilidad y las limitaciones de cada método son analizados con cierto detalle. A través de estos métodos se derivan varios resultados nuevos, algunos exactos y otros aproximados, que permiten entender algunas propiedades genéricas características de procesos estocásticos que incluyen términos con retraso.
Se obtienen los siguientes resultados generales:
- En procesos sin retroalimentación (feedback) cuando el retraso aparece en el paso de creación, éste resulta totalmente irrelevante (siendo la situación equivalente a un sistema sin retraso). Si el retraso aparece en la degradación, es posible resolver exactamente el proceso para distribuciones de retraso generales y se encuentra que la probabilidad a un tiempo es equivalente a un sistema sin retraso, pero aparecen diferencias a nivel de la función de correlación, que no obstante, siempre decrece monótonamente.
- En procesos con retraso en la degradación y retroalimentación la situación depende de la forma particular en la que el retraso y la retroalimentación son introducidos, pero en muchas situaciones el efecto es similar al caso sin retroalimentación.
- Cuando el retraso aparece en el proceso de creación y existe feedback positivo, el retraso disminuye la magnitud de las fluctuaciones y la función de correlación puede ser no monótona pero siempre es positiva. Con retroalimentación negativa, las fluctuaciones aumentan con la magnitud del retraso, superando el nivel obtenido cuando no hay retroalimentación e invirtiendo así el efecto de la retroalimentación negativa (que en ausencia de retroalimentación reduce las fluctuaciones) y la función de correlación se vuelve oscilante. Estos efectos disminuyen cuando la magnitud del retraso se hace más variable.

El cuarto capítulo se centra en el desarrollo de un marco general para el estudio de sistemas estocásticos de partículas en interacción donde los elementos no son idénticos, presentando un cierto grado de diversidad o heterogeneidad.
Si bien la mayoría de los sistemas estudiados tradicionalmente en física están formados por elementos idénticos (como moléculas, átomos o electrones), recientemente se han aplicado métodos y herramientas de la física para el estudio

de sistemas habitualmente estudiados en otras disciplinas, como ecología, epidemiología, economía, etc. Estas nuevas aplicaciones requieren la consideración de sistemas que están caracterizados por un alto grado de heterogeneidad entre sus componentes y que muy a menudo sólo pueden ser modelados a nivel estocástico (ya que el conocimiento completo de todas las variables, la dinámica precisa de los componentes y la interacción con el entorno no está disponible). Sin embargo, el efecto de la heterogeneidad en sistemas estocásticos no ha sido estudiado de forma sistemática.
En la tesis, se analiza el efecto de la heterogeneidad en la magnitud de las fluctuaciones en sistemas generales, comparando con el caso de partículas idénticas. Se estudia la posibilidad de inferir la presencia y la magnitud de la heterogeneidad existente en un sistema a partir de medidas referentes a variables globales únicamente, indicando diferentes formas de conseguir esto. Se desarrolla un método aproximado de validez general para el análisis de sistemas de elementos heterogéneos con dinámicas estocásticas. El método es aplicado para el estudio de dos modelos particulares de interés en la literatura y que se aplican a contextos en donde la asunción de partículas idénticas difícilmente es justificable: mercados financieros (modelo de Kirman) y propagación de epidemias (modelo SIS). En estos casos particulares se derivan varios resultados, exactos y aproximados, y se discute el efecto general de la heterogeneidad sobre las fluctuaciones, dependiendo del modo en el que aparece.
Se encuentra que la heterogeneidad en la "susceptibilidad" (propensión a cambiar de estado debido a interacción con otras partículas) o en la preferencia de estados típicamente disminuye las fluctuaciones, mientras que heterogeneidad en la "influencia" (presencia de la partícula en un estado aumenta la propensión de otras partículas estar un este estado) o en el nivel de estocasticidad de las partículas aumenta las fluctuaciones. Dependiendo de la dinámica y del tipo de heterogeneidad, es posible detectarla midiendo los primeros momentos de la variable global o la función de correlación de ésta.

El quinto capítulo de la tesis consiste en el análisis de las propiedades de sincronización en un sistema particular de elementos excitables acoplados no idénticos, rotores activos cerca del umbral de excitabilidad, en un sistema similar al modelo de Kuramoto.
El fenómeno de la sincronización juega un papel importante en muchos campos científicos (desde sistemas neuronales y células cardiacas hasta circuitos electrónicos y reacciones químicas). Los modelos de fase, en los que las unidades se describen a partir de un ángulo que determina su posición en el ciclo de oscilaciones, constituyen una descripción genérica que puede derivarse a partir de sistemas generales de osciladores de ciclo límite acoplados débilmente. Entre ellos, el modelo de Kuramoto se ha convertido en un paradigma para el estudio del fenómeno de la sincronización. Este modelo muestra cómo la sincronización

puede aparecer cuando los efectos competitivos de acoplamiento y diversidad entre los elementos del sistema están presentes. La diversidad de los osciladores es introducida asignando la frecuencia natural de cada oscilador a partir de una cierta distribución de probabilidad. Estudios previos en este campo a menudo han considerado una distribución de frecuencias lorentziana, porque permite un tratamiento analítico más completo. Generalmente se asume que los resultados relativos a la sincronización son cualitativamente independientes de la forma concreta de la distribución de frecuencias utilizada, ya que éste es el caso para algunas situaciones básicas.
En el trabajo se estudia el papel de la forma particular de la distribución de parámetros en una variante del modelo de Kuramoto en la que las unidades son excitables. Se demuestra que la distribución lorentziana da lugar a resultados no genéricos. En concreto, las distribuciones con primer momento bien definido muestran un régimen de oscilaciones colectivas inducido por la diversidad, mientras que este régimen está totalmente ausente para la distribución lorentziana. Este resultado cuestiona el uso indiscriminado de algunos métodos propuestos recientemente cuya validez se basa en el uso de distribuciones lorentzianas. Así mismo, se desarrolla un nuevo método para el análisis del sistema, no limitado a una forma particular de la distribución de parámetros, que permite entender el origen del régimen de oscilaciones colectivas y analizarlo en cierto detalle.

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Summary of the thesis

This thesis is focused on the development of mathematical methods suitable for the study of stochastic process of interest in physics and other sciences.

In the first part of the work there is a brief exposition of the ways in which randomness enters in the scientific description of nature. Some basic elements of the theory of probability and stochastic processes are presented afterwards, introducing the notation and some results that will be used later in the thesis.

The second chapter consists on the analysis of a general approximation method, the Gaussian approximation, often used in the context of stochastic processes due to its simplicity and wide application range.
Stochastic processes can seldom be solved exactly, specially when the system presents non-linearities or interactions. Because of this fact, the development of approximated methods becomes specially important. In this chapter we derive upper bounds for the error introduced when using the Gaussian approximation and we show that this error is indeed smaller than that introduced with other more elaborated methods. In this way the usefulness of the Gaussian approximation is highlighted.

The third chapter is focused on the development of mathematical methods suitable for the analysis of stochastic processes that include delay terms, in the context of interacting particle systems.
Delay terms appear generically due to the finite times for the propagation of information and response, as well as when a reduced description in terms of a few variables of a more complicated system is performed. Delay and stochasticity appear together in many situations of interest such as gene regulation, physiological processes or posture control. However, the combined effect of stochasticity and delay is not completely understood. From a mathematical point of view, stochastic processes including delay terms are difficult to analyze due to their non-Markovian character, since many of the results derived in the field of stochastic processes are only valid for Markovian systems.
In this respect, we develop several mathematical methods suitable for the study of this kind of systems, focusing on birth and death processes. The application range and limitations of the methods are analyzed in some detail. With these methods, several new results are derived, both exact and approximated, that shed light into some generic properties of stochastic processes with delay. The following general results are derived:
-In processes without feedback, when delay appears in the creation term, it is completely irrelevant (since the system is equivalent to another without delay).

If delay appears in the degradation step, it is possible to solve exactly the process for arbitrary distribution of delay and it is found that the one-time probability is equal to that of a system without delay. The time correlation function changes its form relatively to the no-delay case but it is always monotonically decreasing.
-In processes with delay in the degradation step and feedback the situation depends on the particular form in which the delay and the feedback are introduced, but in many cases the situation is similar to the case with no feedback.
-When the delay appears in the creation step and there is positive feedback, delay decreases the size of the fluctuations and the correlation function may become non-monotonous but it is always positive. With negative feedback, the size of the fluctuations increase with the magnitude of the delay, going beyond the level obtained when no feedback is present, and inverting in this way the effect of the negative feedback (that in the case of no delay decreases the size of the fluctuations); moreover the correlation function becomes oscillatory, signaling the presence of stochastic oscillations. The size of these effects decrease when the magnitude of the delay becomes more irregular.

The fourth chapter is focused on the development of a general framework for the study of stochastic systems of interacting particles where the elements are not identical, showing some degree of heterogeneity or diversity.
Most systems traditionally studied in physics are made of identical units (such as molecules, atoms or electrons). However, in the last years methods and techniques developed in physics have been transferred to other disciplines such as ecology, epidemiology or economy. These new applications require the consideration of systems which are characterized by a large degree of heterogeneity among their constituent units. Furthermore, very often these systems can be modeled only at a stochastic level, since a complete knowledge of all the variables, the precise dynamics of the units and the interaction with the environment is not available. Despite the importance of this issue, the effect of heterogeneity in stochastic systems has not been studied systematically.
In the thesis, we analyze the effect of heterogeneity in the magnitude of fluctuations in general systems, comparing to the case of identical particles. We study the possibility of inferring the presence and magnitude of the heterogeneity of a system from measurements concerning only global variables, indicating different ways to achieve this goal. We develop an approximate method generally applicable to the analysis of heterogeneous systems with dynamic stochastic elements. The method is applied to the study of two particular models of interest in literature that refer to contexts where the assumption of identical particles is hardly justifiable: financial markets (Kirman model) and epidemics spreading (SIS model). For these particular systems several results are derived, both exact and approximate, and the overall effect of heterogeneity on fluctuations is discussed.

It is found that heterogeneity in the "susceptibility" (propensity to change state due to interaction with other particles) or in the preference of states, typically decrease the size of the fluctuations. Heterogeneity in the "influence" (the presence of particle in a given state increases the propensity of other particles to be on that state) or in the level of stochasticity of the individual particles, increases the fluctuations. Depending on the type of dynamics and on the way heterogeneity is introduced, it is possible to detect the presence and the size of the heterogeneity by measuring the first moments of the global variable or its correlation function.

The fifth chapter of the thesis is focused on the analysis of synchronization properties in a particular system of coupled nonidentical excitable elements, active rotors near the excitability threshold, in a system that is a variant of the Kuramoto model.
Synchronization phenomenon play an important role in many scientific fields (from cardiac cells and neuronal systems, to electronic circuits and chemical reactions). Phase models, in which the units are described as an angle that determines their position in the cycle of oscillation, constitute a generic description that is suitable for detailed mathematical analysis. Moreover, under some conditions, they can be derived as a reduced description of general systems of weakly coupled limit-cycle oscillators. Among them, the Kuramoto model has become a paradigm for the study of synchronization phenomena. This model shows how synchronization can occur when the competitive effects of diversity and coupling between the elements of the system are present. The diversity is introduced assigning the natural frequency of each oscillator from a certain probability distribution. Previous studies in this field have often considered a Lorentzian frequency distribution, because it allows a more complete analytical treatment. It is generally assumed that the synchronization properties are qualitatively independent of the particular form of the distribution of frequencies used, as it is the case for some basic situations.
In this chapter we examine the role of the particular form of the distribution of parameters in a variant of the Kuramoto model in which the units are excitable. It is shown that the results obtained using a Lorentzian distribution are not not generic. Specifically, all distributions with a well defined first moment show transition into a regimen of collective oscillations induced by diversity, while this regime is completely absent for the Lorentzian distribution. This result questions the indiscriminate use of some recently proposed methods whose validity is based on the use of Lorentzian distributions. Moreover, we develop a new method for the analysis of the system, not limited to a particular form of the distribution of parameters, which allows us to understand the origin of the regimen of collective oscillations and analyze it in some detail.

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Contents

Part I

Introduction

Chapter 1

Introduction and theoretical background

This thesis is devoted to the development of mathematical methods to analyze problems in which stochasticity is present, of interest in physics and other natural sciences.
We will start by examining the ways in which stochasticity enters in our description of reality.

A prominent characteristic of physical theories is that they allow to make precise quantitative predictions, that can be confronted with observations and experiments.
A physical theory essentially consists on a mathematical model, that indicates how some variables evolve over time, and a correspondence of these variables with measurable properties of (some aspect of) the physical world.

In this setting, randomness can appear in several ways. We distinguish here three main origins of randomness in a physical theory:

(i) Finite precision on the initial conditions.
The initial conditions have to be determined through measurements, which are always subject to errors and finite precision.

(ii) Lack of information about all relevant variables or inability to process them.

(iii) The mathematical model that defines the evolution of the system may itself be stochastic.

In the following section, we analyze in some detail the origins of stochasticity named above. We will make a loose use of terms such as stochastic, randomness

or probability, appealing to the intuitive notions of the reader. Latter on the text we will elaborate on the meaning of these terms.

1.1 Origins of stochasticity

1.1.1 Finite precision on the initial conditions

We analyze first how stochasticity can appear in a situation in which the evolution of a system is deterministic and it is possible to fully compute it.

To be precise, we assume that the state of the system is completely described by a set of variables, collectively denoted as $\boldsymbol{x}$. The set of all possible values for these variables determines the phase space, each possible state of the system corresponding to one point in the phase space. Deterministic evolution implies that the state of the system at time t, $\boldsymbol{x}(t)$, can be univocally assigned from the initial state of the system, $\boldsymbol{x}(0)$, i.e. there exists a function $\boldsymbol{F}$ such that:

$$\boldsymbol{x}(t) = \boldsymbol{F}(\boldsymbol{x}(0), t) \tag{1.1}$$

In most physical theories this relation is given implicitly by a differential equation:

$$\frac{d\boldsymbol{x}(t)}{dt} = \boldsymbol{f}(\boldsymbol{x}(t)), \tag{1.2}$$

the form of this equation is general inside a given theory (for example Newton's second law or Schroedinger's equation), whereas the function $\boldsymbol{F}$ above depends on the specific setting and the initial conditions, so we take (1.2) as starting point.

In order to make a particular prediction, (1.2) has to be supplemented with the initial conditions, $\boldsymbol{x}(0)$. These initial conditions need to be determined through measurements, and those are always subject to errors and finite precision [Dietrich, 1991]. This implies that the initial conditions one should consider are not given by a point in phase space, $\boldsymbol{x}(0)$, but rather by a distribution over this phase space, $\rho(\boldsymbol{x}, 0)$, since this description allows to include in a natural way the uncertainty in the actual value of the initial conditions. Using (1.2), one can see that this distribution in the phase space evolves according to the continuity equation:

$$\frac{\partial \rho(\boldsymbol{x}, t)}{\partial t} = -\nabla(\rho(\boldsymbol{x}, t)\boldsymbol{f}(\boldsymbol{x})). \tag{1.3}$$

In some situations, if the initial condition $\rho(\boldsymbol{x}, 0)$ is sharply peaked around some value $\boldsymbol{x}(0)$, the distribution $\rho(\boldsymbol{x}, t)$ will also be sharply peaked around some value

$x(t)$. In this case, the deterministic picture given by (1.2) is enough to predict the evolution of the system.
However, in other situations the initial condition is not sharply peaked around a given value, or even if it is, through the evolution (1.3) the distribution becomes spread in the phase space. This last phenomena is called sensitivity to the initial conditions[1] and is one of the characteristics of chaotic behavior (the other one being aperiodic behavior)[2]. In these situations, a probabilistic description based on the distribution over the phase space and equation (1.3) is needed.

A physical example of this case is the process of coin-tossing. The outcome of a coin toss is completely determined by the initial conditions of the coin (the way it is tossed), together with the position of the table or surface where it will land (if necessary, the friction with the air can be taken into account, the Brownian-like forces -see below- have typically a negligible effect). The deterministic nature of coin-tossing was shown in Diaconis et al. [2007], were a coin-tossing machine was built.
In a conventional, human-produced, coin toss we do not know precisely the initial conditions (velocity and angular momentum) of the coin, so if we have to predict its outcome, the initial conditions we should plug in Newton's laws would be a distribution, giving us an equation like (1.3). This initial distribution is mapped into a final distribution for heads and tails. Since minute changes in the initial conditions change completely the outcome (specially by changing the precise form in which the coin impacts the surface), points very close in phase space (that will have similar probability of being the actual initial condition if the initial distribution is continuous) will give opposite final results. This will result, if the coin is symmetric, in a final distribution of probability 1/2 heads, probability 1/2 tails.

This finite precision on the initial conditions can be seen as a lack of information about the initial state of the systems, which leads us to consider this lack of information in more generality in the next subsection.

1.1.2 Lack of information about all relevant variables or inability to process them

Effective randomness can appear in the evolution of a system if we do not have access to all the relevant variables. This is clearly illustrated in the following

[1] More precisely: points infinitesimally close in phase space initially diverge exponentially in time

[2] Deterministic description of this type of systems also would require infinite numerical precision, since minute differences as given by roundoff errors lead to large discrepancies, which is impossible in actual computers.

example [Tsonis, 2008]:
Consider a succession of pairs of numbers, (a_t, b_t), defined by the following rule: start with a natural number a_0, then

$$a_{t+1} = \begin{cases} \frac{3}{2}a_t & \text{if } a_t \text{ even,} \\ \frac{3}{2}(a_t + 1) & \text{if } a_t \text{ odd,} \end{cases} \tag{1.4}$$

b_t is equal to 1 if a_t is odd, and is equal to 0 otherwise.
If we start with $a_0 = 1$, we obtain the following sequence for the parir (a_t, b_t):

$$(1,1),(3,1),(6,0),(9,1),(15,1),(24,0),(36,0),(54,0),(81,1),(123,1),(186,0)\ldots$$

Obviously, this sequence is deterministic and we can easily predict one term from the previous one. However, if we only have access to the variable b_t the series looks like $1,1,0,1,1,0,0,0,1,1,0\ldots$, and we are not anymore able to predict the next value. In this case, this happens because the relation that assigns b_t from a_t is not invertible, since many (actually infinite) different values of a_t give the same b_t. This prevents obtaining a_t from b_t, which would allow to predict the following values of b_t. Similarly, a given value of b_t is followed by two possible values 1 and 0, so we cannot predict the next value of b_t from the knowledge of b_t alone.

If we had access only to the series of b_t and we had to characterize it, probably the best we could do would be to study it at an statistical level. We could for example assume that 0's and 1's are produced each one with probability 1/2 and see if the statistical properties of the sequence generated this way match those of the series of b_t. Taken into account how the series is actually generated, we could justify this by the fact that there are the same number of odd and even natural numbers and that the process of a_t does not seem to favor any of these classes[3].

This simple example shows how apparent randomness can appear from purely deterministic dynamics. The situation in which a lack of information prevents predictability is generic, as it is the lack of information itself. One could then argue that the purpose of the scientist should be first of all to obtain all the relevant information, before trying to do any prediction. This however is in many cases impractical. We will exemplify this practical impossibility of taking into account all the relevant variables, examining the Brownian motion, that will also show in some detail how probability and stochastic methods enter in the description of a physical system.

[3] This second observation should be checked more carefully, indeed it poses an interesting number-theoretic problem

The Brownian motion is the erratic movement observed in a small particle when it is immerse in a fluid. This movement is the result of the collisions with the molecules of the fluid. Each collision modifies the velocity of the particle in some amount, that depends on the velocity of the molecule that impacts it. To predict deterministically the evolution of the Brownian particle we would need to take into account the positions and velocities of all the molecules of the fluid. This is clearly not possible in practical terms, since there are of the order of 10^{23} variables. Instead, we assume that the set of velocities and positions of the fluid molecules is described by some probability distribution, that typically is assumed to be independent of the state of the Brownian particle and stationary over time. This allows to compute the probabilities for the changes in velocity of the Brownian particle (assuming that the fluid molecules are hard spheres elastically bouncing with the Brownian particle). We will not be able to predict the specific position and velocity of the Brownian particle (those will depend on the particular fluid molecules that happen to collide with it) but we will be able to derive some statistical properties of its movement, that can be experimentally investigated by repeating a experiment many times or by observing a single Brownian particle during a long time (if our assumption about the stationary distribution for the positions and velocities of the particles is correct, the system would be ergodic and averages over time or over realizations of the experiment will be equivalent).

The crucial step in this line of reasoning is the replacement of the actual positions and velocities of the fluid molecules by some probability distribution. Determining the properties of this distribution is a central problem in statistical physics. Remarkably, for many purposes one does not need to know the details of this distribution. For example, in the case of the Brownian motion, the variance of the position of the Brownian particle grows linearly with time, independently of the form of the distribution, as long as the displacement caused by the collisions of the molecules in a given finite time interval has finite second moment. The value of the diffusion coefficient (the coefficient of proportionality between variance and time) depends only on this second moment, regardless of all other characteristics. The independence of details of these findings justifies our replacement of the actual positions and velocities of the fluid molecules by a particular distribution whose properties we know and that allows to derive results that can then be confronted with experiments.

These ideas are remarkably successful and constitute the basis for Einstein's analysis of Brownian motion [Einstein, 1905], that lead to the experimental determination of Avogadro's number, giving a conclusive evidence of the discrete nature of matter. For thermodynamic systems at equilibrium a formal program, that of equilibrium ensembles, has been developed, constituting the core of sta-

tistical physics and a fundamental piece of our current understanding of Nature. For general systems no formal program exists and direct probabilistic reasoning is needed.

In many instances of many-variable systems, it is possible to select a small set of variables that approximately follow an autonomous deterministic law. All the other eliminated variables will be felt as a superimposed erratic effect, that is usually referred to as fluctuations (and gives name to the present thesis). The existence of these fluctuations and the only approximated validity of a deterministic law is generic for macroscopic systems (like in hydrodynamic equations, Ohm's law or chemical kinetics). The macroscopic law is amenable to a deterministic treatment, but, in the line of the previous reasoning, the fluctuations need to be studied with stochastic methods. In some cases these fluctuations can be neglected and a deterministic approach is enough, but in other cases the fluctuations have an important effect and need to be included. Fluctuations generally play an important role in nano-scale systems (such as molecular motors, electronic transport through nanostructures or gene expression) since the relative size of the fluctuations typically decreases with system size. Moreover, the range of validity of the macroscopic law can only be determined starting from the stochastic description.

Although the situation described in this subsection is the most common origin of stochasticity in physical science, and the one that mainly motivates this thesis, there is yet another level at which stochasticity can appear, that we explore in the next subsection.

1.1.3 Fundamentally stochastic model

In the cases studied above, there is an underlying deterministic dynamics, and unpredictability and effective stochasticity appear only due to our inability to compute the actual (very complicated) evolution.

However there are situations in which stochasticity is a fundamental property of the system. In particular, quantum measurement gives rise to stochastic evolution (at least according to the Copenhagen interpretation). Bell's inequalities [Bell, 1966] show that this stochasticity is fundamental and not due to the lack information about some "hidden variables". Since quantum mechanics is the fundamental theory that underlies macroscopic behavior, this quantum uncertainty may be transmitted to macroscopic behavior. However, the analysis of the emergence of macroscopic behavior from quantum mechanics and the role of stochasticity in this process are beyond the scope of the present thesis.

There is another view of this question, that appears when considering the modeling of a complex system. Lets take an ecological model as an example. It is pretty unlikely that we would be able to find a law that precisely determines the behavior of a given animal. However, it might be possible to derive some stochastic law for the behavior of individual animals, from which the properties of the ecosystem could be derived. It this case, the fundamental model (animal behavior) would already be stochastic. One could argue that the behavior of the animal is the product of the physical and chemical processes that constitute its body and brain, and so the eventual behavioral law would not be fundamental and its stochastic character will come from the procedures commented above. In practice, however, its not possible to derive the animal behavior from physical and chemical considerations alone, so an eventual behavioral law could be consider a fundamental one, and so its stochastic character.
Very often, when modeling a complex system, the fundamental "rules" from which one starts to derive the process are stochastic, which further justifies the usefulness of stochastic methods.

In this thesis we will be mainly concerned with the development of mathematical tools to analyze stochastic processes. The particular problems analyzed are motivated by systems and situations of current interest in physics and other natural sciences. The modeling of particular systems and the justification of the adequacy of probabilistic methods to these particular problems are only loosely considered, centering our attention in the methodology more than in particular applications.

In the next section, we give a basic overview of probability theory, emphasizing the results and tools that will be used through the core part of the thesis.

1.2 Overview of Probability theory

When considering probability theory, we distinguish two main aspects: the logical content of the theory and the interpretation of probability in its relation with the physical world. We will start analyzing the later aspect.

1.2.1 Physical interpretations of probability

There are two main interpretations of the concept of probability, the frequentist interpretation and the Bayesian interpretation.

Von Mises definition of the frequentist concept of probability states [von Mises, 1981]:
"It is possible to speak about probabilities only in reference to a properly defined collective. A collective is a mass phenomenon or an unlimited sequence of observations fulfilling the following two conditions: (i) the relative frequencies of particular attributes within the collective tend to fixed limits; (ii) these fixed limits are not affected by any place selection" (i.e. consideration of only a partial set of the original sequence selected according to a fixed rule). The limiting value of the relative frequency of a given attribute is called the probability of that attribute (within the given collective).
In this way, the probability of an event is reduced to the frequency of appearance of this event. This view considers probabilities as actual properties of given collectives. The idealized concept of collective has approximated realizations in physical situations, like an unlimited set of tossings of a coin, molecules in a gas or large groups of people. To apply probabilistic considerations to a physical situation, one postulates that some aspect of the situation corresponds to a collective and then can use the techniques and results of probability theory. The justification of the adequacy of the concepts of probability to the situation comes by experimentally verifying if the considered aspect indeed forms a collective (relative frequencies tending to fixed values not affected to place selection).

In the Bayesian view [Jaynes, 2003], the probability of an event is a real number between zero and one that quantifies the degree of plausibility of the occurrence of this event (one being sure occurrence, zero being sure non-occurrence). It is shown that the only rules to manipulate and compose these degrees of plausibility that are consistent and correspond qualitatively to common sense [Jaynes, 2003; Cox, 1961] are those of customary probability theory. In this way, probability theory becomes a theory of inference and its scope is greatly enhanced, being an extension of logic to situations with limited information, and not restricted to mas phenomena or unlimited sequences of observations. In this view, the probability is an essentially subjective quantity, associated to the observer and not to a physical system.

There has been a considerable amount of dispute about these two views. We, however, see a way to reconcile the two interpretations.
Let us consider an event to which we assign a given plausibility. We can imagine a (infinite) set of situations that are equal in what regards to our current knowledge about the event but different in everything else. Then, the frequentist probability of the realization of the event in this collective would correspond to the plausibility that we assign to it, i.e. its Bayesian probability. Because the collective depends on our current information, the frequentist probability becomes as well subjective (subjective relatively to the event, yet objective relatively to

the collective). This imaginary collective, reminiscent of the ensembles of statistical mechanics, may seem an artificial construction, and admittedly is difficult to approach experimentally, but we believe is a valuable abstract concept that establishes an equivalence between the two interpretations.

In the present thesis we will some times use nomenclature from the frequentist view, talking about realizations of a process, or ensemble averages. We have not found a case in which a Bayesian interpretation would differ from a frequentist one (with suitably defined collectives).

Whichever the interpretation, the formal content of the theory is the same. In our exposition of some basic aspects of probability theory we aim at being clear and close to intuitive ideas that will be useful when applying these concepts to the particular problems considered later in the thesis. We try to avoid excessive mathematical technicalities, at the expense of losing some generality. For a more formal description of probability theory and stochastic processes, the reader is refered to [Kolmogorov, 1956; Feller, 1957; Gihman and Skorohod, 1974]. For a more concrete description of probabilistic methods, more relevant for the physical sciences, the reader is refered to [van Kampen, 2004; Gardiner, 1985]; our presentation follows mainly these two textbooks.

1.2.2 Mathematical basis and definitions

Probability is formalized in a *probability space*, which is defined by a triplet (Ω, F, P), consisting on a set of elementary *events* Ω (called the *sample space*), a σ-algebra of events F in Ω and a function P from F to the real numbers (P is called the *probability*) satisfying the following properties:
(i) $P(A) \geq 0$, $\forall A \in F$
(ii) $P(\Omega) = 1$
(iii) If $A_i \bigcap A_j = \emptyset$ for $i \neq j$, then $P\left(\bigcup_i A_i\right) = \sum_i P(A_i)$, $\forall A_i \in F$.
The positivity condition (i) agrees with our intuitive idea of probability; (ii) is the normalization condition and (iii) allows us to obtain the probability of any event (included in F) starting only with the knowledge of the probabilities of the elementary events.
We will illustrate these concepts with the example of rolling a die.
The sample space here would be the set $\{1, 2, 3, 4, 5, 6\}$. Beyond the probabilities of these elementary events, we would like to be able to speak about the probabilities of composed events, such as the probability of obtaining an even number or the probability of obtaining a number greater than four. That is why we introduce a σ-algebra, which is a collection of subsets of Ω, containing the empty set, $\emptyset$, and the total set, Ω, and that is closed under (countable) unions and complement

respect Ω. In the die example, the event of obtaining an even number will correspond to $\{2\} \bigcup \{4\} \bigcup \{6\} = \{2, 4, 6\}$, and due to (iii) its probability, $P(\text{even})$, would be $P(\text{even}) = P(2) + P(4) + P(6)$.
In general, (ii) and (iii) implie that the probability that an event does not occur is equal to 1 minus the probability that it does occur.

A *random variable*, X, is defined by an application from the sample space to the real numbers (we will only consider real-valued random variables). This allows to assign probabilities to the several possible values of the random variable. The set of all possible values of a random variable is called its *range*. For a discrete range, $P(x_i)$ will be denoted as the probability that the random variable X takes the value x_i, whereas for a continuous range, $P(x)$ will be called the *probability density* at x, and $P(x)dx$ will be denoted as the probability that the random variable takes a value in the interval $(x, x + dx)$. Those can be derived from the underlaying probability space, but often are postulated directly.
An example of physical quantity which can be described in terms of a random variable with a continuous range is the speed of an ideal gas molecule, whose range would be $[0, \infty)$ and whose probability distribution would be the Maxwell one $P(v) = \sqrt{\frac{2}{\pi}} \left(\frac{m}{kT}\right)^{3/2} e^{-mv^2/2kT}$ (in three dimensions).
A random variable with discrete range can equivalently be described by a continuous range that contains the previous one, and with a probability density that is zero everywhere but contains some Dirac-delta functions at the points of the previous range. Noting this fact, in the following, for notational convenience, we will assume that all the random variables have a continuous range.

The *average* or *expected value* of a function, f, of the random variable X (note that a function of a random variable is another random variable, see below) is:

$$\langle f(X) \rangle := \int dx f(x) P(x). \tag{1.5}$$

In particular, $\langle X^m \rangle$ is called the m-th moment of X. The first moment is called the *average* or *mean* and the *variance*, σ^2, is defined as $\sigma^2 := \langle (X - \langle X \rangle)^2 \rangle = \langle X^2 \rangle - \langle X \rangle^2$. σ is called the *standard deviation* and it is a measure of the dispersion around the mean of the random variable.

A useful construction is the *characteristic function*, $C(k)$, which is essentially the Fourier transform of the probability density:

$$C(k) = \langle e^{ikX} \rangle = \int dx e^{ikx} P(x). \tag{1.6}$$

The coefficients of its Taylor expansion around $k = 0$ are the moments:

$$C(k) = \sum_{m=0}^{\infty} \frac{(ik)^m}{m!} \langle x^m \rangle. \tag{1.7}$$

It is also the basis for defining the *cumulants* κ_m:

$$\log C(k) = \sum_{m=1}^{\infty} \frac{(ik)^m}{m!} \kappa_m. \tag{1.8}$$

The cumulants are combinations of the moments. The moments and the cumulants are used to characterize the random variable.
When X has a discrete range, taking only integer values, one usually works with the *generating function*, $G(s)$, defined as

$$G(s) := \langle s^X \rangle = \sum_n s^n P(n), \tag{1.9}$$

instead of using the characteristic function. In this case, the moments of the random variable are related to the derivatives of the generating function at $s = 1$:

$$\langle n^k \rangle = \left(s \frac{\partial}{\partial s} \right)^k G(s)|_{s=1}. \tag{1.10}$$

As noted above, we can consider a random variable that is defined by a function of another random variable, i.e.

$$Y = f(X) \tag{1.11}$$

so when the random variable X takes the value x, the variable Y takes the value $f(x)$. The probability that Y takes a value in the interval $(y, y + \Delta y)$ is

$$P_Y(y)\Delta y = \int_{y<f(x)<y+\Delta y} dx P_X(x), \tag{1.12}$$

which can also be expressed as

$$P_Y(y) = \sum_{x_i | f(x_i)=y} P_X(x_i) \frac{1}{\frac{df(x)}{dx}|_{x=x_i}}. \tag{1.13}$$

$P_X(\bullet)$ gives the functional dependence of the probability density of the random variable X. We will omit the subscript X when confusion is not foreseen (as has been done above).

More in general, we can define a random variable with several components $X_1, \ldots, X_n$. The range will be the (Cartesian) product of the ranges of each component, and the probability distribution, $P(x_1, \ldots, x_n)$ is defined over this new range and is sometimes called the *joint probability distribution* for the n variables $X_1, \ldots, X_n$.
If we consider a subset, $X_1, \ldots, X_k$, of the variables, the probability that they take some definite values, $x_1, \ldots, x_k$, regardless of the values of the other variables, is

$$P(x_1, \ldots, x_k) := \int dx_{k+1} \ldots dx_n P(x_1, \ldots, x_k, x_{k+1}, \ldots, x_n). \tag{1.14}$$

It is called the *marginal distribution* for the subset. The probability that the variables $X_1, \ldots, X_k$ take the values $x_1, \ldots, x_k$ given some definite values, $x_{k+1}, \ldots, x_n$, for the other variables, $X_{k+1}, \ldots, X_n$ is

$$P(x_1, \ldots, x_k | x_{k+1}, \ldots, x_n) := \frac{P(x_1, \ldots, x_k, x_{k+1}, \ldots, x_n)}{P(x_{k+1}, \ldots, x_n)}. \tag{1.15}$$

It is called the *conditional probability*.

Several random variables are called *independent* if their joint probability factorizes i.e. $P(x_1, \ldots, x_n) = P_{X_1}(x_1) \ldots P_{X_n}(x_n)$, which implies that any conditional probability defined in the set is equal to the corresponding marginal probability. Several random variables are called *identically distributed* if their marginal probability densities are equal. For simplicity of notation, throughout the thesis, independent identically distributed random variables will be sometimes denoted as *i.i.d. r.v.*
The moments and the characteristic function of a multivariate distribution are defined analogously to the single-variable case:

$$\langle X_1^{m_1} \ldots X_n^{m_n} \rangle := \int dx_1 \ldots dx_n x_1^{m_1} \ldots x_n^{m_n} P(x_1, \ldots, x_n), \quad C(k_1, \ldots, k_n) := \langle e^{i(K_1 X_1 + \cdots + k_n X_n)} \rangle.$$

If the variables are independent, the moments and the characteristic function factorize. The *covariance* between the variables X_i, X_j is defined as:

$$\sigma_{i,j} := \langle (X_i - \langle X_i \rangle)(X_j - \langle X_j \rangle) \rangle = \langle X_i X_j \rangle - \langle X_i \rangle \langle X_j \rangle.$$

Two variables are called *uncorrelated* if their covariance is zero.

Often it is useful to consider a random variable, Y, that is the sum of other random variables $Y = X_1 + X_2$. The probability density of Y (letting X denote (X_1, X_2)) is given by:

$$P_Y(y) = \int dx_1 P_X(x_1, y - x_1). \tag{1.16}$$

It is immediate to see that the average of the sum is equal to the sum of the averages i.e. $\langle Y \rangle = \langle X_1 \rangle + \langle X_2 \rangle$. Moreover, if X_1 and X_2 are uncorrelated, the variance is the sum of the variances i.e. $\sigma_Y^2 = \sigma_{X_1}^2 + \sigma_{X_2}^2$. Finally, if X_1 and X_2 are independent, the characteristic (and the generating) function is the product of the singe-variable characteristic (or generating) function, i.e. $C_Y(k) = C_{X_1}(k)C_{X_2}(k)$. Obviously, these properties follow for more than two variables as well.

1.3 Stochastic Processes

A stochastic process can be seen as a family of random variables that depend on a parameter, t, (usually interpreted as time). A stochastic process is determined by the (infinite) hierarchy of joint distributions:

$$P_n(x_1, t_1; x_2, t_2; \ldots; x_n, t_n), \qquad n = 1, \ldots, \infty. \tag{1.17}$$

Due to the properties of joint probability distributions discused in the previous section, the functions P_n have to obey the following conditions:
(i) $P_n \geq 0$.
(ii) $\int dx_n P_n(x_1, t_1; \ldots; x_{n-1}, t_{n-1}; x_n, t_n) = P_{n-1}(x_1, t_1; \ldots; x_{n-1}, t_{n-1})$.
(iii) $\int dx_1 P_1(x_1, t_1) = 1$.
(iv) P_n does not change interchanging two pairs (x_k, t_k) and (x_l, t_l) (this is so because a variable is defined by the value of the parameter t, the time to which it corresponds).
Conversely, any set of functions obeying these four conditions determine a stochastic process. The subindex n (referring to the number of variables in the joint probability) will often be omitted, for notational brevity. Stochastic processes are the appropriate tool to study systems whose evolution over time is known only at a probabilistic level.

A stochastic process, $X(t)$, can also be defined as a function, f, of a random variable, Y, and an additional parameter, t, i.e. $X_Y(t) = f(Y, t)$ is a stochastic process. On inserting for Y one of its possible values, y, and ordinary function of t is obtained $X_y(t) = f(y, t)$. This is called a sample function or a realization of the process.
The equivalence between the two definitions was established by Kolmogorov [Kolmogorov, 1956]. However, the random variable and function corresponding to a given hierarchy may be rather abstract, away from physical intuition and difficult to work with, so in physical applications the specification of the process by the hierarchy P_n is often the more suitable one. This is the approach that will be followed in this thesis.

A stochastic process is called *stationary* when the joint distributions depend on time differences alone, i.e.

$$P(x_1, t_1 + \tau; x_n, t_n + \tau) = P(x_1, t_1; x_n, t_n). \tag{1.18}$$

In addition, the *one time probability*, $P(x, t)$, should be independent of time.

A stochastic process is called *Markov* if the conditional probability satisfies:

$$P(x_n, t_n|x_1, t_1, x_2, t_2; \ldots; x_{n-1}, t_{n-1}) = P(x_n, t_n|x_{n-1}, t_{n-1}), \tag{1.19}$$

for all $t_1 < t_2 < \cdots < t_n$. That is, the conditional probability depends only on the value of the latest condition and is completely independent of the values at previous times. A Markov process is completely determined by two functions, $P(x_1, t_1)$ and $P(x_2, t_2|x_1, t_1)$, since they allow to reconstruct all the hierarchy of distribution functions. For example, we see that:

$$\begin{aligned} P(x_3, t_3; x_2, t_2; x_1, t_1) &= P(x_3, t_3|x_2, t_2; x_1, t_1)P(x_2, t_2; x_1, t_1) \\ &= P(x_3, t_3|x_2, t_2)P(x_2, t_2|x_1, t_1)P(x_1, t_1), \end{aligned} \tag{1.20}$$

and similarly for higher order joint probabilities. Integrating both sides of (1.20) over x_2 and dividing over $P(x_1, t_1)$, we obtain:

$$P(x_3, t_3|x_1, t_1) = \int dx_2 P(x_3, t_3|x_2, t_2)P(x_2, t_2|x_1, t_1). \tag{1.21}$$

This identity is known as the *Chapman-Kolmogorov equation*. Any pair of functions $P(x_1, t_1)$ and $P(x_2, t_2|x_1, t_1)$ that are non-negative and follow the Chapman-Kolmogorov equation plus the relation $P(x_2, t_2) = \int dx_1 P(x_2, t_2|x_1, t_1)P(x_1, t_1)$ completely determine a Markov process.
The Chapman-Kolmogorov equation is the basic (closed) relation obeyed by all Markov processes.

A Markov process whose conditional probability depends only on time differences, i.e. $P(x_2, t_2|x_1, t_1) = P(x_2, t_2 + \tau|x_1, t_1 + \tau)$, $\forall\tau$, is called *homogeneous*.

Often, one knows how the conditional probability behaves for infinitesimal time increments, and is interested in deriving the conditional probability for longer times (which allows to state the probabilities of future events given some initial state). We can assume that the conditional probability has the following expansion around zero time difference:

$$P(x_2, t + \Delta t|x_1, t) = (1 - W(x_1, t)\Delta t)\delta(x_2 - x_1) + W(x_2|x_1, t)\Delta t + o(\Delta t). \tag{1.22}$$

It involves the Dirac-delta function because $P(x_2, t|x_1, t) = \delta(x_1, x_2)$. $W(x_2|x_1, t)\Delta t$ is the probability that the system changes from x_1 to x_2 during the interval

$(t, t+\Delta t)$ (if it starts at state x_1 at time t). $1 - W(x_1,t)\Delta t$ is the probability that the system does not change from x_1 during the interval $(t, t+\Delta t)$, so they are related by:

$$W(x_1,t) = \int dx_2 W(x_2|x_1,t) \tag{1.23}$$

$W(x_2|x_1,t)$ is the probability per unit time that the system changes form x_1 to x_2 (provided it is at x_1). This function is called the *rate*. Setting in the Chapman-Kolmogorov equation (1.21) $t_1 = t_0, t_2 = t, t_3 = t + \Delta t$, we obtain:

$$P(x_3,t+\Delta|x_1,t_0) = P(x_3,t|x_1,t_0)(1-W(x_3,t)\Delta t) + \int dx_2 W(x_3|x_2,t)\Delta t P(x_2,t|x_1,t_0) + o(\Delta t) \tag{1.24}$$

Rearranging, taking the limit $\Delta t \to 0$ and using (1.23), we find:

$$\frac{\partial P(x_3,t|x_1,t_0)}{\partial t} = \int dx_2 \Big[W(x_3|x_2,t)P(x_2,t|x_1,t_0) - W(x_2|x_3,t)P(x_3,t|x_1,t_0) \Big]. \tag{1.25}$$

This is known as the master equation, and is the differential form of the Chapman-Kolmogorov equation. Obviously, the initial condition that has to be considered is $P(x_3,t_0|x_1,t_0) = \delta(x_3 - x_1)$. For a discrete range of states, it takes the form

$$\frac{\partial P(n,t|n_0,t_0)}{\partial t} = \sum_{n'} \Big[W(n|n',t)P(n',t|n_0,t_0) - W(n'|n,t)P(n,t|n_0,t_0) \Big]. \tag{1.26}$$

In this case, the appropriate initial conditions is $P(n,t_0|n',t_0) = \delta_{n,n'}$. This is the main equation one usually needs to solve when considering a stochastic process and it will play a central role in the remaining of the thesis.

Actually, the expansion of the conditional probability (1.22) is not the most general. It assumes that the system (typically) stays at x_1 during a finite time before changing to some other state $x_2 \neq x_1$. If the system may change its state continuously, one has to be more precise when establishing how the conditional probability behaves. In this case we assume the following conditions for all $\epsilon > 0$:

(i) $\lim_{\Delta t \to 0} \frac{1}{\Delta t} p(x_2, t+\Delta t|x_1,t) = W(x_2|x_1,t)$ for $|x_2 - x_1| > \epsilon$, uniformly in x_1, x_2 and t.

(ii) $\lim_{\Delta t \to 0} \frac{1}{\Delta t} \int_{|x_2-x_1|<\epsilon} dx_2 (x_2 - x_1) P(x_2, t+\Delta t|x_1,t) = A(x_1,t) + O(\epsilon)$, uniformly in ϵ, x_1, t.

(iii) $\lim_{\Delta t \to 0} \frac{1}{\Delta t} \int_{|x_2-x_1|<\epsilon} dx_2 (x_2 - x_1)^2 P(x_2, t+\Delta t|x_1,t) = B(x_1,t) + O(\epsilon)$, uniformly in ϵ, x_1, t.

Under these conditions, the differential form of the Chapman-Kolmogorov equation is [Gardiner, 1985]:

$$\begin{aligned}\frac{\partial P(x_3,t|x_1,t_0)}{\partial t} &= \int dx_2\Big[W(x_3|x_2,t)P(x_2,t|x_1,t_0) - W(x_2|x_3,t)P(x_3,t|x_1,t_0)\Big] \\ &- \frac{\partial}{\partial x_3}[A(x_3,t)P(x_3,t|x_1,t_0)] + \frac{1}{2}\frac{\partial^2}{\partial x_3^2}[B(x_3,t)P(x_3,t|x_1,t_0)] \quad (1.27)\end{aligned}$$

It can be shown [Gihman and Skorohod, 1974] that, with probability one, a Markov process in which $\lim_{\Delta t\to 0}\int_{|x_2-x_1|<\epsilon} dx_2 P(x_2,t+\Delta t|x_1,t) = 0$ uniformly in x_1 and t (i.e. the rate $W(x_2|x_1,t)$ of condition (i) above vanishes) has continuous sample paths. Because of this, when equation (1.27) includes only the differential terms it describes Markov stochastic processes with continuous sample paths. Equation (1.27) with $W(x_1|x_2,t) = 0$ is know as the *Fokker-Planck equation*. It can be shown that it is the only finite order linear differential equation that can be obeyed by a probability [Pawula, 1967]. When higher order therms are present, the positivity condition is not respected. The rates $W(x_2|x_1,t)$ give rise to discontinuous sample paths with discrete increments, in the sense that the system may stay for a finite time at x_1 and at given time change (instantaneously) to a state x_2 at a finite distance from x_1.

It can be shown [Gardiner, 1985] that the Fokker-Planck equation is equivalent to a *stochastic differential equation* of the form:

$$\frac{dx}{dt} = A(x,t) + \sqrt{B(x,t)}\xi(t). \quad (1.28)$$

Here, $\xi_(t)$ is a stochastic process such that its integral is equal to the *Wiener process*, i.e.

$$\int_0^t dt'\xi(t') = W(t), \quad (1.29)$$

with $W(t)$ the Wiener process, that is defined as a Markov process with $P_W(x,t=0) = \delta(x)$, $P(x,t|x_0,t_0) = \frac{1}{\sqrt{2\phi(t-t_0)}}e^{-(x-x_0)^2/2/(t-t_0)^2}$. Actually, the sample paths of the Wiener process are not differentiable, and we end up with a somewhat singular property for $\xi(t)$: $\langle\xi(t)\xi(t')\rangle = \delta(t-t')$. The formalization of these ideas lead to the development of stochastic calculus. (1.28) is equivalent to (1.27) with $W(x_2|x_3,t) = 0$, in the Ito interpretation. We refrain from exposing here the details of stochastic calculus because it will not be used in the thesis.
Fokker-Planck equations and stochastic differential equations are powerful tools for the study of stochastic processes with continuous transitions, and also as approximations for processes with discontinuous transitions. Moreover, they suggest a simple way to study the role of randomicity and fluctuations in a

system for which the deterministic counterpart is known [Lanvevin, 1908]. If the deterministic evolution of x is given by $\frac{dx}{dt} = a(x,t)$, then one can include some sources of randomicity by changing the previous equation into another of the form (1.28). This is a rather popular approach, although some times it is used in an ad-hoc manner.

In this thesis we will be considering mainly processes with discrete range of states, for which the expansion (1.22) and the master equation (1.26) are appropriate. Processes satisfying (1.22) are some times referred to as *jump* processes. We will respect as much as possible the discrete nature of the processes we study an only rarely use Fokker-Planck or stochastic differential equations. We prefer this approach because in it the microscopic origins of the stochasticity are more clearly stated, and the macroscopic fluctuations are derived from them. However, the stochastic differential equation (also denoted as Langevin) approach can be very useful and some times preferable, and in general, it complements the master equation approach that we follow and develope in this thesis.

As derived, the master equation is an equation for the conditional probability of a Markov process. More in general, one can derive a similar equation for the one time probability. We illustrate the derivation for the case of a discrete range of states. The case of continuous range in similar, replacing the sums by integrals. For any stochastic process (Markov or not), we have the following identity:

$$P(n,t+\Delta t) = \sum_{n'} P(n,t+\Delta t; n',t) = \sum_{n'} P(n,t+\Delta t|n',t)P(n',t). \tag{1.30}$$

We can now expand $P(n,t+\Delta t|n',t)$ to first order in Δt (this expression should include a Kronecker-delta function since $P(n,t|n',t) = \delta_{n,n'}$). Then, taking the limit $\Delta t \to 0$, it is possible to derive a differential equation for the one-time probability. For non-Markov processes, the expression for $P(n,t+\Delta t|n',t)$ may depend on probabilities conditioned at several previous times, but often one can, at least formally, obtain a differential equation for the one time probability of the form:

$$\frac{\partial P(n,t)}{\partial t} = \sum_{n'} \Big[f(n,n')P(n',t) - g(n,n')P(n,t) \Big]. \tag{1.31}$$

In this case, the initial condition is not fixed, and depends on the particular situation considered. We will use the term master equation to refer to a differential equation for a probability distribution (conditioned or one-time). In this sense, eq.(1.31) and eq.(1.26) are both master equations. Actually, for Markov processes, the one-time probability follows a master equation identical to the one followed by the conditional probability, as can be seen by multiplying both sides of (1.26) by $P(n_0,t_0)$ and summing over all n_0. With this in mind, when analyzing Markov processes, we will some times refer to the master equation

for the one time probability and for the conditional probability interchangeably and we will often write the equation for the former for brevity in the notation. For non-Markov processes, the equations for the one-time probability and the conditional probability are no longer identical, and careful distinction between the two has to be made.

The master equation plays such a central role in this thesis, that we will analyze some of its properties and methods for its solution in the next sections.

1.4 Some basic properties of the master equation

The master equation (1.26) is a system of coupled linear differential equations. It is convenient to write it in matricidal form:

$$\frac{dP_n(t)}{dt} = \sum_{n'} A_{n,n'} P_{n'}(t), \tag{1.32}$$

with the matrix A defined as $A_{n,n'} = W(n|n',t) - \delta_{n,n'} \sum_{n''} W(n''|n,t)$. This is however not a general system of linear differential equations, since the matrix defining it has the following properties:

$$A_{n,n'} \geq 0 \ \forall n \neq n', \tag{1.33}$$

$$\sum_{n} A_{n,n'} = 0 \ \forall n'. \tag{1.34}$$

We now focus on homogeneous processes for which the matrix A is time-independent. (1.34) implies that there is a left eigenvector with zero eigenvalue $((1,1,1,\dots))$ which in turn implies that there exist at least one right eigenvector with zero eigenvalue. Each (right) eigenvector of A is a stationary solution of the master equation. When normalized, it corresponds to a stationary probability distribution of the system (note that due to (1.34) the normalization $\sum_n P_n = 1$ is conserved during the evolution).

A central result of the theory of stochastic processes shows that the stationary solution of the master equation is unique and all time-dependent solutions tend to it [van Kampen, 2004], except in some special circumstances with a clear physical interpretation that we detail below. This implies that, regardless the initial conditions, the system will evolve towards a unique steady state, so we can obtain some of the most important properties of the system by just studying this single steady state.

The matrix A is called *decomposable* if by a simultaneous permutation of rows and columns (which amounts to a relabeling of the states) it can be cast into the following form:

$$A = \begin{pmatrix} \mathbb{U} & 0 \\ 0 & \mathbb{V} \end{pmatrix} \tag{1.35}$$

with $\mathbb{U}, \mathbb{V}$ square matrices of lower dimensionality. It is easy to see that $\mathbb{U}, \mathbb{V}$ follow (1.33, 1.34). In this case, the matrix A has at least two linearly independent eigenvectors with zero eigenvalues, ϕ_u, ϕ_v (corresponding to independent stationary probability distributions) satisfying

$$\begin{pmatrix} \mathbb{U} & 0 \\ 0 & \mathbb{V} \end{pmatrix} \begin{pmatrix} \phi_u \\ 0 \end{pmatrix} = 0 \quad \text{and} \quad \begin{pmatrix} \mathbb{U} & 0 \\ 0 & \mathbb{V} \end{pmatrix} \begin{pmatrix} 0 \\ \phi_v \end{pmatrix} = 0 \tag{1.36}$$

A decomposable matrix corresponds to a system composed by two non-interacting subsystems, the evolution of each one given by the matrix $\mathbb{U}$ and $\mathbb{V}$ respectively. Systems with a decomposable matrix can be analyzed studding the subsystems that compose it independently.
The matrix A is called of *splitting* type if can be cast into the form:

$$A = \begin{pmatrix} \mathbb{U} & 0 & \mathbb{R} \\ 0 & \mathbb{V} & \mathbb{S} \\ 0 & 0 & \mathbb{W} \end{pmatrix} \tag{1.37}$$

with $\mathbb{U}, \mathbb{V}$ following (1.33, 1.34), $\mathbb{W}$ a square matrix and some elements of $\mathbb{R}$ and $\mathbb{S}$ nonzero. In this case, it can be easily shown that the total probability of states corresponding to $\mathbb{W}$ decreases, increasing those of $\mathbb{U}$ and $\mathbb{V}$. States corresponding to $\mathbb{W}$ are called *transient*. Once the transient states are eliminated, in the limit $t \to \infty$, the system is decomposable.

It can be proven that, unless the matrix defining the master equation is decomposable or of splitting type, the stationary solution is unique and any time-dependent solution tends to it [van Kampen, 2004]. The proof is strictly valid only for systems with a finite range. The uniqueness of the stationary state is usually valid also for systems with finite number of states or a continuous range, but exceptions exist (such as the random walk).

A special case of Markov processes whose master equation is particularly easy to be solved are *one-step processes*. One-step processes are characterize by the variable changing only one unit in each fundamental transition. This means that the transition rates $W(n|n',t)$ are of the form $W(n|n',t) = c(n',t)\delta_{n,n'+1} + d(n',t)\delta_{n,n'-1} + [1 - c(n',t) + d(n',t)]\delta_{n,n'}$, so the master equation reads:

$$\frac{\partial P(n,t)}{\partial t} = c(n-1,t)P(n-1,t) + d(n+1,t)P(n+1,t) - [c(n,t) + d(n,t)]P(n,t) \tag{1.38}$$

Equation (1.38) can be written in a more compact way using the step operator E, that acting over a function of n gives the function displaced on one unit, i.e. $Ef(n) = f(n+1)$. (1.38) is equivalent to:

$$\frac{\partial P(n,t)}{\partial t} = (E-1)\left[d(n,t)P(n,t)\right] + (E^{-1}-1)\left[c(n,t)P(n,t)\right]. \tag{1.39}$$

The notation using the step operator E will be employed often in the thesis. If the range of the process is not infinite, some boundary conditions have to be imposed. For example, if the range is the non-negative integers, $n = 0, 1, 2, \ldots$, (as would be the case if n corresponds to the number of a certain kind of molecules in a system, for example) (1.39) has to be supplemented with a boundary condition at $n = 0$. We could replace (1.39) for $n = 0$ by $\frac{\partial P(0,t)}{\partial t} = d(1,t)P(1,t) - [c(n,t)]P(0,t)$. This is not necessary if $d(0,t) = 0, c(-1,t) = 0$; in this case, (1.39) may be considered valid for all n (provided that the initial condition assigns non-zero probabilities only for $n \geq 0$).

When the process is homogeneous i.e. the rates $c(n)$ and $d(n)$ do not depend on t, the system approaches a stationary state, in which the one-time probability $P_{st}(n)$ is also independent of t. The properties of this stationary state, can be obtained imposing $\frac{\partial P(n,t)}{\partial t} = 0 \ \ \forall n$ in the master equation (1.39). We obtain [van Kampen, 2004]:

$$\begin{aligned} &c(n-1)P_{st}(n-1) + d(n+1)P_{st}(n+1) - [c(n)+d(n)]P_{st}(n) = 0 \Rightarrow \\ &d(n)P_{st}(n) - c(n-1)P_{st}(n-1) = d(n+1)P_{st}(n+1) - c(n)P_{st}(n). \end{aligned} \tag{1.40}$$

The last equality implies that $d(n)P_{st}(n) - c(n-1)P_{st}(n-1) = J$ independent of n. In the case of a non-negative range, this equation applied at $n = 0$ implies $J = 0$. Then, by induction, one can show that:

$$P_{st}(n) = P_{st}(0)\prod_{k=0}^{n}\frac{c(k)}{d(k+1)}, \tag{1.41}$$

for $n \neq 0$. $P_{st}(0)$ can be obtained imposing the normalization condition $\sum P_{st}(n) = 1$, obtaining

$$P_{st}(0) = \frac{1}{1 + \sum_{n=1}^{\infty}\prod_{k=0}^{n}\frac{c(k)}{d(k+1)}}. \tag{1.42}$$

If the range is infinite, or if there are some special boundary conditions, it is no longer possible to prove that $J = 0$. The stationary solution depends then on the value of J that depends on the situation under consideration. In many cases of interest, the variable n refers to a number of particles, therefore $n \geq 0$ and the solution with $J = 0$ holds.

1.4.1 Generating function

Sometimes it is possible to obtain the solution of the master equation by making use of the generating function (introduced in section (1.2)). We will illustrate this method by means of an example, that is itself significant for other chapters of the thesis.

We consider a set of particles, X. Each particle has a probability per unit of time γ of being eliminated and there is a probability per unit of time C for a new individual to enter in the population. Schematically, it is described by:

$$\emptyset \xrightarrow{C} X,\ X \xrightarrow{\gamma} \emptyset. \tag{1.43}$$

Note that $X \xrightarrow{\gamma} \emptyset$ means that every present particle has a rate γ of being eliminated, where as $\emptyset \xrightarrow{C} X$ means that there is a total rate C for a new particle to appear. We will often use this notation throughout the thesis.

We are interested in the probability that there are n X-particles at time t. This is known as the birth and death process. Its master equation is given by:

$$\frac{\partial P(n,t)}{\partial t} = \gamma(n+1)P(n+1,t) + CP(n-1,t) - (\gamma n + C)P(n,t) \tag{1.44}$$

This is of the form (1.26) with $W(n|n',t) = \gamma n'\delta_{n',n+1} + C\delta_{n',n-1}$.
Multiplying both sides of (1.44) by s^n and summing over all values of n, we get:

$$\frac{\partial G(s,t)}{\partial t} = \gamma(1-s)\frac{\partial G}{\partial s} + C(s-1)G(s,t) \tag{1.45}$$

This partial differential equation can be solved by the Lagrange method, and its solution with initial condition $G(s,0) = s^N$ (which comes from $P(n,0) = \delta_{n,N}$) is:

$$G(s,t) = e^{\frac{C}{\gamma}(s-1)(1-e^{-\gamma t})}\left(se^{-\gamma t} + 1 - e^{-\gamma t}\right)^N$$

Expanding $G(s,t)$ in powers of s we get the probabilities $P(n,t)$:

$$\begin{aligned} P(n,t) &= e^{-(1-e^{-\gamma t})c/\gamma} \sum_{k=0}^{\min\{n,N\}} \binom{N}{k} e^{-k\gamma t}(1-e^{-\gamma t})^{N-k}\left(\frac{C(1-e^{-\gamma t})}{\gamma}\right)^{n-k}\frac{1}{(n-k)!} \qquad (1.46)\\ &= (1-e^{-\gamma t})^{N-n}\left(\frac{C}{\gamma}\right)^n \frac{[-\gamma e^{-\gamma t}(1-e^{-\gamma t})]^N}{n!} U(-N, n+1-N, -\frac{Ce^{\gamma t}}{\gamma(1-e^{-\gamma t})^2}), \end{aligned}$$

with $U(a,b,c)$ the confluent hyper-geometric function. A simpler expression can be obtained for the moments, using the expression of those in terms of the

generating function (1.10). The first two read:

$$\langle n(t)\rangle = Ne^{-\gamma t} + \frac{C}{\gamma}(1 - e^{-\gamma t}) \tag{1.47}$$

$$\sigma^2(t) = \frac{C}{\gamma}(1 - e^{-\gamma t}) + Ne^{-\gamma t}(1 - e^{-\gamma t}) \tag{1.48}$$

The expression for the probabilities gets much simplified in the stationary state case, when we have:

$$G(s, t \to \infty) = e^{\frac{C}{\gamma}(s-1)}$$

$$P(n, t \to \infty) = P_{st}(n) = \frac{e^{-C/\gamma}}{n!}\left[\frac{C}{\gamma}\right]^n \tag{1.49}$$

a Poisson distribution with parameter $\frac{C}{\gamma}$. This could also be obtained using the results of the previous section, since this is a one-step process. One characteristic of the Poisson distribution is that its variance equal to the its value i.e. $\sigma^2 = \langle n\rangle$. In general processes, if the variance is greater than the mean value, we will say that the fluctuations are super-Poissonian. If the variance is smaller than the mean value, the fluctuations will be called sub-Poissonian.

We have seen that a birth and death process with a creation and annihilation rates that are independent of the state of the system (n), has Poissonian stationary state. If those rates depend on the state of the system, we will say that the system has feedback, and this fact will modify the fluctuations. For negative feedback (creation rate that decreases with the number of particles, or annihilation rate that increases) the size of the fluctuations relatively to the mean value are typically reduced[4]. The opposite is true for positive feedback (creation rate increasing with the state of the system or annihilation rate decreasing with it).

As we have seen, using the generating function we transform a set of coupled first order differential equations into a single partial differential equation. However, in many cases (when $W(n|n')$ are nonlinear functions of n') the equation obtained is a high order partial differential equation with non-constant coefficients and its general solution is not known. In this cases approximated methods are needed.

1.4.2 Van Kampen's expansion

In many cases the master equation depends on a large parameter, Ω, (usually the system size or volume) and the evolution of the system becomes deterministic

[4] this is stricly the case for the first order component of the fluctuations, given by van Kampen's expansion, that we will explain in the next subsection

as this parameter goes to infinity. In this cases a systematic expansion of the master equation in powers of $\Omega^{-1/2}$ is possible. Because is the case most often considered in this thesis, we will explain the expansion method for the case of a discrete range and an homogeneous process.

The expansion is based on the existence of two different scales. On one hand the macroscopic properties of the system are functions of the intensive variable x/Ω, so that we expect that the probability for a transition to take place depends on this variable i. e. as Ω varies the probability remains the same function of n/Ω. On the other hand, the size of the transition jumps are function of the extensive variable n.
Formally, it is assumed that we can write the transition probabilities as:

$$W_\Omega(n|n') = f(\Omega)\left[\Phi_0(\frac{n'}{\Omega}, n-n') + \Omega^{-1}\Phi_1(\frac{n'}{\Omega}, n-n') + \Omega^{-2}\Phi_2(\frac{n'}{\Omega}, n-n') + ...\right] \tag{1.50}$$

The master equation (1.26) can be written as:

$$\frac{\partial P(n,t)}{\partial t} = \sum_k (E^{-k} - 1)W_\Omega(n|n')P(n,t) \tag{1.51}$$

where E is a linear operator such that $E\Big[f(n)\Big] = f(n+1)$.

Next, the following ansatz is formulated:

$$n = \Omega\phi(t) + \Omega^{1/2}\xi \tag{1.52}$$

with $\phi, \xi \sim O(\Omega^0)$. This means that the stochastic variable n has a macroscopic component of order Ω and a fluctuating part of order $\Omega^{1/2}$. This ansatz is the essential step of the expansion and is justified because we will find that $P(n,t)$, when expressed in ξ, does not depend on Ω to first approximation.
Now we proceed performing the time-dependent change of variables from n to ξ in the master equation (1.51) and expanding in powers of Ω. We obtain:

$$\begin{aligned}\frac{\partial \Pi(\xi,t)}{\partial t} &= \Omega^{1/2}\frac{d\phi}{dt}\frac{\partial \Pi}{\partial \xi} + \sum_k \left(-k\Omega^{-1/2}\frac{\partial}{\partial \xi} + \frac{k^2}{2}\Omega^{-1}\frac{\partial^2}{\partial \xi^2} + ...\right)\times \\ &\quad \Big[\Phi_0(\phi,r) + \Omega^{-1/2}\Phi_0'(\phi,r) + \Omega^{-1}\Phi_1(\phi,r) + ...\Big]\Pi\end{aligned} \tag{1.53}$$

where $\Pi(\xi,t) = P(\Omega\phi(t) + \Omega^{1/2}\xi, t)$.
The terms of order $\Omega^{1/2}$ vanish if we choose $\phi(t)$ to satisfy:

$$\frac{d\phi}{dt} = \sum_k k\Phi_0(\phi,k) \tag{1.54}$$

This is the macroscopic equation. Next, the terms of order Ω^0 give:

$$\frac{\partial \Pi}{\partial t} = \frac{\partial}{\partial \xi}\left[\xi \Pi \sum_k k\Phi_0'(\phi,k)\right] + \frac{1}{2}\frac{\partial^2}{\partial \xi^2}\left[\Pi \sum_k k^2 \Phi_1(\phi,k)\right] \tag{1.55}$$

This is a linear Fokker-Planck equation whose coefficients depend on t through $\phi(t)$. Its solution is a Gaussian distribution and therefore is fully determined by the first two moments, which follow:

$$\frac{d\langle\xi\rangle}{dt} = -\langle\xi\rangle \sum_k k\Phi_0'(\phi,k), \tag{1.56}$$

$$\frac{d\langle\xi^2\rangle}{dt} = \langle\xi^2\rangle \sum_k \left[-2k\Phi_0'(\phi,k)\right] + \sum_k k^2\Phi_0(\phi,t). \tag{1.57}$$

The equations for $\langle\xi(t)\rangle$ and$\langle\xi^2(t)\rangle$ are linear and uncoupled, so they can be solved analytically, provided that we can solve the macroscopic equation for $\phi(t)$ (1.54) which in general is nonlinear. In the steady state, ϕ becomes a fixed value, and the equations for the moments can always be solved.If higher order terms are included in (1.55) the Gaussian character is lost. However, these corrections are of order $\Omega^{-1/2}$ and can be neglected in a first approximation. First order van Kampen's expansion is sometimes called the linear noise approximation.

This form of the expansion is valid when the macroscopic equation (1.54) has a fixed point as single attractor, which is the case most often found in practice. However, this is not always satisfied. An example is the case in which $\sum_k k\Phi_0(\phi,k) = 0$. In this situation, the fluctuations given by (1.57) grow linearly, which would mean that after some time they would become larger than the macroscopic part, indicating that the ansatz (1.52) is no longer valid. In this case one assumes that the probability depends on n and Ω only through n/Ω and an expansion in Ω^{-1} can be performed. For critical points in which $\sum_k k\Phi_0(\phi,k) = \sum_k k\Phi_0'(\phi,k) = \sum_k k\Phi_0''(\phi,k) = 0$ but $\sum_k k\Phi_0'''(\phi,k) < 0$, the valid scaling usually is $n = \Omega\phi + \Omega^{3/4}\xi$ and fluctuations are no longer Gaussian.

Van Kampen's expansion is a very valuable method, because it is rather general and provides analytical tractability. For these reasons, it will be employed often in this thesis.

Other expansion methods have been proposed. The approach developed by Kubo et al. [1967] starts assuming that the probability distribution scales with system size as $P(x,t) = C\exp[\Omega g_0(x,t) + g_1(x,t) + O(\Omega^{-1})]$, so that in the limit $\Omega \to \infty$ the distribution becomes a Dirac-delta around $g(0,t)$, obtaining a deterministic limit.

Sometimes, the master equation is written in terms of the intensive variable $x = n/\Omega$, so that the operator $(E^{-k} - 1)$ in (1.51) becomes $-k\Omega^{-1}\frac{\partial}{\partial x} + \frac{1}{2}k^2\Omega^{-2}\frac{\partial^2}{\partial x^2} + \dots$ and then the series is truncated at the desired order of Ω^{-1} [Sood et al., 2008]. In this approach, however, one is implicitly assuming that $\phi(x,t) = P(\frac{n}{\Omega}, t)$ does not depend on Ω, and the formalization of this idea leads to one of the methods explained above.

1.4.3 Gillespie method

An exact (in the sense of not biased) numerical algorithm for simulating realizations of a jump Markov process was proposed by Gillespie [1977].
The method is based on computing the time at which the next transition will take place, and then computing which transition will it be. It works for continous-time processes, generating exact sample paths of the process, with the appropriate probabilities.

In order to explain the method, we first note that the probability $p(t)$ that a transition that happens at a rate $w(t)$ occurs (for the first time) at time t (assuming it did not happen before $t = t_0$) follows:

$$\frac{dp(t)}{dt} = [1 - P(t)]w(t) \Rightarrow p(t) = w(t)e^{-\int_{t_0}^{t} w(t')dt'}, \tag{1.58}$$

with $P(t) = \int_0^t dt' p(t')$ the cumulative probability. This is so because the rate can be seen as the conditional probability that the transition happens at time t provided it did not happen before i.e. $w(t) = \frac{p(t)}{1-P(t)}$. In the case of a constant rate, this reduces to an exponential $p(t) = we^{-w(t-t_0)}$

If there are k possible transitions, each one with a rate $w_i(t), i = 1, \dots k$, the time at which transition i will actually happen is given by (1.58). In principle, we could simulate all these individual transitions (generating a sample of a random variable distributed according to (1.58) with the appropriate rate for each process), and then select the one that happens first and execute it. If the rates depend on the state of the system, we would have to simulate again all the possible transitions each time the state of the system is changed. The Gillespie method allows to avoid simulating all the transitions, simulating instead only the one that will happen first.
For this, we note that the time (τ) at which the first transition will take place is the minimum of the times of the individual transitions and is, then, distributed

according to the following probability density:

$$\begin{aligned} p(\tau = t) &= \sum_{i=1}^{k} p(t_i = t) \prod_{j \neq i} [1 - P(t_j)] = \sum_{i=1}^{k} w_i(t) e^{-\int_{t_0}^{t} dt' w_i(t')} e^{\sum_{j \neq i} - \int_{t_0}^{t} dt' w_j(t')} \\ &= w_{tot}(t) e^{-\int_{t_0}^{t} dt' w_{tot}(t')}, \end{aligned} \tag{1.59}$$

with $w_{tot}(t) = \sum_{i=1}^{k} w_i(t)$. For constant rates, it again reduces to an exponential. We have used the fact that the individual transitions are independent.
In the case of the birth and death process commented in a previous section, there are two possible transitions:
(i) Birth of and individual at a rate C, (ii) death of an individual at a rate $n\gamma$ (n being the number of alive individuals).
Once we know when the first transition will take place, we need to know which transition will it be. The probability for transition i can be calculated as follows:

$$\begin{aligned} &P(i \text{ happens at } t | \text{fist reaction happed at } t) \\ &= \frac{P(\text{no reaction happens before t; } i \text{ happens at } t)}{P(\text{fist reaction happed at } t)} \\ &= \frac{e^{-\int_{t_0}^{t} dt' w_{tot}(t')} w_i(t)}{w_{tot}(t) e^{\int_{t_0}^{t} dt' w_{tot}(t')}} = \frac{w_i(t)}{w_{tot}(t)}, \end{aligned} \tag{1.60}$$

so we see it is just proportional to its rate $w_i(t)$.

The Gillespie algorithm, then, works as follows:
1. Compute the transition rates, $\omega_i(t)$, (which depend on the state of the system) and the total rate, $w_{tot}(t) = \sum_{i=1}^{k} w_i(t)$.
2. Obtain the time, τ, at which a transition takes place, from a random number distributed following $p(\tau = t) = w_{tot}(t) e^{-\int_{t_0}^{t} dt' w_{tot}(t')}$.
3. Establish which transition takes place, each of them having a probability proportional to it's rate.
4. Update the state of the system according to the transition chosen, and the time adding the value τ.
Go back to 1.

We can go from 4 to 1 because the rate of a transition tells us precisely the probability that the transition will happen provided it did not happen yet. If there are two possible reactions (a and b) and 3 tells us that a happens at time t, then the probability that b happens from t can be calculated using its rate from time t, going back to 1.

In the case of constant rates, step 2 can be calculated from $\tau = -\frac{1}{w_{tot}} log(u)$, with u a random number uniformly distributed between 0 and 1. For time-dependent rates it can be numerically generated using different methods [Gillespie, 1992].

To obtain mean values of arbitrary functions we can perform M different realizations of the process via this method and average the corresponding results. The sample average, S_{av}, of a random variable X is defined as:

$$S_{av} = \sum_{i=1}^{M} \frac{x_i}{M}, \tag{1.61}$$

where x_i is the value of the variable X in realization i. S_{av} is a *non-biased estimator* of the mean of the variable X, since $\langle S_{av} \rangle = \langle x \rangle$. Moreover, its variance is $\sigma^2[S_{av}] = \frac{\sigma^2[x]}{M}$, so we see that as M (the number of realizations) grows, the variance of S_{av} decreases, approaching a Dirac-delta around the actual mean of X, $\langle x \rangle$. Moreover, due to the central limit theorem, S_{av} is Gaussian-distributed, so confidence intervals can be provided.
If the process is ergodic, the averages can be taken over time instead of over realizations. The considerations above assume that the different values of x_i are uncorrelated, so to apply when one does averages over time, one has to choose a time difference such that the correlation between the points can be neglected. When the different values x_i are correlated, the variance of S_{av} is larger if the correlations are positive. Assuming that the correlations between different measures decreases exponentially with distance i.e. $\langle x_i x_j \rangle - \langle x_i \rangle \langle x_j \rangle = \sigma^2 e^{-|i-j|/\tau}$, with τ the correlation length, we obtain that the variance of the sample mean is: $\sigma^2[S_{av}] = \frac{\sigma^2[x]}{M}(1 + \frac{2}{e^{1/\tau}-1}) - \frac{\sigma^2[x]}{M^2} 2 \frac{e^{1/\tau} - e^{(1-M)/\tau}}{(e^{1/\tau}-1)^2} \simeq \frac{\sigma^2[x]}{M}(1 + 2\tau)$, the last equality bein valid for τ moderatelly larger than 1 and $M >> \tau^2$.

We see that the error in the averages obtained in this way decays as $M^{-1/2}$, so when high accuracy is needed this numerical method can be slow.

Part II

The Gaussian approximation

Chapter 2

Gaussian approximation for Master equations

In this chapter, we will analyze the Gaussian approximation as a method to obtain the first and second moments of a stochastic process described by a master equation. The use of this approximation is justified by ideas coming from van Kampen's expansion approach (the fact that the probability distribution is Gaussian at first order). We will analyze the scaling of the error with a large parameter of the system and compare it with van Kampen's method. Our theoretical analysis and the study of several examples shows that the Gaussian approximation turns out to be more accurate than van Kampen's expansion at first order. This could be specially important for problems involving stochastic processes in systems with a small number of particles.

2.1

Introduction

Master equations are a convenient tool to treat stochastic Markov processes [van Kampen, 2004; Gardiner, 1985]. In some cases, they constitute the differential form of the Chapman-Kolmogorov equation and have been used extensively in discrete-jumps, or birth-death, processes, such as chemical reactions (including those happening inside a cell) [Gillespie, 1977], population dynamics or other ecology problems [Pigolotti et al., 2005], opinion formation and cultural transmission in the field of sociophysics [Castellano et al., 2009], etc. In all these cases, it is important to consider that the population number (whether molecules, in-

dividuals, agents, etc.) might not be very large (maybe ranging in the tens or hundreds) and the fluctuations, whose relative magnitude typically scales as the square root of the inverse of this number, can not be considered as negligible. It is therefore, of the greatest importance to derive evolution equations for the average behavior and the fluctuations. The important work by van Kampen [van Kampen, 2004] offers a systematic way of deriving these equations from an expansion of the master equation in a parameter Ω, typically the system volume. The Ω-expansion is mostly used in its lowest order form, in which one can prove that the error in the average value, the second moment and the fluctuations (the variance), scale at most as Ω^0, Ω^1 and $\Omega^{1/2}$, respectively. The van Kampen Ω-expansion, furthermore, shows that, at this lowest order, the fluctuations follow a Gaussian distribution. Here, we take this result of van Kampen's theory and, considering from the very beginning that fluctuations are Gaussian, we derive a closed system of equations for the average value and the second moment. This Gaussian closure of the hierarchy of moments turns out to be more accurate than the Ω-expansion as the above-mentioned errors scale at most as $\Omega^{-1/2}$, $\Omega^{1/2}$ and $\Omega^{1/2}$, respectively. Furthermore, the Gaussian closure scheme is very simple to carry on in practice and can be easily generalized to systems described by more than one variable. An alternative approach to deal with master equations (specially useful in spatially extended systems) consist on mapping the master equation to a Schrödinger equation in imaginary time in the second quantization formalism [Doi, 1976; Peliti, 1985].

The chapter is organized as follows: In the following section, we will briefly review the Ω-expansion and derive the main equations for the Gaussian closure approximation. The errors of both methods are discussed in section 2.3. In sections 2.4 and 2.5, we will give examples of the application of the method in the cases of a binary chemical reaction and an autocatalytic reaction. The results of these two examples confirm the error-analysis performed before. For both processes we compare with the results coming from the exact solution of the master equation in the stationary regime (derived in the appendix for the binary chemical reaction), and the results of numerical simulations using the Gillespie algorithm in the time-dependent evolution. In section 2.6 we present an application to a recently introduced model for opinion formation which requires two variables for its full description. Finally, in section 2.7 we end with a brief summary of the work.

2.2 Formulation

Let $P(n,t)$ be the probability that at time t the population number takes the value n. We consider that it evolves according to a general master equation of the form:

$$\frac{\partial P(n,t)}{\partial t} = \sum_k (E^k - 1)\left[C_k(n;\Omega)P(n,t)\right], \tag{2.1}$$

where k runs over the integer numbers. Besides n, the coefficients $C_k(n;\Omega)$ depend on Ω, which is a large parameter of the system (typically the system volume). We consider that these functions are polynomials or can be expanded in power series of n as $C_k(n;\Omega) = \sum_a C_k^a(\Omega)n^a$ where the coefficients $C_k^a(\Omega)$ scale as
$C_k^a(\Omega) = \Omega^{1-a}\left(c_{k,0}^a + c_{k,1}^a\Omega^{-1} + c_{k,2}^a\Omega^{-2} + \dots\right)$. Master equations of this form appear in the description of chemical reactions [Gillespie, 1977], ecological systems [Pigolotti et al., 2005] and opinion dynamics [de la Lama et al., 2006], among many other cases. More specific examples will be considered in the next sections.

In his seminal work, van Kampen [van Kampen, 2004] (section 1.4.2) has given a way of finding an approximate solution of Eq. (2.1). The approximation is based upon the splitting of the variable n using the ansatz $n = \Omega\phi(t) + \Omega^{\frac{1}{2}}\xi$, where $\phi(t) \sim O(\Omega^0)$ is a function of time accounting for the deterministic part of n and $\xi \sim O(\Omega^0)$ corresponds to the fluctuations. Changing variables from n to ξ in Eq. (2.1), and expanding in powers of Ω one obtains a Fokker-Planck equation for the probability distribution $\Pi(\xi,t)$ of the new variable ξ:

$$\frac{\partial \Pi(\xi,t)}{\partial t} = \left[\sum_{a,k} c_{k,0}^a ka\phi^{a-1}\right]\frac{\partial(\xi\Pi)}{\partial\xi} + \left[\sum_{a,k} c_{k,0}^a \frac{k^2}{2}\phi^a\right]\frac{\partial^2\Pi}{\partial\xi^2} + O(\Omega^{-\frac{1}{2}}), \tag{2.2}$$

where the macroscopic variable ϕ satisfies

$$\frac{d\phi(t)}{dt} = \sum_{a,k} kc_{k,0}^a\phi^a. \tag{2.3}$$

From Eq.(2.2) we obtain the first and second moments of the fluctuations:

$$\frac{\partial\langle\xi\rangle}{\partial t} = -\left[\sum_{a,k} c_{k,0}^a ka\phi^{a-1}\right]\langle\xi\rangle, \tag{2.4}$$

$$\frac{\partial\langle\xi^2\rangle}{\partial t} = -2\left[\sum_{a,k} c_{k,0}^a ka\phi^{a-1}\right]\langle\xi^2\rangle + 2\left[\sum_{a,k} c_{k,0}^a \frac{k^2}{2}\phi^a\right]. \tag{2.5}$$

CHAPTER 2. GAUSSIAN APPROXIMATION FOR MASTER EQUATIONS

As proven by van Kampen, the solution of the Fokker-Planck equation (2.2) is a Gaussian distribution. Therefore, the Ω-expansion method tells us that, up to corrections of order $\Omega^{-\frac{1}{2}}$, the fluctuations of the variable n follow a Gaussian distribution. It suffices, then, to know the first and second moments of this distribution. Our intention is to use from the very beginning the Gaussian property in order to obtain a closed system of equations for the first two moments $\langle n\rangle$ and $\langle n^2\rangle$.

From (2.1) we get the (exact) equations for these first two moments, as:

$$\frac{d\langle n\rangle}{dt} = -\sum_k \langle kC_k(n;\Omega)\rangle\,, \qquad \frac{d\langle n^2\rangle}{dt} = \sum_k \langle k(k-2n)C_k(n;\Omega)\rangle\,. \tag{2.6}$$

After substitution of the series expansion $C_k(n;\Omega) = \sum_a C_k^a(\Omega)n^a$ in the right hand side of these equations, one obtains higher order moments $\langle n^m\rangle$ for $m \geq 3$. The Gaussian closure replaces these higher order moments with the expressions $\langle n^m\rangle_G$ that hold in the case of a Gaussian distribution, i.e. $\langle n\rangle_G = \langle n\rangle$, $\langle n^2\rangle_G = \langle n^2\rangle$ and

$$\langle n^m\rangle_G = \langle n\rangle^m + \sum_{k=1}^{\left[\frac{m}{2}\right]} \binom{m}{2k}(2k-1)!!\langle n\rangle^{m-2k}\left[\langle n^2\rangle - \langle n\rangle^2\right]^k \tag{2.7}$$

for $m \geq 3$. The first moments are explicitly shown in table 2.1.

Moment	Gaussian approximation
$\langle n^3\rangle$	$3\langle n^2\rangle\langle n\rangle - 2\langle n\rangle^3$
$\langle n^4\rangle$	$3\langle n^2\rangle^2 - 2\langle n\rangle^4$
$\langle n^5\rangle$	$15\langle n^2\rangle^2\langle n\rangle - 20\langle n^2\rangle\langle n\rangle^3 + 6\langle n\rangle^5$
$\langle n^6\rangle$	$15\langle n^2\rangle^3 - 30\langle n^2\rangle\langle n\rangle^4 + 45\langle n\rangle^6$
$\langle n_1^2 n_2\rangle$	$\langle n_1^2\rangle\langle n_2\rangle + 2\langle n_1\rangle\langle n_1 n_2\rangle - 2\langle n_1\rangle^2\langle n_2\rangle$
$\langle n_1^2 n_2^2\rangle$	$\langle n_1^2\rangle\langle n_2^2\rangle + 2\langle n_1 n_2\rangle^2 - 2\langle n1\rangle^2\langle n2\rangle^2$
$\langle n_1^3 n_2\rangle$	$3\langle n_1^2\rangle\langle n_1 n_2\rangle - 2\langle n1\rangle^3\langle n2\rangle$
$\langle n_1^3 n_2^2\rangle$	$6\langle n_1 n_2\rangle^2\langle n_1\rangle + 6\langle n1\rangle^3\langle n2\rangle^2 + 6\langle n_1 n2\rangle\langle n_2\rangle(\langle n_1\rangle^2 - 2\langle n_1\rangle^2$ $-6\langle n_1^2\rangle\langle n_2\rangle^2\langle n_1\rangle + 3\langle n_1^2\rangle\langle n_2^2\rangle\langle n_1\rangle - 2\langle n_1\rangle^3\langle n_2^2\rangle$

Table 2.1: Gaussian moments

The van Kampen ansatz $n = \Omega\phi(t) + \Omega^{\frac{1}{2}}\xi$ allows us to find the error of this approximation. It follows that:

$$\frac{\langle n^m\rangle}{\Omega^{m-1}} = \sum_{l=0}^{m}\binom{m}{l}\Omega^{1-l/2}\phi^{m-l}\langle\xi^l\rangle. \tag{2.8}$$

In the Gaussian approximation, the first three terms of the sum, $l = 0, 1, 2$ are exact and the term $l = 3$ scales as $\Omega^{-1/2}$, or:

$$\frac{\langle n^m \rangle}{\Omega^{m-1}} = \frac{\langle n^m \rangle_G}{\Omega^{m-1}} + O(\Omega^{-1/2}). \tag{2.9}$$

If we use this result in each of the terms of Eq.(2.6) and $C_k(n;\Omega) = \Omega^{1-a}(c^a_{k,0} + O(\Omega^{-1}))$ we obtain

$$\frac{d\langle n \rangle}{dt} = g_1(\langle n \rangle, \langle n^2 \rangle) + O(\Omega^{-1/2}), \tag{2.10}$$

with $g_1 \equiv -\sum_k \langle k C_k(n;\Omega) \rangle_G$. Similarly, one finds

$$\frac{d\langle n^2 \rangle}{dt} = g_2(\langle n \rangle, \langle n^2 \rangle) + O(\Omega^{1/2}), \tag{2.11}$$

with $g_2 \equiv \sum_k \langle k(k-2n) C_k(n;\Omega) \rangle_G$.

This Gaussian approximation scheme (or equivalently, finding a hierarchy of equations for the cumulants and neglecting those of order greater than two) has been used many times in the literature in different contexts [Desai and Zwanzig, 1978; Cubero, 2008]. We will show in the next section that the direct use of Eqs. (2.10,2.11) has a smaller error that the use of Eqs. (2.3-2.5). Before showing this, we will generalize this procedure for the case of two-variable problems. Let us consider a master equation of the following form:

$$\frac{\partial P(n_1, n_2, t)}{\partial t} = \sum_{k_1,k_2} (E_1^{k_1} E_2^{k_2} - 1) \left[C_{k_1,k_2}(n_1, n_2; \Omega) P(n_1, n_2, t) \right]. \tag{2.12}$$

The evolution equations for the first, second order moments and the correlations are:

$$\frac{d\langle n_i \rangle}{dt} = -\sum_{k_1,k_2} \langle k_i C_{k_1,k_2}(n_1, n_2; \Omega) \rangle, \tag{2.13}$$

$$\frac{d\langle n_i^2 \rangle}{dt} = \sum_{k_1,k_2} \langle k_i(k_i - 2n_i) C_{k_1,k_2}(n_1, n_2; \Omega) \rangle, \tag{2.14}$$

$$\frac{d\langle n_1 n_2 \rangle}{dt} = \sum_{k_1,k_2} \langle (k_1 k_2 - k_2 n_1 - k_1 n_2) C_{k_1,k_2}(n_1, n_2; \Omega) \rangle, \tag{2.15}$$

($i = 1, 2$). Again, the Gaussian closure consists in replacing $\langle n_1^{m_1} n_2^{m_2} \rangle$ by the expression $\langle n_1^{m_1} n_2^{m_2} \rangle_G$ that holds assuming that the joint distribution $P(n_1, n_2, t)$ is Gaussian. This can be computed using Wick's theorem [Amit and Martin-Mayor, 2005]. In table (2.1) we write the expression of some of the terms.

2.3

Error of the method

We now calculate the error of the Gaussian approximation and compare it with the one of the Ω-expansion. In Eqs. (2.10-2.11) we have shown that the errors we introduce in the equations for the moments when performing the Gaussian approximation are of order $O(\Omega^{-1/2})$ for $\langle n\rangle$ and $O(\Omega^{1/2})$ for $\langle n^2\rangle$. The Gaussian approximation scheme proceeds by considering approximations $\mu_1(t)$, $\mu_2(t)$ to the true moments $\langle n(t)\rangle$, $\langle n^2(t)\rangle$. These approximations are defined as the solution of the evolution equations (2.10,2.11):

$$\frac{d\mu_1}{dt} = g_1(\mu_1,\mu_2), \qquad \frac{d\mu_2}{dt} = g_2(\mu_1,\mu_2). \tag{2.16}$$

Defining the errors ϵ_1, ϵ_2 as: $\langle n\rangle = \mu_1 + \epsilon_1$, $\langle n^2\rangle = \mu_2 + \epsilon_2$; expanding in first order in ϵ_1 and ϵ_2, and using equations (2.10-2.11) and (2.16) we get:

$$\frac{d\epsilon_1}{dt} = \frac{\partial g_1(\mu_1,\mu_2)}{\partial \mu_1}\epsilon_1 + \frac{\partial g_1(\mu_1,\mu_2)}{\partial \mu_2}\epsilon_2 + O(\Omega^{-1/2}), \tag{2.17}$$

$$\frac{d\epsilon_2}{dt} = \frac{\partial g_2(\mu_1,\mu_2)}{\partial \mu_1}\epsilon_1 + \frac{\partial g_2(\mu_1,\mu_2)}{\partial \mu_2}\epsilon_2 + O(\Omega^{1/2}). \tag{2.18}$$

Taking into account that $\mu_1, g_1 \sim O(\Omega)$, $\mu_2, g_2 \sim O(\Omega^2)$, we have:

$$\frac{d\epsilon_1}{dt} = O(\Omega^0)\epsilon_1 + O(\Omega^{-1})\epsilon_2 + O(\Omega^{-1/2}), \tag{2.19}$$

$$\frac{d\epsilon_2}{dt} = O(\Omega)\epsilon_1 + O(\Omega^0)\epsilon_2 + O(\Omega^{1/2}). \tag{2.20}$$

If we set $\epsilon_1 \sim O(\Omega^a)$, $\epsilon_2 \sim O(\Omega^b)$, and the initial conditions are known, so that initially $\epsilon_1 = \epsilon_2 = 0$, equations (2.19), (2.20) imply that $a \leq -1/2$ and $b \leq 1/2$, a scaling respected during the time evolution.

In conclusion, solving equations (2.10-2.11), we get $\langle n\rangle$ and $\langle n^2\rangle$ with errors of order $\epsilon_1 = O(\Omega^{-1/2})$ and $\epsilon_2 = O(\Omega^{1/2})$, or smaller. Using the equations (2.3-2.5) of first order van Kampen's expansion the error is of higher order in both cases: $O(\Omega^0)$ for $\langle n\rangle$ and $O(\Omega^1)$ for $\langle n^2\rangle$. However, for the variance, $\sigma^2 \equiv \langle n^2\rangle - \langle n\rangle^2$, both approximations have an error of order $O(\Omega^{1/2})$. We will show in the next sections that the Gaussian approximation has the extra advantage that it is easier to derive for many problems of practical interest.

One might be tempted to go to higher order schemes, where one neglects all the cumulants of order greater than m with $m > 2$, and in this way obtain a

closed set of equations for the first m moments. For example, if we neglect all the cumulants of order greater than 3, applying the same analysis as before, it is possible to derive that the errors in the first, second and third moments are of order $O(\Omega^{-1}, \Omega^0, \Omega^1)$, respectively.

A word of caution is needed here. When truncating beyond the second cumulant, it is not ensured that the resulting probability distribution is positive definite [Hänggi and Talkner, 1980]. This means that one could get from such an scheme inconsistent results, e.g. a negative variance. Nevertheless, according to our analysis, the importance of these spurious results would decrease with Ω as indicated, so one can still get useful results from higher order schemes.

The Gaussian approximation approach has two main limitations.
First, if the transition rates are not polynomials, the expansion in terms of moments can be rather cumbersome. One could also replace directly terms of the form $\langle f(n) \rangle$ by the expression one would obtain if $P(n)$ was Gaussian (that will only depend on $\langle n \rangle$ and σ^2) but this expression may diverge or give some misleading results due to the fact that a Gaussian distribution also accepts negative values, so care must be taken.
Second, the system of two differential equations obtained is non-linear, which implies that an analytical solution is generally not available. This is in contrast with first order van Kampen's expansion, that gives a system of linear differential equations that can always be solved (the equation for the macroscopic component ϕ may, however, be non-linear). This is specially useful when the method is employed as a part of a larger calculation and analytical expressions are needed to proceed (this is the case we will often face latter in the thesis, and the reason why van Kampen's expansion will be employed).
However, if one is interested only in the moments and requires higher precision and the rates are suitable, the Gaussian approximation is preferable to first order van Kampen's approach.

Van Kampen's expansion assumes that the average and the variance scale both linearly with Ω. This implies that the relative size of the standard deviation goes to zero as Ω grows, since $\sigma/\langle n \rangle = \Omega^{-1/2}$. In some cases this assumption may not be satisfied but the distribution could still be well approximated by a Gaussian (which allows arbitrary scaling for average and variance). Then the Gaussian approximation is expected to give better results than van Kampen's approach.

In the following sections we will compare the Gaussian approximation presented here with the first order Ω-expansion in some specific examples.

2.4 Binary reaction $A + B \underset{\omega}{\overset{\kappa}{\rightleftarrows}} C$

Chemical reactions are suitable processes for a stochastic description. The stochastic approach is specially necessary when the number of molecules considered is small, as it is the frequently addressed case of chemical reactions inside a cell, because in this situation fluctuations can be very important.

We consider the general process $A + B \underset{\omega}{\overset{\kappa}{\rightleftarrows}} C$, limited by reaction. This means that any two particles A and B have the same probability of reaction. Denoting by $A(t)$ and $B(t)$, respectively, the number of molecules of the A and B substances, the rate for the $A + B \longrightarrow C$ reaction is $\frac{\kappa}{\Omega}A(t)B(t)$. For the reverse reaction, it is assumed that C has a constant concentration, and hence the rate is $\omega\Omega$. In these expressions Ω is proportional to the total volume accessible. Since $B(t) - A(t) \equiv \Delta$ is a constant, one only needs to consider one variable, for example, the number of A molecules at time t. Let us denote by $P(n,t)$ the probability that there are n A-molecules at time t. The master equation describing the process is:

$$\frac{dP(n,t)}{dt} = \frac{\kappa}{\Omega}\left[(n+1)(\Delta+n+1)P(n+1,t) - n(n+\Delta)P(n,t)\right] + \omega\Omega[P(n-1,t) - P(n,t)], \tag{2.21}$$

which is the basis of the subsequent analysis. Note that this equation can be written in the form (2.1) setting $C_1(n;\Omega) = \frac{\kappa}{\Omega}n(n+\Delta)$, $C_{-1}(n;\Omega) = \omega\Omega$.

In the irreversible case, $\omega = 0$, this master equation can be solved exactly using the generating function technique. In the general case, $\omega \neq 0$, an exact solution can also be found for the stationary state $\frac{\partial P(n,t)}{\partial t} = 0$. Details of the calculation are given in the appendix. We will compare the results obtained from the Gaussian approximation and the first order Ω-expansion with the exact results, when available.

The equations for the first two moments, using (2.6), are:

$$\frac{d\langle n\rangle}{dt} = -\frac{\kappa}{\Omega}\left(\langle n^2\rangle + \Delta\langle n\rangle\right) + \Omega\omega, \tag{2.22}$$

$$\frac{d\langle n^2\rangle}{dt} = \frac{\kappa}{\Omega}(-2\langle n^3\rangle + (1-2\Delta)\langle n^2\rangle + \Delta\langle n\rangle) - 2\Omega\omega\langle n\rangle + \Omega\omega. \tag{2.23}$$

Using the Gaussian approximation, the evolution equations for the moments are:

$$\frac{d\mu_1}{dt} = -\frac{\kappa}{\Omega}(\mu_2 + \Delta\mu_1) + \Omega\omega, \tag{2.24}$$

$$\frac{\mu_2}{dt} = \frac{\kappa}{\Omega}(4\mu_1^3 - 6\mu_2\mu_1 + (1-2\Delta)\mu_2 + \Delta\mu_1) + 2\Omega\omega\mu_1 + \Omega\omega. \tag{2.25}$$

And the first order Ω-expansion gives:

$$\frac{d\phi}{dt} = -\kappa\phi(\phi+\delta) + \omega, \tag{2.26}$$

$$\frac{d\langle n\rangle}{dt} = \kappa\Omega\phi^2 - \kappa(\delta + 2\phi)\langle n\rangle + \Omega\omega, \tag{2.27}$$

$$\frac{d\langle n^2\rangle}{dt} = -2\kappa(2\phi+\delta)\langle n^2\rangle + \Omega\Big[\kappa\phi(\phi+\delta)(1-2\langle n\rangle) + 2(\kappa\Omega\phi^2(2\phi+\delta) + \omega(\langle n\rangle + 1 + \omega\phi))\Big], \tag{2.28}$$

where $\delta = \frac{\Delta}{\Omega}$.

We compare the two approximations in the time-dependent case with results obtained by averaging over single realizations of the process, obtained numerically using the Gillespie algorithm [Gillespie, 1977]. In the next figures we compare the exact results with those obtained from the Gaussian approximation (computed by numerical integration of equations 2.24, 2.25) and Ω-expansion (equations 2.26-2.28).

Figure (2.1) shows that the Gaussian approximation reproduces better the exact results for the first two moments; for the variance, the Ω-expansion gives more accurate results but both approximations differ from the exact values. Figure (2.2) shows that the errors in the stationary state, coming from the Gaussian approximation for the mean value, the second moment and the variance scale as (Ω^{-1}, Ω^0, Ω^0), respectively, while the errors of the Ω-expansion at first order scale as (Ω^0, Ω^1, Ω^0). This scaling is consistent with the previous analysis, as the exponents of the errors are smaller than the obtained bounds.

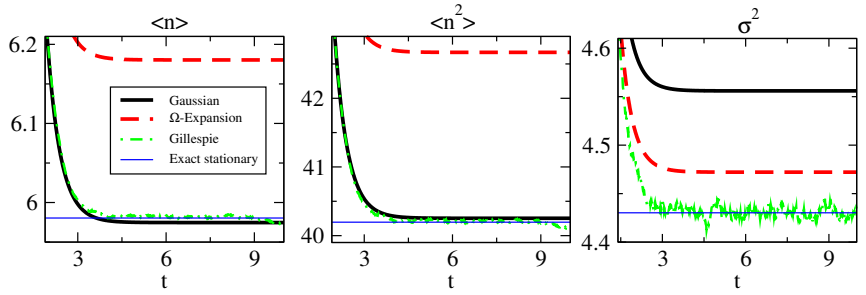

Figure 2.1: $\langle n(t)\rangle$, $\langle n^2(t)\rangle$ and $\sigma^2(t)$ for the binary reaction $A + B \underset{\omega}{\overset{\kappa}{\rightleftarrows}} C$ with parameters $\kappa = 1$, $\omega = 1$, $\Omega = 10$ and initial conditions $n(0) = 100$, $\delta = 1$. For the first two moments the Gaussian approximation (solid) is very close to the results obtained with the Gillespie algorithm (dot-dashed, obtained averaging over one million realizations) and the exact stationary value (thin line), while 1^{st} order Ω-expansion (dashed) gives clearly different values. For σ^2, the Ω-expansion gives more accurate results but both approximations differ from the exact values.

2.5 Autocatalytic reaction $A \overset{k}{\rightarrow} X$, $2X \overset{k'}{\rightarrow} B$

The master equation describing this process is [van Kampen, 2004]:

$$\frac{\partial P(n,t)}{\partial t} = \Omega\phi_A k[P(n-1,t) - P(n,t)] + \frac{k'}{\Omega}[(n+2)(n+1)P(n+2,t) - n(n-1)P(n,t)], \tag{2.29}$$

where the concentration of A particles is consider to be constant with a value ϕ_A. This equation if of the form (2.1) with $C_{-1}(n;\Omega) = \Omega k\phi_A, C_2(n;\Omega) + \frac{k'}{\Omega}n(n-1)$. The general solution for this equation is not known, but the stationary solution $P^{st}(n)$ can be obtained using the generating function technique [van Kampen, 2004]. The exact equations for the first moments are:

$$\frac{d\langle n\rangle}{dt} = \Omega k\phi_A + 2k'\frac{\langle n\rangle}{\Omega} - 2k'\frac{\langle n^2\rangle}{\Omega}, \tag{2.30}$$

$$\frac{d\langle n^2\rangle}{dt} = \Omega k\phi_A(2\langle n\rangle + 1) - \frac{k'}{\Omega}(4\langle n^3\rangle - 8\langle n^2\rangle + 4\langle n\rangle). \tag{2.31}$$

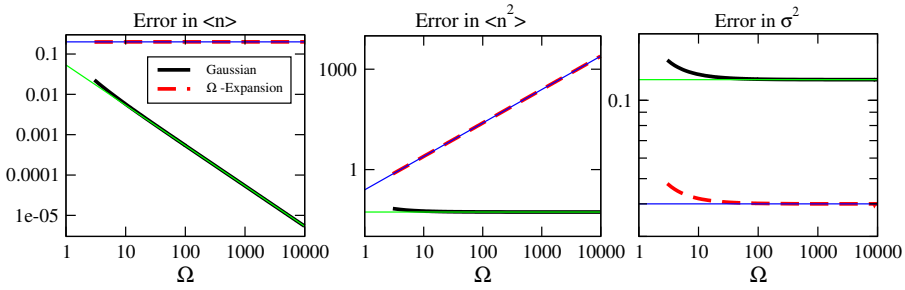

Figure 2.2: Error in $\langle n \rangle$, $\langle n^2 \rangle$ and σ^2 in the stationary state in the same case than in Fig.2.1. The straight thin lines are fits to the data and have slope -1, 0 or 1. For the Gaussian approximation (solid), the errors in ($\langle n \rangle$, $\langle n^2 \rangle$, σ^2) scale as (Ω^{-1}, Ω^0, Ω^0). For the Ω-expansion (dashed), the errors scale as (Ω^0, Ω^1, Ω^0).

Performing the Gaussian approximation, we get:

$$\frac{d\mu_1}{dt} = \Omega k \phi_A + 2k' \frac{\mu_1}{\Omega} - 2k' \frac{\mu_2}{\Omega}, \tag{2.32}$$

$$\frac{d\mu_2}{dt} = \Omega k \phi_A (2\mu_1 + 1) - \frac{k'}{\Omega}(12\mu_2\mu_1 - 8\mu_1^3 - 8\mu_2 + 4\mu_1). \tag{2.33}$$

While first order Ω-expansion approach leads to:

$$\frac{d\phi}{dt} = k\phi A - 2k'\phi^2, \tag{2.34}$$

$$\frac{d\langle n \rangle}{dt} = \Omega(k\phi_A + 2k'\phi^2) - 4k'\phi\langle n \rangle, \tag{2.35}$$

$$\frac{d\langle n^2 \rangle}{dt} = -8k'\phi\langle n^2 \rangle + \Omega(2k\phi_A + 4k'\phi^2)\langle n \rangle + \Omega(k\phi_A + 4k'\phi^2). \tag{2.36}$$

In the next figures we show the results obtained with the Gaussian approximation (computed by numerical integration of equations 2.32-2.33), Ω-expansion (equations 2.34-2.36), the Gillespie algorithm, and the exact stationary solution.

As in the previous example, we see that the Gaussian approximation fits better the evolution of the moments, but the variance is somehow better approximated by the first order Ω-expansion. In figure (2.4) we show the errors in the stationary state for the two approximations as a function of Ω. We see that the errors in ($\langle n \rangle$, $\langle n^2 \rangle$, σ^2) decay as (Ω^{-1}, Ω^{-1}, Ω^0) for the Gaussian approximation, while the first-order Ω-expansion leads to errors that scale as (Ω^0, Ω^1, Ω^0). Again, this scaling is consistent with the analysis of the approximations performed.

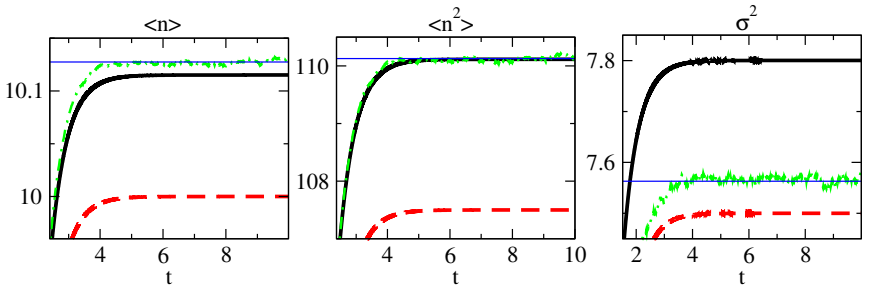

Figure 2.3: $\langle n(t)\rangle$, $\langle n(t)^2\rangle$ and $\sigma^2(t)$ for the autocatalytic reaction $A \xrightarrow{k} X$, $2X \xrightarrow{k'} B$ with $k\phi_A = 1$, $k' = 1/2$, $\Omega = 10$ and initial condition $n(0) = 0$. For the first two moments the Gaussian approximation (solid) is very close to the results coming from the Gillespie algorithm (dot-dashed) and the exact value in the stationary case (thin line) whereas the Ω-expansion result (dashed) is clearly different, although for σ^2 the Ω-expansion provides more accurate results.

2.6 Opinion formation

In the last few years there has been a growing interest in the application of methods and techniques coming from statistical physics to the study of complex phenomena in fields traditionally far from physics research, particularly in biology, medicine, information technology or social systems. In particular the application of the physical approach to social phenomena has been discussed in several reviews [Weidlich, 2002; Stauffer et al., 2006; Castellano et al., 2009]. As an example of the use of master equations in this field, we mention a recent paper [de la Lama et al., 2006] in which the process of opinion formation in a society is modeled as follows: Society is divided in two parties, A and B, plus an "intermediate" group of undecided agents I. The supporters of A and B do not interact among them, but only through their interaction with the group I, convincing one of its members with a given probability. In addition there is a nonzero probability of a spontaneous change of opinion from I to the other two parties and vice-versa. More specifically, if $n_{A(B)}$ is the number of supporters of party A(B), n_I is the number of undecided agents and Ω is the total number of individuals, the possible transitions are:

spontaneous change $A \to I$, occurring with a rate $\alpha_1 n_A$,

spontaneous change $I \to A$, occurring with a rate $\alpha_2 n_I$,

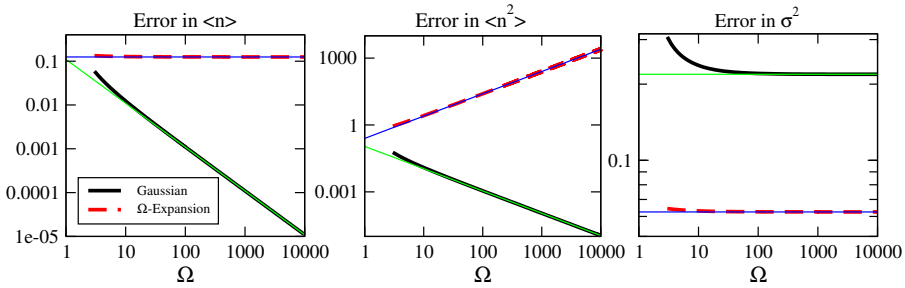

Figure 2.4: Error in $\langle n\rangle, \langle n^2\rangle$ and σ^2 in the stationary state as a function of Ω in the same case than in Fig.2.3. The thin lines have slope -1, 0 or 1. For the Gaussian approximation (solid), the errors in $(\langle n\rangle, \langle n^2\rangle, \sigma^2)$ scale (asymptotically) as $(\Omega^{-1}, \Omega^{-1}, \Omega^0)$. For the Ω-expansion, the errors scale as $(\Omega^0, \Omega^1, \Omega^0)$.

spontaneous change $B \to I$, occurring with a rate $\alpha_3 n_B$,

spontaneous change $I \to B$, occurring with a rate $\alpha_4 n_I$,

convincing rule $A + I \to 2A$, occurring with a rate $\frac{\beta_1}{\Omega} n_A n_I$,

convincing rule $B + I \to 2B$, occurring with a rate $\frac{\beta_2}{\Omega} n_B n_I$.

As the total number of individuals ($\Omega = n_A + n_B + n_I$) is fixed, there are only two independent variables, say n_A and n_B. The master equation of the process is:

$$\begin{aligned}\frac{\partial}{\partial t}P(n_A,n_B,t) &= \alpha_1(n_A+1)P(n_A+1,n_B,t) + \alpha_3(n_B+1)P(n_A,n_B+1,t) \quad (2.37)\\ &+\alpha_2(\Omega-n_A-n_B+1)P(n_A-1,n_B,t) + \alpha_4(\Omega-n_A-n_B+1)P(n_A,n_B-1,t)\\ &+(\Omega-n_A-n_B+1)\left[\frac{\beta_1}{\Omega}(n_A-1)P(n_A-1,n_B,t) + \frac{\beta_2}{\Omega}(n_B-1)P(n_A,n_B-1,t)\right]\\ &-\left[\alpha_1 n_A + \alpha_3 n_B + (\alpha_2+\alpha_4)(\Omega-n_A-n_B) + \frac{\beta_1 n_A + \beta_2 n_B}{\Omega}(\Omega-n_A-n_B)\right]\times\\ &\qquad P(n_A,n_B,t).\end{aligned}$$

We note that this master equation can be written in the general form (2.12) by setting $C_{1,0} = \alpha_1 n_A$, $C_{0,1} = \alpha_3 n_B$, $C_{-1,0} = (\Omega - n_A - n_B)(\alpha_2 + \frac{\beta_1}{\Omega} n_A)$ and $C_{0,-1} = (\Omega - n_A - n_B)(\alpha_4 + \frac{\beta_2}{\Omega} n_B)$.

An exact solution of this master equation is not known. In the following, we will apply to this problem the Gaussian approximation scheme and compare it with the results of the Ω-expansion. The exact equations for the first moments are:

$$\frac{d\langle n_A(t)\rangle}{dt} = -(\alpha_1+\alpha_2-\beta_1)\langle n_A\rangle + \alpha_2(\Omega-\langle n_B\rangle) - \frac{\beta_1}{\Omega}\langle n_A^2\rangle - \frac{\beta_1}{\Omega}\langle n_A n_B\rangle, \tag{2.38}$$

$$\frac{d\langle n_B(t)\rangle}{dt} = -(\alpha_3+\alpha_4-\beta_2)\langle n_B\rangle + \alpha_4(\Omega-\langle n_A\rangle) - \frac{\beta_2}{\Omega}\langle n_B^2\rangle - \frac{\beta_2}{\Omega}\langle n_A n_B\rangle, \tag{2.39}$$

$$\frac{d\langle n_A^2(t)\rangle}{dt} = (\alpha_1+\alpha_2(2\Omega-1)+\beta_1)\langle n_A\rangle + \alpha_2(\Omega-\langle n_B\rangle) - 2(\alpha_1+\alpha_2-\beta_1+\frac{\beta_1}{2\Omega})\langle n_A^2\rangle - (2\alpha_2+\frac{\beta_1}{\Omega})\langle n_A n_B\rangle - \frac{2\beta_1}{\Omega}\langle n_A^3\rangle - \frac{2\beta_1}{\Omega}\langle n_A^2 n_B\rangle, \tag{2.40}$$

$$\frac{d\langle n_B^2(t)\rangle}{dt} = (\alpha_3+\alpha_4(2\Omega-1)+\beta_2)\langle n_B\rangle + \alpha_4(\Omega-\langle n_A\rangle) - 2(\alpha_3+\alpha_4-\beta_2+\frac{\beta_2}{2\Omega})\langle n_B^2\rangle - (2\alpha_4+\frac{\beta_2}{\Omega})\langle n_A n_B\rangle - \frac{2\beta_2}{\Omega}\langle n_B^3\rangle - \frac{2\beta_2}{\Omega}\langle n_A n_B^2\rangle, \tag{2.41}$$

$$\frac{d\langle n_A(t)n_B(t)\rangle}{dt} = -(\alpha_1+\alpha_2+\alpha_3+\alpha_4-\beta_1-\beta_2)\langle n_A n_B\rangle + \alpha_2(\Omega\langle n_B\rangle - \langle n_B^2\rangle) + \alpha_4(\Omega\langle n_A\rangle - \langle n_A^2\rangle) - \frac{\beta_1+\beta_2}{\Omega}(\langle n_A^2 n_B\rangle + \langle n_A n_B^2\rangle). \tag{2.42}$$

Denoting by A_1, A_2, B_1, B_2, C the Gaussian approximations to the moments $\langle n_A\rangle$, $\langle n_A^2\rangle$, $\langle n_B\rangle$, $\langle n_B^2\rangle$ and the correlation $\langle n_A n_B\rangle$, respectively, and using the results in

table 2.1, we obtain:

$$\frac{dA_1}{dt} = -(\alpha_1+\alpha_2-\beta_1)A_1+\alpha_2\Omega-\alpha_2B_1-\frac{\beta_1}{\Omega}A_2-\frac{\beta_1}{\Omega}C, \tag{2.43}$$

$$\frac{dB_1}{dt} = -(\alpha_3+\alpha_4-\beta_2)B_1+\alpha_4\Omega-\alpha_4A_1-\frac{\beta_2}{\Omega}B_2-\frac{\beta_2}{\Omega}C, \tag{2.44}$$

$$\begin{aligned}\frac{dA_2}{dt} &= (\alpha_1+\alpha_2(2\Omega-1)+\beta_1)A_1+\alpha_2(\Omega-B_1)-2(\alpha_1+\alpha_2-\beta_1+\frac{\beta_1}{2\Omega})A_2\\ &\quad -(2\alpha_2+\frac{\beta_1}{\Omega})C-\frac{2\beta_1}{\Omega}(3A_1A_2-2A_1^3)-\frac{2\beta_1}{\Omega}(A_2B_1+2A_1C-2A_1^2B_1),\end{aligned} \tag{2.45}$$

$$\begin{aligned}\frac{dB_2}{dt} &= (\alpha_3+\alpha_4(2\Omega-1)+\beta_1)B_1+\alpha_4(\Omega-A_1)-2(\alpha_3+\alpha_4-\beta_2+\frac{\beta_2}{2\Omega})B_2\\ &\quad -(2\alpha_4+\frac{\beta_2}{\Omega})C-\frac{2\beta_2}{\Omega}(3B_1B_2-2B_1^3)-\frac{2\beta_2}{\Omega}(B_2A_1+2B_1C-2B_1^2A_1),\end{aligned} \tag{2.46}$$

$$\begin{aligned}\frac{dC}{dt} &= -(\alpha_1+\alpha_2+\alpha_3+\alpha_4-\beta_1-\beta_2)C+\alpha_2(\Omega B_1-B_2)\\ &\quad +\alpha_4(\Omega A_1-A_2)-\frac{\beta_1+\beta_2}{\Omega}\left[B_1A_2+B_2A_1+2(A_1+A_2)C-2A_1^2A_2-2B_1^2B_2\right].\end{aligned} \tag{2.47}$$

In van Kampen's expansion method, we define $\phi_{A(B)}, \xi_{A(B)}$ such that $n_{A(B)} = \Omega\phi_{A(B)} + \Omega^{1/2}\xi_{A(B)}$.

The equations for the macroscopic components are [de la Lama et al., 2006]:

$$\frac{d\phi_A}{dt} = -\alpha_1\phi_A+[\alpha_2+\beta_1\phi_A](1-\phi_A-\phi_B), \tag{2.48}$$

$$\frac{d\phi_B}{dt} = -\alpha_3\phi_B+[\alpha_4+\beta_2\phi_B](1-\phi_A-\phi_B), \tag{2.49}$$

and for the fluctuations:

$$\frac{d\langle\xi_A\rangle}{dt} = -[\alpha_1+\alpha_2+\beta_1(2\phi_A+\phi_B)-\beta_1]\langle\xi_A\rangle-(\alpha_2+\beta_1\phi_A)\langle\xi_B\rangle, \quad (2.50)$$

$$\frac{d\langle\xi_B\rangle}{dt} = -[\alpha_3+\alpha_4+\beta_2(2\phi_B+\phi_A)-\beta_2]\langle\xi_B\rangle-(\alpha_4+\beta_2\phi_B)\langle\xi_A\rangle, \quad (2.51)$$

$$\frac{d\langle\xi_A^2\rangle}{dt} = -2\alpha_1\langle\xi_A^2\rangle-2(\alpha_2+\beta_1\phi_A)(\langle\xi_A^2\rangle+\langle\xi_A\xi_B\rangle)+2\beta_1\langle\xi_A^2\rangle(1-\phi_A-\phi_B) +\alpha_1\phi_A+(\alpha_2+\beta_1\phi_A)(1-\phi_A-\phi_B), \quad (2.52)$$

$$\frac{d\langle\xi_B^2\rangle}{dt} = -2\alpha_3\langle\xi_B^2\rangle-2(\alpha_4+\beta_2\phi_B)(\langle\xi_B^2\rangle+\langle\xi_A\xi_B\rangle)+2\beta_2\langle\xi_B^2\rangle(1-\phi_A-\phi_B) +\alpha_3\phi_B+(\alpha_4+\beta_2\phi_B)(1-\phi_A-\phi_B), \quad (2.53)$$

$$\frac{d\langle\xi_A\xi_B\rangle}{dt} = -(\alpha_1+\alpha_3)\langle\xi_A\xi_B\rangle-(\alpha_2+\beta_1\phi_A)(\langle\xi_A\xi_B\rangle+\langle\xi_B^2\rangle) -(\alpha_4+\beta_2\phi_B)(\langle\xi_A\xi_B\rangle+\langle\xi_A^2\rangle)+(1-\phi_A-\phi_B)(\beta_1+\beta_2)\langle\xi_A\xi_B\rangle. \quad (2.54)$$

From those we can recover the original variables $n_{A(B)}(t)$.

In figure (2.5) we compare the results coming from both approximations (obtained by numerical integration of the previous equations) and from simulations of the process using the Gillespie algorithm, for some representative values of the parameters and initial conditions. Again, the Gaussian approximation reproduces better the values for the average and the second moment whereas in this case both methods perform very similarly for the fluctuations and correlation.

2.7 Conclusions

In this chapter, we have given explicit expressions for the equations for the first and second moments of a stochastic process defined by a general class of master equations using the Gaussian approximation closure. The approach is motivated by van Kampen's Ω-expansion result that, at lowest order, the fluctuations are Gaussian. The main difference is that while in van Kampen's approach one introduces the ansatz that the fluctuations are of the order of the square root of the macroscopic value, and then checks that this ansatz is consistent, in the Gaussian approximation scheme one uses the ansatz that the distribution is Gaussian and then derive the order of the fluctuations. We have shown that the Gaussian closure is simple to perform and leads to errors in the average value, the second moment and the fluctuations (the variance), that scale at most as

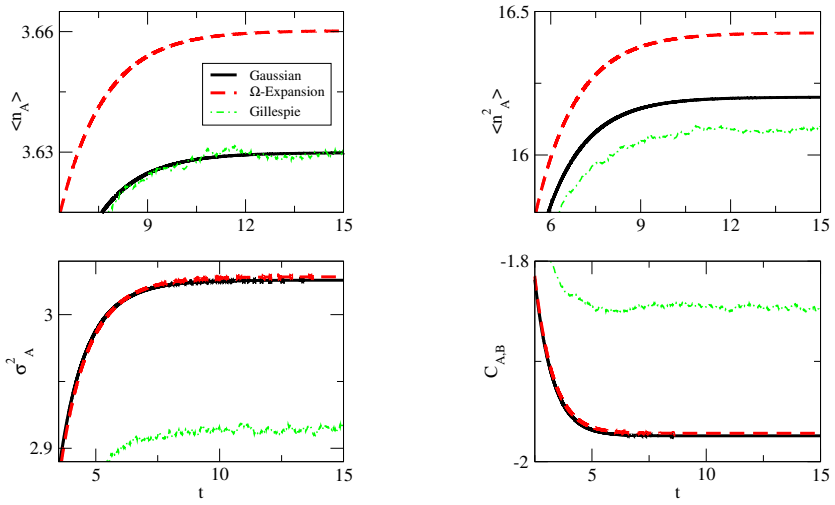

Figure 2.5: $\langle n_A(t)\rangle, \langle n_A^2(t)\rangle$, $\sigma_A^2(t)$ and $C_{AB}(t) \equiv \langle n_A n_B\rangle - \langle n_A\rangle\langle n_B\rangle$ for the opinion formation model of reference [de la Lama et al., 2006], for $\alpha_i = \beta_i = 1, \Omega = 10$, and initial conditions $n_A(0) = 0$, $n_B(0) = \Omega$. For the average $\langle n_A(t)\rangle$, the Gaussian approximation (solid) follows very accurately the Gillespie simulation results (dot-dashed), whereas the Ω-expansion (dashed) differs clearly. For the second moment $\langle n_A(t)^2\rangle$ the Gaussian approximation performs clearly better as well, while for the variance $\sigma_A^2(t)$ and correlations $C_{AB}(t)$, the Gaussian approximation and the Ω-expansion give very similar results, although both are far from the simulation data.

$(\Omega^{-1/2}, \Omega^{1/2}, \Omega^{1/2})$, respectively. This is to be compared with the Ω-expansion result in which the respective errors scale at most as $(\Omega^0, \Omega^1, \Omega^{1/2})$. Therefore, the Gaussian approximation is more accurate, which turns out to be important, specially for small values of Ω. This scaling of the errors is valid for all times provided that the macroscopic law (2.3) has a fixed point as a single attractor [van Kampen, 2004]. In both schemes the validity of the approximations might be limited for large times when there is more than one absorbing state, or a single one different from the attractor of the macroscopic law, since in those cases the distribution eventually approaches a sum of delta-functions. Very recently, an analysis of the accuracy of the Gaussian approximation for chemical kinetics (which voils down to considering at most bimolecular reactions) was developed [Grima, 2012], finding errors of the order Ω^{-1} for the average and Ω^0 for the variance, more accurate but consistent with the bounds found in this work. The same scaling of the errors was found for a truncation of the master equation to

second order in the Kramers-Moyal expansion (Fokker-Planck approximation) [Grima et al., 2011].

We have checked these results by comparing the performance of the two methods in three examples: (i) a binary chemical reaction, (ii) an autocatalytic reaction and (iii) a model for opinion formation. In all cases studied, the Gaussian closure has given a better approximation to the average and the second moment, although the Ω-expansion, due to a cancellation of errors, yields a somehow smaller numerical error in the variance. In general, and compared to other field-theoretical methods available in the litrature [Doi, 1976; Peliti, 1985], the Gaussian closure scheme is very simple to carry on in practice and this simplicity and the improvement of the predictive power is more apparent in many-variable systems. We believe that this method can be usefully applied to the study of other problems of recent interest in the literature involving stochastic processes in systems with a small number of particles.

2.8 Appendix: Reaction-limited process

We now find the solution of the master equation (2.21) in the equilibrium state for the general case, and the full dynamical solution for the irreversible case $\omega = 0$. Without loss of generality, let us rescale $t \to \kappa t/\Omega$ and $\omega \to \omega\Omega^2/\kappa$ to get the simpler equation:

$$\frac{dP(n,t)}{dt} = (n+1)(\Delta+n+1)P(n+1,t) - n(n+\Delta)P(n,t) + \omega[P(n-1,t) - P(n,t)]. \quad (2.55)$$

Furthermore, only the case $\Delta \geq 0$ needs to be considered. If $\Delta < 0$ the change $n' = n - \Delta$ leaves invariant the previous equation provided that we make the identification $P(n,t) \to P(n+\Delta,t)$. This means that the solutions in both cases are related by $P(n,t;\Delta) = P(n-\Delta,t;-\Delta)$.

The generating function

$$f(s,t) = \sum_{n=0}^{\infty} P(n,t)s^n, \quad (2.56)$$

satisfies the partial differential equation:

$$\frac{\partial f}{\partial t} = (1-s)\left[s\frac{\partial^2 f}{\partial s^2} + (1+\Delta)\frac{\partial f}{\partial s} - \omega f\right]. \quad (2.57)$$

Let us first discuss the equilibrium solution in the general case.

2.8.1 The equilibrium solution

By setting $\frac{\partial f}{\partial t} = 0$ one gets the differential equation:

$$s\frac{\partial^2 f}{\partial s^2} + (1+\Delta)\frac{\partial f}{\partial s} - \omega f = 0. \tag{2.58}$$

The solution around the singular regular point $s = 0$ can be found by the Frobenius method as a power series $\sum_{n=0}^{\infty} a_n s^{n+\nu}$. The regular solution satisfying the boundary condition $f(s=1) = 1$ is[1]:

$$f(s) = \frac{s^{-\Delta/2} I_\Delta\left(2\sqrt{\omega s}\right)}{I_\Delta\left(2\sqrt{\omega s}\right)}, \tag{2.59}$$

where $I_n(z)$ is the modified Bessel function of the first kind [Abramowitz and Stegun, 1972]. The equilibrium probabilities, rescaling back to the original parameters, are:

$$P(n) = \frac{(\omega\Omega^2/\kappa)^{n+\Delta/2}}{I_\Delta\left(2\Omega\sqrt{\omega/\kappa}\right) n!(n+\Delta)!}, \tag{2.60}$$

from where the first two moments can be computed as:

$$\langle n\rangle = \frac{I_{\Delta+1}\left(2\Omega\sqrt{\omega/\kappa}\right)}{I_\Delta\left(2\Omega\sqrt{\omega/\kappa}\right)}\Omega\sqrt{\omega\kappa}, \qquad \langle n^2\rangle = \Omega^2\omega/\kappa - \frac{I_{\Delta+1}\left(2\Omega\sqrt{\omega/\kappa}\right)}{I_\Delta\left(2\Omega\sqrt{\omega/\kappa}\right)}\Delta\Omega\sqrt{\omega/\kappa}. \tag{2.61}$$

2.8.2 The time-dependent solution

We now study how the system relaxes towards equilibrium. We will restrict ourselves to the irreversible case $\omega = 0$. This corresponds to the process $A+B \to 0$, inert. The partial differential equation (2.57) can be solved by the technique of separation of variables by trying solutions of the form $f(s,t) = f_1(s)f_2(t)$. This leads to the pair of ordinary differential equations:

$$s(1-s)f_1'' + (1-s)(1+\Delta)f_1' + \lambda^2 f_1 = 0, \tag{2.62}$$

$$f_2' + \lambda^2 f_2 = 0, \tag{2.63}$$

[1] There is another solution to this equation, but it contains a term in $\ln s$ and it has to be discarded since it can not be expanded in a power series of s.

being λ^2 the constant arising from the method of separation of variables. The solution of the time dependent function is $e^{-\lambda^2 t}$ and the solution of the s-function is the hypergeometric function[2] $F(-\mu_1, \mu_2; \Delta + 1; s)$. The explicit series is:

$$F(-\mu_1, \mu_2; \Delta + 1; s) = \sum_{n=0}^{\infty} \frac{(-\mu_1)_n (\mu_2)_n}{(\Delta + 1)_n} \frac{s^n}{n!}. \tag{2.64}$$

$(a)_n$ is the Pochhammer's symbol: $(a)_n = \frac{\Gamma(a+n)}{\Gamma(a)}$, or $(a)_0 = 1$, $(a)_n = a(a+1)\dots(a+n-1)$ for $n > 0$, and we have introduced

$$\mu_1 = \frac{-\Delta + \sqrt{\Delta^2 + 4\lambda^2}}{2}, \qquad \mu_2 = \frac{\Delta + \sqrt{\Delta^2 + 4\lambda^2}}{2}. \tag{2.65}$$

The solution for the function $f(s,t)$ is obtained by linear combination of the elementary solutions found above:

$$f(s,t) = \sum_{\lambda} C_\lambda F(-\mu_1, \mu_2; \Delta + 1; s) e^{-\lambda^2 t}. \tag{2.66}$$

This function is, in general, an infinite series on the variable s. In fact the coefficients, according to (2.56) are nothing but the time-dependent probabilities. However, in this irreversible case, the probability of having more A-molecules that the initial number at $t = 0$, say M, has to be zero. Therefore the series must be truncated after the power s^M. This implies that in the previous expression only hypergeometric functions that represent a polynomial in s can be accepted. This is achieved by forcing $\mu_1 = k = 0, 1, 2 \dots, M$, since the series (2.64) becomes then a polynomial of degree k. The condition $\mu_1 = k$ is equivalent to the parameter λ adopting one of the possible values $\lambda_k = \sqrt{k(k+\Delta)}$. Finally, noticing that $\mu_2 - \mu_1 = \Delta$, the solution can be written as:

$$f(s,t) = \sum_{k=0}^{M} \sum_{n=0}^{k} C_k(\Delta, M) e^{-k(k+\Delta)t} B_{n,k}(\Delta) s^n. \tag{2.67}$$

The notation emphasizes that C_k depends both on Δ and M but $B_{n,k}$ depends only on Δ:

$$B_{n,k}(\Delta) = \frac{(-k)_n (k+\Delta)_n}{n!(\Delta+1)_n}. \tag{2.68}$$

All that remains is to impose the initial condition. We start with M A-molecules at time $t = 0$, such that $f(s, t = 0) = s^M$. This implies that the coefficients C_k must

[2]There is another solution to the second-order differential equation. As before, this solution has to be discarded since it can not be expanded in powers of s.

satisfy:

$$\sum_{k=n}^{M} B_{n,k} C_k = \delta_{n,M}, \tag{2.69}$$

for $n = 0, 1, \ldots, M$. The solution starts by finding first $C_M = 1/B_{M,M}$ and then proceeds backwards to find $C_{M-1}, C_{M-2}, \ldots, C_0$ in a recursive manner. After some lengthy algebra, the result is:

$$C_k(\Delta, M) = (-1)^k \frac{2k+\Delta}{k+\Delta} \frac{(k+1)_\Delta}{\Delta!} \frac{(M-k+1)_k}{(M+\Delta+1)_k}, \tag{2.70}$$

(in the case $\Delta = k = 0$ the correct interpretation of the undetermined expression is $C_0 = 1$). Going back to the original time variable, we now give the expression for the probabilities:

$$P(n,t) = \sum_{k=n}^{M} C_k(\Delta, M) B_{n,k}(\Delta) \mathrm{e}^{-k(k+\Delta)\kappa t/\Omega}. \tag{2.71}$$

To the best of our knowledge, this and the stationary solution Eq.(2.60), are original results. The normalization condition $\sum_{n=0}^{M} P_n(t) = 1$ is verified with the help of the relation $\sum_{n=0}^{k} B_{n,k} = \delta_{k,0}$. The relation $\displaystyle\sum_{n=0}^{k} n B_{n,k} = (-1)^k k \frac{\Delta!}{(k)_\Delta}$ (the indetermination arising when $\Delta = k = 0$ must be resolved as 0) helps to find the average of the number of particles:

$$\langle n(t) \rangle = \sum_{k=1}^{M} (2k+\Delta) \frac{(M-k+1)_k}{(M+\Delta+1)_k} \mathrm{e}^{-k(k+\Delta)\kappa t/\Omega}. \tag{2.72}$$

The second moment $\langle n(t)^2 \rangle$ can be found with the help of Eq.(2.23) as $\langle n(t)^2 \rangle = -\frac{\Omega}{\kappa} \frac{d\langle n(t) \rangle}{dt} - \Delta \langle n(t) \rangle$, or:

$$\langle n(t)^2 \rangle = \sum_{k=1}^{M} (2k+\Delta)(k^2 + (k-1)\Delta) \frac{(M-k+1)_k}{(M+\Delta+1)_k} \mathrm{e}^{-k(k+\Delta)\kappa t/\Omega}. \tag{2.73}$$

Part III

Delay in stochastic processes

Chapter 3

Delay in stochastic processes

3.1 Introduction

Stochastic modeling plays an important role in many areas of science, such as physics, ecology or chemistry [van Kampen, 2004]. Stochasticity may appear due to the lack of complete knowledge about all the relevant variables, the precise dynamics of the system or the interactions with the environment. In some cases, one can obtain a compact description of a complicated system considering only a few relevant variables but at the expense of losing deterministic predictability. Often, probabilities for some fundamental processes can be assigned on the basis of symmetries and other considerations, or on empirical analyis, and the dynamics of the process can be derived bottom-up.

Stochasticity appears together with delay terms in many situations of interest, such as gene regulation [Lewis, 2003; Barrio et al., 2006; Bratsun et al., 2005], physiological processes [Longtin et al., 1990] or postural control [Milton et al., 2009; Boulet et al., 2010]. The combined effects of stochasticity and delay are, however, not completely understood. From the mathematical point of view, stochastic processes including delay are difficult to analyze due to the non-Markovian character. Most of the previous approaches have focused on stochastic differential equations, that consider continuous variables [Küchler and Mensch, 1992; Guillouzic et al., 1999; Frank, 2002; Frank et al., 2003; Ohira and Yamane, 2000], or random walks in discrete time [Ohira and Milton, 1995; Milton et al., 2008], where delay can be taken into account increasing the number of variables. Models with discrete variables but continuous time are the natural description of many systems such as chemical reactions, population dynamics or epidemic

spreading. In some cases, discreteness can be a mayor source of fluctuations, not well captured by continuous models [Aparicio and Solari, 2001]. The approach with discrete variables and continuous time was used in [Bratsun et al., 2005; Galla, 2009; Miekisz et al., 2011; Lafuerza and Toral, 2011b]. Most often, the delay time is taken to be a constant with zero fluctuations. This is not very realistic in the applications, since it is unusual to have a deterministic delay when the rest of the dynamics is stochastic. This issue has been overlooked in theoretical analyses. We will take this consideration into account by allowing the delay times to be random variables with arbitrary probability density functions.

In this chapter we study some simple, yet general, stochastic birth and death processes including delay. We will develop three different approaches to the analytical study of this kind of non-Markovian processes, in the general case of stochastically distributed delay: (i) a direct approach in subsection (3.2.1), (ii) an effective Markovian reduction in subsections (3.2.2), (3.2.3) and (3.2.4), (iii) and a master equation approach, together with a time-reversal invariance assumption, in section (3.3). The first direct approach method is interesting for its simplicity, but its application is limited to systems with first order reactions and without feedback. The second one, effective Markovian reduction, is rather flexible and general and its development is one of the main advances of this chapter. The last master equation approach complements the previous one, giving information about the full probability distribution. Initially, we will assume that completion times for delayed reactions are independent random variables (independent of each other and of other variables of the system), but we will show that the effective Markovian reduction allows to considier non-independent delay times as well. Although our methodology is rather general, we present it here using specific examples that have been grouped in two categories: delay in the degradation (section 3.2) and delay in the creation (section 3.3). Some more technical details are left for the two appendices.

3.2 Delayed degradation

We will start by studying simple stochastic birth and death processes that include delay in the degradation step. A process of this type was proposed in [Bratsun et al., 2005] as a model for protein level dynamics with a complex degradation pathway.

3.2.1 Simple delayed degradation without feedback

We consider first the simplest possible process including delayed degradation:

$$\emptyset \overset{C}{\longrightarrow} X,\ X \underset{\tau}{\Longrightarrow} \emptyset, \tag{3.1}$$

that is, a particle X is created at a rate C and disappears ("dies" or "degrades") a time τ after created. We allow the delay time τ to be randomly distributed i.e. the lifetimes τ of the created particles are random variables, that for simplicity we consider independent and identically distributed, with probability density $f(\tau)$. Although not considered here, the case of non-identically distributed delay times, in particular a probability density that depends on the time from creation, can also be treated.

We note first that distributed delay is completely equivalent to degradation at a rate that depends on the "age" a (time form creation) of the particle, i.e. processes

$$X \underset{\tau}{\Longrightarrow} Y, \qquad \text{and} \qquad X \overset{\gamma(a)}{\longrightarrow} Y, \tag{3.2}$$

are equivalent if the rate $\gamma(a)$ and the probability density of the delay $f(\tau)$ are related by:

$$\gamma(a) = \frac{f(a)}{\hat{F}(a)} \Rightarrow f(\tau) = \gamma(\tau) e^{-\int_0^\tau da \gamma(a)}, \tag{3.3}$$

with $\hat{F}(t) = 1 - F(t)$ being $F(t) = \text{Prob}(\tau < t) = \int_0^\tau d\tau f(\tau)$ the cumulative distribution of the delay-time. This is so because $\gamma(a)da$ is the probability of dying at the time interval $(a, a + da)$, if the particle is still present at a, and so it is nothing but the probability $f(a)da$ that the delay time τ belongs to that same interval conditioned to the particle still being alive at time a, an event with probability $\hat{F}(a)$. In the notation of Papoulis and Pillai [2011], $\gamma(a)$ is nothing but the *conditional failure rate*. When the rate of a reaction does not depend on the sate of the system, it is called a first order reaction. A multi-step reaction with all steps being first-order reactions is equivalent to a single reaction with a delay distribution, i.e. processes

$$X \underset{\tau}{\Longrightarrow} Y, \qquad \text{and} \qquad X \overset{\gamma_1}{\longrightarrow} X_1 \overset{\gamma_2}{\longrightarrow} X_2 \dots X_{m-1} \overset{\gamma_m}{\longrightarrow} Y, \tag{3.4}$$

are equivalent if the probability density of the delay, $f(\tau)$, has a Laplace transform given by:

$$\mathcal{F}(s) \equiv \int dt e^{-st} f(t) = \prod_{i=1}^{m} \frac{\gamma_i}{\gamma_i + s}. \tag{3.5}$$

In the particular case that all the rates are equal, this corresponds to a gamma distribution of the form $f(\tau) = \frac{\gamma^m \tau^{m-1}}{(m-1)!} e^{-\gamma\tau}$. Note that this "multi-step" procedure is not completely general, since the distributions of delay that can be obtained are always given by (3.5) (which corresponds to a superposition of exponentials). This implies that the variance is bounded respect the mean value, since

$$\frac{\sigma[\tau]}{\langle\tau\rangle} = \frac{\sqrt{\sum \frac{1}{\gamma_i^2}}}{\sum \frac{1}{\gamma_i}} \leq 1. \tag{3.6}$$

Mimicking a delay distribution with a multi-step process is convenient because the process is Markovian and usual methods can be employed [Morelli and Jülicher, 2007]. However we see that the multi-step procedure is not completely general. It is the goal of this chapter to develop methods to analyze this kind of non-Markovian processes, valid for general delay distributions.

We take $t = 0$ as the time origin, so the number of particles present at time t is $n(t) = 0$ for $t \leq 0$. Let $P(n,t)$ the probability of n particles being present at time t. In the remaining of this subsection we assume that there is no feedback, in the sense that the creation rate C is independent on the number of particles n, but, for the sake of generality, we do allow it to be a function of time $C(t)$. The non-feedback assumption allows us to obtain a full analytical solution. As shown in Appendix 1, independently of the form of the delay distribution, $P(n,t)$ follows a Poisson distribution

$$P(n,t) = e^{-\langle n(t)\rangle} \frac{\langle n(t)\rangle^n}{n!}, \tag{3.7}$$

with average $\langle n(t)\rangle = \int_0^t dt' C(t') \hat{F}(t-t')$. If the creation rate, $C(t)$, is independent of time, a steady state is reached, in which the average number of particles is $\langle n\rangle_{\text{st}} = C\langle\tau\rangle$, again independently of the form of the delay distribution.

We will now compute the two-times joint probability distribution, which in particular, allows to derive the time correlation function. We shall see that the analytical expression of the correlation function does depend on the form of the delay distribution (and not only on the average delay, as we have seen is the case for the average number of particles), which opens the possibility to determine the presence and the form of the delay distribution from macroscopic data (by macroscopic we mean based on n and not on the lifetime of individual particles). We start from the relation:

$$n(t+T) = n_{new}(t+T) + n_{old}(t+T), \tag{3.8}$$

where we have split the particles present at time $t+T$ into those that were already present at time t, $n_{old}(t+T)$, and those that were created in the interval $(t, t+T)$.

n_{new} can be computed exactly as before (now taking t as the time origin), so we have:

$$P(n_{new} = m, t+T|n,t) \equiv P_{new}(m, t+T|n,t) = \frac{\langle n_{new}(t+T)|n(t)\rangle^m}{m!} e^{-\langle n_{new}(t+T)|n(t)\rangle}, \quad (3.9)$$

with

$$\langle n_{new}(t+T)|n(t)\rangle = \int_0^T dt' C(t+t')\hat{F}(T-t'), \quad (3.10)$$

which is actually independent of $n(t)$. The evolution of the number of particles that were already present at t depends on the age a of each one of these particles. The survival probability until time $t+T$ of one of these particles can be written as:

$$\begin{aligned} &P(\text{alive at } t+T|\text{alive at } t) \\ &= \int_0^t da P(\text{age} = a|\text{alive at } t) P(\text{lifetime} > a+T|\text{lifetime } > a) \\ &= \int_0^t da \frac{C(t-a)\hat{F}(a)}{\int_0^t dt' C(t')\hat{F}(t-t')} \frac{\hat{F}(a+T)}{\hat{F}(a)} = \frac{\int_0^t dt' C(t')\hat{F}(t+T-t')}{\int_0^t dt' C(t')\hat{F}(t-t')}, \\ &\equiv g(t,T), \end{aligned} \quad (3.11)$$

where we have used $P(a|b) = \frac{P(a;b)}{P(b)}$. Since the different particles are independent, n_{old} follows a binomial distribution:

$$P_{old}(n, t+T|n_0, t) = \binom{n_0}{n} g(t,T)^n [1-g(t,T)]^{n_0-n}, 0 \le n \le n_0. \quad (3.12)$$

Using (3.8) and that n_{new} and n_{old} are statistically independent, we obtain the expression for the two-times probability:

$$P(n, t+T; n_0, t) = \sum_{m=0}^{n} P_{old}(m, t+T|n_0, t) P_{new}(n-m, t+T|n_0, t) P(n_0, t), \quad (3.13)$$

with $P(n_0, t)$ given by (3.7). A more explicit formula is found for the generating function:

$$G(s, t+T; s_0, t) = \sum_{n=0, n_0=0}^{\infty} s^n s_0^{n_0} P(n, t+T; n_0, t) = e^{\langle n_{new}(t+T)\rangle(s-1)} e^{\langle n(t)\rangle\{s_0[g(t,T)s+1-g(t,T)]-1\}}. \quad (3.14)$$

The correlation function, $K[n](t,T) = \langle n(t)n(t+T)\rangle - \langle n(t)\rangle\langle n(t+T)\rangle$, can be easily obtained using that $\langle n(t)n(t+T)\rangle = \frac{\partial^2 G(s,t+T;s_0,t)}{\partial_s \partial_{s_0}}|_{s=s_0=1}$:

$$K[n](t,T) = \int_0^t dt' C(t')\hat{F}(t+T-t'), \tag{3.15}$$

If $C(t) = C$, independent of time, a steady-state can be reached with correlation function $K_{\text{st}}[n](T) = \lim_{t\to\infty} K[n](t,T)$. For a constant rate γ, which would be equivalent to an exponential delay distribution $f(\tau) = \gamma e^{-\gamma\tau}$, it has the usual exponential decay $K_{\text{st}}[n](T) = (C/\gamma)e^{-\gamma T}$. For a fixed delay time τ_0, corresponding to $f(\tau) = \delta(\tau - \tau_0)$, the correlation function is a straight line $K_{\text{st}}[n](T) = C(\tau_0 - T)$ for $T < \tau_0$ and $K_{\text{st}}[n](T) = 0$ for $T \geq \tau_0$. For other distributions of delay time, the correlation function adopts different forms, but it is always monotonically decreasing. In figure (3.1) we plot the correlation function for two different types of distribution of delay, for different values of the variance of the delay. We see that the distribution with fatter tail displays a slower asymptotic decay, and that the decay is slower as the variance of the delay increases. Numerical simulations, performed with a conveniently modified version of the Gillespie algorithm [Cai, 2007] (see Appendix 3 for details about the numerical simulations), are in perfect agreement with this exact result, providing a check of its correctness. We remark that the functional form of the decay of the correlation function does depend on the functional form of the delay distribution and can differ from the exponential decay found in systems without delay.

3.2.2 Instantaneous plus delayed degradation

We now consider a process including both instantaneous and delayed degradation steps:

$$\emptyset \xrightarrow{C} X,\ X \xrightarrow{\gamma} \emptyset,\ X \xrightarrow{D} \underset{\tau}{\Longrightarrow} \emptyset, \tag{3.16}$$

this is, particles are created at a rate C and each particle can be eliminated by two processes: i) instantaneous degradation at a rate γ; ii) delayed degradation, initiated at a rate D but completed only a time τ after initiation. Again, we will allow the delay-degradations times to be random variables with probability density function $f(\tau)$.

For the process to be completely defined, one has to specify if a particle that initiates delayed-degradation at time t and thus will disappear at $t+\tau$ (this kind of particles will be called "infected"), can also disappear before the completion of this reaction, through instantaneous degradation. In the most general case, this can happen at a rate γ', not necessarily equal to γ. Note that, in the case

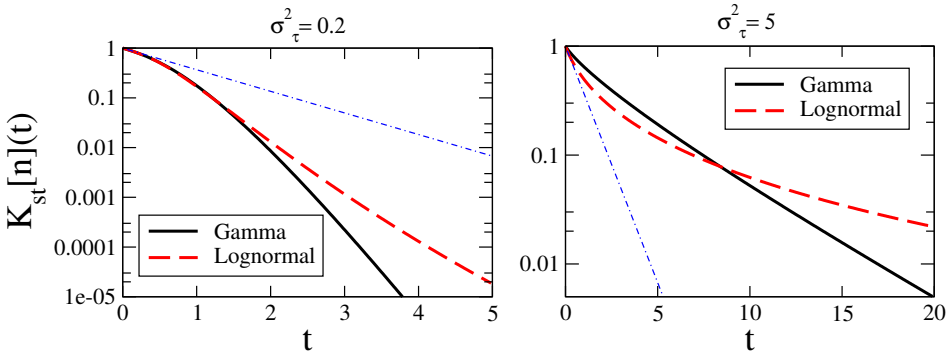

Figure 3.1: Steady state correlation function, Eq.(3.15), as a function of time, plotted in logarithmic scale, for two different types of delay distribution, gamma and lognormal, for two values of the variance of the delay: $\sigma_\tau^2 = 0.2$ (left panel) and $\sigma_\tau^2 = 5$ (right panel); in both cases the average delay is $\langle\tau\rangle = 1$ and the creation rate is $C = 1$. We also plot a exponential decay with exponent one (dot-dashed line), for comparison. Note that delay distributions with larger variance and fatter tayls display slower asymptotic decay.

of first-order degradation (γ' not dependent on the number of particles n), this instantaneous degradation is completely equivalent to a system with $\gamma' = 0$, after modifying the distribution of the delayed-degradation times in the following way:

$$f(\tau) \to e^{-\gamma'\tau} f(\tau) + e^{-\gamma'\tau}\gamma'\hat{F}(\tau). \tag{3.17}$$

That is, when instantaneous degradation is added to infected particles, the probability that the lifetime is equal to τ has two contributions: (i) a particle initially has a lifetime τ (probability density $f(\tau)$) and survives up to this time (an event with probability $e^{-\gamma'\tau}$); (ii) a particle has a lifetime larger than τ (probability $\hat{F}(\tau)$), but survives up to τ (probability $e^{-\gamma'\tau}$) and then undergoes instantaneous degradation (at rate γ'). The consideration of these two contributions leads straightforwardly to Eq.(3.17). We see that omitting first order instantaneous degradation of infected particles comprises no loss of generality, given that the treatment is valid for general distributions of delay.

If D and γ are independent of n, the process is equivalent to the one-variable system discussed in the previous subsection (3.23.2.1) with a conveniently modified distribution of delay:

$$f(\tau) \to e^{-(\gamma+D)\tau}\gamma + \int_0^\tau dt' e^{-(\gamma+D)t'} D f(\tau - t'). \tag{3.18}$$

This comes from the fact that a particle may disappear at time τ through two different processes: (i) a particle does not disappear or is infected before τ and is degraded instantaneously at time τ (probability density $e^{-(\gamma+D)\tau}\gamma$); (ii) a particle gets infected at some previous time (t') with an appropriate lifetime ($\tau - t'$, probability density $\int_0^\tau dt' e^{-(\gamma+D)t'} D f(\tau - t')$). This includes as particular cases the ones studied in [Miekisz et al., 2011; Lafuerza and Toral, 2011a]. The results of subsection (3.2.1) allows us to obtain the full solution also in the more general case of distributed delay. If D or γ depend on n the processes are not anymore equivalent, two variables are necessary and a new approach is needed for the analysis. In the following we develop this method. We will also consider the case in which the creation rate C depends on the number of particles, and denote this situation as having feedback.

The full process corresponds to the following two-variable system:

$$\emptyset \overset{C}{\longrightarrow} X_A,\ X_A \overset{\gamma}{\longrightarrow} \emptyset,\ X_A \overset{D}{\longrightarrow} X_I + Z,\ X_I \underset{\tau}{\Longrightarrow} \emptyset, \tag{3.19}$$

where we have split the proteins into two types: X_I are infected particles that will die precisely at a time τ (itself a stochastic variable) after being infected and X_A are non-infected ("active") particles (so $X = X_A \cup X_I$). We allow the rates to depend on n_A, the number of X_A, active, particles, but not on n_I, the number of X_I, infected, particles which are considered to be "inert"; this condition will be relaxed in the next subsection. Following [Miekisz et al., 2011], we have introduced the auxiliary particles Z whose number is given by the stochastic variable $n_Z(t)$. The introduction of Z will allow us to obtain the properties of n_I by using the relation:

$$n_I(t) = \int_{-\infty}^{t} dt' \frac{dn_Z(t')}{dt'} s(t', t), \tag{3.20}$$

where the discrete process $n_Z(t)$ is a sequence of step (Heaviside) functions and its derivative must be understood as a series of Dirac-delta functions. Here we have introduced the family of "survival" stochastic processes $s(t', t)$ defined in the following way: first, for each t' we obtain a value of $\tau(t')$ independently drawn from the distribution $f(\tau)$. Next, we set $s(t', t) = 1$, if $t \in (t', t' + \tau(t'))$, and $s(t', t) = 0$, otherwise. This can be considered as the indicator function of a virtual [1] particle that is infected at t' and survives up to a time $t' + \tau(t')$. It follows

[1] $s(t', t)$ is defined for all t', regardless if a particle is actually infected a time t'. However it only contributes to (3.20) if a particle is actually infected at time t', since only then $\frac{dn_Z(t')}{dt'} \neq 0$

from the definition that:

$$\langle s(t_1,t)\rangle = \hat{F}(t-t_1), \tag{3.21}$$

$$\langle s(t_1,t)s(t_2,t')\rangle = \begin{cases}\langle s(t_1,t)\rangle\langle s(t_2,t')\rangle & \text{if } t_1 \neq t_2\\ \langle s(t_1,\max\{t,t'\})\rangle & \text{if } t_1 = t_2,\end{cases} \tag{3.22}$$

Expressions (3.20-3.22) are the main advances of this section and provide us with the necessary tools to derive the main properties of the stochastic process (3.16). In the case considered in [Miekisz et al., 2011] there is a fixed delay ($f(\tau) = \delta(\tau-\tau_0)$) and no instantaneous degradation of infected particles ($\gamma' = 0$), so one has simply $n_I(t) = n_Z(t) - n_Z(t-\tau)$. The inclusion of the survival process $s(t',t)$ allows us to consider the general case of distributed delay and rates depending on the state of the system.

Note that the process followed by $\{n_A, n_Z\}$ is Markovian as the delay only appears in variable n_I, so the properties of n_Z can be obtained using Markovian methods, and the properties of the variable n_I can be derived afterwards using (3.20-3.22). In particular, the first moments follow:

$$\langle n_I(t)\rangle = \int_{-\infty}^{t} dt' \frac{d\langle n_Z(t')\rangle}{dt'}\langle s(t',t)\rangle, \tag{3.23}$$

$$\langle n_I(t)n_I(t+T)\rangle = \int_{-\infty}^{t} dt_1 \int_{-\infty}^{t+T} dt_2 \frac{d^2\langle n_Z(t_1)n_Z(t_2)\rangle}{dt_1 dt_2}\langle s(t_1,t)s(t_2,t+T)\rangle \tag{3.24}$$

Using standard Markovian methods [van Kampen, 2004] (subsection 1.4.2), one can see that the process $\{n_A, n_Z\}$ is described by the master equation:

$$\begin{aligned}\frac{dP(n_A,n_Z,t)}{dt} &= (E_A^{-1}-1)C(n_A)P(n_A,n_Z,t) + (E_A-1)\gamma(n_A)P(n_A,n_Z,t)\\ &+ (E_A E_Z^{-1})D(n_A)P(n_A,n_Z,t),\end{aligned} \tag{3.25}$$

with E_i the step operator, $E_i f(n_i,n_j) = f(n_i+1,n_j)$. In this section, we allow the creation rate C to depend on the number of X_A-particles, constituting a feedback term on the number of "active" particles. From the master equation one easily

derives the equations for the moments, the first of them read:

$$\frac{d\langle n_A\rangle}{dt} = \langle C(n_A)\rangle - \langle(\gamma + D)n_A\rangle, \tag{3.26}$$

$$\frac{d\langle n_Z\rangle}{dt} = \langle Dn_A\rangle, \tag{3.27}$$

$$\frac{d\langle n_A^2\rangle}{dt} = 2\langle 2(n_A+1)C(n_A)\rangle - \langle(2n_A-1)n_A(\gamma+D)\rangle), \tag{3.28}$$

$$\frac{d\langle n_Z^2\rangle}{dt} = 2\langle Dn_An_Z\rangle + \langle Dn_A\rangle \tag{3.29}$$

$$\frac{d\langle n_An_Z\rangle}{dt} = \langle C(n_A)n_Z\rangle - \langle(\gamma+D)n_An_Z\rangle + \langle D(n_A^2 - n_A)\rangle). \tag{3.30}$$

In the case that $C(n_A)$ is a linear function of n_A and γ and D do not depend on n_A (and none of them depend on n_I or n_Z), the system of equations is closed and can be solved. For non-linear systems, we will make use of van Kampen's expansion [van Kampen, 2004] (subsection 1.4.2). The equations for the macroscopic components are:

$$\frac{d\phi_A}{dt} = C(\phi_A) - [\gamma(\phi_A) + D(\phi_A)]\phi_A, \tag{3.31}$$

$$\frac{d\phi_z}{dt} = D(\phi_A)\phi_A. \tag{3.32}$$

The stochastic contributions, to first order in $\Omega^{-1/2}$, read:

$$\frac{d\langle\xi_A\rangle}{dt} = -\left[\widetilde{\gamma} + \widetilde{D} - C'(\phi_A)\right]\langle\xi_A\rangle, \tag{3.33}$$

$$\frac{d\langle\xi_Z\rangle}{dt} = \widetilde{D}\langle\xi_A\rangle, \tag{3.34}$$

$$\frac{d\langle\xi_A^2\rangle}{dt} = -2\left[\widetilde{\gamma} + \widetilde{D} - C'(\phi_A)\right]\langle\xi_A^2\rangle + \left(\widetilde{\gamma} + \widetilde{D}\right)\phi_A + C(\phi_A), \tag{3.35}$$

$$\frac{d\langle\xi_Z^2\rangle}{dt} = 2\widetilde{D}\langle\xi_A\xi_Z\rangle + \widetilde{D}\phi_A, \tag{3.36}$$

$$\frac{d\langle\xi_A\xi_Z\rangle}{dt} = -\left[\widetilde{\gamma} + \widetilde{D} - C'(\phi_A)\right]\langle\xi_A\xi_Z\rangle + \widetilde{D}(\langle\xi_A^2\rangle - \phi_A), \tag{3.37}$$

with $\widetilde{D} \equiv D(\phi_A) + D'(\phi_A)\phi_A$, $\widetilde{\gamma} \equiv \gamma(\phi_A) + \gamma'(\phi_A)\phi_A$. Usually, for the ansatz about the scaling of the variables to work (and so the expansion), the equations for the macroscopic components must have a single stable fixed point. In this case, however, the equation for ϕ_z does not have a fixed point, and $\phi_z(t)$ and $\langle\xi_Z^2(t)\rangle$

grow without bound. This grow, nevertheless, is consistent with $\frac{\sigma^2[n_Z](t)}{\langle n_Z(t)\rangle} = O(\Omega^0)$ ($\frac{\sigma^2[n_Z](t)}{\langle n_Z(t)\rangle} \to \frac{\widetilde{D}}{D}[1 + \widetilde{D}\phi_{A,st}\frac{2C'-D'-\gamma'}{(\widetilde{D}+\widetilde{\gamma}-C')^2}]$ asymptotically, with all functions evaluated at $\phi_{A,\text{st}}$ which will be specified latter), and the expansion can still be applied.

(3.33-3.37) is a system of closed linear equations and so can always be solved. To compute the time correlations of n_I from Eq.(3.24) we need the time correlations of n_Z. We note that:

$$\begin{aligned}\langle n_Z(t_1)n_Z(t_2)\rangle &= \sum_{n_{Z1},n_{Z2}} n_{Z1}n_{Z2}P(n_{Z2},t_2;n_{Z1},t_1)\\ &= \sum_{n_{Z1},n_{Z2},n_A} n_{Z1}n_{Z2}P(n_{Z2},t_2|n_{Z_1},n_A,t_1)P(n_{Z,1},n_A,t_1)\\ &= \langle\langle n_Z(t_2)|n_Z(t_1),n_A(t_1)\rangle n_Z(t_1)\rangle\,, \end{aligned} \tag{3.38}$$

and that $\langle n_Z(t_2)|n_Z(t_1),n_A(t_1)\rangle$ (for $t_2 > t_1$) can be obtained integrating (3.26-3.27) or (3.33-3.34). In the general, non-linear, case, using first order van Kampen's expansion, one obtains, at the steady state:

$$\langle n_Z(t_1)n_Z(t_2)\rangle_{\text{st}} = \Omega^2\phi_z(t_1)\phi_z(t_2) + \Omega\left[\langle\xi_Z^2(\min\{t_1,t_2\})\rangle + \frac{\widetilde{D}}{u}\langle\xi_A\xi_Z\rangle_{st}\left(1-e^{-u|t_1-t_2|}\right)\right], \tag{3.39}$$

with $u \equiv \widetilde{\gamma} + \widetilde{D} - C'(\phi_{A,st})$ and $\phi_{A,st}$ the solution of $C(\phi_A) = (\widetilde{\gamma}+\widetilde{D})\phi_A$. The derivative that appears in (3.24) is:

$$\frac{d^2\langle n_Z(t_1)n_Z(t_2)\rangle_{\text{st}}}{dt_1dt_2} = \Omega^2D^2\phi_{A,st}^2 + \Omega\left[\widetilde{D}u\langle\xi_A\xi_Z\rangle_{st}e^{-u|t_1-t_2|} + \widetilde{D}\phi_{A,st}\delta(t_1-t_2)\right], \tag{3.40}$$

with $\langle\xi_A\xi_Z\rangle_{st} = \frac{\widetilde{D}\phi_{A,st}^2}{2u^2}[2\frac{C'}{\phi_{A,st}} - \gamma' - D']$. Putting all the pieces together, one finally obtains:

$$\begin{aligned}&K_{\text{st}}[n_I](t) = \langle n_I(t_0)n_I(t_0+t)\rangle_{\text{st}} - \langle n_I\rangle_{\text{st}}^2 \qquad (3.41)\\ &= \Omega\widetilde{D}\phi_{A,st}\int_0^\infty dt'\hat{F}(t+t') + \Omega\widetilde{D}u\langle\xi_A\xi_Z\rangle_{\text{st}}\int_0^\infty ds\int_0^\infty dr\hat{F}(s)\hat{F}(r)e^{-u|t+s-r|}.\end{aligned}$$

Proceeding in a similar way, one can derive:

$$K_{\rm st}[n_A, n_I](t) = \Omega\langle\xi_A\xi_Z\rangle_{\rm st} u \int_0^\infty dt' e^{-u(t+t')}\hat{F}(t') \tag{3.42}$$

$$K_{\rm st}[n_I, n_A](t) = \Omega\langle\xi_A\xi_Z\rangle_{\rm st} u \int_0^\infty dt' e^{-ut'}\hat{F}(t+t') + \Omega\widetilde{D}\langle\xi_A^2\rangle_{\rm st}\int_0^t dt' e^{-ut'}\hat{F}(t-t'), \tag{3.43}$$

$$K_{\rm st}[n_A](t) = \Omega\langle\xi_A^2\rangle_{\rm st} e^{-ut}, \tag{3.44}$$

with $K_{\rm st}[n_u, n_v](t) \equiv \langle n_u(t_0+t)n_v(t_0)\rangle_{\rm st} - \langle n_u\rangle_{\rm st}\langle n_v\rangle_{\rm st}$. This finally allows to express the correlation function for the total number of particles, $n = n_A + n_I$, as:

$$K_{\rm st}[n](t) = K_{\rm st}[n_I](t) + K_{\rm st}[n_A, n_I](t) + K_{\rm st}[n_I, n_A](t) + K_{\rm st}[n_A](t). \tag{3.45}$$

In this case, the average of n again depends only on the average delay, $\langle n\rangle_{\rm st} = \Omega\phi_A(1 + D\langle\tau\rangle)$. The second moment, when interactions are present (signaled by C', D' or $\gamma' \neq 0$), depends on the delay distribution in a more complicated way, through factors involving the integral of $\hat{F}(t)$; if there are no interactions, this case reduces to the previous and we again obtain a Poisson distribution. The time correlation typically decreases monotonically but it can increase over some time range if the correlation between n_Z and n_A is negative, which can be obtained with $C'(\phi_{A,\rm st}) < 0$ (negative feedback) or $\gamma'(\phi_{A,\rm st})$ or $D'(\phi_{A,\rm st}) > 0$, and also if $C'(\phi_{A,\rm st}) - \widetilde{\gamma}(\phi_{A,\rm st}) > 0$. In figure (3.2) expression (3.45) is compared with numerical simulations, showing a very good agreement. Note that the treatment of the delayed reactions is exact, the only approximation coming from the use of van Kampen's expansion, which is needed when non-linearities are present, but whose error scales as $\Omega^{-1/2}$. Like in the previous case, the process in which the distribution of delay has fatter tail and higher variance shows slower decay for the correlation function.

3.2.3 Full feedback

We now consider the case in which the creation rate depends on all present particles

$$\emptyset \overset{C(n)}{\longrightarrow} X,\ X \underset{\tau}{\Longrightarrow} \emptyset, \tag{3.46}$$

with n the total (inert+active) number of X-particles. As noted before, this single-variable model can account for instantaneous plus delayed degradation, in the case that the degradation and "contagion" rates, denoted as γ and D in the

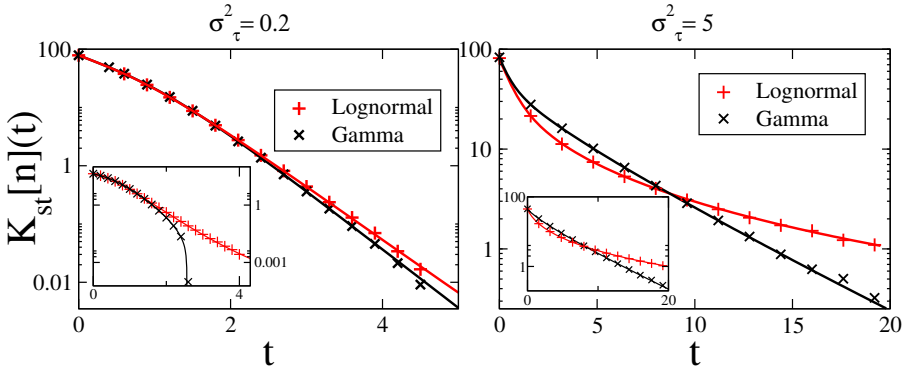

Figure 3.2: Steady state correlation function for the total number of particles as a function of time, plotted in logarithmic scale, for two different types of delay distribution, gamma and lognormal, for two values of the variance of the delay: 0.2 (left panel) and 5 (right panel); in both cases the average delay is $\langle\tau\rangle = 1$. The insets show the time correlation for the number of "infected" particles, X_I, which gives the largest contribution to the difference between different distributions. Symbols come from numerical simulations and lines from the theoretical analysis Eqs.(3.42-3.45). The creation rate is $C(n_A) = \frac{c\Omega}{1+\left(\epsilon\frac{n_A}{\Omega}\right)^2}$, parameters values are: $\Omega = 100, c = 1, \epsilon = 0.4$ and $D = \gamma = 1$.

previous subsection, do not depend on the state of the system. For simplicity, we restrict our attention to this case. This process can be treated with the approach of the previous subsection introducing the additional variable Z,

$$\emptyset \overset{C(n)}{\longrightarrow} X + Z,\ X \underset{\tau}{\Longrightarrow} \emptyset, \tag{3.47}$$

with $n_Z(t)$ the corresponding random variable giving the number of Z particles. We see that:

$$n(t) = \int_{-\infty}^{t} dt' \frac{dn_Z(t')}{dt'} s(t', t), \tag{3.48}$$

with $s(t', t)$ the same "survival" function as in the previous section. The probability distribution for $\{n, n_Z\}$ follows a master equation of the form:

$$\frac{dP(n_Z, n, t)}{dt} = (E^{-1}E_Z^{-1} - 1)C(n)P(n_Z, n, t) + (E - 1)g(n_Z, n)P(n_Z, n, t). \tag{3.49}$$

Details of the derivation of the master equation in systems with delay are given in Appendix 2. Here, $g(n_Z, n) = \int_0^\infty dt' \langle C(n(t - t'))|n_Z(t), n(t)\rangle f(t')$, with $f(t)$

the probability density of the delay distribution, although, since we are only interested in the properties of variable n, we will not be using this expression. The key step in this case is to note that Eq.(3.49) allows us to derive the statistical properties (moments and correlations) of $n_Z(t)$ as a function of those of $n(t)$. Then, using (3.48) we will be able to self-consistently derive the properties of n. More specifically, the approach proceeds as follows:
Summing Eq.(3.49) over n, we can obtain an equation for the evolution of $P(n_Z, t)$, but that still depends on n (in this step the contribution of the second term in Eq.(3.49) vanishes):

$$\frac{dP(n_Z,t)}{dt} = (E_Z^{-1} - 1)\sum_n C(n)P(n_Z, n, t) = (E_Z^{-1} - 1)\langle C(n(t))|n_Z, t\rangle P(n_Z, t). \quad (3.50)$$

The two times probability distribution $P(n_{Z_1}, t_1; n_{Z_2}, t_2)$ follows a similar equation, details are given in Appendix 2:

$$\begin{aligned}\frac{d^2P(n_{Z_1},t_1;n_{Z_2},t_2)}{dt_1dt_2} &= (E_{Z_1}^{-1} - 1)(E_{Z_2}^{-1} - 1)\langle C(n_A(t_1))C(n_A(t_2))|n_{Z_1}, t_1; n_{Z_2}, t_2\rangle \times \\ &\quad P(n_{Z_1}, t_1; n_{Z_2}, t_2) + \\ &\quad \delta(t_1 - t_2)\left[(1 - E_{Z_2})\delta_{n_{Z_1},n_{Z_2}}E_{Z_1}^{-1} + (1 - E_{Z_2}^{-1})\delta_{n_{Z_1},n_{Z_2}}\right] \times \\ &\quad \langle C(n_A)|n_{Z_1}\rangle P(n_{Z_1}, t_1)\end{aligned} \quad (3.51)$$

From (3.48) we easily obtain:

$$\langle n(t)\rangle = \int_{-\infty}^{t} dt_1 \frac{d\langle n_Z(t_1)\rangle}{dt_1}\langle s(t_1, t)\rangle \quad (3.52)$$

$$\langle n(t)n(t')\rangle = \int_{-\infty}^{t} dt_1 \int_{-\infty}^{t'} dt_2 \frac{d^2\langle n_Z(t_1)n_Z(t_2)\rangle}{dt_1dt_2}\langle s(t_1, t)s(t_2, t')\rangle. \quad (3.53)$$

While (3.50, 3.51) imply:

$$\frac{d\langle n_Z\rangle}{dt} = \langle C(n(t))\rangle, \quad (3.54)$$

$$\frac{d^2\langle n_Z(t_1)n_Z(t_2)\rangle}{dt_1dt_2} = \langle C(n(t_1))C(n(t_2))\rangle + \delta(t_1 - t_2)\langle C(n(t_1))\rangle \quad (3.55)$$

And we finally obtain the following set of integral equations for the moments:

$$\langle n(t)\rangle = \int_{-\infty}^{t} dt_1\langle C(n(t_1))\rangle\hat{F}(t - t_1) \quad (3.56)$$

$$\begin{aligned}\langle n(t)n(t')\rangle &= \int_{-\infty}^{t} dt_1 \int_{-\infty}^{t'} dt_2\langle C(n(t_1))C(n(t_2))\rangle\hat{F}(t - t_1)\hat{F}(t' - t_2) \\ &\quad + \int_{-\infty}^{t} dt_1\langle C(n(t_1))\rangle\hat{F}(\max\{t, t'\} - t_1),\end{aligned} \quad (3.57)$$

In the case of linear feedback, $C(n) = a+bn$, this system of equations is closed. For non-linear systems, one can use van Kampen's expansion as explained above. In the steady state, one finds:

$$\begin{aligned} \langle n\rangle_{st} &= \Omega\phi_{\rm st}, \qquad \phi_{\rm st} = C(\phi_{\rm st})\langle\tau\rangle && (3.58)\\ K_{\rm st}[n](t) &= \int_0^\infty dx \int_0^\infty dy K_{\rm st}[n](t+x-y)\hat{F}(x)\hat{F}(y) + \\ &+ \Omega C(\phi_{\rm st})\int_0^\infty dx\hat{F}(t+x) && (3.59)\end{aligned}$$

Eq. (3.58) shows that the steady state number of particles depends only on the average delay. Eq. (3.59) shows that the correlations depend on the delay distribution in a non-trivial way. The analysis of this equation is left for future work.

3.2.4 Non-independent delay times

In this subsection we will study the case in which the delay times depend on the state of the system. We will indicate how the method developed can account for this situation as well.

For simplicity, we consider the process analyzed in subsection (3.2.1):

$$\emptyset \overset{C}{\longrightarrow} X + Z,\ X \underset{\tau}{\Longrightarrow} \emptyset, \tag{3.60}$$

but in this case, the delay times are not independent random variables. As noted in subsection (3.2.1), a reaction with a given delay distribution is equivalent to an instantaneous reaction whose rate depends on the age of the particle. We will consider, then, that the particles are eliminated at a rate, r, that depends on the age, a, of the particle and on the current number of present particles $n(t)$, i.e. $r = r(a, n(t))$. As seen before, the survival probability of a particle created at t_1 to survive until time t_2 is:

$$\hat{F}(t_1, t_2) = e^{-\int_{t_1}^{t_2} dt' r(t'-t_1, n(t'))}. \tag{3.61}$$

This fact allows to analyze this case exactly as the previous one. Again the number of particles n can be expressed as a function of the number of the auxiliary variable Z:

$$n(t) = \int_0^t dt' \frac{dn_z(t')}{dt'} s(t', t), \tag{3.62}$$

with the survival stochastic process defined as before. Note that now, due to (3.61) the survival probability depends on previous values of n. For the average, one obtains:

$$\langle n(t)\rangle = \int_0^t dt' C\langle e^{-\int_{t'}^{t} dt'' r(t''-t',n(t''))}\rangle, \tag{3.63}$$

(the factor C appears because we are considering the simple case of no feedback). And similarly for higher order moments. Assuming van Kampen's splitting of the variable n and that the rate r depends on n only throug n/Ω at first order, it is possible to obtain closed equations for the mean value and fluctuations, but in this case they are integral equations.

3.3 Delayed creation

We now turn our attention to the case in which the creation reaction, that is initiated stochastically, takes a finite time to be completed. For simplicity, we initially assume that the degradation reaction is instantaneous. Schematically, we have:

$$\emptyset \overset{C(n)}{\longrightarrow} \underset{\tau}{\Longrightarrow} X, \qquad X \overset{\gamma(n)}{\longrightarrow} \emptyset. \tag{3.64}$$

In this case, if the creation rate does not depend on the number of particles, n, then the delay in the creation is completely irrelevant, since the probability that a new particle appears at time t is equal to the probability that its creation started at a time $t-\tau$, but this equal to the probability that a particle starts its creation at time t. If the creation rate, C, is time dependent and the delay is fixed, (with a shift in the time if C is time-dependent), so the process is completely equal to one with instantaneous creation.
We will see that the case of delayed creation with feedback shows an interesting delay-dependent phenomenology, that we will analyze in some detail.

We will adopt here an approach different from that of the previous sections [Lafuerza and Toral, 2011b], that, besides the moments, will allow us to obtain an expression for the full probability distribution. In Appendix 2 it is shown that the master equation of the process (3.64) is:

$$\begin{aligned}\frac{\partial P(n,t)}{\partial t} &= (E-1)[\gamma(n)nP(n,t)] \\ &+ (E^{-1}-1)\left[\sum_{n'=0}^{\infty}\int_0^{\infty} d\tau C(n')P(n',t-\tau;n,t)f(\tau)\right],\end{aligned} \tag{3.65}$$

(we remind that $f(\tau)$ is the probability density of the delay). The master equation (3.65) can be written as:

$$\frac{\partial P(n,t)}{\partial t} = (E-1)[\gamma(n)nP(n,t)] + (E^{-1}-1)[\tilde{C}(n,t)P(n,t)], \tag{3.66}$$

where the effective creation rate, $\tilde{C}(n,t)$, is given by:

$$\tilde{C}(n,t) = \int_0^\infty d\tau f(\tau)\langle C(n'(t-\tau))|n(t)\rangle. \tag{3.67}$$

The conditional probability $P(n,t|n_0,t_0)$ follows a master equation identical to (3.65) with all the probabilities conditioned to n_0 at time t_0. From it, and using that $\langle n(t)|n(t_0)\rangle = \sum_n nP(n,t|n(t_0),t_0)$, we obtain the following evolution equation for the conditional average:

$$\frac{d\langle n(t)|n(t_0)\rangle}{dt} = -\langle\gamma(n(t))n(t)|n(t_0)\rangle + \int_0^\infty d\tau f(\tau)\langle C(n(t-\tau))|n(t_0)\rangle, \tag{3.68}$$

for $t \geq 0$, with initial condition $\langle n(t_0)|n(t_0)\rangle = n(t_0)$.

The knowledge of the steady value $\tilde{C}_{\rm st}(n) \equiv \lim_{t\to\infty}\int d\tau\langle C(n'(t-\tau))|n,t)\rangle f(\tau) = \int d\tau\langle C(n'),-\tau|n\rangle_{\rm st} f(\tau)$ [2], allows the calculation of the steady-state probabilities $P_{st}(n)$, obtained by imposing $\frac{\partial P(n,t)}{\partial t} = 0$ in Eq.(3.66), as (see section 1.4):

$$P_{\rm st}(n) = P_{\rm st}(0)\prod_{k=0}^{n-1}\frac{\tilde{C}_{\rm st}(k)}{(k+1)\gamma(k+1)} = \frac{P_{\rm st}(0)}{\gamma^n n!}\prod_{k=0}^{n-1}\tilde{C}_{st}(k), \tag{3.69}$$

$P_{\rm st}(0)$ is fixed by the normalization condition, and the second equality holds when the degradation rate, γ, does not depend on n. In the remaining of this section we focus in the constant γ case to obtain more explicit results; the extension to the case in which γ depends on n is straightforward. All is left to do now is to compute the effective creation rate $\tilde{C}_{\rm st}(n)$.

The effective creation rate will be computed using expression (3.68). In the general case of nonlinear creation rate, we will use van Kampen's expansion (see section 1.4.2) to linearize $C(n)$ around the macroscopic component of n. We have: $C(n) = \Omega C(\phi) + \Omega^{1/2}C'(\phi)\xi$, so

$$\langle C(n'(t-\tau))|n(t)\rangle = \Omega C(\phi(t-\tau)) + \Omega^{1/2}C'(\phi(t-\tau))\langle\xi'(t-\tau)|\xi(t)\rangle \tag{3.70}$$

[2] A necessary condition for the existence of this steady state is that C and γ do not explicitly depend on time or reach an asymptotic constant value; in the following we assume that this condition is satisfied and C and γ will refer to those steady state expressions.

using (3.68) we obtain:

$$\frac{d\phi(t)}{dt} = -\gamma\phi(t) + \int_0^\infty d\tau f(\tau) C\left(\phi(t-\tau)\right), \tag{3.71}$$

$$\frac{d\langle\xi(t')|\xi(t)\rangle}{dt'} = -\gamma\langle\xi(t')|\xi(t)\rangle + \int_0^\infty d\tau f(\tau) C'\left(\phi(t-\tau)\right)\langle\xi(t')-\tau|\xi(t)\rangle \tag{3.72}$$

Equation (3.71) is in general a non-linear integro-differential equation, that can be difficult to solve. Here, however, we will focus on the cases in which (3.71) has a stable steady state as a single attractor, which is the solution of $\gamma\phi = C(\phi)$. This is the regimen in which the validity of van Kampen's expansion is guaranteed.

We reach now a delicate point. Eq.(3.72) is a (linear) integro-differential equation. To solve it, we would need an initial condition in the whole interval $(-\infty, t)$ but we only know a one-time condition $\langle\xi(t'=t)|\xi(t)\rangle = \xi(t)$. We will circumvent this difficulty by assuming that, over the steady state, the system is statistically invariant under time-reversal, which implies $\langle\xi(t+t_1)|\xi(t)\rangle = \langle\xi(t-t_1)|\xi(t)\rangle$. This condition, together with the value of ξ at time t, allows to find the solution of (3.72). The time-reversal invariance assumption in the steady state is fulfilled by any Markovian system that follows detailed balance. Our system follows detailed balance (as any one-step process [van Kampen, 2004]), but, due to the presence of delay, it is not Markovian. So the time-reversal invariance is an assumption, whose validity needs to be checked. In Fig. (3.3) we plot the correlations $\langle n, \tau|k\rangle_{st}$ and $\langle n, -\tau|k\rangle_{st}$ as a function of k, using a negative feedback loop $C(n) = \frac{c}{1+\epsilon n}$ for two different sets of parameters, in the case of constant delay, $f(t) = \delta(t-\tau)$ (that we will see is the case for which the delay has greatest effect). In the same figure we plot the stationary probability distribution $P_{st}(k)$. As it can be seen from this figure, it is not true that these two correlations are identical for all values of k. However, it has to be noticed that the larger discrepancies occur for those values of k which have a low probability of appearance, so the time-reversal invariance is approximately valid.

In the case of constant delay, equation (3.71) for the macroscopic component becomes a nonlinear delayed differential equation. As in the general delay-distributed case, the steady state value ϕ_{st} is readily accessible as the solution of $\gamma\phi_{st} = C(\phi_{st})$. The stability of this fixed point is found by linearization around it. A standard analysis of the resulting linear delay differential equation, tells us that a sufficient (but not necessary) condition for stability is $|\alpha| < \gamma$, where we have defined $\alpha \equiv -C'\left(\phi_{st}\right)$.

Once in the steady state, we replace $\phi(t)$ by its stationary value ϕ_{st} and Eq. (3.72) becomes a delay linear differential equation with constant coefficients, and we are looking for the time-symmetric solution of this equation satisfying the initial

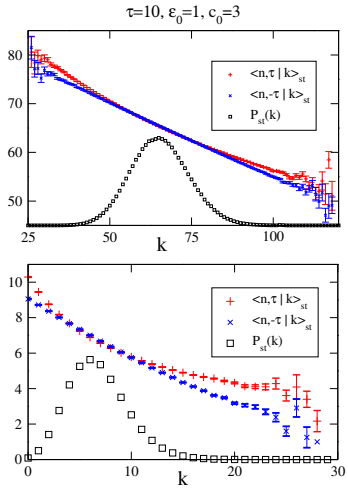

Figure 3.3: Conditional averages in the steady state, $\langle n, \tau | k \rangle_{st}$ (+ symbols) and $\langle n, -\tau | k \rangle_{st}$ (× symbols) coming from numerical simulations of the process with delay schematized in Eq.(3.64) using a creation rate $C(n) = \frac{c_0 \Omega}{1 + \frac{c_0}{\Omega} n}$, with a constant delay of $\tau = 10, \epsilon_0 = 1, c_0 = 3$ and two different values of $\Omega = 50$ (top) and $\Omega = 5$ (bottom) (Ω gives a measure of system size). In the same figures, we also plot with square symbols, the (arbitrarily rescaled) stationary probability distribution $P_{st}(k)$. Note that the discrepancy between $\langle n, \tau | k \rangle_{st}$ and $\langle n, -\tau | k \rangle_{st}$ is larger in those cases that the particular value of k is less probable, and that this discrepancy becomes smaller as the system size increases.

condition $\langle \xi', t | \xi, t \rangle = \xi$. This can be written as $\langle \xi', t + \Delta | \xi, t \rangle = \xi g(\Delta)$, being $g(t)$ the symmetric solution $g(-t) = g(t)$ of the equation $\dot{g}(t) = -\gamma g(t) - \alpha g(t - \tau)$ and $g(0) = 1$ (see Appendix 4). From Eq.(3.70) we get the effective creation rate $C(n) = \Omega C(\phi_{st}) + \Omega^{1/2} C'(\phi_{st}) \xi g(\tau) = \Omega \phi_{st} (\gamma - C'(\phi_{st}) g(\tau)) + C'(\phi_{st}) g(\tau) n$ after replacing $\xi = \Omega^{-1/2} n - \Omega^{1/2} \phi_{st}$ and $\gamma \phi_{st} = C(\phi_{st})$. From Eq.(3.69) one can obtain the steady-state probabilities $P_{st}(n)$. Their functional form depends on the sign of $C'(\phi_{st}) g(\tau)$: (i) If $C'(\phi_{st}) g(\tau) < 0$, the distribution is a binomial distribution $P_{st}(n) = \binom{M}{n} p^n (1 - p)^{M-n}$ with $p = \frac{-C'(\phi_{st}) g(\tau)}{\gamma - C'(\phi_{st}) g(\tau)}$ and $M = \Omega C(\phi_{st}) \left(\frac{\gamma}{-C'(\phi_{st}) g(\tau)} - 1 \right)$ and $0 \leq n \leq M$; (ii) if $C'(\phi_{st}) g(\tau) = 0$, the distribution has a Poisson form $P_{st}(n) = e^{-\chi} \frac{\chi^n}{n!}$ with $\chi = \Omega C(\phi_{st})$; (iii) finally, if $C'(\phi_{st}) g(\tau) > 0$, the distribution is a negative binomial, $P_{st}(n) = \binom{M+n-1}{n} (1 - q)^M q^n$, with $q = \frac{C'(\phi_{st}) g(\tau)}{\gamma}$ and $M = \Omega C(\phi_{st}) \left(\frac{\gamma}{C'(\phi_{st}) g(\tau)} - 1 \right)$. In all cases, however, they can be approximated up to terms of order $\Omega^{-1/2}$ by a Gaussian distribution. Despite the differences in the

functional form, in all three cases the mean value and variance are given by:

$$\langle n \rangle_{st} = \Omega \phi_{st} \tag{3.73}$$

$$\sigma^2_{st} = \frac{\langle n \rangle_{st}}{1 - \gamma^{-1} C'(\phi_{st}) g(\tau)}, \tag{3.74}$$

An equivalent expression for the variance taking as a starting point a linear Langevin differential equation including delay was obtained in [Küchler and Mensch, 1992; Frank et al., 2003].

In the case of a negative feedback loop, we have $\alpha = -C'(\phi_{st}) > 0$. It can then be seen from the expression in the Appendix 4 that $g(\tau)$ monotonically decreases from the value 1 at $\tau = 0$ to the value $-\frac{\gamma-\lambda}{\alpha} < 0$ at $\tau \to \infty$ ($\lambda = \sqrt{\gamma^2 - \alpha^2}$, see Appendix 4, recall that $|\alpha| < \gamma$ is a sufficient condition for the stability of the fixed point ϕ_{st}). In this case the fluctuations are sub-Poissonian if $g(\tau) > 0$ (small τ) and super-Poissonian if $g(\tau) < 0$ (large τ). The threshold between the two cases is the value τ_P at which $g(\tau_P) = 0$ or $\tau_P = -\lambda^{-1} \ln \zeta$ in the notation of the Appendix 4. As explained before, the probability distribution is binomial for $\tau < \tau_P$, Poissonian for $\tau = \tau_P$ and a negative binomial for $\tau > \tau_P$. This is illustrated in figure (3.4), where we also plot the Hopf bifurcation into a limit cycle that the macroscopic part ϕ undergoes due to the presence of delayed negative feedback, for a particular creatin rate of the form $\frac{c}{1+(\epsilon\phi)^2}$. We see that the transition from sub-Poissonian to super-Poissonian happens way before the bifurcation for the macroscopic component takes place. Moreover, for moderately large delays, a small amount of negative feedback is enough to induce super-Poissonian fluctuations, indicating that for large delays, negative feedback almost always increases the fluctuations (we remind that fluctuations are Poissonian when no feedback is present).

In the case of positive feedback, $\alpha = -C'(\phi_{st}) < 0$, $g(\tau)$ monotonically decreases from 1 at $\tau = 0$ to $-\frac{\gamma-\lambda}{\alpha} > 0$ at $\tau \to \infty$, and in this case the fluctuations are always super-Poissonian, but their magnitude is reduced as the delay is increased. The steady-state probability distribution is always a negative binomial distribution.

We conclude that the delay can have opposite effects: in a negative feedback loop it enhances the fluctuations, whereas in a positive feedback loop it reduces them. On the other hand, it is well known that, in the non-delay scenario, a negative feedback reduces the magnitude of the fluctuations [Thattai and van Oudenaarden, 2001] when compared to the n-independent creation rate. We find it remarkable that the presence of delay can reverse the usual fluctuations-reducing effect of the negative feedback loop, and, instead, enhance the fluctuations.

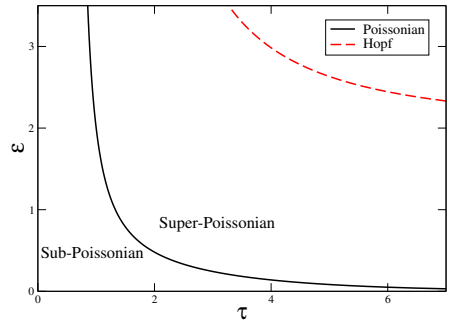

Figure 3.4: Relative size of the variance respect mean value for the number of particles, in the $\tau - \epsilon$ plane, for creation with constant delay and a negative feedback given by a creation rate of the form $\frac{c}{1+(\epsilon\phi)^2}$ (note that ϵ is the strength of the negative feedback). The "Poissonian line", $\sigma^2[n] = \langle n \rangle$, obtained through the approximation (3.74), marks the transition from sub-Poissonian to Super-Poissonian fluctuations, while the Hopf line marks the Hopf transition into oscillatory behavior in the deterministic system. Parameters values are: $c = 1$, $D = \gamma = 1$.

The correlations in the steady state can be obtained from $K[n](t) = \langle n(t)\langle n(t' + t)|n(t'))\rangle_{st}\rangle_{st} - \langle n\rangle_{st}^2$, as:

$$K[n](t) = \sigma_{st}^2 g(t). \tag{3.75}$$

Note that, as can be seen from the alternative definition $K[n](t) = \lim_{t'\to\infty}\langle n(t + t')n(t')\rangle - \langle n\rangle_{st}^2$, the correlation function is a time-symmetric function $K[n](-t) = K[n](t)$. However, and contrary to previous assumptions[Bratsun et al., 2005], this does not imply that the conditional expectation value $\langle n', t|n\rangle_{st}$ has to be a symmetric function. In fact, it is not for an arbitrary value of n, as shown in Fig.3.3. The analytical expression of $g(t)$ (given in Appendix 4) shows that in the case of negative feedback the correlation function becomes non-monotonic, developing peaks of alternating sign at approximately multiples of the delay, signaling the presence of stochastic oscillations. For positive feedback, the time correlation is always positive, but not necessarily monotonic.

We apply these results to specific functional dependences of $C(n)$. Let us first comment that in the linear case $C(n) = c - \epsilon n$, Eq.(3.68) is already a closed equation and our treatment, not surprisingly, can be carried out without assuming the expansion (3.70). However, we do not find this case very interesting as it turns out that the problem is ill-defined as the rate $C(n)$ might become negative when the number of molecules n exceeds c/ϵ.

A more interesting case, used in the protein transcription problem [Tyson, 2004], is the rate $C(n) = \frac{c}{1+\epsilon n}$, that we write in the form $C(n) = \Omega C\left(\frac{n}{\Omega}\right)$ with $C(z) = \frac{c_0}{1+\epsilon_0 z}$ and $c_0 = c/\Omega$, $\epsilon_0 = \epsilon\Omega$ where Ω is a large parameter, typically proportional to the cell volume. This corresponds to a negative feedback loop. Note that the condition $|a| < \gamma$ is always satisfied for such a creation rate and the steady state ϕ_{st} is always stable no matter how large the delay time τ.

In Fig.(3.5) we compare the average and variance obtained from numerical simulations with those obtained from the theoretical analysis. The agreement is, in general, very good and improves as Ω becomes large. In Fig.(3.6) we compare the correlation function obtained numerically with the analytical expression (3.75). Its non-monotonic character due to the delay is apparent.

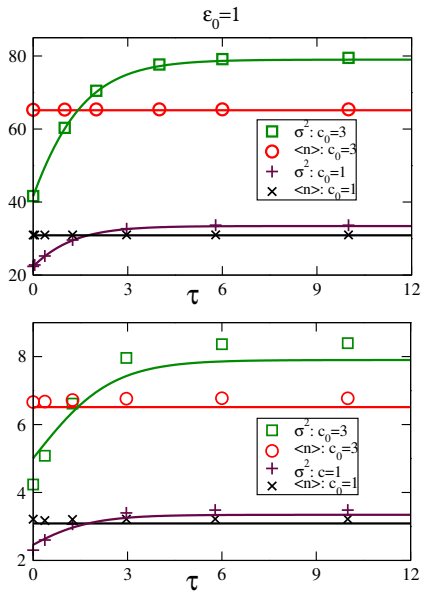

Figure 3.5: Steady state average $\langle n \rangle_{st}$ (dashed lines) and variance σ^2_{st} (full lines), for process defined in (3.64), as a function of the delay time τ, for a creation rate $C(n) = \frac{c_0\Omega}{1+\frac{c_0}{\Omega}n}$ with $c_0 = 3$ (upper part of each panel) and $c_0 = 1$ (lower part of each panel), and two system sizes (Ω) (upper and lower panel) and $\epsilon_0 = 1$ in both cases. In each case, we plot with symbols the results coming from numerical simulations and by lines the theoretical expressions, Eqs. (3.73) and (3.74).

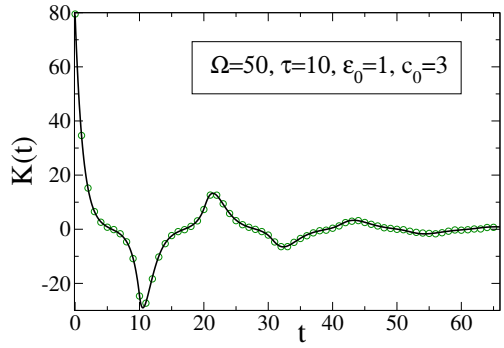

Figure 3.6: Correlation function in the steady state, for the delayed process (3.64) with creation rate $C(n) = \frac{c_0\Omega}{1+\frac{\epsilon_0}{\Omega}n}$. Simulations (circles) and theory, equation (3.75) (solid line).

For $C(n) = \frac{c_0\Omega}{1+\epsilon_0\left(\frac{n}{\Omega}\right)^l}$ with $l > 1$, (negative feedback loop with cooperativity) the equation for the macroscopic variable (3.71) has a Hopf bifurcation into a limit cycle attractor, as we noted earlier. For parameters below the Hopf bifurcation, the situation is qualitatively equal to the previous case, and the discussion applies. For parameters above the Hopf bifurcation, the macroscopic variable becomes oscillatory. Still the stochastic system will have a stationary distribution (but with a correlation time that increases with system size, Ω, [Gaspard, 2002], corresponding to stochastic oscillations). In the regimen with stochastic oscillations, at a given "phase" of the cycle the time reversal invariance will not be satisfied. However, when we consider the conditional average $\langle n, t \pm \Delta | k, t\rangle$, we average over different phases with the same instantaneous value for the number of particles, k, some phases will be "increasing" others will be decreasing and by averaging we can expect the time inversion invariance to be approximately fulfilled (at least for symmetric cycles).

3.3.1 Distributed delay

The case of distributed delay presents some additional technical difficulties. The master equation has the same form as before, so the mean value, variance and

correlation function are given by:

$$\langle n\rangle_{st} = \Omega\phi_{st}, \tag{3.76}$$

$$\sigma^2_{st} = \frac{\langle n\rangle_{st}}{1-\gamma^{-1}C'(\phi_{st})\int d\tau f(\tau)g(\tau)}, \tag{3.77}$$

$$K(t) = \sigma^2_{st}g(t), \tag{3.78}$$

but now $g(t)$ is the solution of the integro-differential equation (remember $f(\tau)$ is the probability density of the delay)

$$\frac{dg(t)}{dt} = -\gamma g(t) + C'\left(\phi_{st}\right)\int \mathrm{d}\tau f(\tau)g(t-\tau) \tag{3.79}$$

satisfying $g(-t) = g(t)$ and $g(0) = 1$. There is no general method that can be applied to find the solution of this complicated equation. A reduction to a set of linear differential equations can be achieved if we adopt the Gamma probability distribution: $f(\tau;k) = A\tau^{k-1}e^{-\frac{k}{\overline{\tau}}\tau}$, depending on two parameters: k and $\overline{\tau}$, for $k \in \mathbb{N}^+$. The average value is $\overline{\tau}$ and the root-mean-square is $\sigma_\tau = \frac{\overline{\tau}}{\sqrt{k}}$. Increasing k for fixed $\overline{\tau}$ decreases the fluctuations of τ, and in the limit $k \to \infty$ the distribution approaches a Dirac-delta and τ becomes a deterministic variable (fixed delay). As pointed out in section (3.2.1) this form of the delay is equivalent to a reaction composed by k steps each one with a rate $k/\overline{\tau}$. The alternative solution method, known as the linear-chain trick[Smith, 2011], begins by defining a family of time-dependent functions $Z_l(t) = \int \mathrm{d}\tau f(\tau;l)g(t-\tau)$, $l = 1,\ldots,k$. After some algebra, one can prove that (3.72) is equivalent to the system of linear ordinary differential equations:

$$\frac{dg(t)}{dt} = -\gamma g(t) + C'\left(\phi_{st}\right)Z_k(t), \tag{3.80}$$

$$\frac{dZ_1}{dt} = \frac{k}{\overline{\tau}}(g(t) - Z_1), \tag{3.81}$$

$$\frac{dZ_l}{dt} = \frac{k}{\overline{\tau}}(Z_{l-1} - Z_l), \qquad l = 2,\ldots,k. \tag{3.82}$$

which, besides $g(0) = 1$, require a set of initial conditions for $Z_l(t=0)$, $l = 1,\ldots,k$. These can be determined in a self-consistent manner. First, note that the symmetry condition $g(t) = g(-t)$ implies:

$$Z_l(t=0) = \int \mathrm{d}\tau f(\tau;l)g(\tau), \qquad l = 1,\ldots,k. \tag{3.83}$$

One then solves (3.80-3.82) with arbitrary initial conditions for $Z_l(t=0)$ and imposes (3.83). This yields an algebraic system of k linear equations for $Z_l(t=0)$.

The solution of the linear differential equations (3.80-3.82) and the solution of the algebraic equations (3.83) can be obtained, either analytically for small k, or numerically, but with a very high precision, for large k. Note that in order to compute the variance, Eq.(3.77), all we need to know is $\int d\tau f(\tau;k)g(\tau) = Z_k(t = 0)$.

In Fig.(3.7) we plot the ratio $\sigma^2_{st}/\langle n\rangle_{st}$ as a function of σ_τ for fixed mean delay $\overline{\tau}$. We see that as the delay distribution becomes wider (decreasing k), the fluctuations of the process decrease, so that the effect of the delay becomes less important. The results for the Gamma probability distribution are qualitatively equal to other distributions for the delay times such as uniform or Gaussian (truncated in order not to produce negative values). This results suggests that a natural or artificial system should have a rather precise delay if it is to make use of the effects that delay induces in the fluctuations, or it should have an irregular delay to avoid those effects.

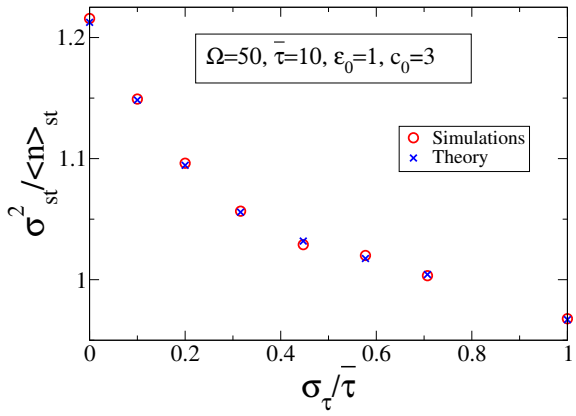

Figure 3.7: Variance normalized to the mean value $\sigma^2_{st}/\langle n\rangle_{st}$, for the process with distributed delay defined in (3.64) and a creation rate $C(n) = \frac{c_0\Omega}{1+\frac{c_0}{\Omega}n}$, for a delay distributed according to a gamma distribution $p(\tau;k) = A\tau^{k-1}e^{-\frac{k}{\overline{\tau}}\tau}$, as a function of the relative size of the fluctuations in the delay $\frac{\sigma_\tau}{\overline{\tau}} = k^{-1/2}$. Results coming from numerical simulations (○) and from the theoretical method (×) as explained in the main text.

3.3.2 Two-step creation model

So far, we have considered simple one-step birth and death processes. Now we will analyze a system in which the creation takes two steps to be completed. The particular model is motivated by gene regulation, where the protein production involves two major steps (transcription and translation). In this context, it is well known that the combined effect of the two steps can enhance significantly protein fluctuations [Thattai and van Oudenaarden, 2001]. Here we will consider the effect of delay in the process, a very relevant question since transcription and translation reactions take significant times to be completed [Voliotis et al., 2008].The process can be schematized as follows:

$$\emptyset \xrightarrow{C} Y^* \underset{\tau_1}{\Longrightarrow} Y, \qquad Y \xrightarrow{\omega} X^* \underset{\tau_2}{\Longrightarrow} X, \qquad X \xrightarrow{\gamma_n} \emptyset, \qquad Y \xrightarrow{\gamma_m} \emptyset. \tag{3.84}$$

Now X corresponds to the protein (with n the current number) and Y to the mRNA. We denote by m the number of mRNA molecules at time $t-\tau_2$. In doing so, the translational delays τ_1 and τ_2 can be absorbed in a total delay $\tau \equiv \tau_1 + \tau_2$. The master equation for the process is:

$$\begin{aligned} \frac{\partial P(m,n,t)}{\partial t} &= (E_n - 1)[\gamma_n n P(m,n,t)] + (E_m - 1)[\gamma_m m P(m,n,t)] \\ &+ (E_n^{-1} - 1)\left[\omega m P(n,m,t)\right] + (E_m^{-1} - 1)\left[\sum_{n'=0}^{\infty} C(n') P(n', t-\tau; m, n, t)\right] \end{aligned} \tag{3.85}$$

being E_n and E_m the step operators for the number of proteins, n, and the number of mRNA, m, respectively. As before, we will allow for feedback loops by letting the creation rate C to become a function on n. For simplicity, though, the translation rate ω, as well as the degradations rates γ_n and γ_m will be considered constant, and we also assume a fixed delay τ.

The general formal expression for the stationary solution of the master equation (3.85) is not known. To proceed in this case, we will apply van Kampen's expansion, which assumes that both n and m can be split in deterministic and stochastic contributions as $n = \Omega\phi_n + \Omega^{1/2}\xi_n$ and $m = \Omega\phi_m + \Omega^{1/2}\xi_m$. This expansion in the inverse of the system size has been applied to other stochastic systems [Mackane and Newman, 2005; de la Lama et al., 2006; Galla, 2009]. [de la Lama et al., 2006] The probability density function $\Pi(\xi_n, \xi_m)$ for the stochastic variables satisfies a Fokker-Planck equation that is found by expanding the

master equation in powers of Ω:

$$\begin{aligned}\frac{\partial \Pi(\xi_m,\xi_n,t)}{\partial t} &= \frac{\partial}{\partial \xi_m}\{\Big[\gamma_m\xi_m - f'(\phi_n(t-\tau))\langle\xi_n',t-\tau|\xi_m,\xi_n,t\rangle\Big]\Pi\} \\ &+ \frac{1}{2}\Big[\gamma_m\phi_m + f(\phi_n(t-\tau))\Big]\frac{\partial^2}{\partial\xi_m^2}\Pi + \frac{\partial}{\partial\xi_n}\{\big[\gamma_n\xi_n - \omega\xi_m\big]\Pi\} \\ &+ \frac{1}{2}\Big[\gamma_n\phi_n + \omega\phi_m\Big]\frac{\partial^2}{\partial\xi_n^2}\Pi. \end{aligned} \tag{3.86}$$

The deterministic contributions ϕ_n, ϕ_m and the averages of the fluctuation terms obey the following system of delayed differential equations:

$$\frac{d\phi_m}{dt} = -\gamma_m\phi_m + \Phi(\phi_n(t-\tau)), \tag{3.87}$$

$$\frac{d\phi_n}{dt} = -\gamma_n\phi_n + \omega\phi_m, \tag{3.88}$$

$$\begin{aligned}\frac{d\langle\xi_m',t'|\xi_n,\xi_m,t\rangle}{dt'} &= -\gamma_m\langle\xi_m',t'|\xi_n,\xi_m,t\rangle \\ &+ \Phi'(\phi_n(t-\tau))\langle\xi_n',t'-\tau|\xi_n,\xi_m,t\rangle,\end{aligned} \tag{3.89}$$

$$\frac{d\langle\xi_n',t'|\xi_n,\xi_m,t\rangle}{dt'} = -\gamma_n\langle\xi_n',t'|\xi_n,\xi_m,t\rangle + \omega\langle\xi_m',t'|\xi_n,\xi_m,t\rangle. \tag{3.90}$$

The solutions for the average of the fluctuations with appropriate initial conditions, after replacing $\phi_m(t)$ and $\phi_n(t)$ by their stationary values $\phi_{n,st}$ and $\phi_{m,st}$ coming from the fixed-point solution of Eqs.(3.87,3.88) can be solved under the assumption of time-reversal invariance, to obtain:

$$\langle\xi_n',t|\xi_m,\xi_n\rangle_{st} = f_n(t)\xi_n + f_m(t)\xi_m \tag{3.91}$$

(see Appendix 4 for explicit expressions of the functions $f_n(t)$ and $f_m(t)$). We replace again $\phi_m(t)$ and $\phi_n(t)$ by $\phi_{n,st}$ and $\phi_{m,st}$ and use the time reversal approximation $\langle\xi_n',-\tau|\xi_m,\xi_n\rangle_{st} = \langle\xi_n',\tau|\xi_m,\xi_n\rangle_{st}$ to reduce Eq.(3.86) to a linear Fokker-Planck equation whose solution is well known to be a Gaussian distribution [van Kampen, 2004]. The corresponding steady state values for the average and fluctuations in protein levels are given by:

$$\langle n\rangle_{st} = \Omega\phi_{n,st} \tag{3.92}$$

$$\frac{\sigma^2_{n,st}}{\langle n\rangle_{st}} = 1 + \frac{\frac{\omega}{\gamma_m}}{1+\frac{\gamma_n}{\gamma_m}+\frac{\alpha}{\gamma_m}f_m(\tau)}\frac{1-\frac{\alpha}{\gamma_n}f_n(\tau)(1+\frac{\alpha}{\gamma_m}f_m(\tau))}{1+\frac{\alpha}{\gamma_m}\left(\frac{\omega}{\gamma_n}f_n(\tau)+f_m(\tau)\right)} \tag{3.93}$$

In the case of no delay ($\tau = 0$), this expression reduces to the one obtained in [Thattai and van Oudenaarden, 2001]. In Fig.(3.8) we compare the average and

variance of this transcription-translation model as a function of the delay for a creation rate of the form $C(n) = \frac{c_0\Omega}{1+\frac{c_0}{\Omega}n}$. Again, in this negative feedback loop setting, the delay significantly enhances the fluctuations, up to a level well over the value without feedback (marked in the figure by a dashed line), leaving the mean value $\langle n\rangle_{st}$ essentially unchanged. So again in this case, the delay reverts the effect of the negative feedback, from fluctuation-reducing (for low values of the delay) to fluctuation-amplifying (for large values of the delay).

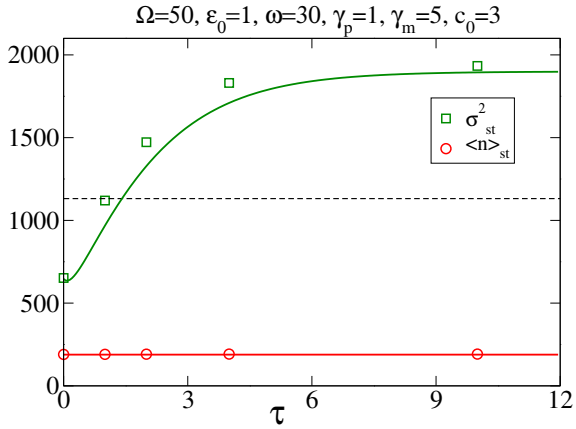

Figure 3.8: Stationary values for the average $\langle n\rangle_{st}$ and variance σ^2_{st} for the protein levels as a function of the total delay, for the transcription-translation model schematized in (3.84) for a creation rate of the form $C(n) = \frac{c_0\Omega}{1+\frac{c_0}{\Omega}n}$. Values from numerical simulations (symbols) and theory (solid lines, Eq. (3.93)). Values of parameters in top of figure. The dashed line corresponds to the variance of a system without feedback, with the same average.

We will finish by noting that the "effective Markovian reduction" method used in the previous section can also be used for the case of delay in the creation with feedback. Moreover it allows to consider the general case of delay both in the creation and in the degradation step in a simple way. We consider two independent delays, one in the creation (with probability density $f_c(t)$), and one in the degradation (with probability density $f_d(t)$). The process is schematized as follows:

$$\emptyset \overset{C(n)}{\longrightarrow} \underset{\tau_c}{\Longrightarrow} X, \qquad X \underset{\tau_d}{\Longrightarrow} \emptyset, \tag{3.94}$$

with $\tau_{c/d}$ random variables distributed according to $f_{c/d}(t)$. With the addition of two new variables, the process can be rewritten as:

$$\emptyset \overset{C(n)}{\longrightarrow} Z + Y, \qquad Y \underset{\tau_c}{\Rightarrow} X, \qquad X \underset{\tau_d}{\Rightarrow} \emptyset, \tag{3.95}$$

which allows us to note that:

$$n(t) = \int_{-\infty}^{t} dt' \frac{dn_Z(t')}{dt'} \tilde{s}(t', t). \tag{3.96}$$

In this case, the survival process $\tilde{s}(t', t)$ is defined as: $\tilde{s}(t', t) = 1$, if $t \in (t' + \tau_c(t'), t' + \tau_c(t') + \tau_d(t'))$, and $\tilde{s}(t', t) = 0$, otherwise, being $\tau_c(t')$ and $\tau_d(t')$ random times obtained from the corresponding pdf's $f_c(\tau_c)$ and $f_d(\tau_d)$. $\tilde{s}(t', t)$ is equal to 1 if a virtual particle that initiated its creation at time t' finished it at some intermediate time $t'' < t$ and since then had a lifetime greater that $t - t''$, so that it is still alive at t, being 0 otherwise. It follows that:

$$\langle \tilde{s}(t_1, t) \rangle = \int_0^{t-t_1} dt' f_c(t') \hat{F}_d(t - t_1 - t') \tag{3.97}$$

$$\langle \tilde{s}(t_1, t)\tilde{s}(t_2, t') \rangle = \begin{cases} \langle \tilde{s}(t_1, t) \rangle \langle \tilde{s}(t_2, t') \rangle, & \text{if } t_1 \neq t_2, \\ \int_0^{\min\{t,t'\}-t_1} dt'' f_c(t'') \hat{F}_d(\max\{t, t'\} - t_1 - t''), & \text{if } t_1 = t_2. \end{cases} \tag{3.98}$$

In the case that the creation rate $C(n)$ does not depend on the number of X-particles, the number of Z-particles follows a Markovian process (Poisson process), and the properties of n can be derived from (3.96). If the creation rate depends on the number of X-particles i.e. if feedback is present, the properties of n_Z can be derived formally as a function of n and then the properties of n can be derived self-consistently trough (3.96), as done in subsection (3.2.3).

3.4 Comments and conclusions

In this chapter we have analyzed general stochastic birth and death models that include delay. We have presented three different methods that together constitute a general toolbox to study stochastic models including delay.

In sub-section (3.2.1) we have shown that when the creation rate is independent of the state of the system (no feedback) and the initiation of the delayed degradation and the instantaneous degradation are first order reactions (rate not depending

on the state of the system), the process can be solved fully in an exact fashion for general distributions of delay, showing always Poissonian character and a monotonically decreasing time correlation function given by (3.15), contrary to previous results [Bratsun et al., 2005].

In sub-sections (3.2.2), (3.2.3) we have considered a more general process with delay in the degradation step, allowing the initiation of the delay degradation and the instantaneous degradation to be higher order reactions, as well as the presence of feedback in the creation rate. The developed method method allows us to reduce the system to a Markovian one, where usual techniques can be used. Explicit expressions for the time correlation for general delay distributions were obtained. In this case the correlation might be non-monotonic, if feedback is present, but typically decreases monotonically.

Section (3.3) shows that when the delay appears in the creation reaction and feedback is present, the delay typically has more dramatic consequences. When a stochastic process has negative feedback, the fluctuations are decreased; however, if this feedback is delayed, the fluctuations can be actually enhanced, depending on the magnitude of the delay. A positive feedback loop enhances the fluctuations, but if the feedback is delayed, this enhancement is decreased. We have also shown that the effect of the delay is less apparent if the delay itself has relative large fluctuations, so for this mechanism to work, the delay has to be controlled precisely. This may be relevant for example in gene-regulatory networks, where delay times are typically broadly distributed but several regulatory mechanisms may act to control this [Voliotis et al., 2008]. The analytical theory allows us to understand and predict this phenomenology in a general way. For negative feedback, an in the case of constant delay, we have shown that the time correlation function becomes oscillatory, alternating positive and negative values at approximately multiples of the delay. In the positive feedback case, again for fixed delay, the time correlation function remains always positive. Finally, we have pointed out that systems with delay are not, in general, statistically invariant under time reversal over the steady state, even if they fulfill the detailed balance condition.

3.5 Appendix 1: Calculation of $P(n,t)$ in the simple case of delayed degradation

We start by considering the case $n = 0$. For the sake of simplicity, we focus on the case with creation rate, C, independent of time, but the generalization

to time-dependent C is straightforward. Since the time origin is taken at $t = 0$, the probability of observing zero particles at time $t > 0$ is equal to the following limit:

$$P(0,t) = \lim_{M\to\infty} \prod_{i=0}^{M-1} [1 - C\Delta t + C\Delta t F(t - t_i) + o(\Delta t)] \equiv \lim_{M\to\infty} \prod_{i=0}^{M-1} \left[1 - C\hat{F}(t - t_i)\Delta t o(\Delta t)\right], \tag{3.99}$$

with $\Delta t \equiv \frac{t}{M}$ playing the role of a small time-increment, $t_i \equiv i\Delta t$ and $\hat{F}(t) \equiv 1 - F(t)$. This expression follows from the fact that, in order to find the system with zero particles at time t, in every previous infinitesimal time interval ($t' \in [t_i, t_{i+1}), i = 0, \ldots, M-1$) one of the following two (incompatible) events must take place: either a particle is not created (probability $1 - C\Delta t$) or a particle is created with a lifetime smaller that $t - t_i$ (probability $C\Delta t F(t - t_i)$). We now have:

$$\log P(0,t) = \lim_{M\to\infty} \sum_{i=0}^{M-1} \left[-C\hat{F}(t - t_i) + o(\Delta t)\right] \Delta t = -C \int_0^t dt' \hat{F}(t - t'), \tag{3.100}$$

so we find

$$P(0,t) = e^{-C\int_0^t dt' \hat{F}(t-t')}. \tag{3.101}$$

Following a similar line of reasoning, $P(n,t)$ can be computed as:

$$P(n,t) = \lim_{M\to\infty} \sum_{i_1=0}^{M-1} \sum_{i_2=i_1+1}^{M-1} \cdots \sum_{i_n=i_{n-1}+1}^{M-1} \prod_{l=1}^{n} \left[C\Delta t \hat{F}\left(t - t_{i_l}\right)\right] \prod_{\substack{0\le j\le M-1 \\ j\neq i_1, i_2, \ldots, i_n}} \left[1 - C\Delta t \hat{F}(t - t_{i_j})\right] \tag{3.102}$$

This expression results from the consideration of choosing the times $(t_{i_1}, \ldots, t_{i_n})$ at which the n particles are created and survive up to t. The l-th particle is created with probability $C\Delta t$ and survives up to t with probability $\hat{F}\left(t - t_{i_l}\right)$. The other factor comes from the fact that at the other time intervals either a particle is not created or it is created but dies before t.

Using

$$\lim_{M\to\infty} \prod_{\substack{0\le j\le M-1 \\ j\neq i_1, i_2, \ldots, i_n}} \left[1 - C\Delta t \hat{F}(t - t_{i_j})\right] = e^{-C\int_0^t dt' F(t-t')} \tag{3.103}$$

and replacing the sums by integrals in the limit $M \to \infty$

$$\int_0^t dt_1 C\hat{F}(t - t_1) \int_{t_1}^t dt_2 C\hat{F}(t - t_2) \ldots \int_{t_{n-1}}^t dt_n C\hat{F}(t - t_n) = \frac{C^n}{n!} \left[\int_0^t dt' F(t - t)\right]^n \tag{3.104}$$

we finally obtain:

$$P(n,t) = e^{-C\int_0^t dt'\hat{F}(t-t')}\frac{C^n\left[\int_0^t dt'\hat{F}(t-t')\right]^n}{n!}, \tag{3.105}$$

that is, a Poisson distribution with average $\langle n(t)\rangle = C\int_0^t dt'\hat{F}(t-t')$. In the steady state (found as the limit $t\to\infty$), the average becomes $\langle n(t)\rangle = C\langle\tau\rangle$. Remarkably, this Poissonian character is completely independent of the form of the delay distribution. As commented above, this result can be easily generalized to the case in which the creation rate depends on time, $C\to C(t)$, obtaining again a Poisson distribution with average $\int_0^t dt'C(t')\hat{F}(t-t')$.

3.6 Appendix 2: derivation of the master equation in a system with delay

Here we derive the master equation of the process (3.64). We consider first the case of fixed delay τ. We start with the following identity:

$$\begin{aligned} P(n,t+\Delta) &= \sum_{n'} P(n,t+\Delta;n',t) = P(n,t+\Delta;n+1,t) + P(n,t+\Delta;n-1,t) \\ &+ P(n,t+\Delta;n,t) + o(\Delta). \end{aligned} \tag{3.106}$$

It is immediate to see that $P(n,t+\Delta;n+1,t) = \gamma(n+1)\Delta P(n+1,t)$. In the case of fixed delay, the second sum can be evaluated introducing a three-times probability as:

$$\begin{aligned} P(n,t+\Delta;n-1,t) &= \sum_{n'} P(n,t+\Delta;n-1,t;n',t-\tau) \\ &= \sum_{n'} P(n,t+\Delta|n-1,t;n',t-\tau)P(n',t-\tau;n-1,t). \end{aligned} \tag{3.107}$$

Now, $P(n,t+\Delta|n-1,t;n',t-\tau) = C(n')\Delta + o(\Delta)$. Expanding in a similar way the term $P(n,t+\Delta;n,t)$, and taking the limit $\Delta\to 0$, we can obtain the master equation of the process:

$$\frac{\partial P(n,t)}{\partial t} = (E-1)[\gamma n P(n,t)] + (E^{-1}-1)\left[\sum_{n'=0}^{\infty} C(n')P(n',t-\tau;n,t)\right], \tag{3.108}$$

3.6. APPENDIX 2: DERIVATION OF THE MASTER EQUATION IN A SYSTEM WITH DELAY

In the case of distributed delay, we start considering a discrete distribution of delays i.e. $\tau = \tau_1, \ldots, \tau_M$ with corresponding probabilities $f(\tau_1), \ldots f(\tau_M)$. The continuum limit can then be obtained making $M \to \infty$. The creation term in (3.106) can be written as:

$$P(n, t+\Delta; n-1, t) = \sum_{n_1,\ldots n_M} P(n, t+\Delta; n-1, t; n_1, t-\tau_1; \ldots; n_M, t-\tau_M)$$
$$= \sum_{n_1,\ldots,n_M} P(n, t+\Delta | n-1, t; n_1, t-\tau_1; \ldots; n_M, \tau_m) \times$$
$$P(n_1, t-\tau_1; \ldots; n_M, t-\tau_M; n-1, t). \tag{3.109}$$

Now, $P(n, t+\Delta | n-1, t; n_1, t-\tau_1, \ldots, n_M, \tau_m) = \sum_{i=1}^{M} C(n_i) f(\tau_i)\Delta + o(\Delta)$, that is, the probability that a particle started its creation at time $t-\tau_i$ with a creation time equal to τ_i. Replacing in the previous equation and performing the appropriate sums we obtain:

$$P(n, t+\Delta; n-1, t) = \sum_{n'} \sum_{i=1}^{M} C(n') f(\tau_i) P(n', t-\tau_i; n-1, t)\Delta + o(\Delta) \tag{3.110}$$

that in the continuum limit reduces to $\sum_{n'} \int_0^\infty d\tau C(n') f(\tau) P(n', t-\tau; n-1, t)$. Considering in a similar way the other terms in (3.106) and taking the limit $\Delta \to 0$ one can obtain the master equation for distributed delay (3.65). We will now derive the master equation for the two-times probability distribution of process (3.47) $\emptyset \overset{C(n)}{\to} X + Z$, $X \underset{\tau}{\Rightarrow} \emptyset$,. We note that:

$$P(n_{Z_1}, t_1 + \Delta t; n_{Z_2}, t_2) = \sum_n \Big[P(n_{Z_1} - 1, n, t_1; n_{Z_2}, t_2) C(n) \Delta t \tag{3.111}$$
$$+ P(n_{Z_1}, n, t_1; n_{Z_2}, t_2)(1 - C(n)\Delta t) \Big] + o(\Delta t),$$

which leads to:

$$\frac{\partial P(n_{Z_1}, t_1; n_{Z_2}, t_2)}{\partial t_1} = (E_1^{-1} - 1) \sum_n P(n_{Z_1}, n, t_1; n_{Z_2}, t_2) C(n) \tag{3.112}$$
$$= (E_1^{-1} - 1) \langle C(n(t_1)) | n_{Z_1}, t_1; n_{Z_2}, t_2 \rangle P(n_{Z_1}, t_1; n_{Z_2}, t_2),$$

expression (3.50) of the main text. Now we use

$$\frac{\partial P(n_{Z_1}, t_1; n_{Z_2}, t_2 + \Delta t)}{\partial t_1} = (E_1^{-1} - 1) \sum_{n,n'} P(n_{Z_1}, n, t_1; n_{Z_2} - 1, n', t_2) C(n) C(n') \Delta t$$
$$+ (E_1^{-1} - 1) \sum_{n,n'} P(n_{Z_1}, n, t_1; n_{Z_2}, n', t_2) C(n) [1 - C(n')\Delta t]$$
$$+ o(\Delta t), \tag{3.113}$$

which leads us to

$$\begin{aligned}\frac{\partial^2 P(n_{Z_1},t_1;n_{Z_2},t_2)}{\partial t_1 \partial t_2} &= (E_1^{-1}-1)(E_2^{-1}-1)\sum_{n,n'} P(n_{Z_1},n,t_1;n_{Z_2},n',t_2)C(n)C(n') \\ &= (E_1^{-1}-1)(E_2^{-1}-1)\langle C(n(t_1))C(n(t_2))|n_{Z_1},t_1;n_{Z_2},t_2\rangle \times \\ &\qquad P(n_{Z_1},t_1;n_{Z_2},t_2). \quad (3.114)\end{aligned}$$

This expression is only valid for $t_1 \neq t_2$, since in (3.113), for simplicity, we have implicitly assumed $t_1 \neq t_2$. Actually, one has to consider terms of the form $P(n_{Z_1},t_1+\Delta t;n_{Z_1}-1,n,t_1;n_{Z_2},t_2+\Delta t;n_{Z_2}-1,n',t_2)$, which is equal to

$$C(n)C(n')\Delta t^2 P(n_{Z_1},n,t_1;n_{Z_2},n',t_2)+o(\Delta t^3)$$

only if $t_1 \neq t_2$, since for $t_2 = t_1$ the "birth" events are not independent, they are the same, so the probability is proportional to Δt instead of Δt^2. The case $t_1 = t_2$ can be considered more easily using the definition of derivative and that $P(n_{Z_1},t;n_{Z_2},t) = \delta_{Z_1,Z_2}P(n_{Z_1},t)$:

$$\begin{aligned}&\frac{\partial^2 P(n_{Z_1},t_1;n_{Z_2},t_2)}{\partial t_1 \partial t_2}|_{t_1=t_2} = \lim_{\Delta t\to 0}\frac{1}{\Delta t^2}\Big[P(n_{Z_1},t_1+\Delta t;n_{Z_2},t_1+\Delta t) \\ &\qquad -P(n_{Z_1},t_1+\Delta t;n_{Z_2},t_1)-P(n_{Z_1},t_1;n_{Z_2},t_1+\Delta t)+P(n_{Z_1},t_1;n_{Z_2},t_1)\Big] \\ &= \lim_{\Delta t\to 0}\frac{1}{\Delta t^2}\sum_n \Big\{\delta_{n_{Z_1},n_{Z_2}}[P(n_{Z_1}-1,t_1)C(n)\Delta t + P(n_{Z_1},t_1)(1-C(n)\Delta t)] \\ &-\delta_{n_{Z_1},n_{Z_2}}(1-C(n)\Delta t)P(n_{Z_2},t_1)-\delta_{n_{Z_1},n_{Z_2}+1}C(n)\Delta t P(n_{Z_2},t_1) \quad (3.115) \\ &-\delta_{n_{Z_1},n_{Z_2}}(1-C(n)\Delta t)P(n_{Z_1},t_1)-\delta_{n_{Z_1},n_{Z_2}-1}C(n)\Delta t P(n_{Z_1},t_1)+\delta_{n_{Z_1},n_{Z_2}}P(n_{Z_1},t_1)\Big\} \\ &= \delta(t_1-t_2)\Big[(1-E_{Z_2})\delta_{n_{Z_1},n_{Z_2}}E_{Z_1}^{-1}+(1-E_{Z_2}^{-1})\delta_{n_{Z_1},n_{Z_2}}\Big]\langle C(n_A)|n_{Z_1}\rangle P(n_{Z_1},t_1)\end{aligned}$$

which is equal to expression (3.51) of the main text.

Appendix 3: numerical simulations

To perform numerical realizations of the process, we use the following modification of the Gillespie algorithm [Gillespie, 1977; Cai, 2007]:

1: Initialize the state of the system, setting, e.g. $n = 0$.

2: Compute the reaction rates $C(n)$ and γn. Obtain a number Δt exponentially distributed with average $1/(C(n) + \gamma n)$.

3: If $t + \Delta t$ is larger than the time of the next scheduled delayed reaction, go to step 4. Otherwise, update time from t to $t + \Delta t$ and obtain which kind of process (creation or degradation) will take place. To do so, generate a uniform random number between 0 and 1. If this number is smaller than $\gamma n/(C(n) + \gamma n)$, set $n \to n - 1$; otherwise add an entry in the list of scheduled creation processes to happen at time $t + \tau$. Go to step 2.

4: Update the time to that of the next scheduled reaction. Set $n \to n + 1$. Go to step 2.

This procedure is statistically exact, as the original Gillespie algorithm in the case of non-delayed reactions.

In the case with delay, the time until the next reaction is exponentially distributed, with average $C(n) + \gamma n$, only if the state of the system doesn't change during this interval (due to a scheduled delayed reaction). This happens with probability $1 - e^{-(C(n)+\gamma n)t_\tau}$ (with $t + t_\tau$ the time of the next scheduled delayed reaction). The algorithm fulfills this, since the probability that step 3 is completed is precisely $1 - e^{-(C(n)+\gamma n)t_\tau}$. Once a reaction has taken place (delayed or not) the time for the next reaction is again exponentially distributed as long as no delayed reaction takes place, and the procedure can be iterated.

Appendix 4: solution of the delay-linear equations

We consider the following linear delayed differential equation:

$$\frac{dg(t)}{dt} = -\alpha g(t - \tau) - \gamma g(t). \tag{3.116}$$

We are looking for a symmetric solution $g(-t) = g(t)$. We summarize here for completeness the treatment of reference [Bratsun et al., 2005]. We make the ansatz $g(t) = ae^{\lambda|t|} + be^{-\lambda|t|}$, valid only for $-\tau \leq t \leq \tau$. Inserting in (3.116), equating the coefficients of $e^{\lambda t}$ and $e^{-\lambda t}$, and imposing $g(0) = 1$, we obtain λ, a, b. Once we know $g(t)$ for $|t| \leq \tau$, we can obtain $g(t)$ for $|t| > \tau$ iteratively integrating (3.116).

The solution for $t \geq 0$ is:

$$\begin{aligned} \lambda &\equiv \sqrt{\gamma^2 - \alpha^2}, \qquad \zeta \equiv \frac{\gamma - \lambda}{\alpha}, \\ g(t) &\equiv \begin{cases} \frac{e^{-\lambda t} - \zeta e^{\lambda(t-\tau)}}{1 - \zeta e^{-\lambda\tau}}, & \text{if } 0 \leq t \leq \tau \\ e^{-\gamma(t-k\tau)} g(k\tau) - \alpha \int_{k\tau}^{t} dt'\, g(t'-\tau) e^{\gamma(t'-t)}, & \text{if } k\tau \leq t \leq (k+1)\tau, k = 1, 2, \cdots \end{cases} \end{aligned} \tag{3.117}$$

Note that $g(\tau) = \dfrac{e^{-\lambda\tau} - \zeta}{1 - \zeta e^{-\lambda\tau}}$. Using the symbolic manipulation program Mathematica [Wolfram Research, 2008] to perform the integrals of the iterative process, we have been able to find explicit expressions for $g(t)$ up to $|t| \leq 10\tau$.

We apply a similar approach to the case of two coupled linear delayed differential equations:

$$\frac{dx_m(t)}{dt} = -\gamma_m x_m(t) - \alpha x_m(t-\tau), \tag{3.118}$$

$$\frac{dx_n(t)}{dt} = -\gamma_n x_n(t) + w x_m(t). \tag{3.119}$$

Due to the linearity, the solution has the form:

$$x_n(t) = x_n(0) f_n(t) + x_m(0) f_m(t), \tag{3.120}$$

with $f_n(0) = 1$, $f_m(0) = 0$. To find this solution, we use the ansatz $x_n(t) = a_1 e^{\lambda_+|t|} + b_1 e^{-\lambda_+|t|} + a_2 e^{\lambda_-|t|} + b_2 e^{\lambda_-|t|}$, $x_m(t) = c_1 e^{\lambda_+|t|} + c_2 e^{-\lambda_+|t|} + d_1 e^{\lambda_-|t|} + d_2 e^{\lambda_-|t|}$, for $-\tau \leq t \leq \tau$. Equating the coefficients of the exponentials and imposing the initial condition we obtain the expression valid in $0 \leq t \leq \tau$:

$$f_n(t) = \left[\gamma_n \frac{1 - b_-(t)}{b(t)} + \lambda_- \frac{1 + b_-(t)}{b(t)}\right]\left(e^{\lambda_+ t} - b_+(t) e^{-\lambda_+ t}\right) \tag{3.121}$$

$$- \left[\gamma_n \frac{1 - b_+(t)}{b(t)} + \lambda_+ \frac{1 + b_+(t)}{b(t)}\right]\left(e^{\lambda_- t} - b_-(t) e^{-\lambda_- t}\right), \tag{3.122}$$

$$f_m(t) = \omega \frac{1 - b_+(t)}{b(t)}\left[e^{\lambda_- t} - b_-(t) e^{-\lambda_- t}\right] - \omega \frac{1 - b_-(t)}{b(t)}\left[e^{\lambda_+ t} - b_+(t) e^{-\lambda_+ t}\right] \tag{3.123}$$

$$\lambda_\pm = \sqrt{\frac{\gamma_m^2 + \gamma_n^2}{2} \pm \frac{1}{2}\sqrt{(\gamma_m^2 - \gamma_n^2)^2 + 4\omega^2\alpha^2}}, \tag{3.124}$$

$$b_\pm(t) = \frac{\lambda_\pm^2 + (\gamma_m + \gamma_n)\lambda_\pm + \gamma_n \gamma_m}{\omega\alpha} e^{\lambda_\pm t}, \tag{3.125}$$

$$b(t) = \lambda_-(1 + b_-(t))(1 - b_+(t)) - \lambda_+(1 - b_-(t))(1 + b_+(t)). \tag{3.126}$$

Part IV

Heterogeneity in stochastic interacting-particle systems

Chapter 4

Role of heterogeneity in interacting-particle systems

4.1

Introduction

In recent years, methods and ideas developed in statistical physics have been transferred to other disciplines, such as ecology, epidemiology, sociology, economy, etc. [Stauffer et al., 2006; Castellano et al., 2009], focusing on collective and emergent phenomena in what is known as complexity science. Unlike the systems traditionally studied by physics, which consist of identical (some times even indistinguishable) units (molecules, atoms, electrons), the new applications require the consideration of systems which are characterized by a large degree of heterogeneity among their constituent units. Furthermore, very often these systems can be modeled only at a stochastic level since a complete knowledge of all the variables, the precise dynamics of the units and the interaction with the environment is not available. One way to include heterogeneity is to consider that the interactions between the units are not homogeneous but mediated by some complex network, an approach that has attracted enormous attention in the last years [Newman et al., 2006; Boccaletti et al., 2006]. An issue that has been less studied is the heterogeneity in the behavior of the particles themselves. The effect of heterogeneity in deterministic systems has been considered before [Tessone et al., 2006; Young, 2009; Novozhilov, 2012], but the combined effects of stochasticity and heterogeneity has not been studied systematically with few exceptions, e.g. reference [Masuda et al., 2010] analyzes the effect of heterogeneous transition rates on consensus times in the voter model.

In this chapter we will show that the combined effect of stochasticity and heterogeneity can give rise to unexpected results. While, based on naïve arguments, one should conclude that fluctuations increase in heterogeneous systems, we will show that in some cases fluctuations in systems of stochastic interacting particles actually decrease with the degree of heterogeneity. Moreover, we will see that it is possible to infer the degree of heterogeneity in the system by measuring only global variables. We will study first the simple case of independent particles; then we will consider the general case of interacting particles and develop an approximated method of general validity to analytically study this systems; next, as a way of example, this method will be applied to two particular models of interest in economy and epidemiology.

We start by considering a stochastic description of a system composed by N non-identical units, which we call generically "particles" or "agents". Each particle is characterized by a constant parameter λ_i ($i = 1, \ldots, N$); the value of this parameter differs among the particles and it is the source of heterogeneity considered. Throughout the chapter we will use the terms heterogeneity or diversity interchangeably. There are more general ways of including heterogeneity, for example that each particle has a different functional form of some underlaying dynamical equations, but here we will stick to parametric heterogeneity [Dushoff, 1999] because it is simple and we regard it as general enough. For simplicity, we assume that each particle can be in one of two possible states and define $s_i(t) = 0, 1$ as the variable describing the state of particle i at time t (the two-states assumption will be relaxed latter). The collective state of the system is given by the total number $n(t) = \sum_{i=1}^{N} s_i(t)$ of particles in state 1. Sometimes, one does not have access to the individual dynamics and can only access experimentally the value of $n(t)$. We are interested in the statistical properties of this global variable and how do they depend on the degree of heterogeneity in the system. We will often refer to n as the macroscopic variable and to the s_i's as the microscopic ones.

4.2 Independent Particles

We study first the case in which particles jump independently from state 0 to 1 and vice-versa, schematically:

$$0 \xrightarrow{r_i^+} 1, \qquad 1 \xrightarrow{r_i^-} 0, \tag{4.1}$$

with rates that depend on the value of the heterogeneity parameter, $r_i^\pm = r^\pm(\lambda_i)$. The probability $p_i(t)$ for particle i to be in state 1 at time t obeys the linear rate

equation $\frac{dp_i}{dt} = -r_i^- p_i + r_i^+(1-p_i)$. In the case of constant rates, the solution is: $p_i(t) = \frac{r_i^+}{r_i}(1-e^{-r_i t}) + p_i(0)e^{-r_i t}$, with $r_i \equiv r_i^+ + r_i^-$. The results below apply equally if the rates depend on time or on the time that the particle has been in its current state [1] Using particle independence and that the moments with respect to realizations of the stochastic process of the random variable s_i are given by $\langle s_i^k \rangle = 1^k p_i + 0^k(1-p_i) = p_i$, one obtains that the average and variance of the global variable n are:

$$\langle n(t) \rangle = \sum_{i=1}^{N} p_i(t) = N\overline{p(t)}, \tag{4.2}$$

$$\sigma^2[n(t)] = \sum_{i=1}^{N} \left(p_i(t) - p_i(t)^2 \right) = N\left(\overline{p(t)} - \overline{p(t)^2} \right), \tag{4.3}$$

where the overline denotes an average over the population, $\overline{g} \equiv \frac{1}{N}\sum g_i$. If we consider a system where all particles are identical (i.e. have the same values for the internal parameter $\lambda_i = \lambda_j, \forall i, j$), and keep the same average value $\langle n(t) \rangle$ for the global variable at time t, the variance would be $\sigma^2_{\text{id}}[n(t)] = N\overline{p(t)}\left(1 - \overline{p(t)}\right) \geq \sigma^2[n(t)]$. We conclude that a system of heterogeneous independent particles displays smaller fluctuations in its collective variable than another system with identical particles. The reduction in the variance of the collective variable is N times the variance of p_i over the population:

$$\sigma^2_{\text{id}}[n(t)] - \sigma^2[n(t)] = N\left(\overline{p(t)^2} - \overline{p(t)}^2 \right), \tag{4.4}$$

which is of the same order, $O(N)$, as the variance itself, giving a non-negligible correction. We obtain the somehow counterintuitive result that the heterogeneity of a population of independent particles reduces the magnitude of the collective fluctuations. This effect is illustrated in figure (4.1).
Reading this formula backwards, one realizes that the moments of the collective variable give information about the degree of heterogeneity in the system:

$$\overline{p(t)^2} - \overline{p(t)}^2 = \frac{\langle n(t) \rangle - \langle n(t) \rangle^2 / N - \sigma^2[n(t)]}{N}. \tag{4.5}$$

This expression is general, regardless the specific form in which p_i is distributed over the population. Higher moments of the heterogeneity distribution are

[1] If the rate depends on the time a that the particle has been on its current state, the steady-state probability of finding the particle at state 1 is $p_{i,\text{st}} = \frac{\Lambda_i^-}{\Lambda_i^+ + \Lambda_i^-}$ with $\Lambda_i^\pm = \int_0^\infty dt\, e^{-\int_0^t da\, r_i^\pm(a)}$.

also related to higher moments of the collective variable. This allows to infer the skewness, kurtosis and higher order characteristics of the heterogeneity distribution by measuring only global variables and their fluctuations. As we show below, an equivalent result is obtained generically for k-state systems for $k > 2$.

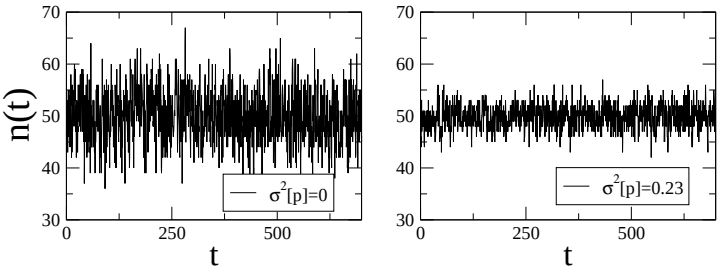

Figure 4.1: Time series for the global variable $n(t)$ of a system of identical (left panel) and heterogeneous (right panel) particles, for a system of $N = 100$ particles. The parameters were set as $r_i^+ = 1, r_i^- = 1/p_i - 1$, with $p_i = 1/2$ in the case of identical particles (left panel) and p_i chosen from a symmetric Beta distribution $f(p) = \frac{\Gamma(\alpha)^2}{\Gamma(2\alpha)}[p(1-p)]^{\alpha-1}$, with $\alpha = 0.05$, being the sample mean and variance equal to $\overline{p} = 0.501$, $\sigma^2[p] = 0.23$, respectively. Note that the fluctuations of the average state are larger in the case of identical particles.

Besides the moments, one can derive the full probability distribution of the global variable. We will do this by deriving the generating function of the single-particle variables and then using that the generating function of the sum of independent random variables is the product of the generating functions. The generating function for the one particle is $g_i(s) = \sum_{n_i=0}^{1} s^{n_i} P(n_i) = 1 - p_i + p_i s$, so the generating function for the global variable n is:

$$G(s) = \prod_{i=1}^{N} g_i(s). \tag{4.6}$$

Expanding in powers of s we can obtain the probability distribution for n: $P(n) = \sum_{\mathbf{i}\in S_N} \prod_{l=1}^{n} \frac{p(\lambda_{i_l})}{n!} \prod_{l=n+1}^{N} \frac{1-p(\lambda_{i_l})}{(N-n)!}$, where S_N is the group of permutations of N elements.

The model studied in this section may seem a "toy model", too simple to have any real-world relevance. However, it constitutes a reduced description of generic systems of non-interacting multi-stable units subject to noise. If one is interested

in the collective properties of one such system when the units are non-identical, the results obtained here are directly relevant. Moreover, this model presents in isolation a mechanism, spontaneous transitions, that can play a role in more complicated and relevant systems (we will see this latter). The simplicity of the model allows us to understand the effect of heterogeneity in this mechanism, which will give us insight in the role of heterogeneity in the behavior of more complicated systems.

4.2.1 M-states system

We now consider the case in which each particle can be in one of M (instead of 2) possible states. We will show that the results obtained above for 2−state systems also hold in this more general case.

We label the states with the subscript $\alpha = 0, 1, \ldots, M-1$, so in this case the variable describing the state of particle i can take M possible values, $s_i = 0, \ldots, M-1$ (we start the labeling from 0 to be consistent with the previous case, that would correspond to $M = 2$). Let $p_i(\lambda_i, \alpha, t)$ be the probability that particle i, with heterogeneity parameter λ_i, be on state α. It satisfies the evolution equation:

$$\frac{dp_i(\lambda_i, \alpha, t)}{dt} = A_{\alpha,\beta}(\lambda_i) p_i(\lambda_i, \beta, t), \tag{4.7}$$

with $A_{\alpha,\beta}$ a general transition matrix (satisfying $A_{\alpha,\alpha} = -\sum_{\gamma=0}^{N-1} A_{\gamma,\alpha}$), that may depend in principle on time and on the time that the particle has been on its current state. To isolate the role of parameter heterogeneity, we assume that the initial condition is the same for all the particles (or that the initial condition is determined by the value of λ_i) such that the solution $p_i(\lambda_i, \alpha, t) = p(\lambda_i, \alpha, t)$ is the same for all particles sharing the same value of the parameter. The macroscopic state of the system will be described by the set of variables $n_\alpha = \sum_{i=1}^{N} \delta_{\alpha,s_i}$, that is, the number of particles in each state. The averages and variances of this variables are given by:

$$\langle n_\alpha(t) \rangle = \sum_{i=1}^{N} p(\lambda_i, \alpha, t) \tag{4.8}$$

$$\sigma^2[n_\alpha(t)] = \sum_{i=1}^{N} \left[p(\lambda_i, \alpha, t) - p(\lambda_i, \alpha, t)^2 \right]. \tag{4.9}$$

This variance is again smaller that tat of a system of identical particles with same average, the difference given by:

$$\sigma^2[n_\alpha(t)]_{\text{id}} - \sigma^2[n_\alpha(t)] = N\overline{p(\alpha, t)^2} - \overline{p(\alpha, t)}^2, \tag{4.10}$$

a result exactly analogous to the one obtained in the previous case. The heterogeneity among the particles on the probability of occupation of level α can be derived from the first moments of the occupation number of the level:

$$\overline{p(\alpha,t)^2} - \overline{p(\alpha,t)}^2 = \frac{\langle n_\alpha\rangle - \langle n_\alpha\rangle^2/N - \sigma^2[n_\alpha]}{N}. \tag{4.11}$$

Note that, when focusing on the number of particles on state α, the system effectively reduces to a 2−level one, with states α and no-α, so the results of the previous section can be translated directly.

A different and some times relevant question can be considered when the labeling of the states is such that the order is well defined (for example each state corresponds to an energy level or a distance from a reference). Then the average state is meaningful and we can study its statistical properties. Below we show that the variance of this mean level is again always smaller if heterogeneity is present.

The average state of the system is given by $L = \sum_{\alpha=0}^{M-1} \alpha \, \frac{n_\alpha}{N}$. It is a random variable whose average and variance are given by:

$$\begin{aligned}
\langle L\rangle &= = \sum_{\alpha=0}^{M-1} \alpha \frac{\langle n_\alpha\rangle}{N} = \sum_{\alpha=0}^{M-1}\sum_{i=1}^{N} \alpha \frac{p(\lambda_i,\alpha)}{N}, &(4.12)\\
\sigma^2[L] &= \sum_{\alpha,\beta=0}^{M-1} \frac{\alpha\beta}{N^2}(\langle n_\alpha n_\beta\rangle - \langle n_\alpha\rangle\langle n_\beta\rangle)\\
&= \frac{1}{N^2}\sum_{i=1}^{N}\left[\sum_{\alpha=0}^{M-1}\alpha^2 p(\alpha,\lambda_i) - \sum_{\alpha,\beta=0}^{M-1}\alpha p(\alpha,\lambda_i)\beta p(\beta,\lambda_i)\right]. &(4.13)
\end{aligned}$$

We have used $p(\lambda_i,\alpha) = \langle\delta_{\alpha,s_i}\rangle$ and $\langle n_\alpha n_\beta\rangle = \sum_{i,j=1}^{N}\langle\delta_{\alpha,s_i}\delta_{\beta,s_j}\rangle = \langle n_\alpha\rangle\langle n_\beta\rangle + \sum_{i=1}^{N}[\delta_{\alpha,\beta}p(\alpha,\lambda_i) - p(\alpha,\lambda_i)p(\beta,\lambda_i)]$. A system of identical particles that had the same average occupation of the different levels i.e. $p_{id}(\lambda_i,\alpha) = \frac{1}{N}\sum_{j=1}^{N} p(\lambda_j,\alpha,) = \frac{\langle n_\alpha\rangle}{N}\ \forall i,\alpha$, would have and average and variance of the mean level given by:

$$\begin{aligned}
\langle L\rangle_{id} &= \sum_{\alpha=0}^{M-1}\alpha\frac{\langle n_\alpha\rangle}{N} = \langle L\rangle, &(4.14)\\
\sigma^2[L]_{\mathrm{id}} &= \frac{1}{N}\sum_{\alpha=0}^{M-1}\alpha^2\frac{\langle n_\alpha\rangle}{N} - \frac{1}{N}\sum_{\alpha,\beta=0}^{M-1}\alpha\beta\frac{\langle n_\alpha\rangle}{N}\frac{\langle n_\beta\rangle}{N}. &(4.15)
\end{aligned}$$

We now define $g(\lambda_i) \equiv \sum_\alpha \alpha p(\lambda_i, \alpha)$ (the average level of particle i), and note that the first terms in the right-hand side of (4.13) and (4.15) are equal, while the second terms can be written as:

$$\frac{1}{N^2}\sum_{i=1}^{N}\sum_{\alpha,\beta=0}^{M-1}\alpha p(\lambda_i,\alpha)\beta p(\lambda_i,\beta) = \frac{1}{N^2}\sum_{i=1}^{N} g(\lambda_i)^2 = \frac{1}{N}\overline{g^2}, \tag{4.16}$$

$$\frac{1}{N}\sum_{\alpha,\beta=0}^{M-1}\alpha\beta\frac{\langle n_\alpha\rangle}{N}\frac{\langle n_\beta\rangle}{N} = \frac{1}{N}\left[\frac{1}{N}\sum_{i=1}^{N} g(\lambda_i)\right]^2 = \frac{1}{N}\overline{g}^2, \tag{4.17}$$

which implies that $\sigma^2[L]_{\rm id} \geq \sigma^2[L]$, i.e. the variance of the mean level is always smaller in a system of heterogeneous particles, the difference with respect to the case of identical ones being:

$$\sigma^2[L]_{\rm id} - \sigma^2[L] = \frac{1}{N}\left(\overline{g^2} - \overline{g}^2\right) \tag{4.18}$$

$$= \frac{1}{N}\sum_{\alpha,\beta=0}^{M-1}\alpha\beta\left[\sum_{i=1}^{N}\frac{p(\alpha,\lambda_i)p(\beta,\lambda_i)}{N} - \sum_{i,j=1}^{N}\frac{p(\alpha,\lambda_i)p(\beta,\lambda_j)}{N^2}\right] \geq 0.$$

The correction to the variance in this case scales as $1/N$, but again is of the same order as the variance itself, indicating a non-negligible correction. In this case to derive the heterogeneity of $g(\lambda_i)$ over the population one needs to know the average occupation level of each state $\langle n_\alpha\rangle$ and use:

$$\overline{g^2} - \overline{g}^2 = \sum_\alpha \alpha^2\langle n_\alpha\rangle/N - \langle L\rangle^2 - N\sigma^2[L]. \tag{4.19}$$

This can be written in terms of the variance of L in an equivalent system of identical particles, $\sigma^2[L]_{\rm id}$. If this is known, one can directly use

$$\overline{g^2} - \overline{g}^2 = N\left(\sigma^2[L]_{\rm id} - \sigma^2[L]\right). \tag{4.20}$$

Note that, contrary to the two-level case, now the value of $\langle L\rangle$ does not determine $\sigma^2[L]_{\rm id}$.

4.2.2 Intuitive origin of the main result

We have shown that a system of independent heterogeneous particles has smaller fluctuations for the collective variable than an equivalent system of identical ones. The origin of this result is the following (for simplicity we refer to the case of 2-state system):

The average of the global variable is determined by the concentration of the states of the particles around state 1 ($\langle n \rangle = \sum_i \langle s_i \rangle$). The fluctuations (measured by the variance) of the global variable are determined by the stochastic fluctuations of the individual particles alone ($\sigma^2[n] = \sum_i \sigma^2[s_i]$, since the particles are independent).
In a system of heterogeneous particles, the dispersion of the states of the particles is due to the heterogeneity (some prefer to be around sate 0, others prefer to be around sate 1) plus their intrinsic stochasticity. In a system of identical particles, the dispersion comes from the stochasticity alone, so for a system of identical particles to have the same concentration in the states of the particles (global average) than a heterogeneous system, the intrinsic stochasticity has to be larger. This will give rise to larger fluctuations for the global variable.
In particular, any given rational value of $\frac{\langle n \rangle}{N} = \frac{A}{B}$ can be obtained with zero fluctuations, taking A particles that are always at state 1 and $B - A$ particles that are always at state 0.

This explanation is illustrated in figure (4.2). In the identical-particles system both particles fluctuate between 1 and 0. In the heterogeneous case, one particle spends most of the time at 1 and the other spends most of the time at 0. The probability of finding a given particle at 1 is the same in both cases (1/2) but in the heterogeneous case most of the time there is one particle at 1 and one particle at 0, resulting on a value of the average state most often equal to 1/2, and so with smaller fluctuations. The situation is similar for a larger number

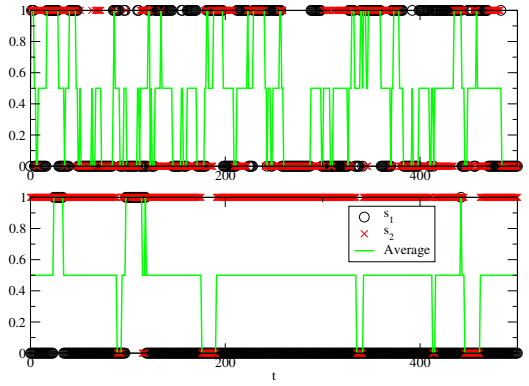

Figure 4.2: Time series of a system of two identical (upper panel) and heterogeneous (lower panel) particles, together with the corresponding average state. Note that the fluctuations of the average state are more pronounced in the case of the identical particles.

of particles, as shown in figure (4.1). An analogous picture emerges when one

considers more that 2 states. Note that in every case we compare a system of heterogeneous particles with another of identical ones that has the same one-particle distribution i.e. $p_i(\alpha)_{id} = \sum_j \frac{p(\alpha,\lambda_j)}{N}$, $\forall i, \alpha$.

4.3 Two types of uncertainties

In this section we will discuss the situation in which the particular values of the parameter of each particle are not known. This will lead us to consider two types of uncertainty, with different origins. For simplicity, we will focus on the 2-level independent particles system considered above, but the discussion is general and applies as well to general systems of interacting particles. This discussion will also allow us to take a closer look at the results obtained and clarify their meaning and relevance in different settings.

Often, one does not know the value of the parameter λ_i of each individual particle, but has some idea about how this parameter is distributed on the population, perhaps its probability distribution (obtained for example by measuring individual behavior in an equivalent system). Here, we will assume that the λ_i's are independent and identically distributed random variables with a given probability density $f(\lambda)$. In this case, $\langle n \rangle$ and $\sigma^2[n]$ are themselves random variables that, as shown above, depend on the particular values of the λ_i's. The expected values of these quantities are obtained by averaging (4.2,4.3) over the distribution of the individual parameters:

$$\widehat{\langle n(t) \rangle} = N\widehat{p(t)}, \quad \widehat{\sigma^2[n(t)]} = N\left(\widehat{p(t)} - \widehat{p(t)^2}\right), \tag{4.21}$$

where the hat denotes an average with respect to $f(\lambda)$, $\widehat{g} \equiv \int g(\lambda) f(\lambda) d\lambda$. Again the variance is smaller than for a system of identical particles with the same mean value, namely, $\sigma^2_{\text{id}}[n(t)] - \widehat{\sigma^2[n(t)]} = N\left(\widehat{p(t)^2} - \widehat{p(t)}^2\right)$.

If we average the generating function (4.6) over the distribution of parameters, and expand in powers of s, we obtain a simple form for the probability of the global variable n:

$$\begin{aligned} \widehat{P(n)} &= \int d\lambda_1 \dots d\lambda_N P(n|\lambda_1, \dots, \lambda_N) f(\lambda_1) \dots f(\lambda_N) \\ &= \binom{N}{n} \widehat{p}^n \left(1 - \widehat{p}\right)^{N-n}, \end{aligned} \tag{4.22}$$

a binomial distribution with parameter the average $\widehat{p} = \int d\lambda p(\lambda) f(\lambda)$ over the distribution f. The variance of this distribution is

$$\sigma^2[n(t)]_{\text{tot}} = N\left(\widehat{p(t)} - \widehat{p(t)}^2\right), \tag{4.23}$$

equal to the variance one would obtain in a system of identical particles with the same average, $N\widehat{p}(t)$, a result in apparent contradiction with (4.21). However, we should note that they refer to different things: Expression (4.21) gives the average variance when the parameter values are given, so measuring the average uncertainty in n due to the stochastic nature of the process. (4.23), in addition to the uncertainty coming from the stochasticity of the process, also includes the uncertainty on the parameter values.

The two expressions are related by the law of total variance:

$$\begin{aligned} \sigma^2[n]_{tot} &= \widehat{\sigma^2[n]} + \sigma^2[\langle n|\lambda_1, \ldots, \lambda_N\rangle] \\ &= N(\widehat{p} - \widehat{p^2}) + \sigma^2\left[\sum_i p_i\right] = N(\widehat{p} - \widehat{p^2}). \end{aligned} \tag{4.24}$$

In $\sigma^2[\langle n|\lambda_1, \ldots, \lambda_N\rangle]$, the variances are taken over the distribution of the λ_i's. If we are considering a particular system, the temporal[2] fluctuations in n will come only from the intrinsic stochasticity, and expressions (4.3,4.21) are the ones that measure it. Expressions (4.22,4.23) are appropriate only if we are considering an ensemble of systems with a distribution of parameters and our different measurements may come from different systems in the ensemble.

4.4 Formulation of the general method

Let us now consider a general system of interacting heterogeneous particles. The stochastic description now starts from a master equation for the N-particle probability distribution:

$$\begin{aligned} \frac{dP(s_1, \ldots, s_N)}{dt} &= \sum_{i=1}^{N} (E_i - 1)\left[s_i r_i^- P(s_1, \ldots, s_N)\right] \\ &+ \sum_{i=1}^{N} (E_i^{-1} - 1)\left[(1 - s_i) r_i^+ P(s_1, \ldots, s_N)\right], \end{aligned} \tag{4.25}$$

[2] All the systems considered in this paper are ergodic, so we can think on averages over time or over the realization of the stochastic process interchangeably.

with step operators defined now as $E_i^k F(s_1, ..., s_i, ...s_N) = F(s_1, ..., s_i + k, ..., s_N)$. The transition rates $r_i^{\pm}$ might now depend on the state of any other particle (this is how interactions enter in the model). From Eq.(4.25) one can derive for the moments and correlations:

$$\frac{d\langle s_i\rangle}{dt} = \langle r_i^+\rangle - \langle (r_i^- + r_i^+)s_i\rangle \tag{4.26}$$

$$\frac{d\langle s_i s_j\rangle}{dt} = -\langle q_{ij}s_j s_i\rangle + \langle r_i^+ s_j\rangle + \langle r_j^+ s_i\rangle + \delta_{i,j}\left[\langle s_i r_i^-\rangle + \langle (1-s_i)r_i^+\rangle\right]. \tag{4.27}$$

with $q_{ij} = r_i^- + r_j^- + r_i^+ + r_j^+$In general, if the transition rates depend on the state variables s_i, these equations are not closed since they involve higher order moments, and some approximation method is needed to proceed. Systematic expansions in $1/N$, including van Kampen's Ω-expansion [van Kampen, 2004] (section 1.4.2), are not applicable, since variables $s_i = 0, 1$ are not extensive. In the following, we introduce an approximation suitable for the analytical treatment of systems of globally coupled heterogeneous particles.

Our main ansatz is that the m-particle correlations $\sigma_{j_1,...,j_m}(t) = \langle \delta_{j_1}(t)\cdots\delta_{j_m}(t)\rangle$ with $\delta_j(t) = s_j(t) - \langle n_j(t)\rangle$ scale with system size as

$$\sigma_{j_1,...,j_m}(t) = O(N^{-m/2}), \quad \text{for } j_k \neq j_l. \tag{4.28}$$

Using this ansatz one can close the system of equations (4.26,4.27) for the mean values and the correlations. This is proven in the appendix (4.9).

While the resulting equations for the average values $\langle s_i(t)\rangle$ coincide with the mean-field rate equations usually formulated in a phenomenological way [Young, 1998; Novozhilov, 2012], our formulation allows to compute the correlations and include, if needed, higher order corrections in a systematic way.

4.4.1 Justification of the Ansatz

The validity of the ansatz (4.28) can be established a posteriori by checking that the results obtained using the ansatz are consistent with it. In this subsection, we will link its validity with the well-known van Kampen's ansatz [van Kampen, 2004], (section 1.4.2) that is the basis for the systematic system-size expansion.

Van Kampen's ansatz consists on assuming that the variable of interest has a deterministic part of order Ω plus a stochastic part of order $\Omega^{1/2}$, i.e. $n = \Omega\phi(t) + \Omega^{1/2}\xi$, where Ω is a parameter of the system that controls the relative size of the changes due to elementary processes, typically the system size.

In our system the role of the parameter Ω is played by the total number of particles N. As briefly stated above, we cannot expect that the single-particle

variables that we are considering obey van Kampen's ansatz, since they are not extensive. Our variables $s_i = 0, 1$ have a deterministic and stochastic part that are both of order zero respect to N (note that $\sigma^2[s_i] = \langle s_i \rangle (1 - \langle s_i \rangle)$). However, the macroscopic variable $n = \sum s_i$ is indeed extensive and we can expect that it will follow van Kampen's ansatz: $n = N\phi(t) + N^{1/2}\xi$. This implies that the m-th central moment of n will scale as $N^{m/2}$, i.e:

$$\langle (n - \langle n \rangle)^m \rangle = \sum_{j_1,\ldots,j_m} \sigma_{j_1,\ldots,j_m} = O(N^{m/2}). \tag{4.29}$$

Now, assuming that $\sigma_{j_1,\ldots,j_m} = f_m(N)\tilde{\sigma}_{j_1,\ldots,j_m}$ for $j_k \neq j_l$, with $\tilde{\sigma}_{j_1,\ldots,j_m}$ independent of N i.e. the m-particle correlations are all or the same order in N, so that $\sum_{j_1 \neq j_2 \neq,\ldots,\neq j_m} \tilde{\sigma}_{j_1,\ldots,j_m}$ scales as N^m (note that there are of the order of N^m terms in the sum), we obtain our main ansatz, $\sigma_{j_1,\ldots,j_m} = O(N^{-m/2})$ for $j_k \neq j_l$. We have only considered terms with $j_k \neq j_l$ in the sum (4.29); terms with repeated sub-indexes can be expressed as lower order ones. For example, if the index j_1 is present k times, and the others are all different, we find:

$$\begin{aligned}
&\sigma_{j_1,j_1,\ldots,j_1,j_2,\ldots j_{m-k+1}} = \langle (s_{j_1} - \langle s_{j_1} \rangle)^k \delta_{j_2} \ldots \delta_{j_{k-k+1}} \rangle \\
&= \sigma_{j_2,\ldots j_{m-k+1}} (-\langle s_{j_1} \rangle)^k + \langle \delta_{j_2} \ldots \delta_{j_{m-k+1}} \sum_{i=0}^{k-1} \binom{k}{i} (-\langle s_{j_1} \rangle)^i s_{j_1} \rangle \\
&= \sigma_{j_2,\ldots j_{m-k+1}} [(1 - \langle s_{j_1} \rangle)^k \langle s_{j_1} \rangle + (1 - \langle s_{j_1} \rangle)(-\langle s_{j_1} \rangle)^k] \\
&+ \sigma_{j_1,\ldots,j_{m-k+1}} [(1 - \langle s_{j_1} \rangle)^k - (-\langle s_{j_1} \rangle)^k]
\end{aligned} \tag{4.30}$$

as can be see expanding $(s_{j_1} - \langle s_{j_1} \rangle)^k$ and keeping in mind that $s_i^2 = s_i$. The number of such terms in the sum (4.29) is $O(N^{m-k+1})$, so they give smaller contribution that terms with all sub-indexes different. Proceeding order by order from $k = 1$, we see that our main ansatz (4.28) follows from (4.29).
We point out that in systems of heterogeneous particles we do not have a closed description for the global, extensive, variable n so van Kampen's expansion cannot be used. Instead we derive the implications of van Kampen's ansatz over the correlations of the microscopic variables. (4.28) is a simple and convenient expression that in general allows to close the equation for the moments (4.26,4.27). Often, however it is not necessary, and a weaker condition of the form (4.29), that directly follows from van Kampen's ansatz without further assumptions, is sufficient.

Van Kampen's ansatz is generally valid when the macroscopic equations have a single attracting fixed point, when the system displays small fluctuations around the macroscopic state. The general method explained here is expected to be valid under similar conditions. An interesting topic for future research will

be whether a system that has a single attracting fixed point in the absence of diversity always maintains this globally stable state when diversity is present, and whether a system that does not posses this globally stable fixed point can acquire it when diversity is added.

4.5 Variable number of particles

For simplicity, we have assumed a constant number of particles. The case of variable, but bounded, number of particles can be included straightforwardly by considering an extra state. In the case of binary variables, we would have 3 states: "dead" particle, particle in state 0, particle in state 1. The case of unbounded total number of particles can be treated as a limit of the previous case. As an illustration, we will consider a simple birth and death process of the form:

$$\emptyset \overset{C(\gamma)d\gamma}{\longrightarrow} X(\gamma), \qquad X(\gamma) \overset{\gamma}{\longrightarrow} \emptyset, \tag{4.31}$$

that is, a particle is created at a rate $C = \int C(\gamma)d\gamma$; this particle has a parameter γ chosen according to the probability density $F(\gamma) = C(\gamma)/C$; a particle with parameter γ disappears at a rate γ. This process can be obtained as the limit $N \to \infty$ of the following one:

$$\emptyset \overset{C_i/N}{\longrightarrow} X(\gamma_i), \qquad X(\gamma_i) \overset{\gamma_i}{\longrightarrow} \emptyset, \tag{4.32}$$

where N is the total number of particles of this 2-state system. Following section 4.2, we see that the logarithm of the generating function for the total number of "alive"particles is given by:

$$\log G(s) = \sum_{i=1}^{N} \log\left(1 + \frac{C_i/N}{\gamma_i}(s-1)\right) \tag{4.33}$$

In the limit $N \to \infty$, we have:

$$\begin{aligned} \log G(s) &= \lim_{N\to\infty} \sum_{i=1}^{N} \frac{C_i/N}{\gamma_i}(s-1) = \overline{\left(\frac{C}{\gamma}\right)}(s-1), \\ G(s) &= e^{(s-1)\overline{\left(\frac{C}{\gamma}\right)}}, \end{aligned} \tag{4.34}$$

a Poisson distribution with average $\overline{\left(\frac{c}{\gamma}\right)} \equiv \int \frac{C(\gamma)}{\gamma} d\gamma$.

This corresponds to a system with unbounded number of particles but with only one state for the "alive" particles. The inclusion of more states for the "alive" particles is straight forward. The description at the level of moments can also be performed, and the $N \to \infty$ limit can be taken, which allows to treat systems of interacting particles. In such case, the ansatz for the scaling of the correlations (4.28) has to be modified to include, a part from N that will be taken $N \to \infty$, another parameter Ω that controls the relative size of the changes of the global variable due to elementary processes.

We will proceed by applying the presented method to analyze the role of heterogeneity in two models previously considered in the literature that apply to contexts in which the assumption of identical agents can hardly be justified: stock markets and disease spreading.

4.6 Application to Kirman Model

We now consider Kirman's model [Kirman, 1993], proposed to study herding behavior in the context of stock markets and collective dynamics on ant colonies. In the stock market context, agent i can be in two possible states (e.g. $0 \equiv$"pessimistic- with regard to future market price- and $1 \equiv$"optimistic") and they can switch from one to the other through two mechanisms: spontaneous transitions at a rate ϵ, and induced transitions at a rate $N^{-1} \sum_j \lambda_j (1 - \delta_{s_i, s_j})$, being λ_j the "influence" of agent j on other agents. In the original formulation of the model, all agents have the same influence, i.e. $\lambda_i = \lambda_j, \forall i, j$. We generalize the model allowing the parameter λ_i to vary between agents. In [Alfarano and Milaković, 2009], the effect of heterogeneity was explored numerically, but not in a systematic way.

This model is interesting for us because it incorporates in a simple way two basic processes: spontaneous transitions and induced transitions. As we will see, due to its simplicity, a full analytical treatment is possible that will, in turn, allow us to obtain a deeper insight into the general effect of heterogeneity in systems of interacting particles.

The master equation for the process is of the form (4.25), with rates given by:

$$r_i^+ = \epsilon + N^{-1} \sum_k \lambda_k s_k, \; r_i^- = \epsilon + N^{-1} \sum_k \lambda_k (1 - s_k) \tag{4.35}$$

From (4.26) the averages and correlations obey:

$$\frac{d\langle s_i\rangle}{dt} = \epsilon - (2\epsilon + \overline{\lambda})\langle s_i\rangle + N^{-1}\sum_k \lambda_k\langle s_k\rangle, \tag{4.36}$$

$$\frac{d\sigma_{i,j}}{dt} = -2(2\epsilon + \overline{\lambda})\sigma_{i,j} + N^{-1}\sum_k \lambda_k\left(\sigma_{i,k} + \sigma_{j,k}\right) + \delta_{i,j}\left[\epsilon + a + (\overline{\lambda} - 2a)\langle s_i\rangle - 2\sum_k \frac{\lambda_k\sigma_{i,k}}{N}\right] \tag{4.37}$$

with $a \equiv \sum_k \frac{\lambda_k\langle n_k\rangle}{N}$. Note that, due to the particular form of the rates, these equations are indeed closed. The first equation leads to a steady state value $\langle s_i\rangle_{\rm st} = \frac{1}{2}$, which implies $\langle n\rangle_{\rm st} = \frac{N}{2}$ (a property that comes from the symmetry $0 \leftrightarrow 1$). (4.37) is a linear system of equations for the correlations. The steady state correlations can always be obtained by inverting the matrix that gives the couplings. Obtaining a closed expression for $\sigma^2[n]$ in terms of the moments of λ is, however, not completely straightforward. From (4.37), we see that in the steady state:

$$\sigma_{i,j} = \frac{\sum_k \lambda_k\frac{\sigma_{i,k}+\sigma_{j,k}}{N} + \delta_{i,j}\left[\epsilon + \overline{\lambda}/2 - 2\sum_k \frac{\lambda_k\sigma_{i,k}}{N}\right]}{2(2\epsilon + \overline{\lambda})}$$

$$\Rightarrow \quad \sigma^2[n] = \sum_{i,j}\sigma_{i,j} = \frac{N(\epsilon + \overline{\lambda}/2) + 2C(1 - 1/N)}{2(2\epsilon + \overline{\lambda})}, \tag{4.38}$$

with $C \equiv \sum_{i,j}\lambda_j\sigma_{i,j}$. Again from (4.37), and after simple algebra, we obtain:

$$C = \frac{d(1 - 2/N) + (\epsilon + \overline{\lambda}/2)\overline{\lambda}N}{4\epsilon + \overline{\lambda}}, \tag{4.39}$$

$$d = \frac{(\epsilon + \overline{\lambda}/2)\langle\lambda^2\rangle N - 2\epsilon/N}{4\epsilon}, \tag{4.40}$$

where $d \equiv \sum_{i,j}\lambda_i\lambda_j\sigma_{i,j}$, $e \equiv \sum_{i,j}\lambda_i^2\lambda_j\sigma_{i,j}$. Using the ansatz $\sigma_{i,j} = O(N^{-1})$ we see that the last term of (4.40) is $O(N^0)$ (while the other are of $O(N)$), so to the first order we obtain :

$$\sigma^2_{\rm st}[n] = \frac{N}{4}\left[1 + \frac{\overline{\lambda}}{2\epsilon} + \frac{\sigma^2[\lambda]}{2\epsilon\left(4\epsilon + \overline{\lambda}\right)}\right] + O(N^0), \tag{4.41}$$

with $\sigma^2[\lambda] = \overline{\lambda^2} - \overline{\lambda}^2$. In this case, it is possible to include all higher order terms to obtain an exact expression for d (which gives the exact expression for $\sigma^2[n]$

trough (4.39,4.38)), details are given in the appendix (4.9.1):

$$d = \frac{N(\epsilon + \overline{\lambda}/2)\sum_{k=0}^{\infty}\left(\frac{-2}{N(4\epsilon+\overline{\lambda})}\right)^k \overline{\lambda^{2+k}}}{4\epsilon + \overline{\lambda} - \sum_{k=0}^{\infty}\left(\frac{-2}{N(4\epsilon+\overline{\lambda})}\right)^k \overline{\lambda^{1+k}}} = \frac{N(\epsilon + \overline{\lambda}/2)\overline{\frac{\lambda^2}{1+\frac{2\lambda}{N(4\epsilon+\overline{\lambda})}}}}{4\epsilon + \overline{\frac{2\lambda^2}{N(4\epsilon+\overline{\lambda})+2\lambda}}} \tag{4.42}$$

The second equality holds as long as $\lim_{m\to\infty} \overline{\frac{\lambda^{m+2}}{1+\frac{2\lambda}{N(4\epsilon+\overline{\lambda})}}}\left(\frac{2}{N(4\epsilon+\overline{\lambda})}\right)^m = 0$. A sufficient condition for this is $\frac{2\lambda_{max,N}}{N(4\epsilon+\overline{\lambda})} < 1$, with $\lambda_{max,N} \equiv \max\{\lambda_i\}, i = 1, ..., N$. When the λ_i's are i.i.d. random variables, this last condition is typically satisfied for large enough N, relative to $\overline{\lambda}$, since $\langle\lambda_{max,N}\rangle$ usually scales slower than N. This condition is actually necessary and sufficient for the first equality in (4.42) to hold (see appendix).
We finally obtain the following exact expression for the variance:

$$\sigma^2_{\text{st}}[n] = \frac{N}{4}\left[1 + \frac{2\overline{\lambda}(1-1/N)}{4\epsilon+\overline{\lambda}} + (N-3+2/N)\frac{\overline{\frac{\lambda^2}{N(4\epsilon+\overline{\lambda})+2\lambda}}}{2\epsilon + \overline{\frac{\lambda^2}{N(4\epsilon+\overline{\lambda})+2\lambda}}}\right] \tag{4.43}$$

We see from (4.43) that higher order corrections to $\sigma^2[n]$ depend on higher order moments of the distribution of λ over the population. An equivalent exact expression can be obtained in the case in which the interacting term is not divided by system size.

Expressions (4.41, 4.43) refer to the variance of n in a population with given values for the parameters of each agent, λ_i, so the averages are population averages i.e. $\overline{f(\lambda)} = \sum_{i=1}^{N} f(\lambda_i)/N$. In the case that the parameters of the agents are random variables, the population averages themselves, $\overline{f(\lambda)}$, become random variables. To compute the expected (average) value of (4.41, 4.43), $\widehat{\sigma^2[n]}$, one has to average over the distribution of $\overline{f(\lambda)}$, which depends on the distribution $f(\lambda)$ of the $\lambda_i's$ (we are assuming $\lambda_i's$ i.i.d. random variables). This averages were obtained numerically, by evaluating expressions (4.41, 4.43) over the same realizations of the λ_i's that were used in the numerical simulations. One can use the approximation $\widehat{\overline{f(\lambda)}} \simeq \widehat{f(\lambda)}$, that works better the larger the N and the lower the variance σ^2_λ, and that, due to the law of large numbers, is valid in the limit $N \to \infty$. In Fig.4.3 we compare the average of the analytical expression (4.43) with results coming from numerical simulations. We find perfect agreement and see that at first order the dependence of $\sigma^2[n]$ with $\sigma^2_\lambda \equiv \widehat{\lambda^2} - \widehat{\lambda}^2$ is linear and independent of the form of the distribution, as indicated by (4.41,). Higher order

corrections are noticeable for higher levels of diversity. We also note that the diversity gives a change of the variance some times as high as a factor of 3, so in some cases, heterogeneity cannot be neglected. The raw expression (4.43), taking $\overline{\lambda^k} = \widehat{\lambda^k}$, works well for moderate values of diversity and better as system size increases (note that as $N \to \infty$ $\overline{\lambda^k}$ tends to a Dirac-delta around $\widehat{\lambda^k}$).

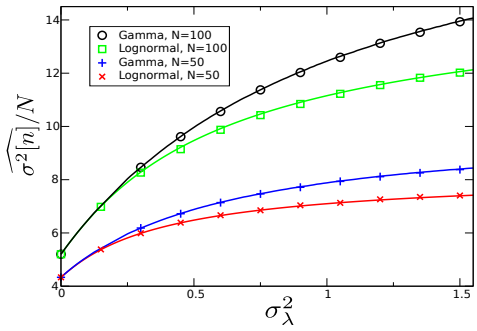

Figure 4.3: Variance of the number of agents in state 1 as a function of the variance of the influence parameter in Kirman's model. Results coming from numerical simulations (symbols) and theoretical analysis (solid lines, Eq.4.43), for different number of agents N and $\epsilon = 0.01$. λ_i are independent random variables distributed according to a log-normal or a Gamma distribution with mean $\widehat{\lambda} = 0.5$ and variance, σ^2_λ. The results have been averaged over $2 * 10^4$ for $N = 50$ and 10^4 for $N = 100$ realizations of the distribution of parameters.

We now realize that, in this case, the knowledge of $\langle n \rangle$ and $\sigma^2[n]$ alone does not allow to infer the degree of heterogeneity present in the system, unless one knows the values of $\overline{\lambda}$ and ϵ. Hence, from observing only the average and variance of the global variable, it is not possible to conclude whether the observed fluctuations have a contribution due to the heterogeneity of the agents. However, the steady-state correlation function $K[n](t) \equiv \langle n(t)n(0)\rangle_{\text{st}} - \langle n\rangle^2_{\text{st}}$, does include a term that allows to infer the possible heterogeneity. $K[n](t)$ is obtained integrating Eq.(4.36) and carefully conditioning (see appendix 4.9.1):

$$K[n](t) = \left(\sigma^2[n] - \frac{C}{\overline{\lambda}}\right) e^{-(2\epsilon+\overline{\lambda})t} + \frac{C}{\overline{\lambda}} e^{-2\epsilon t}. \tag{4.44}$$

C is obtained from (4.38) as $C = \frac{2\epsilon+\overline{\lambda}}{1-1/N}(\sigma^2 - N/4)$. The departure from a pure exponential decay signals the presence of heterogeneity (for identical particles $\frac{C}{\overline{\lambda}} = \sigma^2[n]$). Fitting this expression to data, one can obtain the parameters ϵ, $\overline{\lambda}$

and $\sigma^2[\lambda]$. In Fig.4.4 we show that the numerical simulations indeed support the existence of two exponential decays for the correlation function, which allows to detect the presence of diversity directly from data about the global variable, without any knowledge about parameter values.

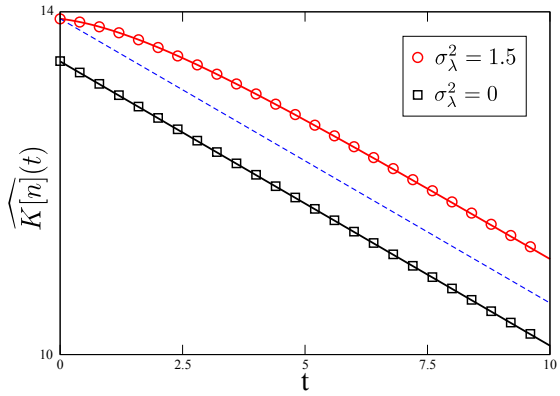

Figure 4.4: Correlation function (in log-linear scale) for Kirman's model. Results coming from numerical simulations (symbols) and theory (Eq.(4.44), solid lines). Note that when heterogeneity is present ($\sigma^2_\lambda = 1.5$) the correlation function departs from purely exponential decay (displayed as a dashed line). Data for $\sigma^2_\lambda = 0$ have been moved 5.5 units vertically for better visualization. Parameters values are $\epsilon = 0.01$, $N = 100$. λ_i are independent random variable distributed according to a gamma with mean $\widehat{\lambda} = 0.5$ and variance, σ^2_λ, indicated in the figure. A simple fit of expression (4.44) to the data with $\sigma^2_\lambda = 1.5$ gives $\overline{\lambda} = 0.50, \epsilon = 0.0099$

4.6.1 Other ways to introduce heterogeneity

Interestingly, other ways to introduce heterogeneity in the system have different effects:
-First, we can assume that the rate of induced change is different for different particles, even if all have the same influence. Measuring this difference in "susceptibility" (to induced change) with a parameter γ_i, we would have that the rate of induced change in agent i is $\gamma_i \sum_j \lambda_j(1-\delta_{s_i,s_j})/N$. The effect of heterogeneity in γ_i (keeping now $\lambda_j = \lambda \ \forall j$ to isolate effects) is that the collective fluctuations decrease with the degree of heterogeneity in the "susceptibility" γ_i.

-If the heterogeneity is introduced in the spontaneous transition rate, $\epsilon \to \epsilon_i$, making some particles more prone to spontaneous transitions that others, it increases the collective fluctuations.
-Setting some heterogeneous preference for the states among the particles, i.e. making ϵ_i^+, the spontaneous rate from 0 to 1 of particle i, different from ϵ_i^-, the spontaneous rate from 1 to 0 of the same particle, decreases global fluctuations. In this last case, in order to vary the preference for one state keeping constant the global "intrinsic noise" of this particle, we set $\epsilon_i^+ = 2\epsilon - \epsilon_i^-$ as i.i.d. random variables with a distribution with support contained in the interval $[0, \epsilon]$ (to avoid negative values). We say that keeping $\epsilon_i^+ + \epsilon_i^- = 2\epsilon$ constant fixes the "intrinsic noise" of this particle because an independent particle has a correlation time given by $\epsilon_i^+ + \epsilon_i^-$. We explore this last case in detail:
The equations for the first moments are:

$$\frac{d\langle s_i\rangle}{dt} = \epsilon_i^+ - (\epsilon_i^+ + \epsilon_i^- + \lambda)\langle s_i\rangle + N^{-1}\lambda\langle n\rangle, \tag{4.45}$$

$$\begin{aligned}\frac{d\sigma_{i,j}}{dt} &= -(\epsilon_i^+ + \epsilon_i^- + \epsilon_j^+ + \epsilon_j^- + 2\lambda)\sigma_{i,j} + N^{-1}\lambda\sum_k\left(\sigma_{i,k} + \sigma_{j,k}\right) \\ &\quad +\delta_{i,j}\left[\epsilon_i^+ + \frac{\lambda\langle n\rangle}{N} + (\epsilon_i^- - \epsilon_i^+ + \lambda - 2a)\langle s_i\rangle - 2\frac{\lambda}{N}\sum_k \sigma_{i,k}\right],\end{aligned} \tag{4.46}$$

Note that, to isolate the effect of diversity in the preference for the states, we have set the influence of each particle equal, i.e. $\lambda_i = \lambda, \forall i$. One can solve this equations to obtain the following exact expression:

$$\langle n\rangle_{st} = N\frac{\overline{\epsilon^+}}{2\epsilon} \tag{4.47}$$

$$\sigma^2[n]_{st} = \frac{N}{4(\epsilon + \frac{2\lambda}{N})}\left[\overline{\epsilon^+}(1 + \frac{\lambda}{\epsilon}) - \overline{\epsilon^+}^2\frac{\lambda}{\epsilon}\left(\frac{1}{2\epsilon} + \frac{1}{2\epsilon + \lambda}\right) - 2\frac{\overline{\epsilon^{+2}}}{2\epsilon + \lambda}\right], \tag{4.48}$$

where we have used $\epsilon_i^+ + \epsilon_i^- = 2\epsilon, \forall i$. If the parameters of the variables, ϵ_i^+, are i.i.d. random variables, then $\overline{\epsilon^+}, \overline{\epsilon^+}^2, \overline{\epsilon^{+2}}$ become themselves random variables. It is easy to compute the expected value of (4.47, 4.48) over the distribution of

parameters, to obtain:

$$\widehat{\langle n\rangle}_{st} = N\frac{\widehat{\epsilon^+}}{2\epsilon} \tag{4.49}$$

$$\widehat{\sigma^2[n]}_{st} = \frac{N}{4(\epsilon+\frac{2\lambda}{N})}\left[\widehat{\epsilon^+}\left(2+\frac{\lambda}{\epsilon}\right)-\widehat{\epsilon^+}^2\left(\frac{\lambda}{2\epsilon^2}+\frac{1}{\epsilon}\right)-\right.$$
$$\left.\sigma^2_{\epsilon^+}\left(\frac{2\epsilon+\lambda/N}{\epsilon(2\epsilon+\lambda)}+\frac{\lambda}{2\epsilon^2 N}\right)\right], \tag{4.50}$$

with $\sigma^2_{\epsilon^+} \equiv \widehat{\epsilon^{+2}} - \widehat{\epsilon^+}^2$. In figure (4.5) we plot the exact expressions (4.49, 4.50) together with numerical simulations. In this case, the correlation function, than

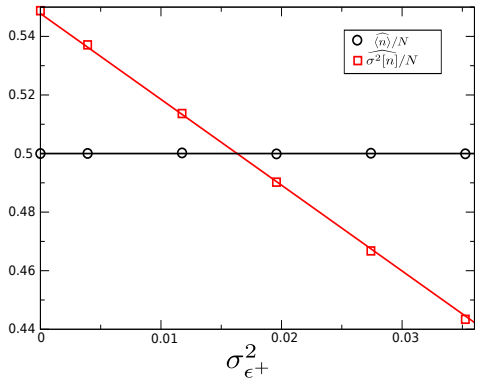

Figure 4.5: Variance and average of the number of agents in state 1 as a function of the variance of the spontaneous transition rate to state 1, ϵ^+, in Kirman's model. Results coming from numerical simulations (symbols) and theoretical analysis (solid lines, Eqs.(4.49, 4.50)), for $N = 50$ agents, $\lambda_i = \lambda = 0.5$ and $\epsilon_+ + \epsilon_- = 2\epsilon = 0.4$. ϵ_i^+ are independent random variables distributed according to a symmetric beta distribution with mean $\overline{\epsilon^+} = 0.2$ and variance, $\sigma^2_{\epsilon^+}$. $P(\epsilon_+) = \frac{\epsilon^{+(\alpha-1)}(1-\epsilon^+)^{\alpha-1}}{B(\alpha,\alpha)}$, $\epsilon_+ \in (0, 2\epsilon)$, with $B(a,b)$ the beta function and $\alpha = \frac{\frac{\epsilon^2}{\sigma^2_{\epsilon^+}}-1}{2}$.

can be obtained integrating (4.45), shows an exponential decay of the form

$$K[n](t) = \sigma^2[n]e^{-2\epsilon t}, \tag{4.51}$$

independently of the degree of heterogeneity, so this form of heterogeneity cannot be inferred by measuring the correlation function. Numerical simulations confirm this result.

In the most general case in which all the parameters $(\epsilon_i^+, \epsilon_i^-, \gamma_i, \lambda_i)$ vary among the particles, the equations for the averages and correlations are:

$$\frac{d\langle s_i\rangle}{dt} = \epsilon_i^+ - (\epsilon_i + \gamma_i\overline{\lambda})\langle s_i\rangle + \gamma_i a, \tag{4.52}$$

$$\frac{d\sigma_{i,j}}{dt} = -[\epsilon_i + \epsilon_j + (\gamma_i + \gamma_j)\lambda]\sigma_{i,j} + \frac{\gamma_i}{N}\sum_k \lambda_k\sigma_{j,k} + \frac{\gamma_j}{N}\sum_k \lambda_k\sigma_{i,k} + \delta_{i,j}\left[\epsilon_i^+ + \gamma_i a + (\epsilon_i^- - \epsilon_i^+ + \overline{\lambda} - 2\gamma_i a)\langle s_i\rangle - 2\frac{\gamma_i}{N}\sum_k \lambda_k\sigma_{i,k}\right], \tag{4.53}$$

we remind that $a \equiv \sum_k \frac{\lambda_k\langle s_k\rangle}{N}, \epsilon_i \equiv \epsilon_i^+ + \epsilon_i^-$. For the average of the global variable, we obtain:

$$\langle n\rangle_{st} = N\left(\overline{\frac{\epsilon^+}{\epsilon + \gamma\overline{\lambda}}} + a_{st}\overline{\frac{\gamma}{\epsilon + \gamma\overline{\lambda}}}\right), \tag{4.54}$$

with $a_{st} = \frac{\overline{\frac{\lambda\epsilon^+}{\epsilon+\gamma\overline{\lambda}}}}{1-\overline{\frac{\lambda\gamma}{\epsilon+\gamma\overline{\lambda}}}}$. The system of equations 4.53 is of the form:

$$\frac{d\vec{\sigma}}{dt} = \vec{v} + M\vec{\sigma}, \tag{4.55}$$

with $\vec{v}$ and M a vector and a matrix of $2N$ dimensions given by (4.53), so the stationary solution is given by $\vec{\sigma_{st}} = -M^{-1}\vec{v}$, from which we obtain the steady state variance of the global variable:

$$\sigma^2[n] = \sum_{i,j}\sigma_{i,j,st}. \tag{4.56}$$

However, an explicit expression in terms of the moments of the parameters has not been obtained.

4.6.2 Intuitive explanation of main result

In the case of distributed "influence", we obtain that heterogeneity increases the size of the fluctuations, in contrast with what was found for independent units. Can we intuitively understand these different effects?

When the influence parameter, λ_i, varies from one unit to the other, there will be some largely influential agents and others with little influence. In the limit of very large heterogeneity we can think of a situation with a single agent with

an extremely large influence and the others having a negligible one (we are keeping a constant average influence). In this case, the highly influential agent drifts from one state to the other, essentially independently (since other agents have negligible influence), but, due to its large influence, all the agents are attracted to its current state. In this “follow the leader" regime, we obtain macroscopic transitions from one state to the other, corresponding to very large global fluctuations.

The situation is the opposite for a non-identical susceptibility parameter ω_i where global fluctuations decrease as the diversity is increased. Again, we can understand this in the limit of very large heterogeneity where a single agent (or a small number of them) has large susceptibility while all the others have a negligible one (in order to keep average susceptibility constant). Then, agents with small susceptibility change essentially independently, in an uncorrelated fashion, resulting in low global fluctuations (note that in order to have large global fluctuations, the fluctuations in the state of the single agents should be correlated).

In the case of diverse spontaneous transition rates, ϵ_i, global fluctuations increase with the degree of heterogeneity. In the limit of large heterogeneity, we would have a small number of agents with very large spontaneous transition rate, whose state would fluctuate in an uncorrelated fashion, and a large number of agents with low spontaneous transition rate, that essentially would only change state through induced transitions, giving rise to correlated fluctuations, resulting in large variance for the global variable.

In the case in which agents display an intrinsic heterogeneous preference for one of the two states, the global fluctuations decrease with heterogeneity degree. We saw this already in the first section for non-interacting agents. Here we see the same effect, suggesting that the phenomenon is robust and still plays a role when interaction is added.

This asymmetry between small number of agents with large value for a parameter and large number of agents with a small value for the parameter, comes from the fact that all the parameters considered are, by definition, positive. If the distribution of the parameter is unbounded (from above), it will necessarily be skewed, showing this effect. However, all the effects of diversity commented are still present if the distribution is symmetric. In this case, nevertheless, the maximum degree of heterogeneity (for constant mean value) is bounded, sometimes greatly limiting the maximum possible value of diversity. For symmetric distributions, a simple explanation is not so clear, but an asymmetry in the effect of increasing and decreasing the value of the parameter seems to be at the heart of the phenomenon.

4.7

Application to the SIS disease spreading model

The previous example could be treated exactly because in the equations for the moments, the interaction, non-linear terms, cancel out. In general, however, this is not the case, and the analytical treatment is more involved. Here we consider a an example of such case. The stochastic susceptible-infected-susceptible (SIS) model and its variants are paradigmatic models for the study of spreading of infectious disease [Anderson, 1982] as well as the diffusion of innovation [Young, 2009] and other types of social influence. Despite its simplicity, it captures interesting phenomenology. The process is schematically described by:

$$S(i) + I(j) \overset{\lambda_j/N}{\longrightarrow} I(i) + I(j), I(j) \overset{\gamma}{\longrightarrow} S(j), S(j) \overset{\epsilon}{\longrightarrow} I(j), \tag{4.57}$$

where $S(i)$ (resp. $I(i)$) denotes agent i being susceptible (resp. infected). There are 3 basic elementary processes: (i) infected agent j infects susceptible agent i at a rate λ_j/N, being λ_j the infectivity parameter of agent j; (ii) infected agent j becomes susceptible a rate γ; (iii) susceptible agent j gets infected spontaneously (due to interactions with agents not considered in the system or other causes) at a rate ϵ. This corresponds to the SIS model with spontaneous contagions and distributed infectivity. In the absence of spontaneous infections $\epsilon = 0$, the system has a trivial steady state with zero infected agents. With $\epsilon \neq 0$ the system has a non-trivial steady state whose properties we analyze in the following. As in the previous case, heterogeneity could appear in any parameter of the agents (for example, in the recovery rate, in a"susceptibility" parameter, etc.).

We study first the case in which only the infectivity, λ_i, can vary from agent to agent. The effect of heterogeneity in the deterministic version of related models was studied recently [Novozhilov, 2012]. The master equation is:

$$\begin{aligned} \frac{dP(n_1,\ldots,n_N,t)}{dt} &= \sum_{i=1}^{N} \left(E_i^{-1} - 1\right)(1-n_i)(\epsilon + \sum_j \frac{\lambda_j n_j}{N})P(n_1,\ldots,n_N,t) \\ &+ \sum_i (E_i - 1)\gamma n_i P(n_1,\ldots,n_N,t) \end{aligned} \tag{4.58}$$

The equations for the averages and correlations are:

$$\frac{d\langle n_i\rangle}{dt} = \epsilon - (\epsilon+\gamma)\langle n_i\rangle + \sum_l \frac{\lambda_l}{N}[\langle n_l\rangle(1-\langle n_i\rangle) - \sigma_{i,l}] \tag{4.59}$$

$$\begin{aligned}\frac{d\sigma_{i,j}}{dt} &= -2(\epsilon+\gamma)\sigma_{i,j} + \sum_l \frac{\lambda_l}{N}[\sigma_{i,l}(1-\langle n_j\rangle) + \sigma_{j,l}(1-\langle n_i\rangle) - 2\sigma_{i,j}\langle n_l\rangle - 2\sigma_{i,j,l}] \\ &+ \delta_{i,j}\left[(1-\langle n_i\rangle)\epsilon + \gamma\langle n_i\rangle + \sum_l \frac{\lambda_l}{N}[\langle n_l\rangle(1-\langle n_i\rangle) - \sigma_{i,l}]\right]\end{aligned} \tag{4.60}$$

These equations can be closed using our main ansatz, to obtain explicit formulas for $\langle n\rangle$ and $\sigma^2[n]$ to any desired order in N^{-1}. In this case, however, the expressions are rather cumbersome and we skip them here. This results are plotted in figure (4.6). To compute the time correlations, we start with the solution of (4.59) (to first order, i.e. neglecting terms with $C_{i,l}$), which reads:

$$\langle n_i(t)|n_i(0)\rangle = n_i(0)e^{-(\gamma+\epsilon+\overline{\lambda})t/2}\frac{sech(c_0+ut)}{sech(c_0)} + \frac{u}{\overline{\lambda}}\tanh(c_0+ut) + \frac{\overline{\lambda}-\epsilon-\gamma}{2\overline{\lambda}}, \tag{4.61}$$

with $c_0 \equiv \tanh^{-1}\left(\frac{a_0}{u} + \frac{\epsilon+\gamma-\overline{\lambda}}{2u}\right), u \equiv \frac{\sqrt{(\epsilon+\gamma-\overline{\lambda})^2+4\epsilon\overline{\lambda}}}{2}, c_0 \equiv \sum_l \frac{\lambda_l n_l(0)}{N}$. Note that the initial condition $n_i(0)$ appears inside the nonlinear functions hyperbolic tangent and hyperbolic secant, which prevents from obtaining a closed expression of the time correlation as a function of lower order moments. In any case, the time correlation $C[n](t) = \langle\langle n(t)|n(0)\rangle n(0)\rangle - \langle n\rangle\langle n\rangle$ changes its functional form, respect to the case of no diversity, where one obtains:

$$\langle n(t)|n(0)\rangle = \frac{N}{\lambda}\left[u\tanh(ut+c_0) + \frac{\lambda-\epsilon-\gamma}{2}\right], \tag{4.62}$$

with $u \equiv \frac{\sqrt{(\epsilon+\gamma-\lambda)^2+4\epsilon\lambda}}{2}, c_0 \equiv \tanh^{-1}\left(\frac{\lambda n_0}{uN} - \frac{\lambda-\epsilon-\gamma}{2u}\right)$

In figure (4.6), we compare the approximation to order $O(N^{-1})$ with results coming from numerical simulations. Here both the average value and the variance are modified by the presence of heterogeneity (the dependence of the average is, however, only in second order in $1/N$, almost unnoticeable in the figure).

In this case, other ways to introduce heterogeneity also have different effects. When heterogeneity appears in the recovery rate γ, the mean number of infected agent increases, with a moderate effect over the variance (resulting in smaller relative fluctuations). Heterogeneity in the susceptibility to infection (which would be introduced with the change $r_i^+ = \epsilon + \sum_l \frac{\lambda_k\langle s_l\rangle}{N} \to \epsilon + \omega_i\sum_l \frac{\lambda_k\langle s_l\rangle}{N}$, with ω_i

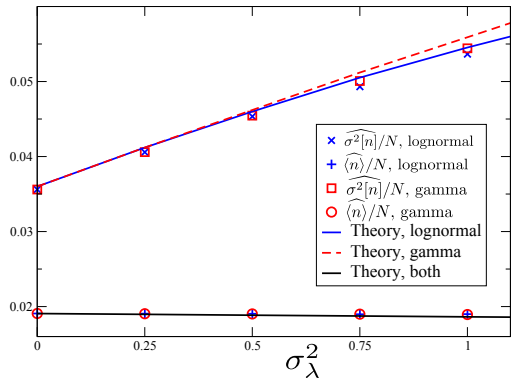

Figure 4.6: Average and variance of the number of infected agents in the SIS model as a function of the variance of the infectivity. Numerical simulations (symbols) and theoretical prediction to first order (lines). Parameters values are $\epsilon = 0.01$, $\gamma = 1$, $N = 200$. λ_i are i.i.d. random variables with average value $\overline{\lambda} = 0.5$ and variance, $\sigma^2[\lambda]$, indicated in the figure. Results were averaged over $3\,10^4$ realizations of the distribution of parameters.

distributed over the population) decreases the fluctuations, with little effect over the mean value. Heterogeneity in the spontaneous infection rate ϵ has almost no effect. The effects of heterogeneity in the infectivity and in the susceptibility are equivalent to those found in the Kirman model, and can be intuitively understood in the same terms. Heterogeneity in the recovery rate is similar to assigning an heterogeneous preference for the state 0 (recovery) and its effect in the (relative) fluctuations is again the same as that in the case of the Kirman model. This suggests that the effects of the heterogeneity found are generic and can be useful to understand the behavior of other systems.

4.8 Conclusions

In this chapter, we have analyzed the combined effect of stochasticity and heterogeneity in interacting-particle systems. We have presented a formulation of the problem in terms of master equations for the individual units, but extracted

conclusions about the fluctuations of collective variables. We have developed an approximation suitable for the analytical study of this general type of systems. We have shown that the heterogeneity can have an ambivalent effect on the fluctuations, enhancing or decreasing them depending on the form of the system and the way heterogeneity is introduced. In the case of independent particles, heterogeneity in the parameters always decreases the size of the global fluctuations. We have also demonstrated that it is possible to obtain precise information about the degree and the form of the heterogeneity present in the system by measuring only global variables and their fluctuations, provided that the underlying dynamical equations are known. In this way stochastic modeling allows to obtain information not accessible from a purely deterministic approach. We have also demonstrated that, in some cases, one can account for the heterogeneity of the particles without losing analytical tractability.

Heterogeneity among the constituent units of a system is a very generic feature, present in many different contexts and this work provides a framework for the systematic study of the effect of heterogeneity in stochastic systems, having thus a wide range of potential applicability. More research in this direction would be welcomed.

4.9 Appendix

We first show how the ansatz (4.28) allows to close the system (4.26, 4.27).
We assume that functional dependence of the rates on the sate variables is of the form $f(s_1/N,\dots,s_N/N)$. This includes, for example, rates of the form $f(\sum \lambda_k s_k/N)$ like the ones used in the examples analyzed. We further assume that the rates can be expanded as a power series:

$$f(s_1/N,\dots,s_N/N) = a_0 + \sum_{i_1=1}^{N} a_{i_1}\frac{s_{i_1}}{N} + \frac{1}{2!}\sum_{i_1,i_2=1}^{N} a_{i_1,i_2}\frac{s_{i_1}s_{i_2}}{N^2} + \dots + \frac{1}{k!}\sum_{i_1,\dots,i_k=1}^{N} a_{i_1,\dots,i_k}\frac{s_{i_1}\cdots s_{i_k}}{N^k} + \dots \tag{4.63}$$

There are N^k terms in the k'th summand, $\sum_{i_1,\dots,i_k=1}^{N}$, giving a total contribution of order $O(N^0)$. The terms in the right hand side of (4.26) are of the form:

$$\frac{\langle s_{i_1}\dots s_{i_k}\rangle}{k!} = \frac{\langle(\delta_{i_1}+\langle s_{i_1}\rangle)\dots(\delta_{i_k}+\langle s_{i_k}\rangle)\rangle}{k!} = \sum_{l=0}^{k}\frac{\delta^l\langle s\rangle^{k-l}}{l!(k-l)!} = \sum_{l=0}^{k}\frac{O(N^{-l/2})}{l!(k-l)!}, \tag{4.64}$$

where δ^l corresponds to a term of the form $\langle \delta_{j_1}(t) \cdots \delta_{j_l}(t) \rangle$, $\langle s \rangle^{k-l}$ corresponds to $\langle s_{i_1} \rangle \cdots \langle s_{i_{k-l}} \rangle$ and the last equality holds due to our ansatz. We see that the dominant terms are those with $l = 0$, which correspond to products of mean values of the form $\langle s_{i_1} \rangle \cdots \langle s_{i_k} \rangle$. We conclude that the ansatz allows to do the substitution $\langle s_{i_1} \dots s_{i_k} \rangle \to \langle s_{i_1} \rangle \cdots \langle s_{i_k} \rangle + O(N^{-1/2})$ in the evolution equations for the mean values.

The evolution equations for the correlations read:

$$\frac{d\sigma_{i,j}}{dt} = \langle (r_i^- + r_i^+) s_i \delta_j \rangle + \langle (r_j^- + r_j^+) s_j \delta_i \rangle + \langle r_i^+ \delta_j \rangle + \langle r_i^+ \delta_j \rangle. \tag{4.65}$$

In this case, the terms are of the form $\langle s_{i_1} \dots s_{i_k} \delta_r \rangle = \langle (\delta_{i_1} + \langle s_{i_1} \rangle) \dots (\delta_{i_k} + \langle s_{i_k} \rangle) \delta_r \rangle$ with $r = i, j$. Due to the presence of δ_s, the term in which only averages appears vanishes. Reasoning as before, we see that the dominant terms are those proportional to $\sigma_{i_l,s}$, while those proportional to higher-order correlations can be neglected. In this case, the ansatz allows to do the substitution $\langle s_{i_1} \dots s_{i_k} \delta_r \rangle \to \langle s_{i_1} \rangle \cdots \langle s_{i_k} \rangle \sum_{l=1}^{k} \frac{\sigma_{i_r}}{\langle s_{i_r} \rangle} + O(N^{-3/2})$. In this way, the evolution equation for the correlations depend, at first order, only on averages and correlations and not on higher order moments.

4.9.1 Details of the calculation in Kirman model

To obtain the exact expression of the variance of the global variable in Kirman model with distributed influence, we start with equation (4.38):

$$\sigma_{i,j} = \frac{\sum_k \lambda_k \frac{\sigma_{i,k} + \sigma_{j,k}}{N} + \delta_{i,j} \left[\epsilon + \overline{\lambda}/2 - 2 \sum_k \frac{\lambda_k \sigma_{i,k}}{N} \right]}{2(2\epsilon + \overline{\lambda})}. \tag{4.66}$$

Using the rescaled variables $\tilde{\sigma}_{i,j} \equiv 4\sigma_{i,j}$, $\tilde{\lambda}_k \equiv \frac{\lambda_k}{2(2\epsilon + \overline{\lambda})N}$, and defining $S_n := \sum_{i,j=0}^{N} \tilde{\lambda}_i{}^n \tilde{\lambda}_j \tilde{\sigma}_{i,j}$, we obtain:

$$S_{n+1} = \frac{N\overline{\tilde{\lambda}} - 1}{2} S_n + \frac{N}{2} \left(\overline{\tilde{\lambda}^n} S_1 + \overline{\tilde{\lambda}^{n+1}} \right). \tag{4.67}$$

Defining now $G_n := \left(\frac{2}{N\overline{\tilde{\lambda}}-1}\right)^n S_n$, $T_M := \sum_{n=1}^{M} G_n$, we arrive to:

$$G_{n+1} = G_n + \left(\frac{2}{N\overline{\tilde{\lambda}}-1}\right)^{n+1} \frac{N}{2}\left[G_1\left(-\frac{\overline{\lambda}+4\epsilon}{4(2\epsilon+\overline{\lambda})}\right)\overline{\tilde{\lambda}^n} + \overline{\tilde{\lambda}^{n+1}}\right], \quad (4.68)$$

$$T_{M+1} - G_1 = T_M + \frac{N}{2}\sum_{n=1}^{M}\left[\left(\frac{2}{N\overline{\tilde{\lambda}}-1}\right)^n\left(\frac{2\overline{\tilde{\lambda}^{n+1}}}{N\overline{\tilde{\lambda}}-1} + G_1\overline{\tilde{\lambda}^n}\right)\right]. \quad (4.69)$$

If $\lim_{M\to\infty} G_M = 0$, we see that:

$$G_1 = -\frac{\frac{N}{2}\sum_{n=1}^{\infty}\left(\frac{2}{N\overline{\tilde{\lambda}}-1}\right)^{n+1}\overline{\tilde{\lambda}^{n+1}}}{1+\frac{N}{2}\sum_{n=1}^{\infty}\left(\frac{2}{N\overline{\tilde{\lambda}}-1}\right)^{n}\overline{\tilde{\lambda}^{n}}}. \quad (4.70)$$

Going back to the original variables, we finally obtain, with the notation of the main text:

$$d = \frac{\frac{N^3(\epsilon+\overline{\lambda}/2)(4\epsilon+\overline{\lambda})}{4}\sum_{n=1}^{\infty}\left(\frac{-2}{(\overline{\lambda}+4\epsilon)N}\right)^n\overline{\lambda^{n+1}}}{1+\frac{N}{2}\sum_{n=1}^{\infty}\left(\frac{-2}{(\overline{\lambda}+4\epsilon)N}\right)^n\overline{\lambda^n}}, \quad (4.71)$$

which can be rewritten in the form (4.42), completing the proof.

The condition of convergence is:

$$\lim_{M\to\infty} G_M = \lim_{M\to\infty}\sum_{i,j=1}^{N}\left(\frac{-2\lambda_i}{(\overline{\lambda}+4\epsilon)N}\right)^M\frac{2\lambda_j}{(2\epsilon+\overline{\lambda})N}\sigma_{i,j}. \quad (4.72)$$

A necessary and sufficient condition for this is $\lambda_i < \frac{(\overline{\lambda}+4\epsilon)N}{2}, \forall i = 1,\dots N$. When the parameters λ_i are i.i.d. r. v. the probability of this typically approaches 1 as N grows.

The correlation function can be derived as follows (we exemplify the derivation in the case of distributed influence, for other types of heterogeneity, the derivation is similar):
(4.36) is an equation for the conditional averages $\langle s_i|\{s_l(t_0)\}\rangle$ if we set $\{s_l(t_0)\}$ as initial conditions. It implies:

$$\frac{da}{dt} = \epsilon\lambda - 2\epsilon a \to a(t_0+t) = \frac{\lambda}{2}(1-e^{-2\epsilon t}) + a(t_0)e^{-2\epsilon t}, \quad (4.73)$$

with $a \equiv \sum_k \lambda_k \langle s_k | \{s_l(t_0)\}\rangle / N$. Noticing that (4.36) is equal to $\frac{d\langle s_i\rangle}{dt} = \epsilon - (2\epsilon + \lambda)\langle s_i\rangle + a(t)$, we obtain:

$$\langle s_i(t_0+t)|\{s_k(t_0)\}\rangle = \frac{1}{2}(1-e^{-(2\epsilon+\overline{\lambda})t}) + \frac{a(t_0)-\overline{\lambda}/2}{\overline{\lambda}} e^{-2\epsilon t}(1-e^{-\overline{\lambda}t}) + s_i(t_0)e^{-(2\epsilon+\overline{\lambda})t}. \quad (4.74)$$

Using now $K_{st}[n](t) = \langle\langle n(t_0+t)|n(t_0)\rangle n(t_0)\rangle_{st} - \langle n\rangle_{st}^2 = \sum_{i,j}\langle\langle s_i(t_0+t)|\{s_k(t_0)\}\rangle s_j(t_0)\rangle - \frac{N^2}{4}$ (remember $\langle n\rangle_{st} = N/2$), and after some straightforward algebra, we obtain:

$$K_{st}[n](t) = (\sigma_{st}^2 - C/\overline{\lambda})e^{-(2\epsilon+\overline{\lambda})t} + C/\overline{\lambda}e^{-2\epsilon t}, \quad (4.75)$$

equal to the expression displayed in the main text.

Part V

Collective firing induced by heterogeneity in coupled excitable systems

Chapter 5

Role of heterogeneity distribution in a system of coupled active rotators

In this chapter we will depart slightly from the main topic of the thesis and consider a system with deterministic evolution. Our main focus here will be, connecting with the previous chapter, the effect of the heterogeneity among the components of the system. We will consider a model very much studied in the literature and we will see that some particular forms of the distribution of heterogeneity can give rise to results qualitatively different from other distributions, warning us about the lack of generality of some results obtained when heterogeneity is present.

5.1

Introduction and background

Synchronization phenomena play a prominent role in many branches of science [Pikovsky et al., 2001]. Phase models successfully describe systems of weakly coupled limit cycle oscillators. Amongst them, the Kuramoto model [Kuramoto, 1984] has become a paradigm for the study of synchronization (for reviews see [Pikovsky et al., 2001; Acebron et al., 2005; Strogatz, 2000]). It shows how synchronization can appear when the competitive effects of coupling and diversity among the individual units are present.

CHAPTER 5. ROLE OF HETEROGENEITY DISTRIBUTION IN A SYSTEM OF COUPLED ACTIVE ROTATORS

In the Kuramoto model each unit, i, is described by a phase variable $\phi_i \in [0, 2\pi)$. In the absence of coupling, the unit just rotates at a frequency ω_i (called the natural frequency of the unit) i.e. its phase increases linearly at a rate ω_i (because ϕ_i is a phase, it is defined mod 2π, i.e. $\phi_i + n2\pi = \phi_i$, $\forall n \in \mathbb{Z}$). The natural frequencies are considered to be slightly different for different units, so, in the absence of coupling, the phase of the different units will diverge. In order to find synchronization a coupling term is added, that tends to make the phases go closer. The original and simplest formulation of the model is:

$$\dot{\phi}_i = \omega_j + \frac{K}{N} \sum_{l=1}^{N} \sin(\phi_l - \phi_j)). \tag{5.1}$$

Here K is the coupling strength. The diversity in the oscillators is introduced by taking their natural frequencies from a probability distribution. This model shows that when the diversity of the oscillators is smaller than some (coupling-dependent) threshold there is some degree of synchronization (measured by a non-zero value of the parameter ρ defined below), but the synchronization is lost when the diversity exceeds this threshold. The transition becomes a well-defined second order phase transition in the limit $N \to \infty$. This behavior, illustrated in figure (5.1), is qualitatively independent of the form of the frequency distribution, as long as it is symmetric and unimodal.

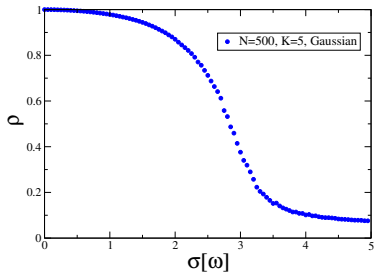

Figure 5.1: Synchronization degree as a function of the standard deviation of the distribution of natural frequencies in the Kuramoto model for a Gaussian distribution, coupling strength $K = 5$ and $N = 500$ units.

Although, on general grounds (central limit theorem), one would expect the distribution of natural frequencies to be well approximated by a Gaussian form, theoretical studies analyzing this model and generalizations of it usually consider a Lorentzian form, since it allows for an easier analytical treatment. It is generally believed that the main results concerning the global synchronization properties are qualitatively independent of the precise form of the distribution,

as long as it is symmetric and unimodal, as is the case in the original model. In this chapter, however, we will show that a variant of the Kuramoto model displays or not a reentrant diversity-induced transition into a state of collective firing, depending on the type of distribution used. This transition is present (for some parameter range) in all the distributions studied (symmetric and unimodal) except in the case of the Lorentzian. The non-generic behavior of the system with a Lorentzian distribution of natural frequencies warns about the indiscriminate use of some recently proposed methods [Ott and Antonsen, 2008] in order to understand generic properties of coupled oscillators.

We consider the following variant of the Kuramoto model which describes the dynamics of an ensemble of globally coupled active rotators $\phi_j(t), j = 1, ..., N$ [Kuramoto, 1975]:

$$\dot{\phi}_j = \omega_j - \sin\phi_j + \frac{K}{N}\sum_{l=1}^{N}\sin(\phi_l - \phi_j)). \tag{5.2}$$

A natural frequency $\omega_j < 1$ (respectively, $\omega_j > 1$) corresponds to an excitable (respectively, oscillatory) behavior of the rotator j when it is uncoupled. K is the coupling intensity. Diversity is introduced by considering that the ω_j's are distributed according to a probability density function $g(\omega)$, with mean value $\overline{\omega}$ and variance σ^2. The model is equivalent to the regular Kuramoto model with zero average frequency and an external periodic driving of frequency $-\overline{\omega}$, as it can be easily seen with the change of variables $\phi_j \to \phi_j - \overline{\omega}t$. Throughout the paper, besides the well-known Gaussian and uniform distributions, we will be considering a general family or Lorentzian-type distributions $L_n^m(\omega)$, for $n > 0, mn > 1$, defined as:

$$L_n^m(\omega) = \frac{n\Gamma(m)}{2\Gamma(m-1/n)\Gamma(1/n)} \cdot \frac{\Delta^{nm-1}}{(|\omega-\overline{\omega}|^n + \Delta^n)^m} \tag{5.3}$$

The variance of these distributions is finite only for $mn > 3$ and it is given by $\sigma^2 = \Delta^2\frac{\Gamma(m-3/n)\Gamma(3/n)}{\Gamma(m-1/n)\Gamma(1/n)}$. The usual Lorentzian distribution corresponds to $n = 2$, $m = 1$ and has, hence, an infinite variance, although we still will use Δ as a measure of diversity.

To characterize the collective behavior of the system we use the time-dependent global amplitude, $\rho(t)$, and phase, $\Psi(t)$ [Kuramoto, 1984, 1975]:

$$r(t) = \rho(t)e^{i\Psi(t)} = \frac{1}{N}\sum_{j=1}^{N} e^{i\phi_j(t)} \tag{5.4}$$

The Kuramoto order parameter $\rho \equiv \langle \rho(t) \rangle$, where $\langle \cdots \rangle$ denotes time average, is known to be a good measure of collective synchronization in coupled oscillators systems, i.e. $\rho \simeq 1$ when the oscillators synchronize ($\phi_j \simeq \phi_l, \forall j, l$), and $\rho \simeq 0$ for desynchronized behavior.

For $\overline{\omega} \lesssim 1$ the system displays three different regimes: (i) for small diversity, almost all units are at rest at similar fixed points; (ii) increasing diversity one enters a dynamical state in which a macroscopic fraction of units fire at (roughly) the same time; (iii) for even larger diversity, the system enters a desynchronized state. To discriminate between static entrainment and collective firing, regimes (i) and (ii), we use the order parameter introduced by Shinomoto and Kuramoto [Shinomoto and Kuramoto, 1986]:

$$\zeta = \langle |\rho(t) e^{i\Psi t} - \langle \rho(t) e^{i\Psi(t)} \rangle | \rangle \tag{5.5}$$

which differs from zero only in the case of synchronous firing.

5.2 Previous results

An approximate theory to describe these three regimes was developed in [Tessone et al., 2007]. The theory was independent of the form of the natural frequencies distribution and was also applicable to identical units subject to noise. A recent method developed by Ott and Antonsen [Ott and Antonsen, 2008, 2009] allows to solve exactly this model (and a large family of related ones) in the infinite number of oscillators limit and in a number of cases that include the Lorentzian distribution of natural frequencies. Childs and Strogatz [Childs and Strogatz, 2008] used this method to obtain the full bifurcation diagram of the model if the case of the Lorentzian distribution. Contrarily to the results of [Tessone et al., 2007], their exact solution implies that there is no transition to collective firing increasing the diversity for $\overline{\omega} < 1$. The non-existence of the transition can be derived from the bifurcation diagram in the $\overline{\omega} - \Delta$ space obtained using the ideas of [Childs and Strogatz, 2008], see Fig.5.2. For $\overline{\omega} < 1$ increasing Δ one never encounters a bifurcation that can lead to oscillatory behavior. This situation is generic for all values of K, since it can be shown that the SNIC bifurcation always starts at $\overline{\omega} = 1, \Delta = 0$ with positive slope. The model was also studied for the Lorentzian case with a different approach in [T.M. Antonsen et al., 2008] and the same results where found.

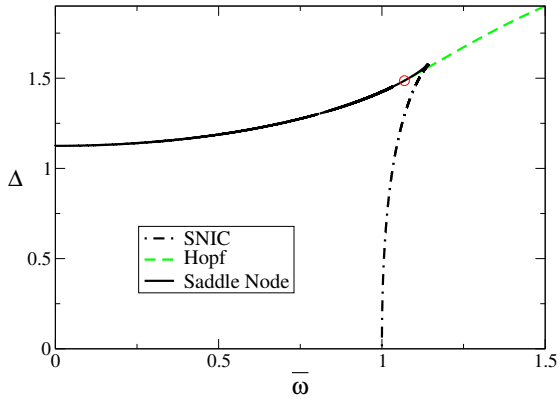

Figure 5.2: Bifurcation diagram for Lorentzian distribution for $K = 5$. There is also an homoclinic bifurcation, not shown in the plot, that goes from the Takens-Bogdanov point (circle) very close to the Hopf bifurcation until the Saddle Node in the Invariant Circle (SNIC) one, but it always has $\overline{\omega} > 1$, so it is not relevant to the present discussion. Note that there is no transition to collective firing (i.e. to a limit cycle attractor) increasing the diversity for $\overline{\omega} < 1$.

5.3 The Ott-Antonsen method

We will give now the main sketches of the Ott and Antonsen method. Quite generally, we will show that the method can be successfully used to numerically study systems with any non-singular distribution $g(\omega)$. Let $f(\omega, \phi, t)$ be the density of oscillators with frequency ω and phase ϕ. This function obeys the continuity equation (conservation of the number of oscillators):

$$\frac{\partial f(\omega,\phi,t)}{\partial t} + \frac{\partial}{\partial \phi}\left[\dot{\phi}(\omega,\phi,r) f\right] = 0 \tag{5.6}$$

with $\dot{\phi}(\omega, \phi, r)$ given by:

$$\dot{\phi}_j = \omega_j - \sin\phi_j + \frac{1}{2}(re^{-i\phi_j} - r^* e^{i\phi_j}) \tag{5.7}$$

Because ϕ is a phase variable $f(\omega, \phi, t)$ has to be periodic in ϕ, so it admits the following Fourier expansion:

$$f(\omega, \phi, t) = \frac{g(\omega)}{2\pi}\left\{1 + \sum_{m=1}^{\infty}\left[f_m(\omega, t)e^{im\phi} + c.c.\right]\right\} \tag{5.8}$$

(*c.c.* denotes complex conjugate). Inserting (5.8) into (5.6) one obtains an equation for the Fourier coefficients $f_m(\omega, t)$, in which lower order coefficients are coupled to higher order ones, giving an infinite hierarchy. However, if these coeficients satisfy the Ott-Antonsen ansatz

$$f_n(\omega, t) = \alpha(\omega, t)^n, \tag{5.9}$$

then the function $\alpha(\omega, t)$ satisfies the following (closed) integro-differential equation:

$$\frac{\partial \alpha}{\partial t} + i\omega\alpha + \frac{1}{2}\{[Kr + 1]\,\alpha^2 - Kr^* - 1\} = 0, \tag{5.10}$$

where the complex order parameter $r(t)$ is given by:

$$r(t) = \int d\omega \int d\phi\, e^{i\phi} f(\omega, \phi, t) = \int d\omega\, \alpha(\omega, t)^* g(\omega). \tag{5.11}$$

The manifold defined by (5.9) is invariant under the evolution of the system, so if the condition is fulfilled by the initial condition, it is fulfilled afterwards. Moreover, in [Ott and Antonsen, 2009; Ott et al., 2011] it is shown that the long time evolution of the order parameter is always described by this reduced manifold, under mild conditions for the distributioin of natural frequencies and the inital condition. If $g(\omega)$ has a finite set of poles $\hat{\omega}_1, \hat{\omega}_2, \ldots$ outside the real axis (as is the case for $L_n^m(\omega)$ for even n and integer m, including the Lorentzian $L_2^1(\omega)$, and $\alpha(\omega, t)$ satisfies certain analyticity conditions, one can obtain (5.11) by contour integration. Then $r(t)$ can be written is terms of $\alpha_k(t) \equiv \alpha(\hat{\omega}_k, t)$ and one can obtain a closed set of ordinary differential equations for $\alpha_k(t)$. In the case of poles with multiplicity larger than one, $r(t)$ depends also on the partial derivatives with respect to ω, $\alpha_k^s(t) \equiv \alpha^{(s)}(\hat{\omega}_k, t)$. Equations for these new functions $\alpha_k^s(t)$ can be obtained by differentiating Eq.(5.10) with respect to ω. For an arbitrary distribution $g(\omega)$, we can obtain an approximate evolution of the system by evaluating integral (5.11) using a finite, though large, set of values of ω and integrate numerically (5.10) for each one of these frequencies.

5.4 New results

In Figs. 5.3 and 5.4 we show the stationary values of the order parameters as a function of the diversity for several frequency distributions, obtained by direct simulation of Eqs. (5.2) and by the above mentioned application of the Ott and Antonsen method. In all the cases except the Lorentzian one, the regimen of collective firing (signaled by a nonzero value of the parameter ζ) is present for intermediate values of the diversity.

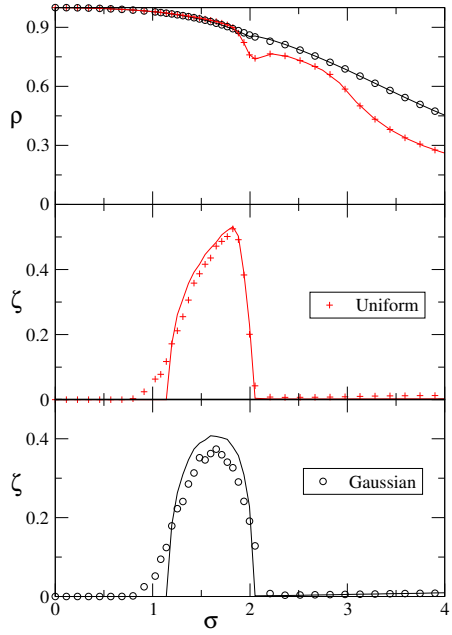

Figure 5.3: Stationary values of ρ (upper panel) and ζ (lower ones) as a function of the diversity for $K = 5$ and $\overline{\omega} = 0.97$. The distribution of natural frequencies is Gaussian (dots) and uniform (crosses). Simulations were done for $N = 10^4$ units. In Ott-Antonsen method 10000 values of ω were considered.

The transition is also present for other symmetric distributions such as symmetric exponential ($g(\omega) = \frac{\alpha}{2} e^{\alpha|\omega - \overline{\omega}|}$) or the family $L_n^m(\omega)$ for all integer values of m and $n \geq 2$ except for the Lorentzian. Even $L_3^1(\omega)$ which has infinite variance (but well-defined first moment) presents this reentrant diversity-induced transition (for

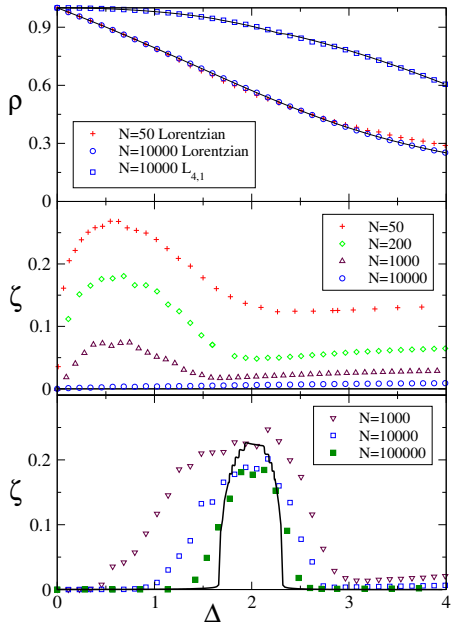

Figure 5.4: Stationary order parameters as a function of the diversity for $K = 5$ and $\overline{\omega} = 0.97$ for Lorentzian (upper and middle panels) and $L_4^1(\omega)$ (upper and lower ones) distributions. For the Lorentzian distribution $L_2^1(\omega)$ the Ott-Antonsen method reduces to two coupled ordinary differential equations, four in the case of $L_4^1(\omega)$.

values of $\overline{\omega}$ close enough to one). Also, if we truncate the Lorentzian distribution at some finite value of ω, i.e. set $g(\omega) = 0$, if $|\omega - \overline{\omega}| > C$, the system shows this reentrant transition (we checked for C=50Δ). Furthermore, Fig. 5.4 shows that for finite size Lorentzian systems the transition is indeed present, being quite visible up to a few thousands of units. In fact, Lorentzian distributions in systems with a finite number of units are effectively truncated, truncation that disappears in the limit $N \to \infty$. Therefore we conclude that the existence of the transition is a truly generic phenomenon and the results obtained using a Lorentzian distributions in the infinite system size limit are pathological and somehow meaningless.

Following Kuramoto's analysis one can get that in the limit of infinitely many units, when $\rho(t)$ and $\Psi(t)$ are time independent, they follow the following (complex) self-consistent equation [Sakaguchi, 1988]:

$$\rho e^{i(\Psi-\phi_0)} = b\left[iJ + \int_{-\pi/2}^{\pi/2} d\theta g(b\sin\theta - \overline{\omega})\cos\theta e^{i\theta}\right] \tag{5.12}$$

where

$$J = \int_0^{\pi/2} d\theta \frac{\cos\theta(1-\cos\theta)}{\sin^3\theta}\left[g(\frac{b}{\sin\theta} - \overline{\omega}) - g(-\frac{b}{\sin\theta} - \overline{\omega})\right]$$

$$\tan\phi_0 = \frac{K\rho\sin\Psi}{b + K\rho\cos\Psi}, b = \sqrt{1 + K^2\rho^2 + 2K\rho\cos\Psi} \tag{5.13}$$

After some algebraic manipulation, we can get the following real equations for the global amplitude and phase:

$$\rho\sin\Psi = \overline{\omega} - \int_{|\omega|>b} \omega\sqrt{1 - \frac{b^2}{\omega^2}}g(\omega)d\omega, \tag{5.14}$$

$$K\rho^2 + \rho\cos\Psi = \int_{-b}^{b} \sqrt{b^2 - \omega^2}g(\omega)d\omega. \tag{5.15}$$

These equations can also be obtained imposing the steady state condition in (5.10, 5.11). In order to obtain a single closed equation that will allow us to derive some results, we now change variables from ρ, Ψ to b, θ defined by:

$$b\sin\theta = \sin\Psi, \tag{5.16}$$

$$b\cos\theta = K\rho + \cos\Psi. \tag{5.17}$$

(5.14, 5.15) expressed in the new variables imply:

$$\tan\theta = \frac{f_1}{f_2}, \tag{5.18}$$

$$\rho^2 b^2 = f_1^2 + f_2^2, \tag{5.19}$$

with

$$f_1(b, K, \overline{\omega}, \sigma) \equiv \overline{\omega} - \int_{|\omega|>b} \omega\sqrt{1 - \frac{b^2}{\omega^2}}g(\omega)d\omega = \rho\sin\Psi, \tag{5.20}$$

$$f_2(b, K, \overline{\omega}, \sigma) \equiv \int_{-b}^{b} \sqrt{b^2 - \omega^2}g(\omega)d\omega = K\rho^2 + \rho\cos\Psi. \tag{5.21}$$

Using (5.16, 5.17) and (5.18), one can express ρ as a function of b: $\rho = \frac{bf_2 - \sqrt{f_2^2 + f_1^2(1-b^2)}}{K\sqrt{f_1^2+f_2^2}}$. Inserting in (5.19) one finally obtains the following closed equation for b:

$$b = \frac{K(f_1^2 + f_2^2)}{bf_2 - \sqrt{f_2^2 + f_1^2(1-b^2)}}, \tag{5.22}$$

This equation will allow us to determine the situation in which a transition takes place. Since b is real ($b^2 = K^2\rho^2 + 2K\rho\cos\Psi + 1 \geq (1 - K\rho)^2$), when the factor inside the square root of (5.22) becomes negative, the solution ceases to exists and a transition takes place. At the transition point the following is satisfied:

$$f_2^2 = f_1^2(b^2 - 1) \Rightarrow K^2\rho^4 + 2K\rho^3\cos\Psi = \rho^2\sin^2\Psi(K^2\rho^2 + 2K\rho\cos\Psi). \quad (5.23)$$

An immediate solution is $\Psi = \pm\pi/2$. To see that this is the only solution with $\rho \neq 0$ (that can correspond, then, to the transition into collective firing), we note that (5.23) is equivalent to:

$$K^2\rho^2(1-\sin^2\Psi) + 2K\rho\cos\Psi(1-\sin^2\Psi) + \cos^2\Psi = 0 \Rightarrow K^2\rho^2 + 2K\rho\cos\Psi + 1 = 0, \quad (5.24)$$

the last equality being valid assuming that $\cos^2\Psi = 1-\sin^2\Phi \neq 0$ (i.e. $\Psi \neq \pm\pi/2$). With this assumption we see that $K^2\rho^2 + 2K\rho\cos\Psi + 1 > (K\rho - 1)^2 \geq 0$, which implies that (5.24) cannot be satisfied and so that $\Psi = \pm\pi/2$ is the only solution of (5.23) with $\rho \neq 0$. Moreover, (5.14) implies that $\sin\Psi \geq 0$, so the transition happens with $\Psi = \pi/2$.
Setting $\Psi = \pi/2$ in (5.14, 5.15) and solving numerically the system for ρ and σ, one can obtain the values of this parameters at the transition. In figure 5.5 we compare the results obtained in this way with those obtained integrating directly equations (5.10, 5.11).

For distributions which decay fast enough we can obtain an approximated analytical expression for the value of σ in which the transition to collective firing appears (σ_c). In this case we can neglect the second term of the right hand side of equation (5.14) (provided that ρ is high enough so that $g(\omega) \simeq 0 \forall \omega | |\omega| > b$) and we see that this equation will not have a (synchronized) solution if $\rho < \overline{\omega}$. Inserting $\rho = \overline{\omega}$ and $\Psi = \pi/2$ in (5.15) and expanding the integrand, we obtain the expression for σ_c. To second order in ω/b, it reads:

$$\sigma_c = \sqrt{\overline{\omega}^2(2K^2 - 2K\sqrt{1 + K^2\overline{\omega}^2} - 1) + 2} \quad (5.25)$$

This expression is independent of the particular distribution, higher order corrections do depend on the specific form of the distribution. The next order in the Gaussian case, gives:

$$\sigma_c^2 = \frac{-\overline{\omega}^2(3 + 2K^2) - 2}{3} + \frac{\sqrt{\overline{\omega}^2[6\overline{\omega}^2 - 24K(1 + K^2\overline{\omega}^2)^{\frac{3}{2}}] + 28(1 + K^2\overline{\omega}^2)^2}}{3} \quad (5.26)$$

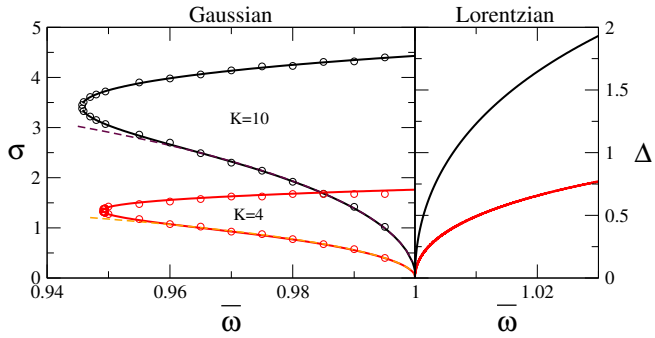

Figure 5.5: (Partial) Bifurcation diagram for Gaussian and Lorentzian distributions. In the Gaussian panel, the dots where obtained using Ott-Antonsen method, the solid lines to numerical solution of equations (5.14),(5.15) (following the program commented in the main text), and the dashed lines to the approximated expression (5.26).

The approximation is better for large coupling (K), since b increases with K.

In the case of the Lorentzian distribution, for $\overline{\omega} \gtrsim 1$ there is a small region limited by the homoclinic and the Hopf bifurcations where there is bistability between a static state and one with collective motion. However in the collective motion state, the order parameter drifts slightly around a fixed value rather than performs collective firing, and the basin of attraction of this state is very small, so the transition if different to the one considered here.

The Lorentzian distribution is a rather pathological one since it has not well-defined moments. Any distribution found in practice has well-defined moments, so this regime of collective firing should be found. From figure (5.5) we see that this discrepancy is due to the fact that, in the Lorentzian distribution, the SNIC bifurcation, which starts at $\omega = 0, \Delta = 0$, has positive slope and never enters the $\omega < 1$ region. This is different for the rest of distributions where the transition (that also starts at $\omega = 0, \Delta = 0$) enters the $\omega < 1$ region. This small quantitative difference has, however, important qualitative consequences when the system is consider as an ensemble of coupled excitable units. Even though the bifurcation diagrams may be topologically equivalent, they have important qualitative differences in some situations.

This non-generic behavior of the Lorentzian distribution also appears in another well-known system wich shows excitable behavior, an ensemble of coupled FitzHugh-Nagumo[Tessone et al., 2004] units, where this reentrant diversity-

induced transition is also present for distributions such as Gaussian or uniform, but not for the Lorentzian one.

5.5 Conclusions

We have shown that for an ensemble on Kuramoto-like active rotators near the excitable regime, a Lorentzian distribution of parameters gives rise to results that are qualitatively different to the ones obtained for other conventional distributions. The origins of the discrepancy lay in the fact that the Lorentzian has a a not well-defined first moment. This non-universality of the Lorentzian distribution is relevant because some powerful recently proposed analytical methods are only applicable for Lorentzian-like distributions. Moreover the Kuramoto model has been extensively studied as a paradigm of synchronization phenomena, but the results derived are only relevant in this sense if they are generic.

For future work it would be interesting to study if this transition is present under other coupling schemes different from all to all and whether other variants of the Kuramoto model also show non-generic results when considering a Lorentzian distribution of parameters.

Part VI

Conclusions and outlook

Chapter 6

Conclusions and outlook

This thesis has been concerned with the development of mathematical methods to analyze stochastic processes of interest in physics and other sciences.

In the second chapter we analyzed the Gaussian approximation as a method to close the hierarchy of evolution equations for the moments of a Markov stochastic process with discrete states. It was found that the method introduces a smaller error that first order van Kampen's expansion (a systematic method usually employed in the literature). In particular, the errors that the Gaussian approximation introduces in the average value, the second moment and the fluctuations (the variance), scale at most as ($\Omega^{-1/2}$, $\Omega^{1/2}$, $\Omega^{1/2}$), respectively (being Ω a large parameter, typically system size or volume), while in first order van Kampen's approach the respective errors scale at most as (Ω^{0}, Ω^{1}, $\Omega^{1/2}$). Therefore, the Gaussian approximation is more accurate, which turns out to be important specially for small values of Ω. This small error and the simplicity of the method are the main advantages of the Gaussian approximation. These results were checked by comparing the performance of the two methods in three examples: (i) a binary chemical reaction, (ii) an auto catalytic reaction and (iii) a model for opinion formation. In all cases studied, the Gaussian closure has given a better approximation to the average and the second moment, although the Ω-expansion, due to a cancellation of errors, yields a somehow smaller numerical error in the variance. In general, and compared to other field-theoretical methods available in the literature [Doi, 1976; Peliti, 1985], the Gaussian closure scheme is very simple to carry on in practice and this simplicity and the improvement of the predictive power is more apparent in many-variable systems.

In the third chapter we considered stochastic birth and death processes with delay, i.e. some reactions, that are initiated stochastically at a given rate, take

a finite time to be completed. We considered the general case of distributed (stochastic) delay, that can also be seen as a process with non-exponential waiting times or age-dependent rates. We developed several analytical approaches and derived various new results, some exact others approximated. We highlight the following:
-When the creation rate is independent of the state of the system (no feedback) and the initiation of the delayed degradation and the instantaneous degradation are first order reactions (rate not depending on the state of the system), the process can be solved fully in an exact fashion for general distributions of delay, showing always Poissonian character and a monotonically decreasing time correlation function.
-We developed a more general method that allows us to reduce the system to a Markovian one. The method was used to analyze the case in which the initiation of the delay degradation and/or the instantaneous degradation are higher order reactions and feedback is present in the creation rate. Explicit expressions for the time correlation for general delay distributions were obtained. It was shown that in this case the correlation might be non-monotonic, if feedback is present, but typically decreases monotonically.
-We then showed that when the delay appears in the creation reaction and feedback is present, the delay typically has more dramatic consequences. When a stochastic process has negative feedback, the fluctuations are decreased; however, if this feedback is delayed, the fluctuations can be actually enhanced, depending on the magnitude of the delay. A positive feedback loop enhances the fluctuations, but if the feedback is delayed, this enhancement is decreased. We have also shown that the effect of the delay is less apparent if the delay itself has relative large fluctuations, so for this mechanism to work, the delay has to be controlled precisely. This may be relevant for example in gene-regulatory networks, where delay times are typically broadly distributed but several regulatory mechanisms may act to control this. The analytical theory allows us to understand and predict this phenomenology in a general way. For negative feedback, and in the case of constant delay, we showed that the time correlation function becomes oscillatory, alternating positive and negative values at approximately multiples of the delay. In the positive feedback case, again for fixed delay, the time correlation function remains always positive. Finally, we pointed out that systems with delay are not, in general, statistically invariant under time reversal over the steady state, even if they fulfill the detailed balance condition.

Chapter four considers the effect of heterogeneity among the components of systems of stochastic interacting particles. we have analyzed the combined effect of stochasticity and heterogeneity in interacting-particle systems. We presented a formulation of the problem in terms of master equations for the individual

units, but extracted conclusions about the fluctuations of collective variables. We developed an approximation suitable for the analytical study of this general type of systems. We showed that the heterogeneity can have an ambivalent effect on the fluctuations, enhancing or decreasing them depending on the form of the system and the way heterogeneity is introduced. In the case of independent particles, heterogeneity in the parameters always decreases the size of the global fluctuations. We also demonstrated that it is possible to obtain precise information about the degree and the form of the heterogeneity present in the system by measuring only global variables and their fluctuations, provided that the underlying dynamical equations are known. In this way stochastic modeling allows us to obtain information not accessible from a purely deterministic approach. We also demonstrated that, in some cases, one can account for the heterogeneity of the particles without losing analytical tractability.

In chapter five we analyzed the role of the particular form of the distribution of heterogeneity in a system of Kuramoto-like coupled active rotators near the excitable regime. We showed that the Lorentzian distribution, often employed in the literature because of its analytical properties, gives rise to non-generic results. In particular, a regimen of collective firing induced by an increase of the heterogeneity of the units is not found for the Lorentzian case, while it is found for all distributions with well-defined moments. The reason of the discrepancy was found on the extremely fat tails of the Lorentzian probability density (that decay as x^{-2}, leading to divergence of all the moments). A new analytical approach that does not rely on a Lorentzian distribution of heterogeneity was developed, to better establish the nature of this transition.

There are several open questions that are left for future work.
In the topic of delay in stochastic processes, the application of the effective Markovian reduction to systems with global feedback and/or non-independent delay times has only been considered superficially in the thesis. This systems typically lead to integro-differential equations that are challenging to analyze and it will be interesting to see how far the analytical approach can be taken. The exploration of the validity of the time reversal invariance approximation in systems with oscillatory macroscopic limits is another interesting question. The application of the techniques developed to particular systems of interest, such as models of disease spreading or neuronal dynamics, is another task I would like to develop.
The topic of heterogeneity in stochastic systems also offers many open questions. First, the exploration of the role of heterogeneity in particular systems of interest is an obvious way forward. The application of the techniques here developed to analyze macroscopic data from real systems in order to infer the presence of heterogeneity is another relevant issue. As seen, the effect of heterogeneity

depends on the particular way it is introduced and on the microscopic dynamics. Determining the generality of the findings and establishing other generic effects of heterogeneity in stochastic systems is a main goal for the next years.

List of Figures

Chapter 7

Curriculum Vitae

Education and training:

October 2012: FOC-CRISIS School on Complex Financial Networks.
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September 2011: Summer School on Statistical Physics of Complex and Small Systems.
Institute for Cross-Disciplinary Physics and Complex Systems (IFISC), Palma de Mallorca, Spain.

Juny 2009: Summer School in Probability.
Pacific Institute for the Mathematical Sciences (PIMS), University of British Columbia, Vancouver, Canada.

2008 – 2009: Master's degree in Physics.
Thesis title: Gaussian approximation to the resolution of Master Equations. Advisor: Raul Toral.
University of Balearic Islands, Palma de Mallorca, Spain.

2003 – 2008 Licenciatura en Física (Honours Degree in Physics).
University of Zaragoza, Zaragoza, Spain.

Research experience

October – December 2011: Research visit.
Fluctuations and plasticity in evolution. Advisor: Kunihiko Kaneko.
Graduate School of Arts and Sciences, Department of Basic Science, The University of Tokyo, Tokyo, Japan.

April – July 2010: Research visit.
Applications of statistical physics to problems of social dynamics. Advisor: Sidney Redner.
Physics department, Boston University, Boston, MA, USA.

2008: Undergraduate research fellowship.
Game dynamics in Complex Networks. Advisor: Mario Floria and Yamir Moreno.
Institute for Biocomputation and Physics of Complex Systems (BiFi), University of Zaragoza, Zaragoza, Spain.

Summer 2007: Undergraduate research fellowship.
Characterization of semiconductor nanostructures with X-ray diffraction.
Microelectronics research institute of Madrid, Spanish National Research Council (CSIC), Madrid, Spain.

Undergraduate research fellowship.
Evolution of inhomogeneities in a scalar field as a model of dark energy.
High Energy Physics group, Department of Theoretical Physics, University of Zaragoza, Zaragoza, Spain.

Publications

- On the role of heterogeneity in stochastic interacting-particle systems.
Submitted (2012). arXiv:1206.3547v2
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