STOCHASTIC PERTURBATION THEORY AND ITS APPLICATION TO COMPLEX BIOLOGICAL NETWORKS
A QUANTIFICATION OF SYSTEMATIC FEATURES OF BIOLOGICAL NETWORKS

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STOCHASTIC PERTURBATION THEORY AND ITS APPLICATION TO COMPLEX BIOLOGICAL NETWORKS
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To my wife,

Lili Hu,

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SUMMARY

The primary objective of this thesis is to make a quantitative study of complex biological networks. Our fundamental motivation is to obtain the statistical dependency between modules by injecting external noise. To accomplish this, a deep study of stochastic dynamical systems would be essential. The first chapter is about the stochastic dynamical system theory. The classical estimation of invariant measures of Fokker-Planck equations is improved by the level set method. Further, we develop a discrete Fokker-Planck-type equation to study the discrete stochastic dynamical systems. In the second part, we quantify systematic measures including degeneracy, complexity and robustness. We also provide a series of results on their properties and the connection between them. Then we apply our theory to the JAK-STAT signaling pathway network.

CHAPTER I

INTRODUCTION

In this dissertation, we shall study the stochastic dynamical systems and investigate their applications to the complex biological networks. Stochastic dynamical systems are dynamical systems subjected to the effects of noise. Non-trivial effects of stochastic perturbation in dynamical systems have been of interest for decades. Besides theoretical problems in stochastic dynamical systems, we are particularly interested in activating complex biology networks by external fluctuations and quantifying their systematic measures. Problems in system biology are often challenging due to the complexity of biological networks. By depicting an overall view of complex biological networks, systematic measures describe the macroscale behaviors of biological networks. We will establish a mathematical framework of systematic measures of complex biological network including degeneracy, complexity and robustness based on our study in stochastic dynamical systems.

This dissertation consists of three chapters. Chapter I serves as the introduction. The main objects of study in chapter II are the stochastic dynamical system theory. Problems in both ODE systems and discrete dynamical systems are extensively studied. Chapter III is dedicated to the systematic measures of complex biological networks. We rigorously characterize the definitions of some systematic measures and prove some theoretical issues like the connection between distinct systematic measures.

1.1 Stochastic Dynamical Systems

A dynamical system consists of a state space and a rule for time evolution on this state space. For more than a century, problems in dynamical systems have emerged from

numerous scientific areas from classical mechanics to cell biology. In the real world, dynamical systems often undergo fluctuations, which leads to the study of stochastic dynamical systems. The stochastic dynamical system theory, or the stochastic perturbation of dynamical systems, has been extensively investigated for decades. We refer the readers to [26, 4, 40] for the stochastic perturbation problems in ODE systems. It has been known for a long time that the time evolution of probability density function in stochastic perturbation problems can be described by Fokker-Planck equation [56]. The Fokker-Planck equation often admits a unique invariant measure [7]. However, most existing results are made by assuming that one or more equilibrium points are fixed. In constrast, when the dynamics of underlying ODE systems become more complex, only limited results concerning the invariant measures of Fokker-Planck equations exist.

Discrete stochastic dynamical system also gains popularity because of its rich mathematical properties and strong relevance in applications. For the stochastic problems on the discrete setting, Markov chains have been studied for more than a century. However, to the best of our knowledge, the Fokker-Planck equation on a graph has not been established. The lack of a proper Fokker-Planck equation on a graph leads to two problems. First, Fokker-Planck equation has rich geometric features; see [37, 52, 70, 71]. Without a discrete Fokker-Planck-type formalism, all these fundamental connections between Fokker-Planck equation, entropy and optimal transport can not be generalized to discrete spaces. Second, if we apply spatial discretization schemes to Fokker-Planck equation to obtain their counterparts for discrete state spaces, many problems will arise. For instance, commonly used linear discretization schemes often lead to steady states that are different from Gibbs density, which contradicts the observations in statistical mechanics.

A variety of problems mentioned above are studied in Chapter II.

1.1.1 Invariant Measures of Stochastic ODE systems

In Chapter II we first consider an ODE system

$$x' = f(x) \tag{1.1.1}$$

for a continuous vector field $f(x)$ on $\mathbb{R}^N$. Let $\sigma(x)$ be a $N \times N$ matrix, dW_t be the N-dimensional white noise, ϵ be a positive constant. Under additive white noise perturbations σdW_t, we obtain a stochastic differential equation (SDE).

$$\mathrm{d}X = f(X) + \epsilon\sigma(x)dW_t\,, \tag{1.1.2}$$

which is also called stochastic ODE system in some literatures.

The time evolution of the probability density function associated with the SDE (1.1.2) satisfies the following Fokker-Planck equation (FPE).

$$\rho_t = \frac{1}{2}\epsilon^2 \sum_{i,j=1}^{n} \partial_{ij}(a_{ij}\rho) - \sum_{i=1}^{n} \partial_i(f\rho) := \mathcal{L}_\epsilon \rho \tag{1.1.3}$$

where $\{a_{ij}(x)\}_{i,j=1}^N := A(x) := \sigma(x)\sigma^T(x)$ is a $N \times N$ symmetric positive semi-definite matrix. The operator $\mathcal{L}_\epsilon$ is called Fokker-Planck operator. Conventionally, scalar functions and vector fields are denoted by lower case letters f, while random variables are written in upper case letters. We also denote the i-th component of x by x_i and the i-th partial derivative of f by $\partial_i f$.

Remark 1.1.1. The so-called white noise is the generalized mean-square derivative of the Brownian motion. A Brownian motion W_t is an independent increment stochastic process with

$$W_0 = 0$$

$$W_t - W_s \sim N(0, t-s)$$

where $N(\mu, \sigma^2)$ is the normal distribution with mean μ and variance σ.

Equation (1.1.2) is a conventional expression of the stochastic process X_t. The formal integral equation of X_t is

$$X_{t+s} - X_t = \int_t^{t+s} f(X_u)\mathrm{d}u + \int_t^{t+s} \epsilon\sigma(x)dW_t$$

where the integral notion with dW_t means the following Ito stochastic integral:

$$\int_0^t H_t dW_t = \lim_{||\pi_n||\to 0} \sum_{[t_{i-1},t_i]\in\pi_n} H_{t_{i-1}}(W_{t_i} - W_{t_{i-1}})$$

in which $\pi_n = \{0 = t_0 \le t_1 \le \cdots \le t_n = T\}$ is a partition of $[0, T]$. $||\pi_n||$ means the length of maximal interval in the partition:

$$||\pi_n|| = \max_i (t_i - t_{i-1})$$

For the rigorous definition of Brownian motion, see [38].

Under certain conditions, Fokker-Planck equation (1.1.3) admits a unique invariant measure μ_ϵ for each $\epsilon > 0$. The existence, uniqueness and regularity of such invariant measure are overviewed in 2.1.1.

Properties of invariant measures μ_ϵ has been extensively studied. The primary approach introduced by the classical theory, or Freidlin-Wentzell theory, is called quasi-potential method. Quasi-potential method proves that for any set $P \subset \mathbb{R}^N$ that does not intersect with any attractor of (1.1.1), a constant $V > 0$ exists such that

$$\lim_{\epsilon\to 0} \epsilon^2 \log \mu_\epsilon(P) = V$$

[26]. Other results, such as the first exit time, can also be obtained by quasi-potential methods [16].

In this dissertation, we improve the study to invariant measures of Fokker-Planck equations by investigating level sets of Lyapunov functions. This method is inspired by [33]. The main results of stochastic ODE problems are outlined as follow.

1. Theorem 2.1.18 proves that invariant measure μ_ϵ concentrates at ϵ-small neighborhood of the global attractor. i.e. For any $\delta > 0$ there exists constant M such that

$$\mu_\epsilon(\{x|\text{dist}(x, \mathcal{K}) \leq M\epsilon\}) \geq 1 - \delta\,.$$

2. In average sense, the mean square displacement is bounded from both below and above. Note that the mean square displacement of μ_ϵ is

$$V(\epsilon) = \int_{\mathbb{R}^N} \text{dist}^2(x, \mathcal{K}) u_\epsilon(x) \mathrm{d}x\,. \tag{1.1.4}$$

   In Theorem 2.1.23 we proved that under certain conditions there exists $V_1, V_2 > 0$ such that

$$V_1\epsilon^2 \leq V(\epsilon) \leq V_2\epsilon^2$$

3. Lastly, the concentration of invariant measure reveals interesting connections between the differential entropy and dimension of attractors. In Theorem 2.1.26 we prove

$$\lim_{\epsilon\to 0} \frac{\text{Ent}(u_\epsilon(x))}{-\log\epsilon} \geq N - d \tag{1.1.5}$$

   for regular attractors, where d is the Minkowski dimension of the global attractor. This entropy-dimension relation will be used in our biological application extensively.

1.1.2 Discrete Fokker-Planck-Type Equations

The rest part of Chapter II is dedicated to the discrete stochastic systems. Consider a finite graph $G = (V, E)$ associated with a potential function $\mathbf{\Psi}$. Assume that V is a finite vertices set $V = \{a_1, \cdots, a_N\}$. Potential function $\mathbf{\Psi}$ generates a "gradient

like" Markov chain X_t naturally with the following transition rate.

$$Pr(X_{t+h} = a_j | X_t = a_i) \tag{1.1.6}$$

$$= \begin{cases} (\Psi_i(t) - \Psi_j(t))h + o(h), & \text{if } j \in N(i), \Psi_j(t) < \Psi_i(t), \\ 1 - \sum_{k \in N(i), \Psi_k(t) < \Psi_i(t)} (\Psi_i(t) - \Psi_k(t))h + o(h) & \text{if } j = i, \\ 0, & \text{otherwise,} \end{cases} \tag{1.1.7}$$

where $N(i) := \{a_j | \{a_i, a_j\} \in E\}$.

How to inject external noise into this "gradient flows" on graphs is an interesting problem. Unlike an ODE system, there is no well recognized "white noise" in the discrete settings. The linear discretization of a continuous Fokker-Planck equation could lead to undesired results, such as the inconsistency of invariant measure proved in 2.2.1.

We solve this problem by discretizing Otto's calculus, which establish the geometric structure about Fokker-Planck equations and free energy functional. Fokker-Planck equation is the gradient flow of free energy functional on 2-Wasserstein metric space [52]. A Fokker-Planck-type equation is proposed on finite graph by taking upwind discretization of Otto's procedure. Let $\rho = \{\rho_{\mathbf{i}}\}_{\mathbf{i=1}}^{\mathbf{N}}$ be the probability distribution on the graph G. We obtain the following Fokker-Planck type equation.

$$\begin{aligned} \frac{d\rho_i}{dt} = & \sum_{j \in N(i), \Psi_j > \Psi_i} ((\Psi_j + \beta \log \rho_j) - (\Psi_i + \beta \log \rho_i))\rho_j \\ & + \sum_{j \in N(i), \Psi_j < \Psi_i} ((\Psi_j + \beta \log \rho_j) - (\Psi_i + \beta \log \rho_i))\rho_i \\ & + \sum_{j \in N(i), \Psi_j = \Psi_i} \beta(\rho_j - \rho_i) \end{aligned} \tag{1.1.8}$$

for $i = 1, 2 \cdots, N$, where β is the magnitude of noise. We prove the following properties of equation (2.2.7).

1. Equation (2.2.7) admits a unique solution $\rho(t)$. As $t \to \infty$, $\rho(t)$ converges to the Gibbs distribution.

2. The convergence rate to Gibbs distribution is exponential.

3. Equation (2.2.7) is the gradient flow of $F(\rho)$ on certain Riemannian manifolds, where $F(\rho) := \sum_{i=1}^{N} \rho_i \Psi_i + \beta \rho_i \log \rho_i$ is the discrete free energy defined on the graph G.

1.2 Systematic Measures of Biological Networks

Chapter III is dedicated to the quantitative study of systematic features of complex biological networks. The concept of modular biology has been proposed and extensively investigated in the past decades. Functional modules in cells are created by interacting molecules that function in a semi-autonomous fashion. In complex biological networks, modules are functionally correlated. To better understand the interactions between modules of complex biological networks, it is necessary to quantitatively study systemic properties such as evolvability, robustness, complexity, degeneracy and redundancy.

The notation of degeneracy was first introduced in [65], and the robustness was studied in [42]. Essentially, the structural complexity measures the magnitude of functional integration and local segregation of sub-systems; the degeneracy measures the capacity of elements that are structurally different to perform the same function, while the robustness measures the capacity of performing similar function under perturbation. Furthermore, these systematic measures are not independent. It has already been observed via numerical simulations for neural networks that high degeneracy not only yields high robustness, but also it is accompanied by an increase in structural complexity [66].

As increasingly biological phenomena are being observed, a rigorous study of systematic measures in biological networks is imperative. Although some features like regulation and robustness of biochemical networks of signal transduction have been studied quantitatively [42, 57], the features of interest here, such as degeneracy and

complexity, have not been formalized mathematically in the general context. Thus, an important theoretical problem is to explore and analyze the role degeneracy plays in general biological networks modeled by differential equations. A mathematical challenge is to generalize the notion of degeneracy and study its connection with robustness and structural complexity of the networks.

The quantifications and further studies of systematic features of biological network rely on our theoretical work in stochastic dynamical systems. Our method of measuring this interconnection is partially inspired by [66]. By injecting external fluctuation into the networks, the connections are activated and the mutual information among modules are able to be measured. The mutual information shared between two modules indicates the level of mutual dependence of them. In ODE based models, such mutual informations are taken between margins of the invariant measure of corresponding stochastic ODEs. Although the invariant measure of ODE systems can be singular, while in most scenarios, the invariant measures of stochastic ODEs are smooth and unique. Take stochastic ODE (1.1.2) for an example. Let μ_1, μ_2 be the margins of μ_ϵ on two subspaces X_1 and X_2. Then the mutual information $MI(X_1; X_2)$ between μ_1 and μ_2 indicates the codependency between modules corresponding to X_1 and X_2.

Such mutual informations are used to quantify degeneracy and complexity. According to [66], the degeneracy is high if the average mutual information between input and output components is greater than what would be expected from a linear change due to subset size; the complexity is high if different input components can behave coherently. The degeneracy and complexity are characterized as combinations of mutual informations between different modules in a following way.

Let $\{I, \mathcal{O}\}$ be an input-output decomposition of the variable set. Then $D(k)$ indicates the degeneracy with respect to a k-decomposition of I: $I = I_k \cup I_k^c$, where

$0 \leq k \leq |I|$.

$$D(k) = MI(I; I_k; \mathcal{O}) = MI(I_k; \mathcal{O}) + MI(I_k^c; \mathcal{O}) - MI(I; \mathcal{O}). \tag{1.2.1}$$

The degeneracy with respect to decomposition $\{I, \mathcal{O}\}$ is

$$D(\mathcal{O}) = \langle MI(I; I_k, \mathcal{O}) \rangle = \sum_{I_k} \frac{1}{2\mathrm{C}_k^n} \max\{MI(I; I_k; \mathcal{O}), 0\}. \tag{1.2.2}$$

In addition, $C(\mathcal{O})$ means the complexity with respect to decomposition $\{I, \mathcal{O}\}$.

$$C(\mathcal{O}) = \langle MI(I_k; I_k^c) \rangle = \sum_{I_k} \frac{1}{2\mathrm{C}_k^n} MI(I_k; I_k^c). \tag{1.2.3}$$

Another systematic feature is the robustness, which is measured by the strength of its attractor, either in a uniform way or in an average way. Further, as suggested by [42], the robustness is not always equivalent to the stability. If the performance function of a system is known, then we can define the functional robustness. The detailed definitions of robustness are made in Section 3.2.2.

The properties of degeneracy, complexity and robustness are also extensively studied in this dissertation. It is believed that degeneracy, complexity and robustness are not isolated concepts. Many simulations and experiments suggest certain internal connections among them (see [19, 63]). We will show that these relationships, already observed in biological experiments, can be verified in our mathematical framework of degeneracy, complexity and robustness. By applying the results in stochastic dynamical systems and information theory, we prove the following main results

1. We prove equation (3.4.1), which says that the complexity is larger than the degeneracy. Hence high degeneracy always yields high complexity.

2. In Theorem 3.4.2 we prove that a robust system with twisted attractor has positive degeneracy.

3. A robust system with stable equilibrium has position degeneracy under certain conditions (Theorem 3.4.7). The conditions are given in Equation (3.4.5).

Another interesting problem is to estimate the systematic measures from the network structure and the reaction parameters. We illustrate by some examples that it is possible to conclude some of its systematic features just from the structure of the network and the rate of the reactions.

We apply our theory in two examples. The first example is a limit cycle in a Lotka-Volterra equation, as an example of twisted attractor. The second example is a JAK-STAT crosstalk network. The JAK-STAT pathway is an intracellular signaling pathway in which a member of the JAK family of kinases is activated by phosphorylation following ligation of the receptor with extra cellular cytokine. In the second example, we find that interacting input sets lead to high degeneracy, while independent or redundant input sets lead to low degeneracy.

In the end, we give some discussions on how to extend our theory to discrete dynamical systems, including space-discretized and time-discretized systems. By introducing external noise, we can eliminate the singularity and non-uniqueness of the invariant measure so that the definition of systematic measures could be extent naturally.

Chapter III is organized in the following way: Section 3.1 outlines the classical theory and recent progress of the biochemical reaction networks. In section 3.2, we introduce the definition of systematic measures, including degeneracy, complexity and robustness. The robustness is particularly discussed in section 3.3. Section 3.4 is dedicated to the connections between degeneracy, complexity and robustness. As a real-world example, the JAK-STAT crosstalk network is studied in section 3.5 and extended discussions are given in section 3.6. In the end, section 3.7 presents a discrete model of biological network.

CHAPTER II

STOCHASTIC PERTURBATION THEORY

This chapter focuses on the theoretical results of stochastic dynamical systems. A stochastic dynamical system is a dynamical system subjected to random perturbations. It can be studied either pathwisely or in an average sense. We will primarily study the Fokker-Planck equations and their invariant measures (i.e. in average sense). Both continuous and discrete cases will be covered.

2.1 Stochastic perturbation to ODE systems and Fokker-Planck equations

2.1.1 Background : existence, uniqueness and regularity of invariant measure

As mentioned in the introduction, we consider the following stochastic ODE systems (1.1.2).

$$\mathrm{d}X = f(X) + \epsilon\sigma(x)dW_t\,, \tag{2.1.1}$$

where $f(x)$ is a vector field on $\mathbb{R}^N$, $\sigma(x)$ is a $N \times N$ matrix, ϵ is a positive parameter and dW_t is a N-dimensional white noise.

Fokker-Planck equation (FPE) (1.1.3) describes the time evolution of the probability density function.

$$\rho_t = \frac{1}{2}\epsilon^2 \sum_{i,j=1}^{n} \partial_{ij}(a_{ij}\rho) - \sum_{i=1}^{n} \partial_i(f\rho) := \mathcal{L}_\epsilon \rho \tag{2.1.2}$$

where $\{a_{ij}(x)\}_{i,j=1}^N := A(x) := \sigma(x)\sigma^T(x)$.

We first study the existence, uniqueness and regularity of invariant measures of the Fokker-Planck equation (1.1.3).

It is known that the stochastic differential equation (1.1.2) admits a stationary density function ρ_ϵ, where ϵ is a positive parameter representing the magnitude of perturbations. ρ_ϵ satisfies the following stationary Fokker-Planck equation.

$$\mathcal{L}_\epsilon \rho_\epsilon = 0\,, \quad \int \rho_\epsilon \mathrm{d}x = 1\,, \qquad u \geq 0\,. \tag{2.1.3}$$

The Fokker-Planck operator $\mathcal{L}_\epsilon$ has an adjoint operator $\mathcal{L}_\epsilon^*$:

$$\mathcal{L}_\epsilon^*(v) = \frac{1}{2}\epsilon^2 \sum_{i,j=1}^{N} a_{ij}\partial_{ij}v + \sum_{i=1}^{N} f_i \partial_i v\,. \tag{2.1.4}$$

If μ_ϵ is a probability measure solve the Fokker-Planck equation in the weak sense. i.e. μ_ϵ satisfies

$$\int \mathcal{L}_\epsilon^* h(x)\mathrm{d}\mu = 0\,, \quad \forall h(x) \in C_0^\infty(\mathbb{R}^N)\,,$$

then μ_ϵ is called a measure solution, or ϵ-invariant measure .

The existence, uniqueness and regularity of the invariant measure of the Fokker-Planck operator in compact set can be obtained by the classical elliptic partial differential equation theory. For the similar results in $\mathbb{R}^n$, things are more complicated. The existence, uniqueness and regularity of the stationary Fokker-Planck equation in $\mathbb{R}^n$ are extensively studied in several publications including [9, 33]. Recall the following Theorem from [33]:

Theorem 2.1.1. *Assume the following conditions*

1. $f_i(x) \in L^p_{loc}(\mathbb{R}^N)$, $a_{ij}(x) \in W^{1,p}_{loc}(\mathbb{R}^N)$ *for all* i, j, *where* $p > N$ *is an integer*

2. *There exists Lyapunov function* $U(x)$ *and Lyapunov constant* $\gamma > 0$ *such that*

$$\mathcal{L}^*_\epsilon U(x) \leq -\gamma$$

   for all x *with sufficient large norm* $|x|$.

3. $U(x) \to \infty$ *as* $|x| \to \infty$.

Then (2.1.3) *admits a unique weak solution with density function* $u_\epsilon(x) \in W^{1,p}_{loc}(\mathbb{R}^N)$.

In this dissertation, we make the following stronger hypotheses about the vector field f and the perturbation coefficient matrix A because we need to study a family of steady-state Fokker-Planck equations with different parameters ϵ.

Assumption (H1).

- $f(x)$ and $\sigma(x)$ is smooth on R^n; and
- $$f(x) \cdot \frac{x}{|x|} \leq -\gamma$$
  for some constant $\gamma > 0$ and for all x with $|x|$ sufficiently large.
- $a_{ij}(x)$ is uniformly bounded.

Then we can conclude the existence, uniqueness and regularity easily:

Theorem 2.1.2. *Assume that (***H***1) holds on equation* (1.1.3)*, then for any* $\epsilon > 0$*,* (2.1.3) *admits a unique measure solution* μ_ϵ *whose density function* $u_\epsilon(x)$ *is also smooth.*

Proof. Let $U(x) = |x|^2$. Then we find that

$$\mathcal{L}_\epsilon^* U(x) \leq \frac{1}{2}\epsilon^2 \mathbf{Tr} A(x) - 2\gamma|x|$$

Since $a_{ij}(x)$ is uniformly bounded, we can always find sufficient large R such that $\mathcal{L}_\epsilon^* U(x) < 0$ for all $|x| > R$. It follows from Theorem 2.1.1 that there exists a unique measure solution with density function $u_\epsilon(x) \in W^{1,p}_{loc}(\mathbb{R}^N)$.

Further, it follows from the well-known higher interior regularity theorem (such as Theorem 8.14 in [29]) that $u_\epsilon(x) \in C^2(\Omega)$ for every compact set Ω with smooth boundary. □

Remark that while the ODE (1.1.1) may have many complicated invariant measures without even having density functions, the steady-state of the SDE (1.1.2) is nevertheless unique and smooth.

2.1.2 Classical results: Freidlin-Wentzell theory

This subsection serves as a review of classical theory of random perturbations of dynamical systems, or Freidlin-Wentzell theory. This classical theory was introduced in the 1970s and 1980s (see [26]), in which the fundamental notion is the quasi-potential function.

As a function associated with stochastic differential equation (1.1.2), quasi-potential function is defined in three steps. First we characterize the Lagrangian and Hamiltonian with respect to the equation (1.1.2). Then we integrate the Lagrangian to obtain the action functional. Lastly, the quasi-potential is the minimum of action functional.

We consider the following Lagrangian

$$L(x,v) = \frac{1}{2}(f(x)-v)^T A^{-1}(f(x)-v) \tag{2.1.5}$$

and the corresponding Hamiltonian

$$H(x,p) = \frac{1}{2}p^T Ap + p^T f(x)\,. \tag{2.1.6}$$

The vector field $f(x)$ above comes from equation (1.1.1) or (1.1.2). Matrix $A = A(x) = \{a_{ij}(x)\}_{i,j=1}^N = \sigma\sigma^T$ is the same matrix as in the Fokker-Planck equation. x means the position. p and v are associated variables that will be explained later.

The action functional is the integral of the above Lagrangian. Let $\phi(t)$ be an absolutely continuous function with $\phi(T_1) = x$, $\phi(T_2) = y$. Then the action functional $S_{T_1T_2}(\phi(x))$ is defined by

$$S_{T_1T_2}(\phi) = \int_{T_1}^{T_2} L(\phi(t),\phi'(t))\mathrm{d}t\,, \tag{2.1.7}$$

where $L(x,v)$ is the Lagrangian from (2.1.5). Action functional plays a fundamental role in the Freidlin-Wentzell theory.

The quasi-potential function is defined as the minimum of action functional.

$$V(x,y) = \inf\{S_{T_1T_2}(\phi)|\phi(T_1) = x, \phi(T_2) = y, T > 0\}\,. \tag{2.1.8}$$

If the ODE systems (1.1.1) admits a unique stable equilibrium position x_0, the following function $V(x)$ is conventionally used as the quasi-potential function.

$$V(x) = \inf\{S_{T_1T_2}(\phi)|\phi(T_1) = x_0, \phi(T_2) = x, T > 0\}\,. \tag{2.1.9}$$

The following two lemmas describe basic properties of the quasi-potential function.

The first one comes from Lemma 2.1 of [26], Ch.3, which gives the existence of minimal path. In this lemma we consider paths in compact set $\Omega \subset \mathbb{R}^n$ and denote the space of continuous function $C([a,b],\bar{\Omega})$ by $C[a,b]$ for simplicity.

Lemma 2.1.3. *For $-\infty < a < b < \infty$, denote*

$$I_a^b = I_a^b(\phi) = \int_a^b L(\phi(t), \phi'(t))\mathrm{d}t\,.$$

Then I_a^b is lower semicontinuous on $C[a,b]$. Moreover, if K is a compact subset of Ω, then the set

$$\{\phi(t) \in C[a,b]| \quad \phi(a) \in K, I_a^b(\phi) \leq s, s > 0\}$$

is compact in $C[a,b]$.

The second lemma characterizes the regularity of quasi-potential function.

Lemma 2.1.4. *In any compact area $\bar{\Omega}$, the quasi-potential function is Lipschitz continuous.*

Proof. It is sufficient to show there exists a number $L > 0$, such that

$$V(x,z) - V(y,z) \leq L|x-y|\,.$$

Without loss of generality, we assume $V(x,z) \leq V(y,z)$. Let $\phi(t)$ be a minimal path connecting z and x such that $\phi(T_1) = 0; \phi(T_2) = x$ (The existence of the minimal path is guaranteed by Lemma 2.1.3). Then we can extend the path from x to y with linear interpolation:

$$\phi(T+t) = x + t\frac{y-x}{|x-y|}; \qquad 0 \leq t \leq |y-x|\,.$$

Suppose $\|A\| \leq M$, $|F(x)| \leq N$ for $x \in \Omega$, then clearly

$$\int_T^{T+t} L(\phi(\tau), \phi'(\tau))\mathrm{d}\tau \leq M(N+1)^2|x-y|$$

It follows that

$$V(y,z) \leq \int_0^{T+t} L(\phi(\tau), \phi'(\tau))\mathrm{d}\tau \leq V(x) + M(N+1)^2|x-y|$$

This implies $L = M(N+1)^2$. Hence $V(x,y)$ is Lipschitz continuous. □

Now we introduce some important results of the Freidlin-Wentzell theory. First we assume the existence of a stable equilibrium.

Assumption (H2). 1. The assumption (**H**1) is satisfied;

2. The system (1.1.1) has a unique stable equilibrium point x_0.

According to [26], the following Theorem (Theorem 4.3, Chapter 3) holds.

Theorem 2.1.5. *Assume (***H***2) holds. Then*

$$\lim_{\epsilon \to 0} \epsilon^2 \ln \mu_\epsilon(D) = - \inf_{x \in D} V(x)$$

for every compact set D.

Theorem 2.1.5 can be extended to more general scenarios. Consider an ODE system (1.1.1) and its stochastic perturbation (1.1.2) that satisfy the following relaxed assumptions.

Assumption (H3).

- The system (1.1.1) is defined on an compact manifold D;
- The system (1.1.1) has k stable invariant sets $K_1, \cdots, K_k$;
- $\forall x \in K_i, y \notin K_i$, the quasi-potential function $V_D(x, y) \neq 0$ for any compact set D, where

  $$V_D(x, y) = \inf\{S_{T_1 T_2}(\phi) | \phi(T_1) = x, \phi(T_2) = y, \phi \subset D, T > 0\},$$

  where $S_{0T}(\phi)$ is the action functional;
- $\forall x \in K_i, y \in K_i$, $V_D(x, y)$;
- Every ω-limit set of the system (1.1.1) lies entirely in one of the K_i.

In addition, for general stochastic dynamical systems, we introduce the following new notations . Let D be a compact set in $\mathbb{R}^n$, then for $x, y \in D$

$$V_D(x, y) = \inf\{S_{0T}(\phi) | \phi(0) = x, \phi(T) = y, T > 0, \phi \subset D\}$$

and

$$V_D(K_i, K_j) = V_D(x, y)|_{x\in K_i, y\in K(j)}$$

$$V_D(x, K_i) = V_D(x, y)|_{y\in K(i)}$$

$$V_D(K_i, y) = V_D(x, y)|_{x\in K(i)}$$

Definition 2.1.1. Assume L is a finite set and let W be a subset of L, then the following directed graph is called a *W-graph* if the following conditions hold:

- It consists of arrows $m \to n, m \in L \setminus W, n \in W$;
- Every point $m \in L/W$ is the initial point of exactly one arrow on the graph.

We denote by $G(W)$ the set of W-graphs. It follows from the definition that there are no closed cycles in the graph.

The invariant sets K_i are labeled by the following function derived from the W-graph.

$$W(K_i) = \min_{g\in G(\{i\})} \sum_{(m\to n)\in g} V_D(K_m, K_n)$$

There exists at least one i such that $W(K_i)$ is minimal. Without loss of generality, assume

$$W(K_{j_1}) = \cdots = W(K_{j_k}) = \min\{W(K_1), \cdots, W(K_n)\}$$

be the sets of minimal attractors. Let $\bar{\mathcal{K}} = \{K_{j_1}, \cdots, K_{j_k}\}$ denote the union of the minimal attractors.

The following theorem in [26] extends Theorem 2.1.5.

Theorem 2.1.6. *Denote*

$$W(x) = \min_i \{W(K_i) + V_D(K_i, x)\}.$$

Let μ_ϵ be the invariant measure of the Fokker-Planck equation (1.1.3) *and let γ be any positive number. then for any open set $A \subset D$ with $A \cap \bar{\mathcal{K}} = \emptyset$, there exists $\epsilon_0 > 0$*

such that for all $\epsilon \leq \epsilon_0$*, we have*

$$exp\{-\epsilon^{-1}(W(A) - M + \gamma)\} \leq \mu_\epsilon(A) \leq exp\{-\epsilon^{-1}(W(A) - M - \gamma)\}$$

where $W(A) = \inf\{W(x)|x \in A\}$ *and* $M = \min_i W(K_i)$.

Note that the original Freidlin-Wentzell theory is established for stochastic dynamical systems on a compact manifold D. But it is trivial to generalize these results to stochastic dynamical systems on $\mathbb{R}^N$. This generalization is guaranteed by the following lemma.

Lemma 2.1.7. *If a system satisfies the general assumption (***H***1), then for any compact set* D*, we can always find a compact set* D_1*, such that* $D \subset D_1$ *and*

$$V_{D_1}(x, y) = \inf\{S_{T_1T_2}(\phi) \,|\, x, y \in D, \phi(T_1) = x, \phi(T_2) = y, T > 0\}$$

Proof. Suppose such compact set does not exist, then we can find a sequence of smooth curves $\phi_n(t)$, such that $\phi_n(-T) = x$, $\phi_n(0) = y$ for each n, and $S_{-T,0}(\phi_{n+1}(t)) \leq S_{0T}(\phi_n(t))$ for all n, and there exist a sequence α_n, such that $\phi_n(\alpha_n) \notin B(0, n)$.

However, from the assmuption (**H**1), there exists $R > 0$ and $\sigma < 0$, such that $f(x) \cdot \frac{x}{|x|} \leq \sigma < 0$ for all $|x| > R$. Let τ_n be the first arrival time of ϕ_n to the circle $||x|| = R$, or

$$\tau_n = \inf_{t<0}\{||\phi_n(t)|| = R\}$$

Denote the "increasing set"

$$\mathcal{T}_n = \{t| - T < t < 0, f(\phi_n(t)) \cdot \phi_n(t) \geq 0\}.$$

for each $n > R$. Then

$$\begin{aligned} S_{-T,0}(\phi_n) &= \int_{-T}^{0} \frac{1}{2}||f(\phi_n(t)) - \phi_n'(t)||^2 \mathrm{d}t \\ &\geq \int_{\tau_n}^{\alpha_n} \frac{1}{2}||f(\phi_n(t)) - \phi_n'(t)||^2 \mathrm{d}t \\ &\geq \int_{[\tau_n,\alpha_n]\cap\mathcal{T}_n} \frac{1}{2}||f(\phi_n(t)) - \phi_n'(t)||^2 \mathrm{d}t \\ &\geq \int_{[\tau_n,\alpha_n]\cap\mathcal{T}_n} \frac{1}{2}||f(\phi_n(t))||^2 \mathrm{d}t \\ &\geq \int_{R}^{n} \frac{1}{2}x^2 \mathrm{d}x = \frac{1}{6}(n^3 - R^3)\,. \end{aligned}$$

It follows from above that $V_D(x,y)$ can be arbitrarily large. On the other hand, $f(x)$ is Lipschitz continuous in D, so $V_D(x,y) \leq Lr(D)$, where $r(D) = \max_{x,y\in D} ||x - y||$. This makes a contradiction. Therefore we can always find bounded set D_1 such that

$$V_{D_1}(x,y) = \inf\{S_{-T,0}(\phi)|x,y \in D, \phi(-T) = x, \phi(0) = y, T > 0\}$$

□

Hence it is safe to generalize Theorem 2.1.6 from compact domains to $\mathbb{R}^n$.

Theorem 2.1.8. *If stochastic dynamical system* (1.1.2) *defined on* $\mathbb{R}^N$ *admits an invariant measure, then Theorem 2.1.6 still holds.*

Proof. To show this, we define a family of compact sets Ω_k such that

$$D_1 \subset \Omega_1 \subset \cdots \Omega_k \subset \cdots$$

and

$$\lim_{k\to\infty} \Omega_k = \mathbb{R}^N$$

Let $u_k(x)$ be the density of invariant measure μ_k of (1.1.2) on Ω_k for each k. Then it is sufficient to show that $\mu_k(K) \to \mu(K)$ for any open set $K \subset \bar{K} \subset D_1$, where μ

is the invariant measure of (1.1.1) on $\mathbb{R}^N$ and $\bar{K}$ is another open set. This is obvious because firstly we have Harnack inequality:

$$\max_{x\in K} u_k(x) \leq C \min_{x\in K} u_k(x)$$

for every k, where C only depends on the operator $\mathcal{L}$ and the set K. Then $\min_{x\in K} u_k(x)$ is bounded by $(\lambda(K))^{-1}$ where λ is the Lebesgue measure. Hence u_k is uniformly bounded.

Secondly, from Holder estimation (e.g. Theorem 8.24 in [29]), we have

$$||u_k||_{C^\alpha(K)} \leq C_1(||u_k||_{L^2(\bar{K})} + m)\,,$$

where C_1 and m are independent of k. So u_k are also equicontinuous. From Arzela-Ascoli Theorem, $\{u_k(x)\}_{k=1}^{\infty}$ have a uniformly convergence subsequence. Since there exists a unique solution u in $\mathbb{R}^N$, we may assume without loss of generality that $u_k \to u$ up to a subsequence, from which the theorem follows. □

Both Theorem 2.1.5 and Theorem 2.1.6 concern the limit case when $\epsilon \to 0$. These results can be used to estimate some rare events such as first passage time. However, they can not provide enough information for more subtle analysis, especially in the small neighborhood of the attractor. The classical theory (Freidlin-Wentzell theory) only gives limited approaches to calculate or approximate the density of invariant measure. Some of them are reviewed below.

Theorem 2.1.9. *If the quasi-potential function has second order derivatives in the neighborhood of the unique attractor $\mathcal{K}$, then there exists a continuous function $z(x)$ with $z(0) = 1$, such that*

$$u_\epsilon(x) = \frac{1}{K} z(x) e^{-V(x)/\epsilon^2} + O(\epsilon^2)\,,$$

where $V(x) = V(\mathcal{K}, x)$ is the quasi-potential function.

Theorem 2.1.9 requires the regularity of quasi-potential function. The regularity issue is partially solved by the next theorem in [15]. If the Hamiltonian system refered in the next theorem has stable manifold of class C_n, then it follows from [15] that the quasi-potential function is of class C_{n+1}.

Theorem 2.1.10. *Suppose $x_0 \in \Omega$ and $\phi(t)$ is a minimizing path such that $\phi(-T) \in \mathcal{M}$ and $\phi(0) = x_0$, and*

$$V(x_0) = \int_{-T}^{0} L(\phi(t), \phi'(t))\mathrm{d}t\,.$$

If $\phi(t) \in \Omega$ for all $t \in [t_1, t_2]$, then on the interval $[t_1, t_2]$, the functions

$$x(t) = \phi(t), \quad p(t) = L_v(\phi(t), \phi'(t))$$

are of C^{n+1} and satisfy the Hamiltonian system

$$\begin{aligned} \frac{\mathrm{d}x}{\mathrm{d}t} &= H_p(x,p) && (2.1.10)\\ \frac{\mathrm{d}p}{\mathrm{d}t} &= -H_x(x,p) && (2.1.11)\\ H(x,p) &\equiv 0\,. \end{aligned}$$

Theorem 2.1.9 can be derived by Theorem 2.1.10 in a following way.

Proof. Let $u_\epsilon(x) = \frac{1}{K} z(x) e^{-V(x)/\epsilon^2}$. Then $\mathcal{L}^* u_\epsilon(x)$ becomes

$$\begin{aligned} \mathcal{L}^* u_\epsilon(x) &= \frac{1}{\epsilon} e^{-V(x)/\epsilon^2} z(x) \Big(\frac{1}{2}\sum_{i,j=1}^{N} a_{ij}\partial_i V \partial_j V + \sum_{i=1}^{N} f_i \partial_i V\Big)\\ &\quad - e^{-V(x)/\epsilon^2}\Big(\Big(\sum_{i=1}^{N}\Big(\sum_{j=1}^{N} a_{ij}\partial_i V + f_i\Big)\partial_i z\Big) + z(x)\Big(\sum_{i,j=1}^{N}\partial_i(a_{ij})\partial_j V\\ &\quad + \frac{1}{2}\sum_{i,j=1}^{N} a_{ij}\partial_{ij} V + \sum_{i=1}^{N}\partial_i(f_i)\Big)\Big)\\ &\quad + O(\epsilon^2 e^{-V(x)/\epsilon^2})\,. \end{aligned}$$

Since $\mathcal{L}_\epsilon^* u_\epsilon(x) = 0$, we obtain two equations. One being

$$\frac{1}{2}\sum_{i,j=1}^{N} a_{ij}\partial_{ij} V + \sum_{i=1}^{N} f_i \partial_i V = 0\,,$$

which is equivalent to

$$H(x, \nabla V) := H(x, p) = 0$$

by the definition of Hamiltonian. The other equation is

$$(\sum_{i=1}^{N}(\sum_{j=1}^{N} a_{ij}\partial_j V + f_i)\partial_i z) + z(x)(\sum_{i,j=1}^{N} \partial_i a_{ij}\partial_j V + \frac{1}{2}\sum_{i,j=1}^{N} a_{ij}\partial_{ij} V + \sum_{i=1}^{N} \partial_i f_i) = 0\,. \quad (2.1.12)$$

Note that $V(x)$ is the quasi-potential function. Hence $H(x, p) = 0$ is always satisfied because of Theorem 2.1.10. Further, $z(x)$ in equation (2.1.12) can be solved locally using the ray method provided in [48] as long as the second order derivatives of $V(x)$ is well defined. That completes the proof. □

For the multi-attractor case, results in Theorem 2.1.6 and Theorem 2.1.9 can be combined.

Proposition 2.1.11. *If the quasi-potential function has continuous second order derivatives, then the density function $\rho_\epsilon(x)$ of invariant measure μ_ϵ has the form*

$$\rho_\epsilon(x) = \frac{1}{K} z(x) e^{-\phi(x)/\epsilon^2} + O(\epsilon^2)\,,$$

where $\phi(x) = W(x) - M$ and $z(x)$ is a continuous function with $z(0) = 1$.

Only limited knowledge about the regularity of quasi-potential function exists. For example, One known result comes from [15, 14].

Theorem 2.1.12. *If $\mathcal{K}$ is a fixed point or a limit cycle and if $f(x), A(x)$ are of C^n continuous, then there exists a compact neighborhood N such that $V(\mathcal{K}, x)$ is of C^{n+1} in N.*

We want to mention that it is difficult to extend the above classical results even to the case of systems with smooth invariant manifolds because it requires too much information about the dynamics of the original dynamical system (1.1.1). Basically, the regularity of quasi-potential function depends on the existence of stable manifold

of the Hamiltonian system (2.1.10). However, such existence requires so much detail about the system (1.1.1), which makes it difficult to conclude any useful results from this approach. That's why we need a series of new theorems by using the level set method inspired by [33] in the next subsection.

2.1.3 More refined analysis: estimation in the vicinity of attractors

In this subsection we introduce a variety of improved results concerning the concentration of invariant measures of Fokker-Planck equation (1.1.3). As mentioned in the last subsection, the classical theory of stochastic dynamical system has certain limitations. Although limit behaviors of invariant measures have been studied, limited information about the invariant measures in the vicinity of attractors can be obtained. To overcome this problem, we adopt the level set method introduced in [33]. Instead of using Ito integrals, level set method studies Fokker-Planck equation on the level sets of a Lyapunov function. New estimations of the invariant measure in the vicinity of attractors will be introduced below.

Consider the ODE system (1.1.1) with an associated Lyapunov function defined as follows.

Definition 2.1.2. A function $U(x)$ is called *Lyapunov function* if

1. $U(x)$ is C^1 continuous, $U(x) \geq 0$;

2. For any $\rho > 0$, there exists a $\tau > 0$, such that

$$\nabla U(x) \cdot f(x) \leq -2\tau$$

   for every $x \in \mathbb{R}^N$ such $U(x) > \rho$;

3. $U(x)$ have finite first and second order derivatives in compact sets. i.e. there exists a constant Γ that depends on K such that

$$|\nabla U(x)| < \Gamma \quad , \quad |U_{ij}(x)| < \Gamma$$

for every $x \in K$ where K is a compact set.

Note that we still assume that condition (**H**1) holds. Hence the ball $B(0, R)$ is invariant with respect to the vector field $f(x)$ in equation (1.1.1). In other words, all ω-limit sets must lay in the ball $B(0, R)$.

To conduct local analysis using level method, we assume the local condition (**H**4) about the attractor of system (1.1.1) as follows.

Assumption (H4). 1. Equation (1.1.1) has a unique strong attractor $\mathcal{K}$;

2. There exists a Lyapunov function as defined in Definition 2.1.2;

3. $\mathcal{K}$ is the ω-limit set;

4. There exist an open set $O \supset \mathcal{K}$, such that in O;

5. $U(x)$ is of class C_2 continuous in O and there exists a positive constant L_1 such that

$$U(x) \geq L_1 \text{dist}^2(x, \mathcal{K}) .$$

6. $\exists \gamma, \kappa > 0$ such that

$$-\kappa |\nabla U(x)|^2 \leq \nabla U(x) \cdot f(x) \leq -2\gamma |\nabla U(x)|^2 .$$

Remark 2.1.13. Note that $U(x)$ takes value 0 at the global attractor and has second order derivatives. From Taylor expansion, we can derive the following properties about $U(x)$ when $x \in O$.

1.

$$\max_{x \in O} U_{x_i x_j}(x) = D < \infty ;$$

2. $\exists \gamma, \kappa > 0$ such that

$$-\kappa |\nabla U(x)|^2 \leq \nabla U(x) \cdot f(x) \leq -2\gamma |\nabla U(x)|^2 ;$$

3. $\exists L_1, L_2 > 0$ such that

$$L_1 \text{dist}^2(x, \mathcal{K}) \leq U(x) \leq L_2 \text{dist}^2(x, \mathcal{K}) ;$$

4. $\exists K_1, K_2 > 0$ such that

$$K_1 \text{dist}(x, \mathcal{K}) \leq |\nabla U| \leq K_2 \text{dist}(x, \mathcal{K}) .$$

2.1.3.1 Concentration of Measure

The concentration of the ϵ-invariant measures will be proved here. First the estimation in [26] is re-derived by a different approach. Then we prove a more accurate estimation that most probability density concentrates in a ϵ-small neighborhood of the strong attractor. Our approach is the level set method introduced in [33].

The first lemma is borrowed from [33] Lemma 2.3:

Lemma 2.1.14. *Assume u is a weak solution of* (1.1.3)*, then for any Lipschitz domain Ω and a function $F \in C^2(\Omega)$ having a constant value on each boundary component of Ω,*

$$\int_\Omega (\sum_{i,j=1}^N \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 F + \sum_{i=1}^N f_i \partial_i F) u \mathrm{d}x = \int_{\partial\Omega} (\sum_{i=1}^N \sum_{j=1}^N \frac{1}{2}\epsilon^2 a_{ij}\partial_i F \nu_j) u \mathrm{d}s \qquad (2.1.13)$$

where $\{\nu_j\}_{j=1}^N$ denotes the unit outward normal vectors.

Rough estimations of ϵ-invariant measures will be given first. The basic strategy is to first use the level sets of $U(x)$ to estimate the invariant measure inside of $B(0, 2R)$, then use $|x|$ as another Lyapunov function to estimate the invariant measure in the complement of $B(0, 2R)$. In some sense, this theorem reproduces the result in [26] by a different approach.

Theorem 2.1.15. *Under the condition (***H***1) and (***H***4), for any open neighborhood N of $\mathcal{K}$, there exists a positive number $\beta > 0$ and a $\epsilon_0 > 0$, such that*

$$1 - \mu_\epsilon(N) \leq e^{-\beta/\epsilon^2}$$

for all $0 < \epsilon < \epsilon_0$.

Proof. Let $U_\rho = \{x \,|\, U(x) \le \rho$, and $\Gamma_\rho = \{x \,|\, U(x) = \rho\}$ be the level sets. We can choose positive M such that $U_{2\rho_M} \subset O$ and $U_{\rho_M} \subset N$. Then it is sufficient to prove $1 - \mu_\epsilon(U_{\rho_M}) \le e^{-\beta/\epsilon^2}$

For any $0 < \rho_0 < 2\rho_M$, let $\Delta\rho$ be a small number such that $\Delta\rho \le \rho_0$. consider a cut-off function

$$\phi(\rho) = \begin{cases} 0 & \rho < \rho_0 \\ \frac{1}{2\Delta\rho}(\rho - \rho_0)^2 & \rho_0 < \rho < \rho_0 + \Delta\rho \\ \rho - \rho_0 - \frac{1}{2}\Delta\rho & \rho > \rho_0 + \Delta\rho \end{cases}$$

From Lemma 2.1.13, we have

$$\begin{aligned} & \int_{U_{2\rho_M}} \phi'(U)(\sum_{i,j=1}^N \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 U \\ + & \sum_{i=1}^N f_i \partial_i U)u\mathrm{d}x + \int_{U_{2\rho_M}} \phi'(U)(\sum_{i,j=1}^N \frac{1}{2}\epsilon^2 a_{ij}\partial_i U \partial_j U)u\mathrm{d}x \\ = & \int_{\Gamma_{2\rho_M}} (\sum_{i=1}^N \sum_{j=1}^N \frac{1}{2}\epsilon^2 a_{ij}\partial_i U \nu_j)u\mathrm{d}x \ge 0\,. \end{aligned} \tag{2.1.14}$$

By the definition of $\phi(\rho)$, it follows that

$$\begin{aligned} & \int_{U_{2\rho_M}} \phi'(U)(\sum_{i,j=1}^N \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 U + \sum_{i=1}^N f_i \partial_i U)u\mathrm{d}x \\ & = \int_{U_{2\rho_M} \setminus U_{\rho_0}} \phi'(U)(\sum_{i,j=1}^N \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 U + \sum_{i=1}^N f_i \partial_i U)u\mathrm{d}x \end{aligned}$$

Note that $\frac{1}{2}\epsilon^2\{a_{ij}\}_{i,j=1}^N$ has a small coefficient ϵ. Let

$$\bar{\sigma} = \max_{ij}\{A_{ij}\}$$

and $M_1 = D\bar{\sigma}/\gamma K_1^2$, Then $M_1 > 0$ and

$$\sum_{i,j=1}^N \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 U \le \gamma |\nabla U|^2$$

for all x with $\mathrm{dist}(x, \mathcal{K}) > \sqrt{M_1}\epsilon$ provided $B(\mathcal{K}, \sqrt{M_1}\epsilon) \subset O$. Note that we can always find $\epsilon_1 > 0$ such that $B(\mathcal{K}, \sqrt{M_1}\epsilon) \subset O$ for all $0 < \epsilon < \epsilon_1$, which means the previous estimation is valid for all sufficient small ϵ.

Since $U(x)$ is a Lyapunov function, we have

$$\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 U + \sum_{i=1}^{N} f_i \partial_i U \leq -\gamma |\nabla U|^2$$

It follows that

$$\begin{aligned}
&\int_{U_{2\rho_M}\backslash U_{\rho_0}} \phi'(U)(\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 U + \sum_{i=1}^{N} f_i\partial_i U) u \mathrm{d}x \\
&\leq -\gamma \int_{U_{2\rho_M}\backslash U_{\rho_0}} \phi'(U)|\nabla U|^2 u \mathrm{d}x \\
\leq\ & -\gamma \int_{U_{2\rho_M}\backslash U_{\rho+\Delta\rho}} u|\nabla U|^2 \mathrm{d}x \\
\leq\ & -\gamma C_1 \max\{|\nabla U(x)|^2 | x \in U_{\rho_0+\Delta\rho}\backslash U_{\rho_0}\} \int_{U_{\rho_M}\backslash U_{\rho_0+\Delta\rho}} u \mathrm{d}x\,,
\end{aligned}$$

where C_1 is a constant that satisfies

$$\min |\nabla U(x)|^2 \geq C_1 \max |\nabla U(x)|^2 \quad ; \quad x \in U_{\rho_0+\Delta\rho}\backslash U_{\rho_0}\,.$$

From the properties of $U(x)$ it is easy to see that

$$C_1 = \frac{K_1^2 L_1}{K_2^2 L_2}$$

satisfies the requirement.

We now have

$$\begin{aligned}
&\int_{U_{2\rho_M}\backslash U_{\rho_0+\Delta\rho}} \phi'(U)(\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 U + \sum_{i=1}^{N} f_i\partial_i U) u \mathrm{d}x \\
&\leq -\gamma C_1 \max\{|\nabla U(x)|^2 | x \in U_{\rho_0+\Delta\rho}\backslash U_{\rho_0}\} \mu_\epsilon(U_{2\rho_M}\backslash U_{\rho_0})
\end{aligned}$$

On the other had, the boundedness of matrix A follows that

$$\begin{aligned}
&\int_{U_{2\rho_M}} \phi''(U) \sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_i U \partial_j U u \mathrm{d}x = \int_{U_{\rho+\Delta\rho}\backslash U_\rho} \phi''(U) \sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_i U \partial_j U u \mathrm{d}x \\
&\leq \frac{1}{2\Delta\rho}\epsilon^2 \bar{A} \max\{|\nabla U(x)|^2 | x \in U_{\rho+\Delta\rho}\backslash U_\rho\} \int_{U_{\rho+\Delta\rho}\backslash U_\rho} u \mathrm{d}x\,,
\end{aligned}$$

where $\bar{A}$ is the upper bound of largest eigenvalue of matrix $A(x)$.

Combine previous two inequalities and equation (2.1.14), we obtain

$$-\gamma C_1 \mu(2U_{\rho_M} \backslash U_{\rho_0+\Delta\rho}) + \frac{1}{2\Delta\rho}\epsilon^2 A\mu(U_{\rho_0+\Delta\rho} \backslash U_\rho) \geq 0$$

Let $F(\rho) = \mu(U_{2\rho_M} \backslash U_\rho)$ and $\rho = \rho_0$, the above becomes

$$-\gamma C_1 F(\rho+\Delta\rho) + \frac{1}{2\Delta\rho}\epsilon^2 \bar{A}(F(\rho) - F(\rho+\Delta\rho)) \geq 0\,.$$

By taking limit $\Delta\rho \to 0$ in the above inequality, we now have

$$-\gamma C_1 F(\rho) + \frac{1}{2}\epsilon^2 \bar{A}(-F'(\rho)) \geq 0$$

For any ρ_1 with $B(\mathcal{K}, \sqrt{M_1}\epsilon) \subset U_{\rho_1}$, the Gronwall's inequality yields

$$F(\rho) \leq F(\rho_1) e^{-\frac{2\gamma C_1}{\epsilon^2 \bar{A}}(\rho-\rho_1)}$$

Let $\rho_1 = L_2 M_1 \epsilon^2$, from Remark 2.1.13, we have $B(\mathcal{K}, \sqrt{M_1}\epsilon) \subset U_{\rho_1}$ and

$$F(\rho_M) \leq F(\rho_1) e^{-\frac{2\gamma C_1}{\epsilon^2 \bar{A}}(\rho_M-\rho_1)} \leq e^{-\frac{2\gamma C_1}{\epsilon^2 \bar{A}}(\rho_M-\rho_1)}\,.$$

There exists a small $\epsilon_2 \leq \rho_M / 2L_1 M_1$ such that

$$F(\rho_M) \leq e^{-\frac{\gamma C_1 \rho_M}{\epsilon^2 \bar{A}}}\,.$$

Note that $F(\rho_M) \leq \mu_\epsilon(U_{2\rho_M} \backslash N)$, we obtain

$$\mu_\epsilon(U_{2\rho_M} \backslash N) \leq e^{-\frac{\gamma C_1 \rho_M}{\epsilon^2 \bar{A}}}\,. \tag{2.1.15}$$

Let us estimate the probability measure $\mu_\epsilon(B(0,2R) \backslash U_{2\rho_M})$. Since $B(0,2R)$ is not a level set of $U(x)$, we consider U_M instead. The constant M is a large number such that $B(0,2R) \subset U_M$. We denote the upper bound norm of first and second order derivatives of U in U_M as Γ. By repeating the cut-off function approach for $\rho_0 > \rho_M$, it follows that

$$\int_{U_M} \phi'(U)(\sum_{i,j=1}^N a_{ij}\partial_{ij}^2 U + \sum_{i=1}^N f_i \partial_i U)u\mathrm{d}x + \int_{U_M} \phi''(U)(\sum_{i,j=1}^N a_{ij}\partial_i U \partial_j U)u\mathrm{d}x \geq 0\,. \tag{2.1.16}$$

i.e.,

$$\int_{U_M} \phi'(U)(\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 U + \sum_{i=1}^{N} f_i \partial_i U)u\mathrm{d}x$$
$$= \int_{U_M \backslash U_{\rho_0}} \phi'(U)(\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 U + \sum_{i=1}^{N} f_i \partial_i U)u\mathrm{d}x$$

Since $\rho_0 > \rho_M$, from Remark 2.1.13 there exists a fixed positive number τ such that $f \cdot \nabla U \leq -2\tau$. Note that $\frac{1}{2}\epsilon^2\{a_{ij}\}_{i,j=1}^N$ is a small matrix. Clearly there always exists an $\epsilon_3 > 0$ such that for sufficiently small $0 < \epsilon < \epsilon_3$,

$$\sum_{i,j=1}^{N} a_{ij}\partial_{ij}^2 U + \sum_{i=1}^{N} f_i \partial_i U \leq -\tau$$

is satisfied. Then we obtain the estimation

$$\begin{aligned}
\int_{U_M \backslash U_{\rho_0}} \phi'(U)(\sum_{i,j=1}^{N} a_{ij}\partial_{ij}^2 U + \sum_{i=1}^{N} f_i \partial_i U)u\mathrm{d}x &\leq -\tau \int_{U_M \backslash U_{\rho_0}} \phi'(U)u\mathrm{d}x \\
&\leq -\tau \int_{U_M \backslash U_{\rho+\Delta\rho}} u\mathrm{d}x \\
&\leq -\tau \int_{U_M \backslash U_{\rho_0}} u\mathrm{d}x \\
&= -\tau\mu_\epsilon(U_M \backslash U_{\rho_0})\,.
\end{aligned}$$

Meanwhile, the second integral in equation (2.1.16) satisfies

$$\int_{U_M} \phi''(U) \sum_{i,j=1}^{N} a_{ij}\partial_i U \partial_j U u\mathrm{d}x = \int_{U_{\rho+\Delta\rho} \backslash U_\rho} \phi''(U) \sum_{i,j=1}^{N} a_{ij}\partial_i U \partial_j U u\mathrm{d}x$$
$$\leq \frac{1}{2\Delta\rho}\epsilon^2 A \max\{|\nabla U(x)|^2 | x \in U_{\rho+\Delta\rho} \backslash U_\rho\} \int_{U_{\rho+\Delta\rho} \backslash U_\rho} u\mathrm{d}x$$
$$\leq \frac{1}{2\Delta\rho}\epsilon^2 \bar{A}\Gamma \int_{U_{\rho+\Delta\rho} \backslash U_\rho} u\mathrm{d}x\,.$$

Combine previous two inequalities derived from (2.1.16), it is easy to see that

$$-\tau\mu(U_M \backslash U_{\rho_0+\Delta\rho}) + \frac{1}{2\Delta\rho}\epsilon^2 \bar{A}\Gamma\mu(U_{\rho_0+\Delta\rho} \backslash U_\rho) \geq 0\,.$$

Denote $H(\rho) = \mu(\mathbb{R}^N \backslash U_\rho)$ and let $\rho = \rho_0$, the above becomes

$$-\tau H(\rho + \Delta\rho) + \frac{1}{2\Delta\rho}\epsilon^2 \bar{A}\Gamma(H(\rho) - H(\rho + \Delta\rho)) \geq 0\,.$$

By taking the limit $\Delta\rho \to 0$, we obtain

$$-\tau H(\rho) + \frac{1}{2}\epsilon^2 \bar{A}\Gamma(-H'(\rho)) \geq 0$$

It follows from the Gronwall's inequality that

$$H(\rho) \leq H(\rho_M) e^{-\frac{2\tau}{\epsilon^2 \bar{A}\Gamma}(\rho - \rho_M)}$$

which means

$$\mu_\epsilon(B(0,2R)\backslash U_{2\rho_M}) \leq \mu_\epsilon(U_M \backslash U_{2\rho_M}) = H(2\rho_M) \leq e^{-\frac{2\tau\rho_M}{\epsilon^2 A\Gamma}}\,. \tag{2.1.17}$$

In the remaining part we will estimate $\mu_\epsilon(\mathbb{R}^N \backslash B(0,2R))$. Let $W(x) = |x|$ be the new Lyapunov function, define the cut-off function $\phi(x)$ in the same way for each $|x| > R$. Note that the absolute value of the second derivatives of $W(x)$ are less than $\frac{1}{|x|}$. By a similar approach one can derive that

$$\int_{\mathbb{R}^N \backslash W_x} \phi'(W)(\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 W + \sum_{i=1}^{N} f_i \partial_i W) u \mathrm{d}x \leq -\frac{\alpha}{2}\int_{\mathbb{R}^N \backslash W_x} u \mathrm{d}x$$

for all $0 < \epsilon < \epsilon_4$, where

$$\epsilon_4 = \sqrt{\frac{\alpha R}{2\bar{\sigma}N^2}}\,.$$

The boundedness of A implies that

$$\int_{W_{x+\Delta x}\backslash W_x} \phi''(W) \sum_{i,j=1}^{N} a_{ij}\partial_i W \partial_j W u \mathrm{d}x \leq \frac{1}{2\Delta x}\epsilon^2 A \int_{W_{x+\Delta x}\backslash W_x} u \mathrm{d}x\,.$$

Let $I(x) = \mu_\epsilon(\mathbb{R}^N \backslash W_x)$. By taking the limit as $\Delta x \to 0$, we obtain

$$I'(x) \leq -\frac{2\alpha}{\epsilon^2 A} I(x)\,.$$

It follows from the Gronwall inequality that

$$I(x) \leq I(R) e^{-\frac{2\alpha}{\epsilon^2 A}(x-R)}\,, \tag{2.1.18}$$

which means

$$\mu_\epsilon(\mathbb{R}^N \backslash B(0,2R)) \leq e^{-\frac{2\alpha R}{\epsilon^2 A}}\,. \tag{2.1.19}$$

Combine equations (2.1.15), (2.1.17) and (2.1.19) all together, now we have

$$1-\mu_\epsilon(N) \le e^{-\frac{\tau\rho_M}{\epsilon^2 A\Gamma}} + e^{-\frac{\gamma C_1 \rho^M}{\epsilon^2 A}} + e^{-\frac{2\alpha R}{\epsilon^2 A}}$$

for all $0<\epsilon<\min\{\epsilon_1,\epsilon_2,\epsilon_3\}$. Since $C_1, \rho_M, A, \gamma, \tau, R$ and Γ are all independent with ϵ, let

$$\beta = \frac{1}{2}\min\{\frac{\tau\rho_M}{\epsilon^2 A\Gamma}, \frac{\gamma C_1 C_2}{\epsilon^2 A}, \frac{2\alpha R}{A}\}$$

and

$$\epsilon_0 \le \min\{\epsilon_1,\epsilon_2,\epsilon_3,\epsilon_4\sqrt{\frac{\beta}{\log 4}}\}\,.$$

Therefore,

$$1-\mu_\epsilon(N) \le e^{-\beta/\epsilon^2}$$

□

Remark 2.1.16. Theorem 2.1.15 is similar but not same as the classical results. As mentioned above, this theorem provides a rough estimation of the ϵ-invariant measure in a fixed area when taking the limit $\epsilon \to 0$. The difference between Freidlin-Wentzell quasi-potential method is that this theorem does not require the attractor laying in any equivalent class of the quasi-potential function. This means the attractor can have more complex structure. In fact, the conditions here are all about the existence and regularity of Lyapunov function instead of the conditions of the attractor itself.

For large constant ρ_M, further estimations can be obtained as in the following Corollary.

Corollary 2.1.17. *For every positive number K, there exists constants $\beta>0$ and $\epsilon_0>0$ such that when $\rho>K$ and $U_\rho \subset B(0,2R)$,*

$$1-\mu_\epsilon(U_\rho) \le e^{-\beta\rho/\epsilon^2}$$

for all $0<\epsilon<\epsilon_0$.

Proof. First we choose a ρ_M such that $U_{2\rho_M} \subset O$. Recall the proof in theorem 2.1.15. When $\rho_1 < \rho < 2\rho_M$, we have

$$1 - \mu_\epsilon(U_\rho) \leq e^{-\frac{2\tau C_1}{\epsilon^2 \bar{A}}(\rho-\rho_1)} + e^{-\frac{\tau\rho_M}{\epsilon^2 \bar{A}\Gamma}} + e^{-\frac{2\alpha R}{\epsilon^2 \bar{A}}}, \tag{2.1.20}$$

where $\rho_1 = L_2 M_1 \epsilon^2$ is a constant depends on ϵ.

Note that $\rho > K$, one can choose small ϵ such that $\rho_1 < K$. Then $\rho > \rho_1$. Some calculation implies that

$$e^{-\frac{2\tau C_1}{\epsilon^2 \bar{A}}(\rho-\rho_1)} + e^{-\frac{\tau\rho_M}{\epsilon^2 \bar{A}\Gamma}} + e^{-\frac{2\alpha R}{\epsilon^2 \bar{A}}} < e^{-\frac{\gamma C_1}{\epsilon^2 \bar{A}}\rho} + e^{-\frac{\tau\rho_M}{\epsilon^2 \bar{A}\Gamma K}\rho} + e^{-\frac{2\alpha R}{\epsilon^2 \bar{A}K}\rho}.$$

Denote

$$\beta_1 = \frac{1}{2}\min\{\frac{\gamma C_1}{\bar{A}}, \frac{\tau\rho_M}{\bar{A}\Gamma K}, \frac{2\alpha R}{\bar{A}K}\}$$

and

$$\epsilon_1 < \min\{\sqrt{\frac{K}{L_2 M_1}}, \sqrt{\frac{\beta}{\log 3}}\}.$$

It is easy to see that $1 - \mu_\epsilon(U_\rho) < e^{-\beta_1/\epsilon^2}$ for all $\epsilon < \epsilon_1$.

Similarly, when $2\rho_M < \rho < M$ where $B(0, 2R) \subset U_M$, the invariant measure is bounded by

$$1 - \mu_\epsilon(U_\rho) < e^{-\frac{2\tau}{\epsilon^2 A\Gamma}(\rho-\rho_M)} + e^{-\frac{2\alpha R}{\epsilon^2 A}} < e^{-\frac{\tau}{\epsilon^2 A\Gamma}\rho} + e^{-\frac{\alpha R}{\epsilon^2 \rho_M A}\rho}.$$

Denote

$$\beta_2 = \frac{1}{2}\min\{\frac{\tau}{A\Gamma}, \frac{\alpha R}{\rho_M A K}\}$$

and

$$\epsilon_2 < \sqrt{\frac{\beta}{\log 2}},$$

then $1 - \mu_\epsilon(U_\rho) < e^{-\beta_2/\epsilon^2}$ for all $\epsilon < \epsilon_2$.

Let $\beta = \min\{\beta_1, \beta_2\}$ and $\epsilon_0 = \min\{\epsilon_1, \epsilon_2\}$. The Corollary follows. □

The next theorem gives more accurate estimations.

Theorem 2.1.18. *For any $0 < \delta < 1$, there exists constants $\epsilon_0 > 0$ and $M > 0$, such that the measure of $M\epsilon$-neighborhood of $\mathcal{K}$ is at least $1 - \delta$. i.e.*

$$\mu_\epsilon(\{x|\text{dist}(x, \mathcal{K}) \leq M\epsilon\}) \geq 1 - \delta$$

Proof. According to Theorem 2.1.15, there exists a positive number ρ_M such that $U_{\rho_M} \subset O$. Then one can find constants $\beta > 0$ and $\epsilon_1 > 0$, such that

$$1 - \mu_\epsilon(U_{\rho_M}) < e^{-\beta/\epsilon^2}$$

for all $0 < \epsilon < \epsilon_1$.

By repeating the approach as in the proof of theorem 2.1.15, we obtain the inequality

$$F(\rho) \leq F(\rho_1) e^{-\frac{2\gamma C_1}{\epsilon^2 A}(\rho - \rho_1)}$$

for any ρ_1 with $B(\mathcal{K}, \sqrt{M_1}\epsilon) \subset U_{\rho_1}$, where $F(\rho) = \mu_\epsilon(U_{\rho_M}) - \mu_\epsilon(U_\rho)$.

Let $\rho_1 = L_2 M_1 \epsilon^2$ and denote a constant

$$M_2 = L_2 M_1 - \frac{A}{2\gamma C_1} \log \frac{\delta}{2}\,.$$

After some calculation, it follows that

$$F(\rho) = \mu_\epsilon(U_{\rho_M}) - \mu_\epsilon(U_\rho) \leq \frac{\delta}{2}$$

for $\rho > M_2 \epsilon^2$.

Note that

$$1 - \mu_\epsilon(U_{\rho_M}) < e^{-\beta/\epsilon^2}\,.$$

Let

$$\epsilon_2 = \frac{\beta}{-\log \frac{\delta}{2}}\,.$$

Clearly we have

$$\mu_\epsilon(U_{M_2\epsilon^2}) \geq 1 - \delta\,.$$

According to the property of $U(x)$ in Remark 2.1.13, by denoting $M = \sqrt{\frac{M_2}{L_1}}$, we can obtain

$$U_{M_2\epsilon^2} \subset \{x|\text{dist}(x,\mathcal{K}) \leq M\epsilon\}\,.$$

Let $\epsilon_0 = \min\{\epsilon_1, \epsilon_2\}$. Now we have

$$\mu_\epsilon(\{x|\text{dist}(x,\mathcal{K}) \leq M\epsilon\}) \geq \mu_\epsilon(U_{M_2\epsilon^2}) \geq 1-\delta$$

for any $0 < \epsilon < \epsilon_0$. The theorem now follows. □

Remark 2.1.19. One intuitive motivation is that, if the vector field (1.1.1) is stable linear equation, then the ϵ-invariant measure can be explicitly given. Further, the ϵ-invariant measure can be approximated by a multivariate normal distribution when the strength of noise ϵ is sufficiently small. It follows from the "three-sigma rule" of normal distribution that the ϵ-invariant measure must concentrate in a small neighborhood whose scale is of the order of ϵ. In more complicated situations, the existing knowledge is usually not enough to approximate the ϵ-invariant measure in such an explicit way. But we can still show that the ϵ-invariant measure concentrates in a ϵ-small neighborhood of strong attractors, as described in Theorem 2.1.18.

Remark 2.1.20. From the proof of theorem 2.1.18, one can find that in fact the constant M grows very slow as δ decreases. For small ϵ there exist some constant C such that

$$\limsup_{\delta\to 0} \frac{M}{\sqrt{-\log\delta}} \leq C\,.$$

Clearly M has an extremely slow growth rate.

In addition to the estimation in Theorem 2.1.18, we can also measure the average effect of stochastic perturbation by the mean square displacement. The mean square displacement of the ϵ-invariant measure μ_ϵ is denoted as follows:

$$V(\epsilon) = \int_{\mathbb{R}^N} \text{dist}^2(x,\mathcal{K}) u_\epsilon(x)\mathrm{d}x\,. \tag{2.1.21}$$

From its definition, $V(\epsilon)$ measures the L^2 average of square of displacement of perturbed system. Both upper bound and lower bound of the mean square displacement can be estimated by our level set method. This implies that under random perturbation, the average displacement of sample path solution of system (1.1.2) near the strong attractor can be neither too large nor too small. We remark that as far as we know, there is no existing lower bound estimation of stochastic perturbation problems.

To estimate $V(\epsilon)$, further local conditions about the Lyapunov function U(x) is required.

Assumption (H5). There exist some ρ_* with $U_{\rho_*} \subset O$ such that

$$\int_{U_{\rho_*}} \sum_{i,j=1}^{N} \frac{1}{2} a_{ij} U_{ij}(x) u \mathrm{d}x \geq D$$

for some D.

Assumption (**H**5) could be implied by some conditions that can be verified in an easier way. We give the following two propositions as examples.

Proposition 2.1.21. *If $U(x)$ is convex in O, then (**H**5) holds for all $0 < \epsilon < \epsilon_0$ and ρ_* with $U_{\rho_*} \subset O$.*

Proof. Choose a ρ_* such that $U_{\rho_*} \subset O$. It follows from Theorem 2.1.15 that there exists a constant ϵ_0 such that $\mu_\epsilon(U_{\rho_*}) > 1/2$ for all $0 < \epsilon < \epsilon_0$.

Since $U(x)$ is convex, we know that the Hessian matrix $J = \{U_{ij}\}_{i,j=1}^N$ is a symmetric positive definite matrix. Note that $A = \{a_{ij}\}_{i,j=1}^N$ is also a symmetric positive definite matrix. It is known that the Hadamard product of two symmetric positive definite matrix is also symmetric positive definite. Let $\vec{e} = \{1, \cdot, 1\}$, we have

$$\sum_{i,j=1}^{N} a_{ij} \partial_{ij}^2 U = \vec{e}^T A J \vec{e} > 2D > 0$$

for some positive number D. Integrating the above expression within U_{ρ_*} yields that

$$\int_{U_{\rho_*}} \sum_{i,j=1}^{N} a_{ij} U_{ij}(x) u \mathrm{d}x \geq D\epsilon^2 \,.$$

□

Proposition 2.1.22. *If $\sigma(x)$ is constant in O, then (**H**5) holds for all $0 < \epsilon < \epsilon_0$ and ρ_* with $U_{\rho_*} \subset O$.*

Proof. This follows directly from integration by parts. For any $\rho_* > 0$ we have

$$\int_{U_{\rho_*}} \sum_{i,j=1}^{N} a_{ij} U_{ij}(x) u \mathrm{d}x = \int_{\Gamma_{\rho_*}} (A \nabla U(x)) \cdot \nu \mathrm{d}s \,.$$

Note that A is positive definite and $\nu = \frac{\nabla U(x)}{U(x)}$ is parallel to ∇U, we are done. □

The following theorem estimates the mean square displacement.

Theorem 2.1.23. *If (**H**5) holds, then there exists positive constants V_1, V_2 and ϵ_0, such that the mean square displacement is bounded from below and above*

$$V_1 \epsilon^2 \leq V(\epsilon) \leq V_2 \epsilon^2$$

for all $0 < \epsilon < \epsilon_0$.

Proof. According to Remark 2.1.13, in the neighborhood O of the strong attractor, we always have

$$K_1 \mathrm{dist}(x, \mathcal{K}) \leq |\nabla U| \leq K_2 \mathrm{dist}(x, \mathcal{K}) \,.$$

Choose a constant ρ_M such that $U_{\rho_M} \subset O$. Denote $G(\rho)$ for $0 < \rho < \rho_M$ by:

$$G(\rho) = \int_{U_{\rho_M} \setminus U_\rho} |\nabla U(x)|^2 u \mathrm{d}x \,.$$

Then clearly we have lower bound

$$V(\epsilon) \geq \int_{U_{\rho_M}} \mathrm{dist}^2(x, \mathcal{K}) u \mathrm{d}x \geq \frac{1}{K_2^2} G(0)$$

and upper bound

$$V(\epsilon) = \int_{U_{\rho_M}} \mathrm{dist}^2(x, \mathcal{K}) u \mathrm{d}x + \int_{\mathbb{R}^N \setminus U_{\rho_M}} \mathrm{dist}^2(x, \mathcal{K}) u \mathrm{d}x$$
$$\leq \frac{1}{K_1^2} G(0) + \int_{\mathbb{R}^N \setminus U_{\rho_M}} \mathrm{dist}^2(x, \mathcal{K}) u \mathrm{d}x \,.$$

It's more convenient to estimate $G(0)$ instead of the mean square displacement.

We can apply Theorem 2.1.18 to estimate the upper bound. Let $\sigma = 1/2$. From Theorem 2.1.18, there exists constants M_4, ρ_4 and ϵ_1 such that $\mu(U_{\rho_4}) \geq 1/2$ and $\mathrm{dist}(\Gamma_{\rho_4}, \mathcal{A}) \leq \sqrt{M_4}\epsilon$ when $0 < \epsilon < \epsilon_1$. That implies

$$\int_{U_{\rho_4}} |\nabla U|^2 u \mathrm{d}x \leq M_2 \epsilon^2$$

for every $0 < \epsilon < \epsilon_1$.

For $\rho > \rho_4$, we have

$$\begin{aligned} \int_{U_{\rho_M} \setminus U_{\rho_4}} |\nabla U|^2 u \mathrm{d}x &\leq -\int_{\rho_4}^{\rho_M} \frac{K_2^2}{L_1} \rho F'(\rho) \mathrm{d}\rho \\ &= -\frac{K_2^2}{L_1} \rho F(\rho) \Big|_{\rho_4}^{\rho_M} + \frac{K_2^2}{L_1} \int_{\rho_4}^{\rho_M} F(\rho) \mathrm{d}\rho \end{aligned}$$

where $F(\rho) = 1 - \mu_\epsilon(U_\rho)$.

In addition, from the proof of Theorem 2.1.15, there exists ϵ_2 such that

$$F(\rho) \leq F(\rho_4) e^{-\frac{2\gamma C_1}{\epsilon^2 \bar{A}}(\rho - \rho_4)} \leq e^{-\frac{2\gamma C_1}{\epsilon^2 \bar{A}}(\rho - \rho_4)}$$

if $0 < \rho < \rho_M$ and $0 < \epsilon < \epsilon_2$.

Let $M_5 = \frac{2\gamma C_1 L_2 M_4}{\bar{A}}$, it follows that

$$F(\rho) \leq e^{M_5} e^{-\frac{2\gamma C_1}{\epsilon^2 \bar{A}} \rho} \,.$$

From above estimations, one can find a constant $C_6 > 0$ such that

$$\begin{aligned}\int_{U_{\rho_M}\setminus U_{\rho_4}} |\nabla U|^2 u \mathrm{d}x &\leq -\frac{K_2^2}{L_1}\rho F(\rho)\Big|_{\rho_4}^{\rho_M} + \frac{K_2^2}{L_1}\int_{\rho_4}^{\rho_M} F(\rho)\mathrm{d}\rho \\ &\leq \frac{K_2^2}{L_1}\rho_4 F(\rho_4) + \frac{K_2^2}{L_1}\int_{\rho_4}^{\infty} e^{M_5} e^{-\frac{2\gamma C_1}{\epsilon^2 \bar{A}}\rho}\mathrm{d}\rho \\ &\leq \frac{K_2^2 L_2}{L_1} M_{4\epsilon^2} + e^{M_5}\int_{\rho_4}^{\infty} e^{-\frac{2\gamma C_1}{\epsilon^2 \bar{A}}\rho}\mathrm{d}\rho \\ &\leq \frac{K_2^2 L_2}{L_1} M_4 \epsilon^2 + e^{M_5} C_6 \epsilon^2 \,.\end{aligned}$$

Let

$$E_2 = \frac{L_2 K_2^2}{L_1} M_4 + e^{M_5} C_6 + M_4$$

be a constant. Then it follows that

$$G(0) = \int_{\mathbb{R}^N} |\nabla U|^2 u \mathrm{d}x \leq E_2 \epsilon^2$$

For the complement set of U_{ρ_M}, we have

$$\begin{aligned}&\int_{\mathbb{R}^N\setminus U_{\rho_M}} \mathrm{dist}^2(x,\mathcal{K}) u \mathrm{d}x \\ &= \int_{\mathbb{R}^N\setminus B(0,2R)} \mathrm{dist}^2(x,\mathcal{K}) u \mathrm{d}x + \int_{B(0,2R)\setminus U_{\rho_M}} \mathrm{dist}^2(x,\mathcal{K}) u \mathrm{d}x \,.\end{aligned}$$

Since $\mathcal{K} \subset B(0,R)$, from Corollary 2.1.17, there exists $\epsilon_3 > 0$ such that

$$\int_{\mathbb{R}^N\setminus B(0,2R)} \mathrm{dist}^2(x,\mathcal{K}) u \mathrm{d}x \leq e^{-\beta/\epsilon^2} 9R^2$$

for $0 < \epsilon < \epsilon_3$.

From the proof of Theorem 2.1.15, we have equation (2.1.18):

$$I(x) \leq I(R) e^{-\frac{\alpha}{\epsilon^2 \bar{A}}(x-R)}$$

when $0 < \epsilon < \epsilon_4$ for some $\epsilon_4 > 0$.

or equivalently,

$$I(x) = \int_{\mathbb{R}^N\setminus B(0,x)} u \mathrm{d}x \leq e^{-\frac{\alpha x}{2\epsilon^2 \bar{A}}}$$

for all $x > 2R$.

Since $\mathrm{dist}(x, \mathcal{K}) < 2|x|$ when $|x| > 2R$, we have

$$\begin{aligned}\int_{B(0,2R)\setminus U_{\rho_M}} \mathrm{dist}^2(x,\mathcal{K})u\mathrm{d}x &\leq \int_{B(0,2R)\setminus U_{\rho_M}} 4|x|^2 u\mathrm{d}x \\ &= 4\int_{2R}^{\infty} Vol(\partial B(0,x))x^2 I'(x)\mathrm{d}x \\ &= 4C(N)\int_{2R}^{\infty} x^{N+1}I'(x)\mathrm{d}x = 4C(N)P(R,\epsilon)e^{-\frac{\alpha R}{\epsilon^2 \bar{A}}},\end{aligned}$$

where $C(N)$ is the volume of the unit N-dimension sphere in $\mathbb{R}^N$, $P(R,\epsilon)$ is a polynomial of R and ϵ with highest degree N.

Note that e^{1/ϵ^2} converges to 0 faster than ϵ^2. Clearly there exists some $\epsilon_5 > 0$ such that

$$4C(N)P(R,\epsilon)e^{-\frac{\alpha R}{\epsilon^2 \bar{A}}} + 9R^2 e^{-\beta/\epsilon^2} < \epsilon^2$$

for any $0 < \epsilon < \epsilon_5$.

Let $\epsilon_1^* = \min\{\epsilon_1, \epsilon_2, \epsilon_3, \epsilon_4, \epsilon_5\}$, it follows that

$$V(\epsilon) \leq (1 + \frac{E_2}{K_1^2})\epsilon^2 := V_2\epsilon^2$$

for all $0 < \epsilon < \epsilon_1^*$. We remark that the constant V_2 is independent with ϵ.

The lower bound can be proved in a similar approach. Let $\phi(\rho)$ be the same cut-off function

$$\phi(\rho) = \begin{cases} 0 & \rho < \rho_0 \\ \frac{1}{2\Delta\rho}(\rho - \rho_0)^2 & \rho_0 < \rho < \rho_0 + \Delta\rho \\ \rho - \rho_0 - \frac{1}{2}\Delta\rho & \rho > \rho_0 + \Delta\rho \end{cases}$$

We modify $U(x)$ to $\bar{U}(x)$ such that

$$\bar{U}(x) = \begin{cases} U(x) & x \in U_{\rho_M} \\ \text{a smooth function} & x \in B(0,2R)\setminus U_{\rho_M} \\ |x| & |x| > 2R \end{cases}$$

The smoothness of $\bar{U}$ yields

$$\int_{\bar{\Gamma}_{2R+t}} (\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_i \bar{U}\nu_j)u_\epsilon \mathrm{d}s \geq -\bar{A}\epsilon^2 \int_{\bar{\Gamma}_{2R+t}} u\mathrm{d}s\,.$$

Theorem 2.1.15 implies

$$1-\mu_\epsilon(B(0,2R)) < e^{\frac{-2\alpha R}{\epsilon^2 \bar{A}}} . \tag{2.1.22}$$

So there always exists $0 < t_0 < 1$ such that

$$\int_{\bar{\Gamma}_{2R+t_0}} u \mathrm{d}s < e^{\frac{-2\alpha R}{\epsilon^2 \bar{A}}} ,$$

otherwise (2.1.22) can not be true.

Then equation (2.1.13) yields

$$\int_{B(0,2R+t_0)} \phi'(\bar{U})(\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 \bar{U} + \sum_{i=1}^{N} f_i \partial_i \bar{U})u + \phi''(\bar{U})(\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_i \bar{U}\partial_j \bar{U})u \mathrm{d}x$$
$$\leq \bar{A}\epsilon^2 e^{\frac{-2\alpha R}{\epsilon^2 \bar{A}}} .$$

Further, when $\rho_0 + \Delta\rho < \rho_M$, we have

$$\begin{aligned}
& \int_{B(0,2R+t_0)} \phi'(\bar{U})(\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 U + \sum_{i=1}^{N} f_i \partial_i \bar{U})u + \phi''(\bar{U})(\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_i \bar{U}\partial_j \bar{U})u \mathrm{d}x \\
= & \int_{B(0,2R+t_0)\setminus U_{\rho_M}} (\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 \bar{U} + \sum_{i=1}^{N} f_i \partial_i \bar{U})u \mathrm{d}x \\
+ & \int_{U_{\rho_M}} \phi'(U)(\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 U + \sum_{i=1}^{N} f_i \partial_i U)u + \phi''(U)(\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_i U\partial_j U)u \mathrm{d}x \\
:= & I_1 + I_2 .
\end{aligned}$$

Recall the definition of $\bar{U}(x)$, let

$$\bar{M} = \max_{x\in B(0,2R+t_0)\setminus U_{\rho_M}} |\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 \bar{U} + \sum_{i=1}^{N} f_i \partial_i \bar{U}|$$

and $V = \mathrm{Vol}(B(0, 2R + t_0))$.

According to Theorem 2.1.15, there exists $E > 0$ and $\epsilon_6 > 0$ such that

$$1-\mu_\epsilon(U_{\rho_M}) < e^{-E/\epsilon^2}$$

for every $0 < \epsilon < \epsilon_5$.

Hence

$$I_1 \geq -\bar{M}Ve^{-E/\epsilon^2} .$$

Further, since assumption (**H**5) holds, for I_2 we have

$$\begin{aligned}
&\int_{U_{\rho_M}} \phi'(U)(\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 U + \sum_{i=1}^{N} f_i \partial_i U)u\mathrm{d}x \\
&= \int_{U_{\rho_M}\setminus U_{\rho_0}} \phi'(U)(\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 U + \sum_{i=1}^{N} f_i \partial_i U)u\mathrm{d}x \\
&\geq -\kappa \int_{U_{\rho_M}\setminus U_{\rho_0}} \phi'(U)|\nabla U|^2 u\mathrm{d}x \\
&\geq -\kappa \int_{U_{\rho_M}\setminus U_{\rho_0}} |\nabla U|^2 u\mathrm{d}x \geq -\kappa G(\rho_0)\,,
\end{aligned}$$

where

$$G(\rho) = \int_{U_{\rho_M}\setminus U_{\rho}} |\nabla U|^2 u\mathrm{d}x\,.$$

On the other hand,

$$\begin{aligned}
\int_{U_{\rho_M}} \phi''(U)(\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_i U \partial_j U)u\mathrm{d}x &= \int_{U_{\rho+\Delta\rho}\setminus U_{\rho}} \phi'(U)(\sum_{i,j=1}^{N} \frac{1}{2}\epsilon^2 a_{ij}\partial_i U \partial_j U)u\mathrm{d}x \\
&\geq \frac{1}{\Delta\rho}\epsilon^2\alpha \int_{U_{\rho+\Delta\rho}\setminus U_{\rho}} |\nabla U|^2 u\mathrm{d}x \\
&= \epsilon^2\alpha \frac{G(\rho_0) - G(\rho_0+\Delta\rho)}{\Delta\rho}\,,
\end{aligned}$$

where $\alpha = 1/2\lambda_{min}$. λ_{min} is the smallest eighevalue of A.

Recall that

$$I_1 + I_2 \leq e^{\frac{-2\alpha R}{\epsilon^2 \bar{A}}}\,.$$

Taking the limit $\Delta\rho \to 0$ yields

$$G'(\rho_0) \geq -\frac{\kappa}{\alpha\epsilon^2} G(\rho_0) - \bar{M}V e^{-E/\epsilon^2} - A\epsilon^2 e^{-\frac{2\alpha R}{\epsilon^2 A}}\,.$$

Denote a new cut-off function $\phi_1(\rho)$ as follows

$$\phi_1(\rho) = \begin{cases} \rho & \rho < \rho_0 \\ \rho_0 + \frac{1}{2}\Delta\rho - \frac{1}{2\Delta\rho}(\rho - \rho_0 - \Delta\rho)^2 & \rho_0 < \rho < \rho_0 + \Delta\rho \\ \rho_0 + \frac{1}{2}\Delta\rho & \rho > \rho_0 + \Delta\rho \end{cases}$$

A similar calculation implies that

$$\int_{\mathbb{R}^n} \phi_1''(U)(\sum_{i,j=1}^N \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 U + \sum_{i=1}^N U_i\partial_i U)u\mathrm{d}x + \int_{\mathbb{R}^n} \phi_1'(U)(\sum_{i,j=1}^N \frac{1}{2}\epsilon^2 a_{ij}\partial_i U\partial_j U)u\mathrm{d}x$$
$$= \int_{\Gamma_{\rho_0+\Delta\rho}} \frac{1}{2}\epsilon^2 a_{ij}\phi_1'(\rho_0+\Delta\rho)\partial U_i\nu_j u\mathrm{d}s = 0\,.$$

For simplicity, let $\rho_N = \rho_0 + \Delta\rho$ be some fixed number such that $\rho_N = \frac{1}{2}\rho_M$ for the ρ_M mentioned above. The convexity of $U(x)$ implies

$$\int_{U_{\rho_N}} \phi'(U)(\sum_{i,j=1}^N \frac{1}{2}\epsilon^2 a_{ij}\partial_{ij}^2 U + \sum_{i=1}^N f_i\partial_i U)u\mathrm{d}x \geq D\epsilon^2 - \kappa\int_{U_{\rho_N}} |\nabla U|^2 v\mathrm{d}x$$

and

$$\int_{\rho_N} \phi''(U)(\sum_{i,j=1}^N \frac{1}{2}\epsilon^2 a_{ij}\partial_i U\partial_j U)v\mathrm{d}x \geq -\frac{1}{2\Delta\rho}\epsilon^2\bar{A}\int_{U_{\rho+\Delta\rho}\setminus U_\rho} |\nabla U|^2 v\mathrm{d}x\,.$$

Let $\Delta\rho \to 0$, similarly, we have

$$\begin{aligned} 0 &\geq D\epsilon^2 - \kappa(G(0) - G(\rho_N)) + \frac{1}{2}\epsilon^2\bar{A}G'(\rho_N) \\ &\geq D\epsilon^2 - \kappa G(0) + \kappa G(\rho_N) + \frac{1}{2}\epsilon^2\bar{A}(-\frac{\kappa}{\alpha\epsilon^2}G(\rho_N) - \bar{M}Ve^{-E/\epsilon^2} - \bar{A}\epsilon^2 e^{-\frac{2\alpha R}{\epsilon^2 A}}) \end{aligned}$$

Recall that

$$G(\rho_N) = \int_{U_{\rho_M}\setminus U_{\rho_N}} |\nabla U|^2 u\mathrm{d}x\,.$$

According to Remark 2.1.13, there exists some $\beta > 0$ and $\epsilon_7 > 0$ such that

$$G(\rho_N) \leq \frac{K_2^2}{L_1}e^{-\beta/\epsilon^2}$$

for $0 < \epsilon < \epsilon_7$.

Then one can find $\epsilon_8 > 0$ such that for any $0 < \epsilon < \epsilon_8$

$$|\kappa(1 - \frac{A}{2\alpha})G(\rho_N) - \bar{M}Ve^{-E/\epsilon^2} - A\epsilon^2 e^{-\frac{2\alpha R}{\epsilon^2 A}}| \leq \frac{D}{2}\epsilon^2\,.$$

Let $\epsilon_2^* = \min\{\epsilon_6, \epsilon_7, \epsilon_8\}$.It follows that for every $0 < \epsilon < \epsilon_2^*$, inequality

$$G(0) \geq \frac{D}{2\kappa}\epsilon^2$$

holds.

By letting $V_1 = \frac{D}{2\kappa}$ and $\epsilon_0 = \min\{\epsilon_1^*, \epsilon_2^*\}$, we arrive at the desired estimation. □

Remark 2.1.24. The above theorems concerns the global attractors, which may not be connected. However, for most dynamical system subject to white noise perturbation, there would be only one "valid" connected component in general. It follows from the classical theory of stochastic dynamical system that if there are finite many connected attractors $\{\mathcal{K}_1, \cdots, \mathcal{K}_n\}$, then one can usually find attractor $\mathcal{K}_i$ with minimal potential, such that for all $j \neq i$, there exists $W_j > 0$, with

$$\mu_\epsilon(\mathcal{K}_j) \leq e^{-W_j/\epsilon^2}$$

for all $0 < \epsilon < \epsilon_0$. This means that as $\epsilon \to 0$, the probability measure of $\mathcal{K}_j$ may be neglected under the weak noise. We call the attractor K_i a *principal attractor*. The rigorous analysis about principal attractor will be done at the end of this subsection.

Moreover, it is known recently that if $\mathcal{K}_i$ is a connected component of the strong attractor, then we can always "set" a perturbation coefficient function $\sigma_i(x)$, such that $\mathcal{K}_i$ becomes the principal attractor. (see [33])

2.1.3.2 The Entropy-Dimension Relationship

The emphasis of the rest part of this section is paid on the entropy-dimension relationship. We will prove that the concentration of ϵ-invariant measure can reveal some information of the attractor of ODE system (1.1.1).

Let $\mathrm{Ent}(u_\epsilon(x)$ be the *differential entropy* of $u_\epsilon(x)$:

$$\mathrm{Ent}(u_\epsilon(x)) = \int_{\mathbb{R}^N} u_\epsilon(x) \log u_\epsilon(x) \mathrm{d}x \tag{2.1.23}$$

Further, we say a set $\mathcal{A} \subset \mathbb{R}^n$ is regular if the volume of its neighborhood is related to its dimension.

Definition 2.1.3. $\mathcal{A} \subset \mathbb{R}^n$ is a *regular set* if

$$\limsup_{r \to 0} \frac{\log(Vol(B(\mathcal{A}, r)))}{-\log r} = \liminf_{r \to 0} \frac{\log(Vol(B(\mathcal{A}, r)))}{-\log r} = N - d$$

for some $d \geq 0$. The set $B(\mathcal{A}, r)$ means the r-neighborhood of $\mathcal{A}$:

$$B(\mathcal{A}, r) = \{x \,|\, \mathrm{dist}(x, \mathcal{A}) \leq r\}$$

Remark 2.1.25. We remark that not all sets are regular. But all smooth manifolds, Cantor-like sets and many fractal structures are regular.

The concentration of invariant measure implies the following inequality.

Theorem 2.1.26. *Assume (***H***1) and (***H***5) holds. We have*

$$\lim_{\epsilon \to 0} \frac{\mathrm{Ent}(u_\epsilon(x))}{-\log \epsilon} \geq N - d \tag{2.1.24}$$

if the attractor is a regular set.

Proof. Theorem 2.1.18 says that for any fixed $0 < \sigma < 1$, one can always find constant $C_2 > 0$ such that

$$\mu_\epsilon(N(\mathcal{A}, C_2\epsilon)) := \mu(\{x | \mathrm{dist}(x, \mathcal{A}) \leq C_2\epsilon\}) \geq 1 - \sigma\,.$$

The entropy functional attain minimum when the measure is uniformly distributed. This implies

$$\begin{aligned} \int_{N(\mathcal{A}, C_2\epsilon)} u \log u \mathrm{d}x &\geq \int_{N(\mathcal{A}, C_2\epsilon)} u_a \log u_a \mathrm{d}x \\ &= (1-\sigma) \log \frac{1-\sigma}{\mathrm{Vol}(N(\mathcal{A}, C_2\epsilon))}\,, \end{aligned}$$

where u_a is the average of u in $N(\mathcal{A}, C_2\epsilon)$. The regularity of the attractor implies

$$\lim_{r \to 0} \frac{\log \lambda(B(\mathcal{A}, r))}{\log r} = N - d\,.$$

Some calculation shows that

$$\begin{aligned} \lim_{\epsilon \to 0} \frac{\mathrm{Ent}(u_\epsilon)}{-\log \epsilon} &\geq \lim_{\epsilon \to 0} \frac{(1-\sigma)(\log(1-\sigma) - \log(\mathrm{Vol}(N(\mathcal{A}, C_2\epsilon))))}{-\log \epsilon} \\ &= (1-\sigma) \lim_{\epsilon \to 0} \frac{\log \mathrm{Vol}(N(\mathcal{A}, C_2\epsilon))}{\log \epsilon} \\ &= (1-\sigma) \lim_{\epsilon \to 0} \frac{\log \mathrm{Vol}(N(\mathcal{A}, C_2\epsilon))}{\log C_2\epsilon} \\ &= (1-\sigma)(N-d)\,. \end{aligned}$$

The above argument is true for any $\sigma > 0$. This implies

$$\lim_{\epsilon \to 0} \frac{\mathrm{Ent}(u_\epsilon)}{-\log \epsilon} \geq N - d$$

□

The other side of entropy-dimension inequality is difficult to prove by the level set method. The reason is that, by the level set method, we can estimate the density of invariant measure on every level sets of the Lyapunov function. However, the probability distributions of μ_ϵ on each level set remain unclear. The entropy-dimension inequality is derived from that fact that the ϵ-invariant measure can not be perturbed too much. On the other side, the fact that the ϵ-invariant measure can not concentrate too much does not imply the inequality directly.

Although general entropy-dimension equality remains open, conclusions can still be made in many situations. The following theorem gives the entropy-dimension equality for gradient flows.

Theorem 2.1.27. *If* (1.1.1) *is a gradient flow*

$$\frac{\mathrm{d}x}{\mathrm{d}t} = -\nabla U(x) \tag{2.1.25}$$

with $U \geq 0$ *and the set* $U_0 = \{x | U(x) = 0\}$ *is a smooth manifold, then*

$$\lim_{\epsilon \to 0} \frac{\mathrm{Ent}(u_\epsilon(x))}{-\log \epsilon} = N - d\,, \tag{2.1.26}$$

where d *is the dimension of the invariant manifold.*

Proof. Note that for gradient flow

$$x' = -\nabla U(x)\,,$$

the density function of the ϵ-invariant measure $v(x)$, or the Gibbs density function has an explicit expression

$$v(x) = \frac{1}{K} e^{-U(x)/2\epsilon^2}\,.$$

Let us calculate the value of K.

Since the global attractor $\mathcal{K} = U_0$ is a smooth manifold, for any r, one can find a continuous function $\Phi(r)$ which is bounded from upper and below. The volume of the level set $\{x|\text{dist}(x,\mathcal{K})) = r\}$ can be denoted by $\Phi(r)r^{N-d-1}$ because $\mathcal{K}$ is a smooth manifold.

For any vector v, we have

$$\int \Phi(r)r^{N-d-1}e^{-L_1 r^2/\epsilon^2}\mathrm{d}r \geq K \geq \int \Phi(r)r^{N-d-1}e^{-L_2 r^2/\epsilon^2}\mathrm{d}r\,.$$

After some calculation, one can find some H_1, H_2 such that

$$H_1\epsilon^{N-d} \geq K \geq H_2\epsilon^{N-d}\,.$$

Taking the entropy implies

$$\begin{aligned}
\text{Ent}(v_\epsilon) &= \int_{\mathbb{R}^N} v(x)\log v(x)\mathrm{d}x \\
&\leq \int_{\mathbb{R}^N} v(x)\log\max_x v(x)\mathrm{d}x = \max_x v(x) = -\log K \\
&\leq -(N-d)\log\epsilon - \log H_1\,.
\end{aligned}$$

This implies

$$\lim_{\epsilon\to 0}\frac{\text{Ent}(v_\epsilon)}{-\log\epsilon} \leq N-d$$

The identity (2.1.26) can be obtained by combining the above inequality and inequality 2.1.24. This completes the proof. □

In fact, the Entropy-dimension equality can be extended to all system with regular invariant measure.

Definition 2.1.4. The invariant probability density function ρ_ϵ is said to be *regular* for the global attractor $\mathcal{K}$ if there exists some function $C(K) > 0$ that is independent with ϵ, such that

$$\min(\rho_\epsilon(x)) \geq C\max(\rho_\epsilon(x)) \quad ; \quad \forall x \text{ with } \text{dist}(x,\mathcal{K}) \leq K\epsilon$$

and $\rho(x)$ is bounded by $\epsilon^{-\alpha}$ for some α whenever $\text{dist}(x, \mathcal{K}) \geq K\epsilon$ for all $0 < \epsilon < \epsilon_0$ and $K > K_0 > 0$.

The definition of regular invariant measure implies the next theorem.

Theorem 2.1.28. *Assume (***H***5) holds and system* (1.1.1) *has regular invariant measure, then*

$$\lim_{\epsilon \to 0} \frac{\text{Ent}(u_\epsilon(x))}{-\log \epsilon} = N - d\,. \tag{2.1.27}$$

Proof. The proof is trivial. According to Theorem 2.1.18, for any $\delta > 0$ one can find $K > 0$ such that $1 - \rho_\epsilon(B(\mathcal{K}, K\epsilon)) < \delta$. From the boundedness of μ_ϵ outside of $B(\mathcal{K}, K\epsilon)$, we have

$$\int_{\mathbb{R}^N \setminus B(\mathcal{K}, K\epsilon)} \rho_\epsilon(x) \log \rho_\epsilon(x) \mathrm{d}x < \alpha\delta(-\log \epsilon)$$

Further, the condition

$$\min(\rho_\epsilon(x)) \geq C \max(\rho_\epsilon(x)) \quad ; \quad \forall x \text{ with } \text{dist}(x, \mathcal{K}) \leq K\epsilon$$

means that $\rho_\epsilon(x)$ is less than $\frac{C}{Vol(B(\mathcal{K}, K\epsilon))}$. So we have

$$\lim_{\epsilon \to 0} \frac{\text{Ent}(u_\epsilon(x))}{-\log \epsilon} < N - d + \delta\alpha$$

for any $\delta > 0$, which means

$$\lim_{\epsilon \to 0} \frac{\text{Ent}(u_\epsilon(x))}{-\log \epsilon} \leq N - d$$

This completes the proof. □

We note that actually making use of the result in Proposition 2.1.9 to make the following proposition:

Proposition 2.1.29. *If the quasi-potential function has second order derivative, them the entropy-dimension identity holds.*

Remark 2.1.30. The entropy-dimension inequality and entropy-dimension equality would be used in the afterward sections when we discuss the properties of degeneracy and complexity.

2.1.3.3 Some Global Analysis

In this section we consider general stochastic dynamical systems with multiple attractors. Recall that condition (**H**5) says that the Lyapunov function $U(x)$ take zero value at the global attractor $\mathcal{K}$. Using level set method, the concentration of invariant measure at attractor $\mathcal{K}$ can be proved. However, if $\mathcal{K}$ is not connected, some information may be lost in the level set analysis.

One illustrative example is the following the gradient system

$$\frac{\mathrm{d}x}{\mathrm{d}t} = -\nabla\Psi(x)\,, \tag{2.1.28}$$

where $\Psi(x)$ has a global minimum at x_0 and a local minimum at x_1 with $\Psi(x_0) < \Psi(x_1)$. It is known that $x = x_1$ is a local attractor that could be ignored in sufficient weak noise. If $\Psi(x)$ is chosen as then Lyapunov function, the standard condition (**H**5) of Lyapunov function could not be satisfied at $x = x_1$. On the other hand, if some other function $\phi(x)$ is selected as the Lyapunov function such that $\phi(x)$ attains its minimum at both $x = x_0$ and $x = x_1$, then Theorem 2.1.15 and 2.1.18 implies concentration of invariant measure at the set $\{x_0, x_1\}$ instead of $\{x_0\}$.

This problem is solved in this subsection. Improved results are given by combining Freidlin-Wentzell quasi-potential function method and level-set method. Recall the definition of quasi-potential function $V_D(x, y)$ and the W-graph that we reviewed in the last section. Theorem 2.1.8 says that one doesn't need to worry about the restriction of set D as long as the system (1.1.1) has a Lyapunov function at infinity. This implies that the results in Theorem 2.1.6 holds for dynamical system in $\mathbb{R}^n$ under the standard assumption (**H**1). Hence the quasi-potential function can be used to exclude some local attractors with high potential.

In the context of global analysis, we consider the local quasi-potential function with respect to the local attractors.

Definition 2.1.5. The function $V(x, \mathcal{K})$ is called the quasi-potential about attractor

$\mathcal{K}$. It takes the value $V(x,\mathcal{K}) = V(x,y)$ for any $y \in \mathcal{K}$.

Remark 2.1.31. Recall that $V(x,y)$ is the quasi-potential function. The previous definition makes sense if $V(x,y) = V(y,x) = 0$ for all pairs $x, y \in \mathcal{K}$. In particular, if ODE system (1.1.1) is ergodic on $\mathcal{K}$ then $V(x,\mathcal{K})$ must be well-defined.

The local quasi-potential function has certain lower bound.

Lemma 2.1.32. *Assume system* (1.1.1) *has a connected strong attractor* $\mathcal{K}$*. Let* O *be an open set with* $\mathcal{K} \subset O$*. Assume* (1.1.1) *is ergodic on* K*. Moreover, assume there exists a Lyapunov function defined in* O *satisfies the assumption (***H***4). Then there exists a positive number* β

$$V(x,\mathcal{K}) \geq \delta d(x)^2 \tag{2.1.29}$$

where $d(x) = \mathrm{dist}(x,\mathcal{K})$

Proof. Consider the level set $\Gamma_\epsilon = \Gamma_{\sqrt{\rho}}$. Let ρ_M be a constant such that the level set $U_{\rho_M} \subset O$. Then the from assumption (**H**4), it is easy to verify that the following properties are ture.

1. Γ_ϵ is a Lipschitz family of continuous hypersurface for all $0 < \epsilon < \sqrt{\rho_M}$ such that $\mathcal{K}$ is the ω-limit set of each Γ_ϵ. We denote the Lipschitz constant as L, so $L = \frac{L_2}{2\sqrt{K_1}}$ is finite;

2. The distance between the boundary $\partial\Gamma_\epsilon$ and $\mathcal{K}$ is less than or equal to $\beta\epsilon$ for $\beta = \sqrt{L_1^{-1}}$:
$$\mathrm{dist}(\partial\Gamma_\epsilon, \mathcal{K}) \leq \beta\epsilon\,;$$

3. $F(x) \cdot \vec{n}(x) \leq -\alpha\epsilon$ for all $0 < \epsilon < \epsilon_0$, where
$$\alpha = \frac{2\gamma K_1}{\sqrt{L_2}}\,.$$

Choose x such that $\mathrm{dist}(x, \mathcal{K}) < \sqrt{\rho_M}$. Denote $\mathrm{dist}(x, A)$ by d and

$$d_0 = \min\{\mathrm{dist}(x, \mathcal{K}) | x \in \Gamma_{\epsilon_0}\}\,.$$

Then there exists a constant $\bar{\epsilon} > 0$ such that $x \in \Gamma_{\bar{\epsilon}}$.

The definition of quasi-potential function says that

$$V(x, \mathcal{K}) = \inf_{T>0} \frac{1}{2} \int_{-T}^{0} |\dot{\phi}(t) - f(\phi(t))|^2 \mathrm{d}t\,.$$

Since the set $\{x | V(x, \mathcal{K}) \leq c\}$ is always compact, an absolute continuous curve $\rho(t)$ could be found such that

$$V(x, \mathcal{K}) = \frac{1}{2} \int_{-T}^{0} |\dot{\rho}(t) - f(\rho(t))|^2 \mathrm{d}t\,,$$

where $\rho(-T) \in A$, $\rho(0) = x$.

Let $\gamma(t) = \{\epsilon | \rho(t) \in \Gamma_\epsilon\}$. Since $\rho(t)$ is absolutely continuous and family Γ_ϵ are Lipschitz continuous, it is easy to see that $\gamma(t)$ is also absolutely continuous.

Let S be a subset of $[-T, 0]$ that contains countable many closed interval

$$\{[a_1, b_1], \cdots, [a_n, b_n], \cdots\}$$

such that $\dot{\gamma(t)} \geq 0$ for almost every $t \in [a_k, b_k]$ for each k. Moreover, $\gamma(b_k) = \gamma(a_{k+1})$. Then

$$\int_{-T}^{0} |\dot{\rho}(t) - f(\rho(t))|^2 \mathrm{d}t \geq \int_{S} |\dot{\rho}(t) - f(\rho(t))|^2 \mathrm{d}t$$

Let $\epsilon = \gamma(t)$. For almost every $t \in S$ we have $\vec{n} \cdot \dot{\rho}(t) \geq 0$ since $\dot{\gamma}(t) \geq 0$. It follows from the definition of Γ_ϵ family that $f(\rho(t)) \cdot \vec{n} \leq \alpha\epsilon$.

Hence

$$|\dot{\rho}(t) - f(\rho(t))| \geq (\dot{\rho(t)} - f(\rho(t))) \cdot \vec{n}\,.$$

Since Γ_ϵ is a smooth manifold, there exist a small constant $dt > 0$ such that

$$d(\rho(t + dt), \rho(t)) = \dot{\rho}(t) \cdot \vec{n} dt + o(dt^2)\,.$$

Let $\Gamma_\epsilon^1 = \Gamma_\epsilon + \alpha dt\vec{n}$. Since the family Γ_ϵ are Lipschitz continuous, if $\Gamma_{\epsilon_1} \cap \Gamma_\epsilon^1 \neq$, we can obtain $\epsilon_1 - \epsilon \leq L\alpha$.

This means

$$\gamma(t+dt) - \gamma(t) \leq L(\dot{\rho}(t) \cdot \vec{n} dt)\,.$$

Hence

$$|\dot{\rho}(t) - f(\rho(t))| \geq (\dot{\rho(t)} - f(\rho(t))) \cdot \vec{n} \geq \frac{1}{L}\dot{\gamma}(t) + \alpha\gamma(t)\,.$$

Integrating about t implies

$$\begin{aligned} \int_{-T}^{0} |\dot{\rho}(t) - f(\rho(t))|^2 \mathrm{d}t &\geq \int_S \frac{1}{L^2}|\dot{\gamma}(t) + L\alpha\gamma(t)|^2 \mathrm{d}t \\ &\geq \frac{1}{L^2} \inf_{y(-T_1)\in\mathcal{K}; y(0)=\bar{\epsilon}} \int_{-T_1}^{0} |\dot{y}(t) + L\alpha y(t)|^2 \mathrm{d}t\,. \end{aligned} \tag{2.1.30}$$

Note that $\inf_{y(-T_1)\in\mathcal{K}; y(0)=\bar{\epsilon}} \int_{-T_1}^{0} |\dot{y}(t)+L\alpha y(t)|^2 \mathrm{d}t$ gives the quasi-potential function of system

$$\frac{\mathrm{d}x}{\mathrm{d}t} = -L\alpha x\,.$$

The quasi-potential function of above equation can be found explicitly, which is $L\alpha x^2/2$.

This implies

$$V(x,\mathcal{K}) \geq \frac{\alpha}{L}\bar{\epsilon}^2 \geq \frac{\alpha}{L} d(x)^2$$

for $x \in O$. Let $\delta = \frac{\alpha}{L}$. This completes the proof. □

With the help of local quasi-potential function, some global results can be proved as follow.

Proposition 2.1.33. *For any open neighborhood N with $\bar{\mathcal{K}} \subset N$, there exists a positive number $\beta > 0$, such that*

$$1 - \mu_\epsilon(N) \leq e^{-\beta/\epsilon^2}$$

for all $0 < \epsilon < \epsilon_0$.

Proof. We can extend N to compact set $\bar{N}$ such that $\mathcal{K} \subset \bar{N}$. Then the Theorem 2.1.15 implies that there exists constants $\beta_1 > 0, \epsilon_1 > 0$, such that

$$1 - \mu_\epsilon(\bar{N}) < e^{-\beta_1/\epsilon^2}$$

for all $\epsilon < \epsilon_1$.

Let $\{O_{j_i}\}$ denote the open neighborhood of $\mathcal{K}_{j_i}$ as described in Lemma 2.1.32, where $\mathcal{K}_{j_i}$ are connected components of $\bar{\mathcal{K}}$. Let $O = \bigcup_i O_i$. Let $N_1 = N \cap O$. It follows from Lemma 2.1.32 that the set ∂N_1 has positive quasipotential with respect to every $\mathcal{K}_{j_i}$. We denote constant δ by

$$\delta = \min_{x \in \partial N_1, 1 \le i \le k} V(x, \mathcal{K}_{j_i}) \,.$$

Clearly we have $\delta > 0$.

According to Theorem 2.1.6, for each $x \notin N_1$, one can find

$$W(x) - M = \min_i \{W(K_i) + V(K_i, x)\} \ge \min\{\min_{K_i \subset (\mathcal{K} \setminus \bar{\mathcal{K}})} W(K_i), \delta\} := \beta_2 > 0 \,.$$

Further, theorem 2.1.6 says that

$$1 - \mu_\epsilon(\bar{N} \setminus N_1) < e^{-\beta_2/2\epsilon^2}$$

for $\epsilon < \epsilon_2$.

Hence

$$1 - \mu_\epsilon(N) < e^{-\beta_1/\epsilon^2} + e^{-\beta_2/2\epsilon^2} \,.$$

Denote

$$\beta = \frac{1}{2} \min\{\beta_1, \frac{1}{2}\beta_2\} \,;$$

and

$$\epsilon_0 = \min\{\epsilon_1.\epsilon_2, \sqrt{\frac{\beta}{\log 2}}\} \,.$$

By letting

$$1 - \mu_\epsilon(N) < e^{-\epsilon/\epsilon^2} \,,$$

we complete the proof. □

Other estimations can also be improved in a similar way.

Proposition 2.1.34. *For any $0 < \delta < 1$, there exists a $\epsilon_0 > 0$ and a $M > 0$, such that the measure of $M\epsilon$-neighborhood of $\mathcal{K}$ is at least $1 - \delta$. i.e.*

$$\mu_\epsilon(\{x|\text{dist}(x, \bar{\mathcal{K}}) \leq M\epsilon\}) \geq 1 - \delta$$

Proposition 2.1.35. *Define generalized mean square displacement function as*

$$\bar{V}(\epsilon) = \int_{\mathbb{R}^N} \text{dist}^2(x, \bar{\mathcal{K}}) u_\epsilon(x) \mathrm{d}x \tag{2.1.31}$$

Then there exist positive constant V_1 and V_2, such that for sufficient small ϵ, the mean square displacement satisfies

$$V_1 \epsilon^2 \leq \bar{V}(\epsilon) \leq V_2 \epsilon^2$$

Proposition 2.1.36. *Assume conditions (**H**1) and (**L1**) holds for $\bar{\mathcal{K}}$, then*

$$\lim_{\epsilon \to 0} \frac{\text{Ent}(u_\epsilon(x))}{-\log \epsilon} \geq N - d \tag{2.1.32}$$

where $N - d$ is the dimension of $\bar{\mathcal{K}}$.

2.2 Extension 1 : Fokker-Planck equations on finite graph

In this section, we will study the stochastic dynamical system theory on finite graph. More precisely, our theory is about the stochastic perturbation of flows on discrete spaces. The work has been published on ARMA [11]. This section is not a copy-past of our published article. Comparing with [11], more focus is paid on the stochasticity on graphs.

Both classical and new developed stochastic perturbation theory of ODE systems have been covered in the last section. However, as mentioned in the introduction, in practice not all systems are modeled by differential equations. Some systems are so complex that the differential equation models are impractical, while some systems are discrete in natural. For example, the biochemical reaction networks in the cell

are often modeled by Markov chain networks instead of ODE systems because the number of reacting molecules is not large enough. In this sense, it is also important to study the stochastic dynamical system and random perturbation theory in discrete state spaces.

It is well known that Fokker-Planck equations play an important role in the study of stochastic differential equations. Recently it is also known that Fokker-Planck equations have very rich geometric features. Despite remarkable development in the theory related to Fokker-Planck equation in continuous state spaces, much less is known when the state space is discrete and finite. Although the Markov chain (1.1.6) can play the role of gradient flows on graphs, the notion of "white noise" is not clear for Markov processes defined on graphs. It is interesting to investigate the counterpart of white noise perturbation in the discrete setting.

We establish discrete Fokker-Planck-type equations in this section. Our study are motivated by the connection among free energy functional, Fokker-Planck equation and stochastic process. Consider a stochastic perturbation of a gradient flow,

$$dx = -\nabla\Psi(x)dt + \sqrt{2\beta}dW_t,\ x \in \mathbb{R}^N, \tag{2.2.1}$$

where $\Psi(x)$ is a potential function, dW_t is the white noise. Then it is known that the following Fokker-Planck equation describes the time evolution of the probability density function $\boldsymbol{\rho}(x,t)$ of the trajectories of the SDE (2.2.1).

$$\frac{\partial \boldsymbol{\rho}(x,t)}{\partial t} = \nabla \cdot (\nabla\Psi(x)\boldsymbol{\rho}(x,t)) + \beta\Delta\boldsymbol{\rho}(x,t), \tag{2.2.2}$$

Free energy means the maximal amount of work that can be extracted from a system ([49, 62, 72] and references therein). Mathematically, a free energy functional is a scalar-valued function defined on the space of probability distributions and expressed as

$$F(\boldsymbol{\rho}) = U(\boldsymbol{\rho}) - \beta S(\boldsymbol{\rho}) = \int_X \Psi\rho + \beta\rho\log\rho \mathrm{d}x \tag{2.2.3}$$

where $\beta > 0$ is a constant, called temperature, and $\boldsymbol{\rho}$ is a probability density function defined on a state space X.

It is well known that the global minimizer of the free energy F is a probability distribution, called Gibbs distribution,

$$\boldsymbol{\rho}^*(x) = \frac{1}{K} e^{-\Psi(x)/\beta}, \qquad \text{where } K = \int_{\mathbb{R}^N} e^{-\Psi(x)/\beta}\, \mathrm{d}x. \tag{2.2.4}$$

Although historical developments of the free energy and Fokker-Planck equation are not directly related, there are many studies that reveal some connection between them. The following two results about the relationship between them are well known [20, 22, 27, 37, 36, 52, 56]:

1. The free energy (2.2.3) is a Lyapunov functional for the Fokker-Planck equation (2.2.2), i.e., if the probability density $\boldsymbol{\rho}(t, x)$ is a solution of (2.2.2), then $F(\boldsymbol{\rho}(t, x))$ is a decreasing function of time.

2. The Gibbs distribution (2.2.4) is the global minimizer of the free energy (2.2.3) and is the unique stationary solution of the Fokker-Planck equation (2.2.2).

We consider similar matters on a discrete state space which is a finite graph. The following standard condition is assumed in this section.

Assumption (H1).

- $G = (V, E)$ is a finite simple graph, with vertex set $V = \{a_1, a_2, \cdots, a_N\}$ and edge set E
- $\boldsymbol{\Psi} = (\Psi_i)_{i=1}^N$ is a potential function on vertex set V
- the neighborhood set of a vertex a_i is defined as

$$N(i) = \{j \in \{1, 2, \cdots, N\} | \{a_i, a_j\} \in E\},$$

On the previous discrete setting, the free energy functional has the following expression:

$$F(\boldsymbol{\rho}) = \sum_{i=1}^N \Psi_i \rho_i + \beta \sum_{i=1}^N \rho_i \log \rho_i, \tag{2.2.5}$$

The discrete free energy functional has a global minimizer, the Gibbs density, given by

$$\rho_i^* = \frac{1}{K} e^{-\Psi_i/\beta}, \qquad \text{where } K = \sum_{i=1}^{N} e^{-\Psi_i/\beta}. \tag{2.2.6}$$

Based on recent results in continuous state spaces, it is natural to apply spatial discretization schemes, such as the central difference scheme, to Fokker-Planck equation (2.2.2) to obtain their counterparts for discrete state spaces. The resulting equation for a discrete state space is a system of ordinary differential equations. However, many problems arise with this approach. Commonly used linear discretization schemes are consistent with Fokker-Planck equation (2.2.2), but they often lead to steady states that are different from Gibbs density (2.2.6), which is the global minimizer of the free energy. Conversely, although Gibbs distribution is the invariant measure of some Markov kernels such as metropolis kernel, the ODE generated by metropolis kernel is not consistent with equation (2.2.2) in short time.

In fact, we prove rigorously that no linear discretization scheme can achieve the Gibbs distribution at its steady state for general potentials in Theorem 2.2.1. This suggests that the stochastic perturbations on graphs are not as trivial as it looks like. Linear discretizations of equation (2.2.2) can not be consistent both in short time and in long time.

We provide the following Fokker-Planck equation as a counterpart of equation (2.2.2) on graph $G = (V, E)$ satisfies (**H**1)

$$\begin{aligned} \frac{d\rho_i}{dt} = & \sum_{j \in N(i), \Psi_j > \Psi_i} ((\Psi_j + \beta \log \rho_j) - (\Psi_i + \beta \log \rho_i))\rho_j \\ & + \sum_{j \in N(i), \Psi_j < \Psi_i} ((\Psi_j + \beta \log \rho_j) - (\Psi_i + \beta \log \rho_i))\rho_i \\ & + \sum_{j \in N(i), \Psi_j = \Psi_i} \beta(\rho_j - \rho_i) \end{aligned} \tag{2.2.7}$$

for $i = 1, 2 \cdots, N$. It is clear that both equation (2.2.7) and its stationary distribution are consistent with (2.2.2) and its stationary distribution respectively.

Intuitively, with additive noise, we get a diffusion term to against the flows on the state space. On $\mathbb{R}^n$, in the viewpoint of probability measure, the diffusion is expressed by a Laplacian. On a graph, From equation (2.2.7), we can find that the diffusion is expressed by a log-formed Laplacian. To "against" the flow, we need a nonlinear term to play the role as the diffusion. In practice, we can follow this motivation to introduce additive stochastic perturbation. In $\mathbb{R}^n$, artificially added noise removes singularity, while on graphs, injected noise can guarantee the uniqueness of the invariant measure. In both cases, external noise provides the possibility of next step analysis.

In the following subsections, we will address three theoretical parts of discrete Fokker-Planck equations: The inconsistency problem of linear equations; the geometrical aspects and the exponential convergence rate of discrete Fokker-Planck equation. In the end, I will explain the effect of injected random perturbation by an example.

2.2.1 Why linear discretizations fail

Comparing the Fokker-Planck equation (2.2.2) in the continuous state space with our Fokker-Planck equations (2.2.7) on graphs, one immediately notices that our equations are nonlinear while (2.2.2) is linear. It is natural to question the nonlinearity in both equations. For example, can one just apply common discretization schemes, such as the well known central difference, to (2.2.2) and obtain linear Fokker-Planck equations in the discrete case? However, in our numerical studies, we encountered many problems. For instance, steady state solutions of linear equations derived from discretization are not the Gibbs distributions. Furthermore, the free energy does not decay along the solutions. On the other hand, if we choose some linear Markov kernels (such as Metropolis kernel) whose steady state is the Gibbs distribution, then we can find that these Markov kernels are even not consistent with the Fokker-Planck equation (2.2.2)

In this section, we prove that these problems occur for all linear systems obtained

from discretizing the continuous Fokker-Planck equation (2.2.2) using consistent linear schemes. Which means we can never get a "good" linear scheme that is consistent both in short time and long time. We want to mention that this is a long-observed phenomenon by many researchers.

To be more precise, any given linear discretization of (2.2.2) can be written as

$$\frac{d\rho_i}{dt} = \sum_j ((\sum_k e^i_{jk}\Psi_k) + c^i_j)\rho_j, \text{ for } i = 1, 2, \cdots, N, \tag{2.2.8}$$

where Ψ is the given potential and $\{e^i_{jk}\}_{N\times N}$ and $\{c^i_j\}_N$ are some constants that are not all zero. Assume that the Gibbs distribution (2.2.6) is the steady state solution of (2.2.8), then we must have

$$\sum_j ((\sum_k e^i_{jk}\Psi_k) + c^i_j)e^{-\frac{\Psi_j}{\beta}} = 0, \text{ for } i = 1, 2, \cdots, N. \tag{2.2.9}$$

Let us denote $\mathcal{A}$ as the collection of potentials Ψ satisfying (2.2.9), i.e.

$$\mathcal{A} = \{(\Psi_1, \cdots, \Psi_N) \in \mathbb{R}^N : \sum_j ((\sum_k e^i_{jk}\Psi_k) + c^i_j)e^{-\frac{\Psi_j}{\beta}} = 0, \text{for } 1 \le i \le N\}. \tag{2.2.10}$$

Theorem 2.2.1. *The set $\mathcal{A}$ has zero measure in $\mathbb{R}^N$, i.e.*

$$\kappa(\mathcal{A}) = 0,$$

where $\kappa(\cdot)$ is the Lebesgue measure on $\mathbb{R}^N$.

To prove this theorem, we need the following lemma.

Lemma 2.2.2. *Let $g(x)$ be a function in $C^1(\mathbb{R}^N)$. Denote $\mathcal{B} = \{x \in \mathbb{R}^N : g(x) = 0\}$, and $\mathcal{B}_j = \{x \in \mathcal{B} : g_{x_j}(x) = 0\}$ for $j = 1, \cdots, N$. Then*

$$\kappa(\mathcal{B}_j) = \kappa(\mathcal{B}). \tag{2.2.11}$$

Proof. This lemma is a special case of a well known fact about functions in Sobolev spaces, see for example, Lemma 7.7 in [29]. □

Now, we are ready to prove Theorem 2.2.1.

Proof. For the convenience of notations, let us denote $\Psi = (\Psi_1, \cdots, \Psi_N)$ and

$$f_i(\Psi) = \sum_j ((\sum_k e^i_{jk}\Psi_k) + c^i_j)e^{-\frac{\Psi_j}{\beta}}.$$

Clearly, we have $f_i \in C^\infty(\mathbb{R}^N)$. Then, we can consider the sets, $\mathcal{A}_\vartheta$, which collect all potentials $\Psi \in \mathcal{A}$ with vanishing ϑ-th derivatives of f_i for all $i = 1, \cdots, N$, that is

$$\mathcal{A}_\vartheta = \{\Psi \in \mathcal{A} : D^\vartheta f_i(\Psi) = 0, \text{for } 1 \leq i \leq N\},$$

where $\vartheta = (\vartheta_1, \cdots, \vartheta_N)$ is a multiple non-negative integer index, and D^ϑ is the partial derivative operator. Obviously, $\mathcal{A}$ and $\mathcal{A}_\vartheta$ are closed subsets.

Using Lemma 2.2.2 recursively, we have

$$\kappa(\mathcal{A}) = \kappa(\mathcal{A}_\vartheta), \tag{2.2.12}$$

for arbitrary multi-index ϑ. Next, we show $\kappa(\mathcal{A}) = 0$ by contradiction.

Assume that $\kappa(\mathcal{A}) > 0$, so we have $\kappa(\mathcal{A}_\vartheta) = \kappa(\mathcal{A}) > 0$ for arbitrary multi-index ϑ. This implies that there must exist a potential $\Psi^0 \in \mathcal{A}$ such that

$$f_i(\Psi^0) = 0 \quad \text{and} \quad D^\vartheta f_i(\Psi^0) = 0,$$

for arbitrary ϑ.

For any $r \in \{1, \cdots, N\}$ and $s \in \{1, \cdots, N\}$ with $r \neq s$, we have

$$\frac{\partial^3 f_i}{\partial \Psi_r^2 \partial \Psi_s}(\Psi) = \frac{e^i_{rs}}{\beta^2} e^{-\frac{\Psi_r}{\beta}}.$$

Therefore,

$$\frac{\partial^3 f_i}{\partial \Psi_r^2 \partial \Psi_s}(\Psi^0) = 0$$

implies $e^i_{rs} = 0$ for $r \neq s$. Thus, we must have

$$f_i(\Psi) = \sum_j (e^i_{jj}\Psi_j + c_j)e^{-\frac{\Psi_j}{\beta}}.$$

It is easy to compute that for any $j \in \{1, \cdots, N\}$,

$$\frac{\partial^l f_i}{\partial \Psi_j^l} = \left(\frac{l e_{jj}^i}{(-\beta)^{l-1}} + \frac{(e_{jj}^i \Psi_j + c_j^i)}{(-\beta)^l} \right) e^{-\frac{\Psi_j}{\beta}},$$

for arbitrary $l \in \mathbb{N}$. Using the fact that

$$\frac{\partial^l f_i}{\partial \Psi_j^l}(\Psi^0) = 0,$$

which is

$$-\beta l e_{jj}^i + (e_{jj}^i \Psi_j^0 + c_j^i) = 0, \quad \text{for all } l \geq 1.$$

This implies $e_{jj}^i = 0$ and $c_j^i = 0$, and it contradicts to the fact that not all of e_{jk}^i and c_j^i are zero. So we must have $\kappa(\mathcal{A}) = 0$. □

Theorem 2.2.1 indicates that one can not expect a linear system obtained by a consistent discretization of the continuous Fokker-Planck equation (2.2.2) to achieve the Gibbs distribution at its steady state for general potentials. It suggests that a Fokker-Planck equation on a graph needs to be nonlinear in general. However, this does not imply that general linear systems can not achieve the Gibbs distribution at their steady states. In fact, it can be verified that for any given probability vector ρ^*, including the Gibbs distribution, there exists a "reaction matrix" A, such that the solution of the ODE system

$$\rho'(t) = \rho A$$

tends to ρ^* as time $t \to \infty$. Furthermore, the choice of A is not unique. One may choose any A with the property of $e^{At} \to P$, where $P = [\rho^*, \rho^*, \cdots, \rho^*]$ is a rank one matrix. For example, taking $A = P - I$ will work in this situation. But such a matrix A can not be obtained by linearly discretizing the continuous Fokker-Planck equation in a consistent way as we explained in Theorem 2.2.1.

2.2.2 The properties of discrete Fokker-Planck equation

This section is about the properties of discrete Fokker-Planck equation (2.2.7). We will show that equation (2.2.7) is well-defined and has a unique invariant measure

which is Gibbs distribution. In fact, we have the following Theorem:

Theorem 2.2.3. *Given a graph $G = (V, E)$ satisfies (**G**), we have*

1. *For all $\beta > 0$, Gibbs distribution $\boldsymbol{\rho}^* = (\rho_i^*)_{i=1}^N$ given by*

$$\rho_i^* = \frac{1}{K} e^{-\Psi_i/\beta} \text{ with } K = \sum_{i=1}^N e^{-\Psi_i/\beta}$$

   is the unique stationary distribution of equation (2.2.7) in $\mathcal{M}$. Furthermore, the free energy F attains its global minimum at Gibbs distribution.

2. *For all $\beta > 0$, there exists a unique solution*

$$\boldsymbol{\rho}(t) : [0, \infty) \to \mathcal{M}$$

   of equation (2.2.7) with initial value $\boldsymbol{\rho}^0 \in \mathcal{M}$, and $\boldsymbol{\rho}(t)$ satisfies:

   (a) the free energy $F(\boldsymbol{\rho}(t))$ decreases as time t increases,

   (b) $\boldsymbol{\rho}(t) \to \boldsymbol{\rho}^*$ under the Euclidean metric of $\mathbb{R}^N$ as $t \to +\infty$.

Proof. (1). It is well known that F attains its minimum at Gibbs density. By a direct computation, we have that Gibbs distribution is a stationary solution. Let $\boldsymbol{\rho} = (\rho_i)_{i=1}^N$ be a stationary solution of equation (2.2.7) in $\mathcal{M}$. For $\boldsymbol{\sigma} = (\sigma_i)_{i=1}^N \in T_\rho \mathcal{M}$, we let $\boldsymbol{\sigma} \simeq [(p_i)_{i=1}^N]$ for some $(p_i)_{i=1}^N \in \mathbb{R}^N$. Since $\boldsymbol{\rho}$ is the stationary solution, it implies that

$$\begin{aligned}
& \sum_{i=1}^N (\Psi_i + \beta(1 + \log \rho_i))\sigma_i \\
= & \sum_{i=1}^N \Bigg\{ \sum_{j \in N(i), \Psi_j > \Psi_i} ((\Psi_i - \Psi_j)\rho_j + \beta(\log \rho_i - \log \rho_j)\rho_j) \\
& + \sum_{j \in N(i), \Psi_j < \Psi_i} ((\Psi_i - \Psi_j)\rho_i + \beta(\log \rho_i - \log \rho_j)\rho_i) \\
& + \sum_{j \in N(i), \Psi_j = \Psi_i} \beta(\rho_i - \rho_j) \Bigg\} p_i \\
= & \ 0.
\end{aligned}$$

We note that for any $(\sigma_i)_{i=1}^{N-1} \in \mathbb{R}^{N-1}$, if we take

$$\sigma_N = -\sum_{i=1}^{N-1} \sigma_i$$

then $(\sigma_i)_{i=1}^{N} \in T_{\boldsymbol{\rho}}\mathcal{M}$. Thus one has

$$\sum_{i=1}^{N-1}\{(\Psi_i + \beta(1+\log\rho_i)) - (\Psi_N + \beta(1+\log\rho_N))\}\sigma_i = 0$$

for any $(\sigma_i)_{i=1}^{N-1} \in \mathbb{R}^{N-1}$. This implies

$$(\Psi_i + \beta\log\rho_i) - (\Psi_N + \beta\log\rho_N) = 0,$$

which is

$$\rho_i = e^{\frac{\Psi_N - \Psi_i}{\beta}}\rho_N$$

for $i = 1, 2, \cdots, N-1$.

Combining this fact with $\sum_{i=1}^{N}\rho_i = 1$, we have $\rho_i = \frac{1}{K}e^{-\Psi_i/\beta} = \rho_i^*$ for $i = 1, 2, \cdots, N$, where $K = \sum_{i=1}^{N} e^{-\frac{\Psi_i}{\beta}}$. This completes the proof of (2).

(2). Let a continuous function

$$\boldsymbol{\rho}(t) : [0, c) \to \mathcal{M}$$

for some $0 < c \leq +\infty$ be a solution of equation (2.2.7) with initial value $\boldsymbol{\rho}^0 \in \mathcal{M}$. For any $\boldsymbol{\rho}^0 \in \mathcal{M}$, there exists a maximal interval of existence $[0, c(\boldsymbol{\rho}^0))$ and $0 < c(\boldsymbol{\rho}^0)) \leq +\infty$. We will show that for any $\boldsymbol{\rho}^0$, $c(\boldsymbol{\rho}^0) = +\infty$. In fact, this follows from the following claim,

Claim: Given $\boldsymbol{\rho}^0 \in \mathcal{M}$, there exists a compact subset B of $\mathcal{M}$ with respect to the Euclidean metric such that $\boldsymbol{\rho}^0 \in \text{int}(B)$, where $\text{int}(B)$ is the interior of B in $\mathcal{M}$. If

$$\boldsymbol{\rho}(t) : [0, c(\boldsymbol{\rho}^0)) \to \mathcal{M}$$

is the solution of equation (2.2.7) with initial value $\boldsymbol{\rho}^0$ on its maximal interval of existence, then $c(\boldsymbol{\rho}^0) = +\infty$ and $\boldsymbol{\rho}(t) \in \text{int}(B)$ for $t > 0$.

Proof of Claim. Let $\boldsymbol{\rho}^0 = (\rho_i^0)_{i=1}^N \in \mathcal{M}$ be fixed and $\boldsymbol{\rho}(t) : [0, c(\boldsymbol{\rho})) \to \mathcal{M}$ be the solution to equation (2.2.7) with initial value $\boldsymbol{\rho}^0$ on its maximal interval of existence. First, we construct a compact subset B of $\mathcal{M}$ with respect to the Euclidean metric such that $\boldsymbol{\rho}^0 \in \text{int}(B)$. Then we show that $c(\boldsymbol{\rho}^0) = +\infty$ and $\boldsymbol{\rho}(t) \in \text{int}(B)$ for all $t > 0$.

Let us denote

$$M = \max\{e^{2|\Psi_i|} : i = 1, 2, \cdots, N\},$$

$$\epsilon_0 = 1,$$

and

$$\epsilon_1 = \frac{1}{2} \min\left\{ \frac{\epsilon_0}{(1 + (2M)^{\frac{1}{\beta}})}, \min\{\rho_i^0 : i = 1, \cdots, N\} \right\}.$$

For $\ell = 2, 3, \cdots, N-1$, we let

$$\epsilon_\ell = \frac{\epsilon_{\ell-1}}{1 + (2M)^{\frac{1}{\beta}}}.$$

We define

$$B = \Bigg\{ \boldsymbol{\rho} = (\rho_i)_{i=1}^N \in \mathcal{M} : \sum_{r=1}^{\ell} \rho_{i_r} \leq 1 - \epsilon_\ell \text{ where } \ell \in \{1, \cdots, N-1\}, \\ 1 \leq i_1 < \cdots < i_\ell \leq N \Bigg\}.$$

Then B is a compact subset of $\mathcal{M}$ with respect to Euclidean metric,

$$\text{int}(B) = \Bigg\{ \boldsymbol{\rho} = (\rho_i)_{i=1}^N \in \mathcal{M} : \sum_{r=1}^{\ell} \rho_{i_r} < 1 - \epsilon_\ell, \text{ where } \ell \in \{1, \cdots, N-1\}, \\ 1 \leq i_1 < \cdots < i_\ell \leq N \Bigg\},$$

and $\boldsymbol{\rho}^0 \in \text{int}(B)$.

Let $t_0 \in [0, c(\boldsymbol{\rho}^0))$ with $\boldsymbol{\rho}(t_0) \in \text{int}(B)$. Then for any $\ell \in \{1, 2, \cdots, N-1\}$ and $1 \leq i_1 < i_2 < \cdots i_\ell \leq N$, one has

$$\sum_{r=1}^{\ell} \rho_{i_r}(t_0) < 1 - \epsilon_\ell.$$

Moreover

$$\sum_{r=1}^{\ell} \rho_{i_r}(t) < 1 - \epsilon_\ell$$

for small enough $t > t_0$ by continuity. Thus $\boldsymbol{\rho}(t) \in \mathrm{int}(B)$ for small enough $t > t_0$.

With the above discussion and the compactness of B, we are ready to prove that $c(\boldsymbol{\rho}^0) = +\infty$. To show this, it is sufficient to prove that $\boldsymbol{\rho}(t) \in \mathrm{int}(B)$ for all $t > 0$. Let us assume this is not true, which means the solution $\boldsymbol{\rho}(t)$ hits the boundary. In this case, there exists $t_1 > 0$ such that $\boldsymbol{\rho}(t_1) \in \partial B$ and $\boldsymbol{\rho}(t) \in \mathrm{int}(B)$ for all $t \in [0, t_1)$. Since $\boldsymbol{\rho}(t_1) \in \partial B$, we can find $1 \le i_1 < \cdots < i_l \le N$ such that $1 \le l \le N-1$ and

$$\sum_{r=1}^{l} \rho_{i_r}(t_1) = 1 - \epsilon_l. \tag{2.2.13}$$

Let $A = \{i_1, i_2, \cdots, i_\ell\}$ and $A^c = \{1, 2, \cdots, N\} \setminus A$. Then for any $j \in A^c$,

$$\rho_j(t_1) \le 1 - \left(\sum_{r=1}^{\ell} \rho_{i_r}(t_1) \right) = \epsilon_\ell. \tag{2.2.14}$$

Since $\boldsymbol{\rho}(t_1) \in B$, we have

$$\sum_{j=1}^{\ell-1} \rho_{s_j}(t_1) \le 1 - \epsilon_{\ell-1},$$

for any $1 \le s_1 < s_2 < \cdots < s_{\ell-1} \le N$. Hence for each $i \in A$,

$$\rho_i(t_1) \ge 1 - \epsilon_\ell - (1 - \epsilon_{\ell-1}) = \epsilon_{\ell-1} - \epsilon_\ell. \tag{2.2.15}$$

Combining equations (2.2.14), (2.2.15) and the fact

$$\epsilon_\ell \le \frac{\epsilon_{\ell-1}}{1 + (2M)^{\frac{1}{\beta}}},$$

one has, for any $i \in A, j \in A^c$,

$$\Psi_j - \Psi_i + \beta(\log \rho_j - \log \rho_i) \le \Psi_j - \Psi_i + \beta(\log \epsilon_\ell - \log(\epsilon_{\ell-1} - \epsilon_\ell)) \le -\log 2. \tag{2.2.16}$$

Since the graph G is connected, there exists $i_* \in A, j_* \in A^c$ such that $\{a_{i_*}, a_{j_*}\} \in E$. Thus

$$\sum_{i \in A, j \in A^c, \{a_i, a_j\} \in E} \Gamma_{ij}^{\boldsymbol{\Psi}}(\boldsymbol{\rho}(t_1)) \ge \Gamma_{i_* j_*}^{\boldsymbol{\Psi}}(\boldsymbol{\rho}(t_1)) > 0. \tag{2.2.17}$$

Now by (2.2.16) and (2.2.17), one has

$$\begin{aligned}
\frac{\mathrm{d}}{dt}\sum_{r=1}^{\ell}\rho_{i_r}(t)\mid_{t=t_1} &= \sum_{i\in A}\sum_{j\in N(i)}\Gamma_{ij}^{\mathbf{\Psi}}(\boldsymbol{\rho}(t_1))\left(\Psi_j-\Psi_i+\beta(\log\rho_j(t_1)-\log\rho_i(t_1))\right)\\
&= \sum_{i\in A}\{\sum_{j\in A\cap N(i)}\Gamma_{ij}^{\mathbf{\Psi}}(\boldsymbol{\rho}(t_1))\left(\Psi_j-\Psi_i+\beta(\log\rho_j(t_1)-\log\rho_i(t_1))\right)\\
&\quad+\sum_{j\in A^c\cap N(i)}\Gamma_{ij}^{\mathbf{\Psi}}(\boldsymbol{\rho}(t_1))\left(\Psi_j-\Psi_i+\beta(\log\rho_j(t_1)-\log\rho_i(t_1))\right)\}\\
&= \sum_{i\in A}\sum_{j\in A^c\cap N(i)}\Gamma_{ij}^{\mathbf{\Psi}}(\boldsymbol{\rho}(t_1))\left(\Psi_j-\Psi_i+\beta(\log\rho_j(t_1)-\log\rho_i(t_1))\right)\\
&\leq -\log 2\sum_{i\in A}\sum_{j\in A^c\cap N(i)}\Gamma_{ij}^{\mathbf{\Psi}}(\boldsymbol{\rho}(t_1))\\
&= -\log 2\sum_{i\in A,j\in A^c,\{a_i,a_j\}\in E}\Gamma_{ij}^{\mathbf{\Psi}}(\boldsymbol{\rho}(t_1))\\
&\leq -\log 2\Gamma_{i_*j_*}^{\mathbf{\Psi}}(\boldsymbol{\rho}(t_1))<0.
\end{aligned}$$

Combining this with (2.2.13), it is clear that

$$\sum_{i=1}^{l}\rho_{i_r}(t_1-\delta)>1-\epsilon_l$$

for sufficiently small $\delta>0$. This implies $\boldsymbol{\rho}(t_1-\delta)\notin B$, and it contradicts the fact that $\boldsymbol{\rho}(t)\in\mathrm{int}(B)$ for $t\in[0,t_1)$. This completes the proof of the Claim.

□

□

As a direct consequence, we have the following result.

Corollary 2.2.4. *Given the graph $G=(V,E)$ satisfies condition (**G**), we have*

1. *If the noise level $\beta=0$, then Fokker-Planck equation I (2.2.7) for the discrete state space is*

$$\frac{d\rho_i}{dt}=\sum_{j\in N(i),\Psi_j>\Psi_i}(\Psi_j-\Psi_i)\rho_j+\sum_{j\in N(i),\Psi_j<\Psi_i}(\Psi_j-\Psi_i)\rho_i \tag{2.2.18}$$

for $i=1,2,\cdots,N$.

2. *In a special case when the potential is a constant at each vertices, this equation is the master equation:*

$$\frac{d\rho_i}{dt} = \sum_{j \in N(i)} \beta(\rho_j - \rho_i) \tag{2.2.19}$$

for $i = 1, 2, \cdots, N$.

Remark 2.2.5. Equation (2.2.18) describes the time evolution of probability distribution due to the potential energy and is also the probability distribution of a time homogeneous Markov process on the graph G. The master equation is a first order differential equation that describes the time evolution of the probability distribution at every vertex in the discrete state space. Its entropy increases along with the master equation. In this sense, Fokker-Planck equation I (2.2.7) is a generalization of master equation. We refer to [68] for more details on the master equation.

The diffusion term in (2.2.7) is a nonlinear discretization of Laplacian. It describes a nonlinear diffusion of probability distribution between adjacent vertices. So it is not proper to treat $\Psi_i - \Psi_j + \beta(\log \rho_i - \log \rho_j)$ as the "transit rate" from a_i to a_j. The approximated transition rate can be obtained by linearization. The readers may find that linearized discrete Fokker-Planck equation is exactly the metropolis kernel. (see [17])

2.2.3 The geometric features of discrete Fokker-Planck equation

This subsection is dedicated to the geometric properties of discrete Fokker-Planck-type equation (2.2.7). It is already known that the Fokker-Planck equation (2.2.2) is a gradient flow of free energy in the 2-Wasserstein space [52]. Like its continuous counterpart, we will show that equation (2.2.7) is also a gradient flow of free energy in some metric space, which is obtained by discretizing Otto's calculus. Note that Otto's calculus describes the Riemannian geometric structure on 2-Wasserstein metric space.

Remark 2.2.6. 2-Wasserstein distance is defined on the space of probability measures.

Definition 2.2.1. on $\mathbb{R}^n$, the 2-Wasserstein distance between probability measures μ_1 and μ_2 is defined by

$$W_2(\mu_1,\mu_2)^2 = \inf_{\lambda\in\mathcal{M}(\mu_1,\mu_2)} \int_{\mathbb{R}^n\times\mathbb{R}^n} d(x,y)^2 d\lambda(x,y), \tag{2.2.20}$$

where $\mathcal{M}(\mu_1,\mu_2)$ is the collection of Borel probability measures on $\mathbb{R}^n\times\mathbb{R}^n$ with marginal measures μ_1 and μ_2 respectively.

For more introductions of 2-Wasserstein space, see [71, 70].

We discretize Otto's calculus in a following way to construct a family of Riemannian metrics: Given a graph $G=(V,E)$ with $V=\{a_1,a_2,\cdots,a_N\}$, we consider all positive probability distributions on V:

$$\mathcal{M}=\left\{\boldsymbol{\rho}=(\rho_i)_{i=1}^N\in\mathbb{R}^N|\sum_{i=1}^N\rho_i=1 \text{ and } \rho_i>0 \text{ for } i\in\{1,2,\cdots,N\}\right\},$$

and its closure,

$$\overline{\mathcal{M}}=\left\{\boldsymbol{\rho}=(\rho_i)_{i=1}^N\in\mathbb{R}^N|\sum_{i=1}^N\rho_i=1 \text{ and } \rho_i\geq 0 \text{ for } i\in\{1,2,\cdots,N\}\right\}.$$

Let $\partial\mathcal{M}$ be the boundary of $\mathcal{M}$, i.e.

$$\partial\mathcal{M}=\left\{\boldsymbol{\rho}=\{\rho_i\}_{i=1}^N\in\mathbb{R}^N|\sum_{i=1}^N\rho_i=1,\rho_i\geq 0 \text{ and } \prod_{i=1}^N\rho_i=0\right\}.$$

The tangent space $T_\rho\mathcal{M}$ at $\rho\in\mathcal{M}$ is defined by

$$T_\rho\mathcal{M}=\left\{\boldsymbol{\sigma}=(\sigma_i)_{i=1}^N\in\mathbb{R}^N|\sum_{i=1}^N\sigma_i=0\right\}.$$

It is clear that the standard Euclidean metric on $\mathbb{R}^N$, d, is also a Riemannian metric on $\mathcal{M}$.

Let

$$\boldsymbol{\Phi}:(\mathcal{M},d)\to(\mathbb{R}^N,d) \tag{2.2.21}$$

be an arbitrary smooth map given by:

$$\boldsymbol{\Phi}(\boldsymbol{\rho})=(\Phi_i(\boldsymbol{\rho}))_{i=1}^N, \qquad \boldsymbol{\rho}\in\mathcal{M}$$

In the following, we will endow $\mathcal{M}$ with a metric $d_{\mathbf{\Phi}}$, which depends on $\mathbf{\Phi}$ and the structure of G.

For technical reasons, we first consider the function

$$\frac{r_1 - r_2}{\log r_1 - \log r_2}$$

where $r_1 > 0$, $r_2 > 0$ and $r_1 \neq r_2$. We want to extend it to the closure of the first quadrant in the plane. In fact, this can be easily achieved by the following function:

$$e(r_1, r_2) = \begin{cases} \frac{r_1 - r_2}{\log r_1 - \log r_2} & \text{if } r_1 \neq r_2 \text{ and } r_1 r_2 > 0 \\ 0 & \text{if } r_1 r_2 = 0 \\ r_1 & \text{if } r_1 = r_2 \end{cases} .$$

It is easy to check that $e(r_1, r_2)$ is a continuous function on

$$\{(r_1, r_2) \in \mathbb{R}^2 : r_1 \geq 0, r_2 \geq 0\}$$

and satisfies

$$\min\{r_1, r_2\} \leq e(r_1, r_2) \leq \max\{r_1, r_2\}.$$

For simplicity, we will use its original form instead of the function $e(r_1, r_2)$ in this paper.

Next, we introduce the following equivalence relation "$\sim$ " in $\mathbb{R}^N$:

$$\boldsymbol{p} \sim \boldsymbol{q} \quad \text{if and only if} \quad p_1 - q_1 = p_2 - q_2 = \cdots = p_N - q_N,$$

and let $\mathcal{W}$ be the quotient space $\mathbb{R}^N / \sim$. In other words, for $\boldsymbol{p} \in \mathbb{R}^N$ we consider its equivalent class

$$[\boldsymbol{p}] = \{(p_1 + c, p_2 + c, \cdots, p_N + c) : c \in \mathbb{R}\},$$

and all such equivalent classes form the vector space $\mathcal{W}$.

For a given $\mathbf{\Phi}$, and $[\boldsymbol{p}] = [(p_i)_{i=1}^N] \in \mathcal{W}$, we define an identification $\tau_{\mathbf{\Phi}}([\boldsymbol{p}]) = (\sigma_i)_{i=1}^N$ from $\mathcal{W}$ to $T_{\boldsymbol{\rho}}\mathcal{M}$ by,

$$\sigma_i = \sum_{j \in N(i)} \Gamma_{ij}^{\Phi}(\boldsymbol{\rho})(p_i - p_j), \tag{2.2.22}$$

where

$$\Gamma_{ij}^{\Phi}(\boldsymbol{\rho}) = \begin{cases} \rho_i & \text{if} \quad \Phi_i > \Phi_j, j \in N(i) \\ \rho_j & \text{if} \quad \Phi_j > \Phi_i, j \in N(i) \\ \frac{\rho_i - \rho_j}{\log \rho_i - \log \rho_j} & \text{if} \quad \Phi_i = \Phi_j, j \in N(i) \end{cases} \tag{2.2.23}$$

for $i = 1, 2, \cdots, N$. With this identification, we can express $\boldsymbol{\sigma} \in T_{\boldsymbol{\rho}}\mathcal{M}$ by $[\boldsymbol{p}] := \tau_{\boldsymbol{\Phi}}^{-1}(\boldsymbol{\sigma}) \in \mathcal{W}$, and denoted it by

$$\boldsymbol{\sigma} \simeq [(p_i)_{i=1}^N].$$

We note that this identification depends on $\boldsymbol{\Phi}$, the probability distribution $\boldsymbol{\rho}$ and the structure of the graph G. In the following lemma, we show that this identification (2.2.22) is well defined.

Lemma 2.2.7. *If each σ_i satisfies* (2.2.22)*, then the map $\tau_\Phi : [(p_i)_{i=1}^N] \in \mathcal{W} \mapsto \boldsymbol{\sigma} = (\sigma_i)_{i=1}^N \in T_\rho\mathcal{M}$ is a linear isomorphism.*

Proof. It is clear that

$$\tau_{\boldsymbol{\Phi}} : [(p_i)_{i=1}^N] \in \mathcal{W} \mapsto \tau_{\boldsymbol{\Phi}}([(p_i)_{i=1}^N]) = (\sigma_i)_{i=1}^N \in T_\rho\mathcal{M}$$

is a well-defined linear map. Furthermore, both $\mathcal{W}$ and $T_{\boldsymbol{\rho}}\mathcal{M}$ are $(N-1)$-dimensional real linear spaces. Thus, in order to prove the map $\tau_{\boldsymbol{\Phi}}$ is an isomorphism, it is sufficient to show that the map $\tau_{\boldsymbol{\Phi}}$ is injective, which is equivalent to the fact that if $\boldsymbol{p} = \{p_i\}_{i=1}^N \in \mathbb{R}^N$ satisfies

$$\sigma_i = \sum_{j \in N(i)} \Gamma_{ij}^{\Phi}(p_i - p_j) = 0, \Longleftrightarrow p_i = \left(\sum_{j \in N(i)} \Gamma_{ij}^{\Phi} p_j \right) / \left(\sum_{j \in N(i)} \Gamma_{ij}^{\Phi} \right)$$

for $i = 1, 2, \cdots, N$, then $p_1 = p_2 = \cdots = p_N$.

Assume this is not true, and let $c = \max\{p_i : i = 1, 2, \cdots, N\}$. Then, there must exists $\{a_\ell, a_k\} \in E$ such that $p_\ell = c$ and $p_k < c$, because the graph G is connected. This gives

$$c = p_\ell = \frac{\sum_{j \in N(\ell)} \Gamma_{\ell j}^{\Phi} p_j}{\sum_{j \in N(\ell)} \Gamma_{\ell j}^{\Phi}} = c + \frac{\sum_{j \in N(\ell)} \Gamma_{\ell j}^{\Phi}(p_j - c)}{\sum_{j \in N(\ell)} \Gamma_{\ell j}^{\Phi}} \leq c - \frac{\Gamma_{\ell k}^{\Phi}(c - p_k)}{\sum_{j \in N(\ell)} \Gamma_{\ell j}^{\Phi}} < c,$$

which is a contradiction. The proof is complete. □

Definition 2.2.2. By the above identification (2.2.22), we define an inner product on $T_{\boldsymbol{\rho}}\mathcal{M}$ by:

$$g^{\boldsymbol{\Phi}}_{\boldsymbol{\rho}}(\boldsymbol{\sigma}^1, \boldsymbol{\sigma}^2) \;=\; \sum_{i=1}^{N} p_i^1 \sigma_i^2 = \sum_{i=1}^{N} p_i^2 \sigma_i^1.$$

It is easy to check that this definition is equivalent to

$$g^{\boldsymbol{\Phi}}_{\boldsymbol{\rho}}(\boldsymbol{\sigma}^1, \boldsymbol{\sigma}^2) = \sum_{\{a_i, a_j\} \in E} \Lambda^{\Phi}_{ij}(p_i^1 - p_j^1)(p_i^2 - p_j^2), \tag{2.2.24}$$

where

$$\Lambda^{\Phi}_{ij}(\boldsymbol{\rho}) = \begin{cases} \rho_j & \text{if} \quad \{a_i, a_j\} \in E, \Phi_i < \Phi_j, \\ \frac{\rho_i - \rho_j}{\log \rho_i - \log \rho_j} & \text{if} \quad \{a_i, a_j\} \in E, \Phi_i = \Phi_j, \end{cases} \tag{2.2.25}$$

for $\boldsymbol{\sigma}^1 = (\sigma_i^1)_{i=1}^N, \boldsymbol{\sigma}^2 = (\sigma_i^2)_{i=1}^N \in T_\rho\mathcal{M}$, and $[(p_i^1)_{i=1}^N], [(p_i^2)_{i=1}^N] \in \mathcal{W}$ satisfying

$$\boldsymbol{\sigma}^1 \simeq [(p_i^1)_{i=1}^N] \text{ and } \boldsymbol{\sigma}^2 \simeq [(p_i^2)_{i=1}^N].$$

In particular,

$$g^{\boldsymbol{\Phi}}_{\boldsymbol{\rho}}(\boldsymbol{\sigma}, \boldsymbol{\sigma}) = \sum_{\{a_i, a_j\} \in E} \Lambda^{\Phi}_{ij}(\boldsymbol{\rho})(p_i - p_j)^2 \tag{2.2.26}$$

for $\boldsymbol{\sigma} \in T_\rho\mathcal{M}$, where $\boldsymbol{\sigma} \simeq [(p_i)_{i=1}^N]$. For any fixed $\boldsymbol{\Psi}$ and $\boldsymbol{\rho}$, the inner product $g^{\boldsymbol{\Psi}}$ is a well-defined inner product according to the following lemma.

Lemma 2.2.8. *For any smooth map $\boldsymbol{\Phi} : (\mathcal{M}, d) \to (\mathbb{R}^N, d)$ and $\boldsymbol{\rho} \in \mathcal{M}$,*

$$g^{\boldsymbol{\Phi}}_{\boldsymbol{\rho}}(\boldsymbol{\sigma}, \boldsymbol{\sigma}) > 0$$

for any tangent vector $\boldsymbol{\sigma} \neq 0$.

Proof. Let $\boldsymbol{\Phi} : (\mathcal{M}, d) \to (\mathbb{R}^N, d)$ be a smooth map. Given $\boldsymbol{\rho} \in \mathcal{M}$, the identification (2.2.22) can be expressed by

$$\boldsymbol{\sigma}^T = A\boldsymbol{p}^T$$

where $\boldsymbol{\sigma} = (\sigma_i)_{i=1}^N \in T_{\boldsymbol{\rho}}\mathcal{M}$ and $\boldsymbol{p} = (p_i)_{i=1}^N \in \mathbb{R}^N$. Since $\sum_{i=1}^N \sigma_i = 0$ for $(\sigma_i)_{i=1}^N \in T_{\boldsymbol{\rho}}\mathcal{M}$, by deleting the last row and last column of the matrix A we obtain a symmetric

diagonally dominant $(N-1)\times(N-1)$-matrix B. Thus, the identification (2.2.22) becomes

$$\boldsymbol{\sigma}_*^T = B\boldsymbol{p}_*^T$$

where $\boldsymbol{\sigma}_* = (\sigma_i)_{i=1}^{N-1}$ and $\boldsymbol{p}_* = (p_i - p_N)_{i=1}^{N-1}$.

The inner products are given as

$$g_{\boldsymbol{\rho}}^{\boldsymbol{\Phi}}(\boldsymbol{\sigma},\boldsymbol{\sigma}) = \boldsymbol{\sigma}\boldsymbol{p}^T = \boldsymbol{\sigma}_*\boldsymbol{p}_*^T = \boldsymbol{\sigma}_* B^{-1}\boldsymbol{\sigma}_*^T$$

for $\boldsymbol{\sigma} \in T_{\boldsymbol{\rho}}\mathcal{M}$. Clearly, $g_{\boldsymbol{\rho}}^{\boldsymbol{\Phi}}(\boldsymbol{\sigma},\boldsymbol{\sigma})$ for every $\boldsymbol{\sigma} \neq 0$. □

Since $\boldsymbol{\rho} \in \mathcal{M} \mapsto g_{\boldsymbol{\rho}}^{\boldsymbol{\Phi}}$ is measurable, using the inner product $g_{\boldsymbol{\rho}}^{\boldsymbol{\Phi}}$, we can define the distance between two points $\boldsymbol{\rho}^1$ and $\boldsymbol{\rho}^2$ in $\mathcal{M}$ by

$$d_{\boldsymbol{\Phi}}(\boldsymbol{\rho}^1,\boldsymbol{\rho}^2) = \inf_{\gamma} L(\gamma(t)) \tag{2.2.27}$$

where $\gamma : [0,1] \to \mathcal{M}$ ranges over all continuously differentiable curve with $\gamma(0) = \boldsymbol{\rho}^1$, $\gamma(1) = \boldsymbol{\rho}^2$. The arc length of γ is given by

$$L(\gamma(t)) = \int_0^1 \sqrt{g_{\gamma(t)}^{\boldsymbol{\Phi}}(\dot{\gamma}(t),\dot{\gamma}(t))}dt.$$

Although $g_{\boldsymbol{\rho}}^{\boldsymbol{\Phi}}$ may or may not be a smooth inner product with respect to $\boldsymbol{\rho}$, the length of any smooth curve is still well defined because $\boldsymbol{\rho} \in \mathcal{M} \mapsto g_{\boldsymbol{\rho}}^{\boldsymbol{\Phi}}$ is measurable. It is shown by Lemma 2.2.8 that $d_{\boldsymbol{\Phi}}$ is a metric on $\mathcal{M}$. Thus we have a metric space $(\mathcal{M}, d_{\boldsymbol{\Phi}})$. In particular, if $\boldsymbol{\Phi}$ is a constant map, then the metric $d_{\boldsymbol{\Phi}}$ is a Riemannian metric on $\mathcal{M}$ since the map $\boldsymbol{\rho} \in \mathcal{M} \mapsto g_{\boldsymbol{\rho}}^{\boldsymbol{\Phi}}$ is smooth. Hence, $(\mathcal{M}, d_{\boldsymbol{\Phi}})$ is a Riemannian manifold.

Remark 2.2.9. The identification (2.2.22) is motivated by a similar identification introduced by F. Otto in [52] for the case of a continuous state space. We replace the differential operator in [52] by a combination of finite differences because our state space V is discrete.

For the discrete Fokker-Planck equation (2.2.7), we let

$$\boldsymbol{\Phi}(\boldsymbol{\rho}) \equiv \boldsymbol{\Psi},$$

where $\boldsymbol{\rho} \in \mathcal{M}$. The identification (2.2.22)

$$\boldsymbol{\sigma} \simeq [(p_i)_{i=1}^N]$$

is given by

$$\sigma_i = \sum_{j \in N(i)} (p_i - p_j) \Gamma_{ij}^{\boldsymbol{\Psi}}(\boldsymbol{\rho}) \tag{2.2.28}$$

and the corresponding norm (2.2.26) is

$$g_{\boldsymbol{\rho}}^{\boldsymbol{\Psi}}(\boldsymbol{\sigma}, \boldsymbol{\sigma}) = \sum_{\{a_i, a_j\} \in E} \Lambda_{ij}^{\boldsymbol{\Psi}}(\boldsymbol{\rho})(p_i - p_j)^2, \tag{2.2.29}$$

for $\boldsymbol{\sigma} \in T_\rho \mathcal{M}$ with $\boldsymbol{\sigma} \simeq [(p_i)_{i=1}^N]$. Note that the map $\boldsymbol{\rho} \in \mathcal{M} \mapsto g_{\boldsymbol{\rho}}^{\boldsymbol{\Psi}}$ is smooth and the inner product $g^{\boldsymbol{\Psi}}$ generates a Riemannian metric space $(\mathcal{M}, d_{\boldsymbol{\Psi}})$, where $d_{\boldsymbol{\Psi}}$ comes from (2.2.27). Similar to the theory developed in [52], we will show that Fokker-Planck equation I (2.2.7) is the gradient flow of free energy on the Riemannian manifold $(\mathcal{M}, d_{\boldsymbol{\Psi}})$.

Theorem 2.2.10. *Given a graph $G = (V, E)$ satisfies condition (**G**), we have*

1. *The gradient flow of free energy F,*

$$F(\boldsymbol{\rho}) = \sum_{i=1}^N \Psi_i \rho_i + \beta \sum_{i=1}^N \rho_i \log \rho_i$$

on the Riemannian manifold $(\mathcal{M}, d_{\boldsymbol{\Psi}})$ of probability densities $\boldsymbol{\rho}$ on V is

$$\begin{aligned} \frac{d\rho_i}{dt} = & \sum_{j \in N(i), \Psi_j > \Psi_i} \left((\Psi_j + \beta \log \rho_j) - (\Psi_i + \beta \log \rho_i) \right) \rho_j \\ & + \sum_{j \in N(i), \Psi_j < \Psi_i} \left((\Psi_j + \beta \log \rho_j) - (\Psi_i + \beta \log \rho_i) \right) \rho_i \\ & + \sum_{j \in N(i), \Psi_j = \Psi_i} \beta(\rho_j - \rho_i) \end{aligned}$$

for $i = 1, 2, \cdots, N$, which is Fokker-Planck equation I (2.2.7).

Proof. Let $\beta \geq 0$ be fixed and the free energy functional F be defined on the space $\overline{\mathcal{M}}$:

$$F(\boldsymbol{\rho}) = \sum_{i=1}^{N} \Psi_i \rho_i + \beta \sum_{i=1}^{N} \rho_i \log \rho_i \tag{2.2.30}$$

where $\boldsymbol{\rho} = \{\rho_i\}_{i=1}^N \in \overline{\mathcal{M}}$. Thus, we have the gradient flow of F on $(\mathcal{M}, g^{\boldsymbol{\Psi}})$ given by,

$$\frac{d\boldsymbol{\rho}}{dt} = -\mathrm{grad}F(\boldsymbol{\rho}), \tag{2.2.31}$$

where $\mathrm{grad}F(\boldsymbol{\rho})$ is in the tangent space $T_{\boldsymbol{\rho}}\mathcal{M}$.

If the differential of F, which is in the cotangent space, is denoted by $\mathrm{diff}F$, then (2.2.31) can be expressed as

$$g^{\boldsymbol{\Psi}}_{\boldsymbol{\rho}}\left(\frac{d\boldsymbol{\rho}}{dt}, \boldsymbol{\sigma}\right) = -\mathrm{diff}F(\boldsymbol{\rho}) \cdot \boldsymbol{\sigma} \qquad \forall \boldsymbol{\sigma} \in T_{\boldsymbol{\rho}}\mathcal{M}. \tag{2.2.32}$$

It is clear that

$$\mathrm{diff}F((\rho_i)_{i=1}^N) = (\Phi_i + \beta(1 + \log \rho_i))_{i=1}^N \tag{2.2.33}$$

for $(\rho_i)_{i=1}^N \in \mathcal{M}$. By (2.2.32) and the identification (2.2.28), we are able to obtain the explicit expression of the vector field on $\mathcal{M}$.

We know that the gradient flow of free energy F on $(\mathcal{M}, d_{\boldsymbol{\Psi}})$ is given by equation (2.2.32),

$$g^{\boldsymbol{\Psi}}_{\boldsymbol{\rho}}(\frac{d\boldsymbol{\rho}}{dt}, \boldsymbol{\sigma}) = -\mathrm{diff}F(\boldsymbol{\rho}) \cdot \boldsymbol{\sigma} \quad \forall \boldsymbol{\sigma} \in T_{\boldsymbol{\rho}}\mathcal{M}.$$

The left hand side of equation (2.2.32) is

$$g^{\boldsymbol{\Psi}}_{\boldsymbol{\rho}}(\frac{d\boldsymbol{\rho}}{dt}, \boldsymbol{\sigma}) = \sum_{i=1}^{N} \frac{d\rho_i}{dt} p_i \tag{2.2.34}$$

where $\boldsymbol{\sigma} = (\sigma_i)_{i=1}^N \simeq [(p_i)_{i=1}^N]$. By (2.2.33), the right hand side of equation (2.2.32) is

$$-\mathrm{diff}F(\rho) \cdot \boldsymbol{\sigma} = -\sum_{i=1}^{N} (\Psi_i + \beta(1 + \log \rho_i))\sigma_i. \tag{2.2.35}$$

Using the identification (2.2.28), we have

$$\begin{aligned}
&\sum_{i=1}^{N}(\Psi_i+\beta(1+\log\rho_i))\sigma_i=\sum_{i=1}^{N}(\Psi_i+\beta\log\rho_i)\sigma_i\\
=&\sum_{i=1}^{N}(\Psi_i+\beta\log\rho_i)(\sum_{j\in N(i)}\Gamma_{ij}^{\boldsymbol{\Psi}}(\boldsymbol{\rho})(p_i-p_j))\\
=&\sum_{\{a_i,a_j\}\in E,\Psi_i<\Psi_j}\{(\Psi_i-\Psi_j)+\beta(\log\rho_i-\log\rho_j)\}\rho_j(p_i-p_j)\\
&+\beta\sum_{\{a_i,a_j\}\in E,\Psi_i=\Psi_j}(\rho_i-\rho_j)(p_i-p_j)\\
=&\sum_{i=1}^{N}\Bigg\{\sum_{j\in N(i),\Psi_j>\Psi_i}((\Psi_i-\Psi_j)\rho_j+\beta(\log\rho_i-\log\rho_j)\rho_j)\\
&+\sum_{j\in N(i),\Psi_j<\Psi_i}((\Psi_i-\Psi_j)\rho_i+\beta(\log\rho_i-\log\rho_j)\rho_i)\\
&+\beta\sum_{j\in N(i),\Psi_j=\Psi_i}(\rho_i-\rho_j)\Bigg\}p_i
\end{aligned}$$

Combining this equation with equations (2.2.32), (2.2.34) and (2.2.35), we have

$$\begin{aligned}
\sum_{i=1}^{N}\frac{d\rho_i}{dt}p_i=\sum_{i=1}^{N}\Bigg\{&\sum_{j\in N(i),\Psi_j>\Psi_i}((\Psi_j-\Psi_i)\rho_j+\beta(\log\rho_j-\log\rho_i)\rho_j)\\
&+\sum_{j\in N(i),\Psi_j<\Psi_i}((\Psi_j-\Psi_i)\rho_i+\beta(\log\rho_j-\log\rho_i)\rho_i)\\
&+\beta\sum_{j\in N(i),\Psi_j=\Psi_i}(\rho_j-\rho_i)\Bigg\}p_i.
\end{aligned}$$

Since the above equality stands for any $(p_i)_{i=1}^N\in\mathbb{R}^N$, we obtain Fokker-Flanck equation (2.2.7) (2.2.7). This completes the proof. □

In the end of this subsection, we will introduce one proposition about the geodesic equation on the Riemannian space $(\mathcal{M},d_{\boldsymbol{\Psi}})$, which is exactly a discretization of geodesic equation given in [45].

Proposition 2.2.11. *The geodesic of metric $d_{\mathbf{\Psi}}$ is given by the following equation*

$$\frac{\mathrm{d}p_i}{\mathrm{d}t} = -\frac{1}{2}\sum_{j\in N(i),\Psi_i>\Psi_j}(p_i-p_j)^2 \tag{2.2.36}$$

$$\frac{\mathrm{d}\rho_i}{\mathrm{d}t} = \sum_{j\in N(i),\Psi_i>\Psi_j}(p_i-p_j)\rho_i + \sum_{j\in N(i),\Psi_i<\Psi_j}(p_i-p_j)\rho_j \tag{2.2.37}$$

Proof It is well known that geodesic is the minimum of distance as well as the minimum of the energy functional

$$E(\gamma) = \frac{1}{2}\int g(\dot{\gamma},\dot{\gamma})\mathrm{d}t$$

This is obvious because geodesic has constant speed, the Holder inequality becomes an equality.

So geodesic is the minimal integral curve of the following Lagrangian

$$L(\vec{\rho},\vec{\sigma}) = \vec{\sigma}^T L(G,\vec{\rho})\vec{\sigma}$$

After Legendre transformation, we can obtain the Hamiltonian equation (2.2.36). □

Remark 2.2.12. In [45], J.Lott gave the geodesic equation on 2-Wasserstein space over $\mathbb{R}^n$:

$$\begin{aligned}\frac{\mathrm{d}\phi}{\mathrm{d}t} &= -\frac{1}{2}|\nabla\phi|^2 \\ \frac{\mathrm{d}\rho}{\mathrm{d}t} &= -\nabla\cdot(\rho\nabla\phi)\end{aligned} \tag{2.2.38}$$

Clearly equation (2.2.36) is exact a discretization of the previous equation (2.2.38). That's another reason why we claim that our metric $d_{\mathbf{\Psi}}$ has certain similarities as the 2-Wasserstein distance on the space of probability measures on $\mathbb{R}^n$.

2.2.4 The exponential convergence of discrete Fokker-Planck equation

We will introduce the results on the exponential convergence of equation (2.2.7) in this subsection. Let $G = (V, E)$ be a graph that satisfies condition (**G**), and μ a

measure supported on V. For any map $f : V \to \mathbb{R}$, recall the $L^2(\mu)$-norm of f with respect to μ, denoted by $||f||_{2,\mu}$, and given by:

$$||f||_{2,\mu}^2 := \sum_{i \in V} (f(i))^2 \mu_i \, .$$

Let ν be a measure on V, then we measure the distance between (the density of) ν and μ as usual using:

$$||\frac{\nu}{\mu} - 1||_{2,\mu}^2 = \sum_{i=1}^{N} (\frac{\nu_i}{\mu_i} - 1)^2 \mu_i \, .$$

The following is our first main result of this subsection.

Theorem 2.2.13. *Let $G = (V, E)$ be a graph that satisfies condition (**G**). If $\boldsymbol{\rho}(t) = (\rho_i(t))_{i=1}^N : [0, \infty) \to \mathcal{M}$ is the solution of the Fokker-Planck equation I (2.2.7), with the initial value $\boldsymbol{\rho}^o = (\rho_i^o)_{i=1}^N \in \mathcal{M}$, then there exists a constant $C = C(\boldsymbol{\rho}^o; G, \Psi, \beta) > 0$ such that*

$$||\frac{\boldsymbol{\rho}(t)}{\boldsymbol{\rho}^*} - 1||_{2,\rho^*}^2 = ||\frac{\boldsymbol{\rho}^o}{\boldsymbol{\rho}^*} - 1||_{2,\rho^*}^2 e^{-Ct} \, , \tag{2.2.39}$$

where $\boldsymbol{\rho}^* = (\rho_i^*)_{i=1}^N$ is the Gibbs distribution given by (2.2.6). In particular, $\boldsymbol{\rho}(t)$ exponentially converges to global equilibrium: the Gibbs distribution $\boldsymbol{\rho}^*$ under the Euclidean metric of $\mathbb{R}^N$ as $t \to \infty$.

Proof. Given initial value $\boldsymbol{\rho}^o = (\rho_i^o)_{i=1}^N \in \mathcal{M}$. Let $\boldsymbol{\rho}(t) = (\rho_i(t))_{i=1}^N : [0, \infty) \to \mathcal{M}$ be the solution of Fokker-Planck equation I (2.2.7) with initial value $\boldsymbol{\rho}^o \in \mathcal{M}$. For $t \geq 0$, we define

$$L(t) = ||\frac{\boldsymbol{\rho}(t)}{\boldsymbol{\rho}^*} - 1||_{2,\rho^*}^2 = \sum_{i=1}^{N} \frac{(\rho_i(t) - \rho_i^*)^2}{\rho_i^*},$$

where $\boldsymbol{\rho}^* = (\rho_i^*)_{i=1}^N$ is the Gibbs distribution given by (2.2.6). Now for $t > 0$ by (2.2.7)

we have

$$\frac{dL(t)}{dt} = \sum_{i=1}^{N} \frac{2(\rho_i(t) - \rho_i^*)}{\rho_i^*} \frac{d\rho_i(t)}{dt}$$

$$= \sum_{i=1}^{N} \frac{2(\rho_i(t) - \rho_i^*)}{\rho_i^*} (\sum_{j \in N(i), \Psi_j > \Psi_i} ((\Psi_j + \beta \log \rho_j(t)) - (\Psi_i + \beta \log \rho_i(t))) \rho_j(t)$$

$$+ \sum_{j \in N(i), \Psi_j < \Psi_i} ((\Psi_j + \beta \log \rho_j(t)) - (\Psi_i + \beta \log \rho_i(t))) \rho_i(t)$$

$$+ \sum_{j \in N(i), \Psi_j = \Psi_i} \beta(\rho_j(t) - \rho_i(t))).$$

Note that $\Psi_j - \Psi_i = -\beta \log \rho_j^* + \beta \log \rho_i^*$ for $i, j \in \{1, 2, \cdots, N\}$ and $\rho_j^* = \rho_i^*$ when $\Psi_j = \Psi_i$. Combing this with the above equality, we have

$$\frac{dL(t)}{dt}$$

$$= \sum_{i=1}^{N} \frac{2(\rho_i(t) - \rho_i^*)}{\rho_i^*} (\sum_{j \in N(i), \Psi_j > \Psi_i} ((-\beta \log \rho_j^* + \beta \log \rho_j(t)) - ((-\beta \log \rho_i^* + \beta \log \rho_i(t))) \rho_j(t)$$

$$+ \sum_{j \in N(i), \Psi_j < \Psi_i} ((-\beta \log \rho_j^* + \beta \log \rho_j(t)) - ((-\beta \log \rho_i^* + \beta \log \rho_i(t))) \rho_i(t)$$

$$+ \sum_{j \in N(i), \Psi_j = \Psi_i} \beta(\frac{\rho_j(t)}{\rho_j^*} - \frac{\rho_i(t)}{\rho_i^*}) \frac{\rho_i^* + \rho_j^*}{2})$$

$$= \sum_{i=1}^{N} \frac{2(\rho_i(t) - \rho_i^*)}{\rho_i^*} (\sum_{j \in N(i), \Psi_j > \Psi_i} \beta(\log \frac{\rho_j(t)}{\rho_j^*} - \log \frac{\rho_i(t)}{\rho_i^*}) \rho_j(t)$$

$$+ \sum_{j \in N(i), \Psi_j < \Psi_i} \beta(\log \frac{\rho_j(t)}{\rho_j^*} - \log \frac{\rho_i(t)}{\rho_i^*}) \rho_i(t) + \sum_{j \in N(i), \Psi_j = \Psi_i} \beta(\frac{\rho_j(t)}{\rho_j^*} - \frac{\rho_i(t)}{\rho_i^*}) \frac{\rho_i^* + \rho_j^*}{2})$$

We denote $\eta_i(t)$ as $\frac{\rho_i(t) - \rho_i^*}{\rho_i^*}$ for $t \geq 0$. Then the above equation can be written as

$$\frac{dL(t)}{dt} = \sum_{i=1}^{N} 2\eta_i(t) (\sum_{j \in N(i), \Psi_j > \Psi_i} \beta(\log(1 + \eta_j(t)) - \log(1 + \eta_i(t))) \rho_j(t)$$

$$+ \sum_{j \in N(i), \Psi_j < \Psi_i} \beta(\log(1 + \eta_j(t)) - \log(1 + \eta_i(t))) \rho_i(t)$$

$$+ \sum_{j \in N(i), \Psi_j = \Psi_i} \beta(\eta_j(t) - \eta_i(t)) \frac{\rho_i^* + \rho_j^*}{2}).$$

For edge $\{a_i, a_j\} \in E$ with $\Psi_j > \Psi_i$, $2\eta_i\beta(\log(1+\eta_j) - \log(1+\eta_i))\rho_j$ will be in the above sum at vertex a_i; $2\eta_j\beta(\log(1+\eta_i) - \log(1+\eta_j))\rho_j$ will be in the above sum at vertex a_j. So we can write the above equality as

$$\begin{aligned}\frac{dL(t)}{dt} = &- \sum_{\{a_i,a_j\}\in E, \Psi_j > \Psi_i} 2\beta(\log(1+\eta_j(t)) - \log(1+\eta_i(t)))(\eta_j(t) - \eta_i(t))\rho_j(t) \\ &- \sum_{\{a_i,a_j\}\in E, \Psi_j = \Psi_i} 2\beta(\eta_j(t) - \eta_i(t))^2 \frac{\rho_i^* + \rho_j^*}{2}. \end{aligned} \tag{2.2.40}$$

Using (2.2.40) and the following inequality

$$min\{\frac{1}{a}, \frac{1}{b}\} \leq \frac{\log a - \log b}{a - b} \leq max\{\frac{1}{a}, \frac{1}{b}\}$$

for $a > 0, b > 0$ with $a \neq b$, we have

$$\begin{aligned}\frac{dL(t)}{dt} \leq &- \sum_{\{a_i,a_j\}\in E, \Psi_j > \Psi_i} 2\beta(\eta_j(t) - \eta_i(t))^2 \min\{\frac{1}{1+\eta_i(t)}, \frac{1}{1+\eta_j(t)}\}\rho_j(t) \\ &- \sum_{\{a_i,a_j\}\in E, \Psi_j = \Psi_i} 2\beta(\eta_j(t) - \eta_i(t))^2 \frac{\rho_i^* + \rho_j^*}{2} \\ = &- \sum_{\{a_i,a_j\}\in E, \Psi_j > \Psi_i} 2\beta(\eta_j(t) - \eta_i(t))^2 \min\{\frac{\rho_i^*}{\rho_i(t)}, \frac{\rho_j^*}{\rho_j(t)}\}\rho_j(t) \\ &- \sum_{\{a_i,a_j\}\in E, \Psi_j = \Psi_i} 2\beta(\eta_j(t) - \eta_i(t))^2 \frac{\rho_i^* + \rho_j^*}{2}. \end{aligned} \tag{2.2.41}$$

For $\mathrm{b} = (b_i)_{i=1}^N \in \mathbb{R}^N$, we let

$$m(\mathrm{b}) = \min\{b_i : 1 \leq i \leq N\} \text{ and } M(\mathrm{b}) = \max\{b_i : 1 \leq i \leq N\}.$$

Put $A(t) = 2\beta\frac{m(\rho(t))}{M(\rho(t))}m(\rho^*)$ for $t \geq 0$. Then $A(t) > 0$ and by (2.2.41) we have

$$\frac{dL(t)}{dt} \leq -A(t)(\sum_{\{a_i,a_j\}\in E} (\eta_j(t) - \eta_i(t))^2). \tag{2.2.42}$$

Next we prove the following claim, relating the above right hand side to the spectral gap of the Laplacian matrix $\mathcal{L}(G)$ of graph G:

$$\mathcal{L}(G) := D - A\,,$$

where D is a diagonal matrix with $d_{ii} = \deg(a_i)$ (number of edges at a_i), and A is the adjacency matrix ($A_{ij} = 1$ if and only if $a_i, a_j \in E$). It is well known that $\mathcal{L}(G)$ has one 0 eigenvalue and $N-1$ positive eigenvalues if G is a connected simple graph.

Claim 1:

$$\sum_{\{a_i,a_j\}\in E} (\eta_j(t) - \eta_i(t))^2 \geq \frac{\lambda_2}{M(\boldsymbol{\rho}^*)} L(t)\,,$$

where $M(\boldsymbol{\rho}^*)$ is the maximal entry of $\boldsymbol{\rho}^*$ which is at most 1, and λ_2 is the second smallest eigenvalue of the Laplacian matrix of G, or the spectral gap of G.

Proof of Claim 1. Indeed we have

$$\sum_{\{a_i,a_j\}\in E} (\eta_j(t) - \eta_i(t))^2 = \eta^T \mathcal{L}(G)\eta \geq \lambda_2 ||\eta||^2$$

and

$$L(t) = \sum_{i=1}^{N} \rho_i^* \eta_i^2(t) \leq M(\boldsymbol{\rho}^*)||\eta||^2\,.$$

Hence

$$\sum_{\{a_i,a_j\}\in E} (\eta_j(t) - \eta_i(t))^2 \geq \frac{\lambda_2}{M(\boldsymbol{\rho}^*)} L(t)\,.$$

□

Remark 2.2.14. In the literature, there are various standard ways to bound the spectral gap of a graph; for example, see [5], for the bound,

$$\lambda_2 \geq d_{max} - \sqrt{d_{max}^2 - d_{min}^2}\,,$$

where d_{max} and d_{min} are the maximum and minimum degrees of vertices in G; similarly see [46], for

$$\lambda_2 \geq \frac{2N}{2 + N(N-1)d - 2Md}\,,$$

where N is the number of vertices, M is the number of edges, and d is the diameter of G; or [67] for the bound,

$$\lambda_2 \geq 2(1-\cos(\frac{\pi}{N}))\,.$$

We define

$$B = \{\boldsymbol{q} = (q_i)_{i=1}^N \in \mathcal{M} : \sum_{r=1}^{\ell} q_{i_r} \leq 1-\epsilon_\ell \text{ where } \ell \in \{1,\cdots,N-1\},$$
$$1 \leq i_1 < \cdots < i_\ell \leq N\}.$$

Then B is a compact subset of $\mathcal{M}$ with respect to the Euclidean metric,

$$\text{int}(B) = \{\boldsymbol{q} = (q_i)_{i=1}^N \in \mathcal{M} : \sum_{r=1}^{\ell} q_{i_r} < 1-\epsilon_\ell, \text{ where } \ell \in \{1,\cdots,N-1\},$$
$$1 \leq i_1 < \cdots < i_\ell \leq N\}.$$

and $\boldsymbol{\rho}^0 \in \text{int}(B)$. We have

Claim 2: $\rho(t) \in B$ for all $t \geq 0$.

Proof of Claim 2. That is the same claim as in Theorem 2.2.3. □

Using Claim 1 and (2.2.42), we have

$$\frac{dL(t)}{dt} \leq -\frac{\lambda_2}{M(\boldsymbol{\rho}^*)} A(t)\ L(t). \tag{2.2.43}$$

We define $C = 2\beta\lambda_2\ \frac{m(\boldsymbol{\rho}^*)}{M(\boldsymbol{\rho}^*)}\ \frac{1-\epsilon_{L-1}}{\epsilon_1}$; clearly $C > 0$ is dependent on $\boldsymbol{\rho}^o$ as well as on G, Ψ, β, that is $C = C(\boldsymbol{\rho}^o; G, \Psi, \beta)$. By the definition of B and Claim 2, we have

$$\begin{aligned} A(t) &= 2\beta \frac{m(\boldsymbol{\rho}(t))}{M(\boldsymbol{\rho}(t))} m(\boldsymbol{\rho}^*) \geq 2\beta m(\boldsymbol{\rho}^*) \min\{\frac{m(\boldsymbol{q})}{M(\boldsymbol{q})} : \boldsymbol{q} \in B\} \\ &\geq 2\beta m(\boldsymbol{\rho}^*) \frac{1-\epsilon_{L-1}}{\epsilon_1} \\ &= \frac{M(\boldsymbol{\rho}^*)}{\lambda_2} C \end{aligned}$$

for $t \geq 0$. Combing this with (2.2.43), we get $\frac{dL(t)}{dt} \leq -CL(t)$ for $t > 0$. This implies that $L(t) \leq L(0)e^{-Ct}$ for $t \geq 0$. Since $L(0) = ||\frac{\boldsymbol{\rho}(0)}{\boldsymbol{\rho}^*} - 1||^2$, we have (2.2.39), completing the proof of the theorem. □

Remark 2.2.15. Given a graph $G = (V, E)$ that satisfies condition (**G**) and a constant $\beta > 0$, the positive constant $C = C(\boldsymbol{\rho}^o; G, \Psi, \beta)$ appearing in Theorem 2.2.13 is dependent on the initial value $\boldsymbol{\rho}^o \in \mathcal{M}$. In fact $C(\boldsymbol{\rho}^o; G, \Psi, \beta) \to 0$, when the initial distribution $\boldsymbol{\rho}^o$ converges to the boundary of $\mathcal{M}$.

2.2.5 Example: Effect of injected noise

An illustrative example will be demonstrated in this subsection. Recall that small injected noises in an ODE system can remove the singularity and non-uniqueness of the invariant measure. We want to do the same thing for networks in discrete setting. The discrete Fokker-Planck equation provides us an approach to inject noise into Markov chain network, which can remove this non-uniqueness of invariant measure. If the Markov network is reducible, then the irreducible sets form a partially ordered set. One can find that the invariant measure of (2.2.7) concentrates on the bottom of partial ordered set. This phenomenon can be seen as a mimic of classical large deviation theory.

Recall the knowledge of continuous-time Markov chain. For a Markov chain network on X $= \{a_1, \cdots, a_n\}$, let ω_{ij} be the transition rate from i to j. Then the Kolmogorov equation is:

$$\frac{\mathrm{d}\rho_i}{\mathrm{d}t} = -\sum_{j,\omega_{ij}\neq 0} \omega_{ij}\rho_i + \sum_{j,\omega_{ji}\neq 0} \omega_{ji}\rho_j \tag{2.2.44}$$

where $\{\rho_i(t)\}_{i=1}^n$ is the probability distribution on X at time t. Follow the idea of discrete Fokker-Planck equation, we add log-diffusion term to equation (2.2.44):

$$\frac{\mathrm{d}\rho_i}{\mathrm{d}t} = -\sum_{j,\omega_{ij}\neq 0} (\omega_{ij} + \epsilon \log \rho_j - \epsilon \log \rho_i)\rho_i + \sum_{j,\omega_{ji}\neq 0} (\omega_{ji} + \epsilon \log \rho_j - \epsilon \log \rho_i)\rho_j \tag{2.2.45}$$

Then we consider the following Markov chain in figure 1 as one example. The numbers on edges demonstrates the transition rate. This markov chain is reducible so there exists infinite many invariant measures. Further, there are two irreducible components, $A = \{a, b, c\}$ and $B = \{f, g, h\}$. If we add some random perturbation

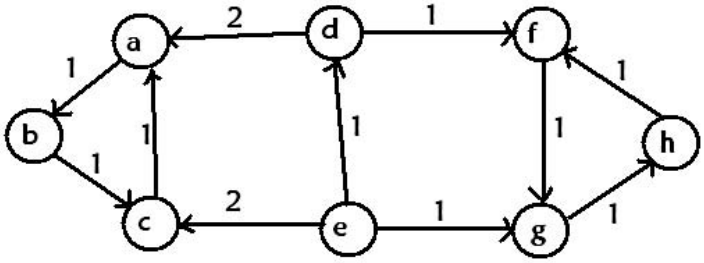

Figure 1: Markov Chain

with strength β to this system, and consider equation (2.2.45) as the time evolution of the probability distributions, then this Markov chain becomes irreducible, while the invariant measure is unique. We can compute the invariant measure μ_ϵ numerically, and numerically experiment suggests that

$$\lim_{\epsilon \to 0} \epsilon \log \frac{\mu_\epsilon(B)}{\mu_\epsilon(A)} = -1$$

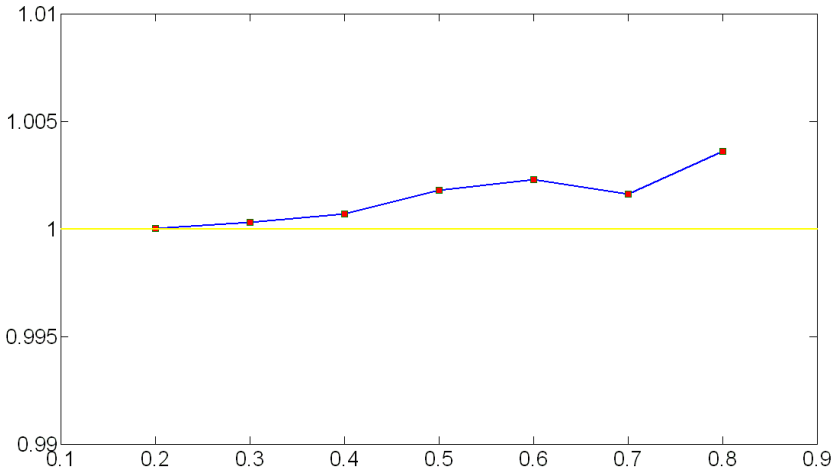

Figure 2: The y-axis is the value of $-\epsilon \log \frac{\mu_\epsilon(B)}{\mu_\epsilon(A)}$, the x-axis is the value of ϵ

2.3 Extension 2 : Fokker-Planck equations of iterative mapping

In this section, the attention will be paid to the time-discrete dynamical system.

Time-discrete dynamical system is an very important and very active research field. Some biological networks are also modeled by time-discrete dynamical systems. The stochastic perturbation theory of time-discrete dynamical systems has already been well-known (See [41] for more detailed reference). Roughly speaking, for stochastic perturbations in the form of Markovian kernel, there has been a large deviation theory that is similar as the stochastic ODE systems.

Although the choices of Markovian kernel can be infinite, one realization of the Markovian kernel is particularly interesting. The Fokker-Planck-type equation of this Markovian kernel can be given explicitly. In addition, this Markovian kernel behaves like Brownian motion perturbation in the vicinity of attractors. This realization of stochastic perturbation of time-discrete dynamical systems was proposed by E.C.Zeeman in article [75]. He use this Markovian kernel to characterize the stability of dynamical system.

We outline his approach as follows. Let X be a smooth compact manifold, $F : X \to X$ be the diffeomorphism, and ϵ be the magnitude of the noise. A smooth Markovian kernel $K_\epsilon(x, y)$ is introduced in [75] to "polish" the probability density function after each iterations of the mapping F. Let

$$K_\epsilon(x, y) = k(y)e^{-d(x,y)/2\epsilon},$$

where $d(x, y)$ is the distance between x and y. The constant $k(y)$ plays the role of a normalizer, such that for each $y \in X$

$$\int K_\epsilon(x, y)\mathrm{d}x = 1\,.$$

In [75], dynamical systems on smooth compact manifolds were considered. A self mapping can be defined on the space of continuous functions over X (denoted by $C(X)$.

We denote

$$S : C(X)^* \to C(X)$$

by

$$S \circ \mu(x) = \mu(K_\epsilon(x, \cdot)) = \int K_\epsilon(x, y)\mu(\mathrm{d}y)\,.$$

Zeeman's approach can be understood easily by recalling the heat equation. Suppose initially we have probability density function $P^n(x)$ after the n-th iteration. Let the diffeomorphism F act on $P^n(x)$ to obtain the push-forward function $P^{n+1/2}(x)$:

$$P^{n+1/2}(x) = F_x^{-1}(F^{-1}(x))P^n(F^{-1}(x))\,.$$

Then push $P^{n+1/2}(x)$ forward by mapping S. Note that map S is nothing but a heat kernel. This is equivalent to the solution at $t = 1$ of the following heat equation:

$$\begin{aligned} \frac{\partial Q}{\partial t} &= \frac{\epsilon}{2}\Delta Q \\ Q(0, x) &= P^{n+1/2}(x)\,. \end{aligned}$$

Denote $P^{n+1}(x)$ by

$$P^{n+1}(x) = Q(1, x)\,. \tag{2.3.1}$$

We obtain the probability density function at the $n + 1$-th iteration.

Essentially, this approach introduces a white noise perturbation after each step. Equivalently, this random perturbation can be written as

$$\bar{F} = F \circ S\,,$$

where S is a noisy map obtained by

$$S(x) = x + \epsilon W_1\,.$$

The random W_1 above is a standard Brownian motion function at time 1. In the other word it is a random variable with standard normal distribution. It is proved in [75] that the map $\bar{F}$ admits a unique invariant probability measure, which is also globally stable.

Similar to the ODE system, the invariant measure of F can be both singular and not unique, while the invariant measure of $\bar{F}$ is nevertheless unique and smooth. Our

definitions of systematic measures rely on the regularity of the invariant measure. Again, the injected noise helps our next step analysis.

The following illustrative example reveals some evidence that the previous mentioned realization of random perturbation behaves similar as the white noise perturbation.

Example 2.3.1. *Consider a contraction mapping with constant rate*

$$X_{n+1} = aX_n \tag{2.3.2}$$

for some $a < 0$. *The orbit of* (2.3.2) *has exponential decay rate to the origin. It behaves like the linear equation*

$$X' = -\mu X \tag{2.3.3}$$

for $\mu > 0$.

It is well known that the white noise perturbation of equation (2.3.3) *is the Ornstein Uhlenbeck process whose invariant measure is a normal distribution. It can also be seen as the gradient flow of potential function* $U = \mu x^2/2$. *Using the same approach, the invariant measure of equation* (2.3.2) *can be found. It is also normally distributed:*

$$\frac{\sqrt{1-a^2}}{2\pi\epsilon^2} e^{\frac{(a^2-1)x^2}{2\epsilon^2}}.$$

Therefore, in the sense of invariant measure, the constant contraction mapping with Zeeman's random perturbation behaves similar as the gradient flow with white noise perturbation.

CHAPTER III

QUANTIFYING SYSTEMATIC MEASURES OF BIOLOGICAL NETWORKS

The emphasis in this chapter will be paid on the quantification of systematic measures of biological networks. This quantification relies on our work in stochastic dynamical systems. We measure the systematic measure of complex biological networks by activating the connections with external noises. Some sections in this chapter come from the published paper [44].

3.1 Review of biochemical reaction network theory

We give an overview of biochemical reaction networks theory in this section as the start of the second part of this dissertation. The modern mathematical theory of biochemical reaction networks was originally developed by Martin Feinberg several decades ago [23]. Implied by his theory, many basic properties of biochemical reaction network can be obtained without solving the reaction equation explicitly, or even without knowing the exact reaction rates. The classical theory introduced in [24, 25] and some modern development in [3, 60] will be covered in three steps. First we characterize biochemical reaction networks in a mathematical way. Then we introduce some notations such as stoichiometric subspace, linkage class and deficiency. Lastly we review the deficiency zero theorem and deficiency one theorem.

A *biochemical reaction network* is a directed graph $G = (V, E) := (\mathcal{C}, \mathcal{R})$ associated with species set $\mathcal{S}$. The set $\mathcal{C} = \{c_1, \cdots, c_n\}$ indicates the complex and $\mathcal{R}$ represents the reaction relation. A biochemical reaction network is also called a reaction diagram. In this section, we denote the species by upper case letters $X_1, X_2, \cdots, X_m$ and the concentration of each species by lower case letters $x_1, x_2, \cdots, x_m$. Further, we always assume $\mathcal{S}$ is a finite set. Let m be the number of species. It is easy to see that each vector of concentration can be written as a vector in the set $\mathbb{R}^m_{\geq 0} := \{(x_1, \cdots, x_m) | x_i \geq 0, 1 \leq i \leq m\}$.

The graph $G = (\mathcal{C}, \mathcal{R})$ represents the topological structure of the biochemical reaction network. The vertices set of G represents the set of complex $\mathcal{C}$. A complex in $\mathcal{C}$ is a linear combination of species in $\mathcal{S}$ with positive integer coefficients. For example, let $\mathcal{S} = \{X_1, X_2, X_3\}$. Then $3X_1, X_1 + 2X_2, X_2, X_1 + X_2 + X_3$ are all complexes. The reaction relation $\mathcal{R}$ is the set of directed edges in G which consists of ordered pairs of complexes $\{c_i, c_j\}$. Each edge represents a reaction in the biochemical

reaction network G, such as

$$3X_1 + X_2 \xrightarrow{k} X_1 + X_2 + X_3\,.$$

Every reaction in $\mathcal{R}$ is associated with a reaction rate function, which is both the consuming rate of the left complex and the producing rate of the right complex. In most cases, we assume the biochemical network is a *mass-action system*. Mass-action system means that the reaction rates are in proportion to the product of concentrations of reactant species on the left hand of the arrows. For example, the reaction rate of the above reaction is ka^3b, where k is some positive constant called rate constant.

Reactions in a biochemical reaction network can be written explicitly. A biochemical reaction network $G = (\mathcal{C}, \mathcal{R})$ with species set $\mathcal{S}$ includes the following set of chemical reactions:

$$\begin{aligned} \alpha_1^1 X_1 + \cdots + \alpha_m^1 X_m \quad &\xrightarrow{k_1} \quad \beta_1^1 X_1 + \cdots + \beta_m^1 X_m \\ &\cdots\cdots \\ \alpha_1^R X_1 + \cdots + \alpha_m^R X_m \quad &\xrightarrow{k_R} \quad \beta_1^R X_1 + \cdots + \beta_m^R X_m\,. \end{aligned} \tag{3.1.1}$$

The above coefficients $\{\alpha_k^r\}$and $\{\beta_k^r\}$, $r = 1, \cdots, R$ $k = 1, \cdots, m$ are non-negative integers that represents the coefficient of species X_k in the reactant complexes of the r-th equation. As mentioned before, we only consider the mass-action system in this thesis. This means that the corresponding differential equations of network (3.1.1) can be written as

$$\frac{\mathrm{d}X_i}{\mathrm{d}t} = \sum_{r=1}^{R} k_r(\beta_i^r - \alpha_i^r) X_1^{\alpha_1^r} \cdots X_m^{\alpha_M^r}\,, \tag{3.1.2}$$

for each $1 \le i \le m$. We want to remark that although the dynamics of ODE system can be complicated, system (3.1.2) usually has simple and nice dynamics. The modern chemical reaction network theory focuses on the properties of mass-action equation (3.1.2) when the rate constant $\{k_r\}$ are not given explicitly. In another word, it is the

topology of chemical reaction network that determines some properties of mass-action system (3.1.2).

Some more notations are required before reviewing the main results. Note that the concentractions of a biochemical reaction network with species size m are vectors in $\mathbb{R}^m_{\geq 0}$. Let $\{\mathbf{e}_1, \cdots, \mathbf{e}_m\}$ be the standard basis of $\mathbb{R}^m$, in which

$$\mathbf{e}_i = [0, \cdots, 0, \overset{i\text{th}}{1}, 0, \cdots, 0] .$$

Let $c = \alpha_1 X_1 + \cdots + \alpha_m X_m$ be a complex. We denote vector $\alpha_1 \mathbf{e}_1 + \cdots + \mathbf{e}_m$ as the *complex vector* of c.

Complex vectors span certain subspaces. Let $\{c_i, c_j\}$ be an edge in $\mathcal{R}$, v_i and v_j be the complex vectors of c_i and c_j respectively. The vector $\mathbf{r}_{ij} = v_j - v_i$ is called the reaction vector of reaction r_{ij}. Denote the spanning set by

$$S = \text{span}\{\mathbf{r}_{ij} | \{c_i, c_j\} \in \mathcal{R}\} .$$

This subspace S is called *stoichiometric subspace*. It is trivial to show that the solution of every mass-action equation lies on the set $S + \mathbf{a}$ for some vector $\mathbf{a} \in \mathbb{R}^m$. Formally, the set $S + \mathbf{a}$ is called *stoichiometric compatibility class*.

The deficiency can be defined by combining the concepts above. Denote the underlying undirected graph of G by G'. The connection components of G' is called *linkage class*. Let c be the size of complex set, l be the number of linkage classes and r be the rank of stoichiometric subspace S. It is showed in [24] that $c - l - r$ is nonnegative. The number $c - l - r$ is called the *deficiency* of the biochemical reaction network.

Take the following chemical reaction network for an example. In this example, the species set $\mathcal{S} = \{A, B, C, D, E, F\}$, complex set $\mathcal{C} = \{3A + B, D, C + E, A + C, E + B, B + C, E + F\}$. There are two linkage classes $\{3A + B, D, C + E, A + C, E + B\}$ and $\{B + C, E + F\}$. Further, it is easy to verify that the rank of stoichiometric subspace is 5. This means the deficiency is $7 - 2 - 5 = 0$.

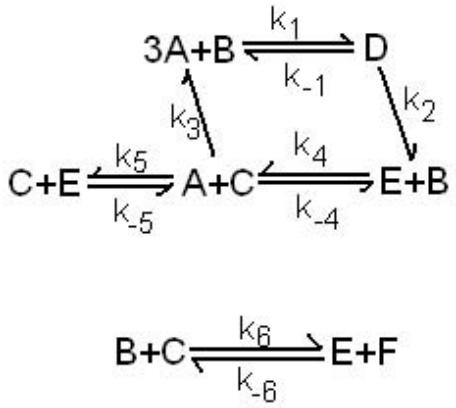

Figure 3: Example of Chemical Reaction Network

Let a, b, c, d, e, f be the concentration of species A, B, C, D, E and F. The mass-action equation can also be written explicity:

$$\begin{aligned}
\frac{\mathrm{d}a}{\mathrm{d}t} &= (2k_3 - k_{-4} - k_5)ac - 3k_1a^3b + 3k_{-1}d + k_4eb + k_{-5}ce \\
\frac{\mathrm{d}b}{\mathrm{d}t} &= (k_{-1} + k_2)d - k_1a^3b + k_2d + k_{-4}ac - k_4eb + k_{-6}ef - k_6bc \\
\frac{\mathrm{d}c}{\mathrm{d}t} &= (-k_3 - k_{-4} - k_5)ac + k_{-5}ce + k_4eb + k_{-6}ef - k_6bc \\
\frac{\mathrm{d}d}{\mathrm{d}t} &= -(k_{-1} + k_2)d + k_1a^3b \\
\frac{\mathrm{d}e}{\mathrm{d}t} &= -k_4eb - k_{-5}ce + (k_5 + k_{-4})ac + k_2d - k_{-6}ef + k_6bc \\
\frac{\mathrm{d}f}{\mathrm{d}t} &= -k_{-6}ef + k_6bc\,.
\end{aligned}$$

The classical theory says that some fundamental properties of mass-action systems do not rely on the parameters too much. This makes lots of sense in practice because the parameters of biochemical biochemical network may be hard to measure. Before reviewing the main theorem of biochemical reaction network, there are several more notations that are necessary to mention.

The first thing is the reversibility of the networks. Without reversibility, if there exists a sink in the biochemical reaction network, then after a sufficient long time, almost all the other complexes will be converted to the complexes in the sink. This will give some degenerated steady-state (steady-state with zero concentration of some

complexes). To avoid this degenerate phenomenon, we need some reversibility of the network. A directed graph is *strongly reversible* if every reaction has its reverse.

Strongly reversibility is too strong in practice. We can relax the requirement to define the weak reversibility. A directed graph is *weakly reversible* if for every pair of complexes which are connected by directed path, there exists a backward directed path on the opposite direction. For example, in Figure 3, $C+E$ and D are connected by the forward path $C + E \rightarrow A + C \rightarrow 3A + C \rightarrow D$ and the backward path $D \rightarrow E + B \rightarrow A + C \rightarrow C + E$. This is also true for all the complex pairs. So the network given in Figure 3 is weakly reversible. However, it is not strongly reversible.

Besides the linkage class, the *terminal linkage class*, which plays the role of sink, is also defined. Formally, a terminal linkage class is a strong connected component with no edge points outside. For example, the two linkage classes in Figure 3 are all terminal linkage classes.

Lastly we are ready to review the famous Deficiency Zero Theorem and Deficiency One Theorem from [24, 25].

Theorem 3.1.1. *(Deficiency Zero Theorem)*
For any weakly reversible reaction network with deficiency zero, there exists a unique positive steady-state on each stoichiometric compatibility class P, which is also global attractor in $P \cap \mathbb{R}^m_{>0}$.

Theorem 3.1.2. *(Deficiency One Theorem)*
For a weakly-reversible biochemical reaction network whose linkage classes are $L_1, \cdots, L_k$. Let δ be the deficiency of the whole network, $\delta_1, \cdots, \delta_k$ be the deficiency of k linkage classes respectively. If

- *Each linkage class contains precisely one terminal linkage class.*
- *$\delta_i \leq 1$ for all $1 \leq i \leq k$*

- $$\sum_{i=1}^{k} \delta_i = \delta$$

Then there exists a unique positive steady-state on each stoichiometric compatibility class P, which is also global attractor in $P \cap \mathbb{R}^m_{>0}$.

Remark 3.1.3. The previous statements are all for closed systems. If a system is open (with material exchange from and to the external environment), then an artificial complex 0 which represents the environment can be added into the network. The concentration of 0 is assumed to be fixed. The difference between open system and closed system is that there is only one stoichiometric compatibility class because the concentration of 0 is already fixed. This means the steady-state is the global steady-state regardless the initial condition.

3.2 Concepts and definitions of degeneracy, complexity and robustness

In this section, we will give rigorous quantitative characterization of systematic measures of biological networks. As we introduced in the Introduction, degeneracy, complexity and robustness are three important systematic features of complex biological network. According to Section 3.1, every biochemical reaction network is associated with an ODE equation called the mass-action kinetic equation. Besides chemical reaction networks, many gene regulation networks, ecological networks can be also modeled by ODE systems. Hence we establish our theoretical framework of ODE systems at first, then extend to more general dynamical systems.

Although mass-action kinetic equations have special structure, to make our characterization universal, from now on we consider the general case of ODE systems.

$$\frac{\mathrm{d}x}{\mathrm{d}t} = f(x) \tag{3.2.1}$$

and its random perturbation

$$\mathrm{d}X_t = f(x)\mathrm{d}t + \epsilon\sigma(x)\mathrm{d}W_t\,, \tag{3.2.2}$$

where $f(x)$ is a continuous vector field in $\mathbb{R}^N$, $\sigma(x)$ is a $N \times N$ matrix function and W_t is the standard n-dimensional white noise. The theory of stochastic differential equations has been covered in the first chapter.

3.2.1 Degeneracy and complexity

Inspired by, but differing from [66], our definition of degeneracy is divided into several steps. In the first step, we define projected density, entropy and mutual information associated with any subspace. Then we fix a subspace as the "output" set and define its associated degeneracy by considering the complementary subspace as the "input" set. Lastly, we define the degeneracy of the entire system by varying the output sets and taking the maximum among all degeneracies of these sets. Our definition are based on the ODE modeled systems, but can be generalized to time-discrete or space-discrete systems naturally.

Let X denote the variable set of ODE system (3.2.1), let $\mathcal{V}$ be the variable subset of X, biologically $\mathcal{V}$ means the set of elements or species of the network.

For simplicity, in this subsection we denote the density function $u_\epsilon(x)$ of the invariant measure of (3.2.2) by ρ when ϵ can be treated as a fixed constant. From the Theorem 2.1.2, we know that ρ is a smooth solution of (2.1.3) for the fixed parameters ϵ, σ. For any subspace I of R^n coordinated by $u \in I$, we define the marginal distribution with respect to I by

$$\rho_I(u) = \int_J \rho(u, v)\mathrm{d}v,$$

where J is the complementary subspace of I coordinated by $v \in J$.

Usually, the coordinates of I is $\mathcal{V}$, which is a subset of the whole variable set X. Biologically I means the subspace spaned by variables in a subset of the whole network.

For instance, in $R^3 = \{(x_1, x_2, x_3)\}$ if $I = \{(0, u, 0)\}$ and $J = \{(v_1, 0, v_2)\}$, then $u = x_2$ and

$$\rho_I(u) = \int_J \rho(x_1, x_2, x_3) dx_1 dx_3.$$

The projected entropy associated with the projected density above is defined by

$$H(\rho_I) = -\int_I \rho_I(u) \log \rho_I(u) du.$$

Entropy is an information theoretical value which measures the uncertainty (amount of information) associated with a random variable. If the probability measure μ is an atomic measure then the entropy could be infinity, which does not make sense for our research. So we must be careful of the regularity of the invariant measure of the system. That is the main reason of the discussion in the first chapter.

For any two subspaces I_1, I_2, the direct sum $I = I_1 \oplus I_2$ is also a subspace. We then define their joint entropy $H(I_1, I_2)$ simply by the projected entropy $H(I_1 \oplus I_2)$ associated with the direct sum, i.e.,

$$H(I_1, I_2) = H(I_1 \oplus I_2) = -\int_{I_1 \oplus I_2} \rho_{I_1, I_2}(u, v) \log \rho_{I_1, I_2}(u, v) du dv,$$

where

$$\rho_{I_1, I_2}(u, v) = \int_J \rho(u, v, w) \mathrm{d}w$$

with J being the complementary subspace of $I_1 \oplus I_2$.

The mutual information among subspaces I_1, I_2 is defined by

$$M(I_1; I_2) = H(I_1) + H(I_2) - H(I_1, I_2).$$

It is easy to see that

$$MI(I_1; I_2) = \int_{I_1 \oplus I_2} \rho_{I_1, I_2}(u, v) \log \frac{\rho_{I_1, I_2}(u, v)}{\rho_{I_1}(u) \rho_{I_2}(v)} \mathrm{d}u \mathrm{d}v \tag{3.2.3}$$

Mutual information is an important information theoretical measure. Originally people use mutual information to measure the efficiency of information channel [13].

Statistically, the mutual information (3.2.3) measures the correlation between marginal distributions with respect to subspaces I_1 and I_2. In a biological network, (3.2.3) measures functional connectivity between two components. If two components could behave coherently, then they share a high mutual information. On the other hand, if two modules are functional independent, then the mutual information between them is fairly low.

We want to mention that mutual information is a better index to measure the connectivity of modules of network than the topological structure of the network it self. The network topology doesn't provide enough information about the functional relationship among elements and components. It is possible that two components are connected by some reactions but still shares low mutual information.

Then we define the *degeneracy*. Let $\mathcal{O}$ be a fixed subspace of R^n, viewed as an output set. We denote I as the complementary subspace to $\mathcal{O}$, viewed as the input set. In other words, the set $\mathcal{O}$ is a fixed set of "observables" when the system (1.1.2) is excited by noise. To measure the noise impacts on all possible components of the input set, we consider any subspace I_k of I and denote its complementary set in I by I_k^c. The multivariate mutual information, or the interacting information among I_k, I_k^c and $\mathcal{O}$ is defined by

$$D(k) = MI(I; I_k; \mathcal{O}) = MI(I_k; \mathcal{O}) + MI(I_k^c; \mathcal{O}) - MI(I; \mathcal{O}). \tag{3.2.4}$$

The interacting information measures how much more correlation the inputs A and B share with output C than expected. Biologically, degeneracy measures how much I_1 and I_2 are structurally different but performs same function at the output set $\mathcal{O}$. In another word, the deficiency between $MI(I; \mathcal{O})$ and the summation of $MI(I_k; \mathcal{O})$ and $MI(I_k^c; \mathcal{O})$ comes from the structural difference between I_k and I_k^c.

We note that unlike the mutual information between two subspaces, the interacting information among three subspaces can take negative values. One example

of negative mutual information is as follows: Let X and Y be independent if Z is unknown, but not independent when conditioning with Z, then $MI(X;Y;Z)$ is negative. Article [64] provides a rigorous proof. Similar to the case of neural networks, we define the degeneracy associated with $\mathcal{O}$ by averaging all the interacting information among all possible subspaces of I, i.e.,

$$D(\mathcal{O}) = \langle MI(I; I_k, \mathcal{O})\rangle = \sum_{I_k} \frac{1}{2\mathrm{C}_k^n} \max\{MI(I; I_k; \mathcal{O}), 0\} \tag{3.2.5}$$

Similiar to degeneracy, *complexity* $C(\mathcal{O})$ associated with $\mathcal{O}$ can be obtained by averaging all the mutual information between I_k and I_k^c, i.e.,

$$C(\mathcal{O}) = \langle MI(I_k; I_k^c)\rangle = \sum_{I_k} \frac{1}{2\mathrm{C}_k^n} MI(I_k; I_k^c). \tag{3.2.6}$$

As we discussed, the mutual information between I_k and I_k^c measures how much the input modules behaves coherently. This complexity of the whole system measures how much the codependency in a network appears among different modules rather than different elements.

Now, for fixed diffusion matrix σ and $\epsilon > 0$, we defined the degeneracy $\mathcal{D}_{\epsilon,\sigma}$ and structural complexity $\mathcal{C}_{\epsilon,\sigma}$ of the system (3.2.1) as

$$\mathcal{D}_{\epsilon,\sigma} = \underset{\mathcal{O}}{Max}\, D(\mathcal{O}),$$

$$C_{\epsilon,\sigma} = \underset{\mathcal{O}}{Max}\, C(\mathcal{O}).$$

We call a differential system (3.2.1) degenerate (resp. complex) with respect to a diffusion matrix σ if there exists ϵ_0, such that $\mathcal{D}_{\epsilon,\sigma} > 0$ (resp. $\mathcal{C}_{\epsilon,\sigma} > 0$) for all $0 < \epsilon < \epsilon_0$. We can only determine whether a system is degenerate when the degeneracy is positive for all small ϵ. That's because the random perturbation is only used to test the interconnection of the network.

We would like to make the following *remarks*

- In many applications, one can often choose $\sigma(x)$ as the identity matrix, so that the noise perturbation becomes purely white. But a variable diffusion matrix $\sigma(x)$, associated with a colored noise perturbation, should play an important role in detecting the key output set mainly responsible for the degeneracy.

- For a particular biological system, one often has a natural choice of "observable" variables to be used as the output set $\mathcal{O}$. If one can select a special subspace I_{k_0} of the complementary subspace I so that the interacting information $MI(I; I_{k_0}; \mathcal{O})$ among the three is positive with respect to a fixed diffusion matrix, then it follows from the definition that the whole system has a certain level of degeneracy. Since the interacting information could be negative, we take the average of $\max\{\mathrm{MI}(I; I_k; \mathcal{O}), 0\}$ to measure the degeneracy of the system.

3.2.2 Uniform robustness, 2-Wasserstein robustness and functional robustness

The robustness (uniform robustness) is defined in a way that reflects the uniform strength of attraction of the global attractor of system (3.2.1). A stronger attractor has better ability to keep stable under stochastic perturbations. Recall that the system (3.2.1) was assumed to be dissipative so that a global attractor already exists. We denote the global attractor by $\mathcal{A}$. Of course robustness should be a broader concept than the stability, the functional robustness reflects such difference between robustness and stability.

To define the robustness, we require in this paper that $\mathcal{A}$ is a strong attractor in the following sense. The attractor $\mathcal{A}$ is said to be a strong attractor with nonnegative index α if there exists a compact neighborhood N with C^1 smooth boundary and a Lyapunov function $V(x)$ such that

$$\frac{\nabla V(x)}{|\nabla V(x)|} \cdot f(x) \leq -\alpha \mathrm{dist}(x, \mathcal{A}), \quad \text{for all } x \in \mathcal{N}.$$

For a strong attractor $\mathcal{A}$, the uniform robustness of $\mathcal{A}$ is the following quantity

$$R = \inf\{\frac{1}{\alpha} : \alpha \text{ is an index of } \mathcal{A}\}.$$

The system is said to be robust if $\mathcal{A}$ is a strong attractor and R is finite.

The definition of robustness is given in a uniform sense. If a system is robustness, then we can find a family of manifolds, which is the level set of the Lyapunov function, such that the vector field points inward on any point of the level set.

The uniform robustness is defined in a straightforward way, which only depends on the strength of the attractor. To provide more information of dynamical system itself or the underlying biological systems, we will discuss the other two variants of robustness. The 2-Wasserstein robustness addresses the stability under stochastic perturbations; while the functional robustness indicates the stability of performance of given biological system.

3.2.2.1 2-Wasserstein Robustness

The average strength againsting the stochastic perturbation can also be used to characterize the robustness. Let $\mathcal{P}(X)$ denote the space of probability measures over the state space. Suppose $\mathcal{P}(X)$ is equipped with 2-Wasserstein metric d_w. The distance between the unperturbed measure and the invariant measure under perturbation can be a good index of the robustness, which is called 2-Wasserstein robustness.

2-Wasserstein metric is derived from the study of optimal transportation problems. In the past decades, geometric features of 2-Wasserstein metric are extensively studied. The definition of 2-Wasserstein metric space is reviewed below.

Definition 3.2.1. Let X be a Polish space, $\mathcal{P}(X)$ be the set of probability measure on X. Let μ, ν be two probability measures on X, then the *2-Wasserstein distance* $\mathcal{W}(\mu, \nu)$ is

$$\mathcal{W}(\mu, \nu)^2 = \inf_{r \in \mathcal{P}(\mu,\nu)} \int_{X \times X} d(x, y)^2 \mathrm{d}r$$

where $\mathcal{P}(\mu,\nu)$ is the set of all probability measures on the space $X\times X$ with marginal μ and ν, and $d(\cdot,\cdot)$ is the distance on X.

r is called the optimal measure if $r\in\mathcal{P}(\mu,\nu)$ and

$$\int_{X\times X} d(x,y)^2 \mathrm{d}r = \mathcal{W}(\mu,\nu)\,.$$

The set of optimal measures is denoted by $\mathcal{P}_0(\mu,\nu)$.

The variational problem in the definition of 2-Wasserstein metric is called the *Kantorovich problem*, which is relaxed from the following *Monge problem*.

$$\mathcal{W}^2(\mu,\nu) = \inf_{T\sharp\mu-\nu}\int |x-T(x)|^2\mathrm{d}x\,.$$

The following two theorems cited from [2] describe some fundamental properties of 2-Wasserstein metric space.

Theorem 3.2.1. *If $\mu,\nu\in\mathcal{P}(\mathbb{R}^d)$, μ is a regular measure (not dirac measure), and*

$$\mu(\{x\in\mathbb{R}^d : \int |x-y|^2\mathrm{d}\nu<\infty\})>0$$

$$\nu(\{x\in\mathbb{R}^d : \int |x-y|^2\mathrm{d}\mu<\infty\})>0$$

then the Kantorovich problem has a unique solution Γ and this solution is induced by an optimal transport. i.e.

$$\Gamma=(i\times r)\sharp\mu$$

for some transport map r, i is the identity map.

Theorem 3.2.2. *For a given sequence $\{\mu_n\}\subset\mathcal{P}(X)$, $\lim_{n\to\infty}\mathcal{W}(\mu_n,\mu)=0$ if and only if $\{\mu_n\}$ converge to μ in the weak* topology and $\{\mu_n\}$ has uniformly finite second moment.*

Remark 3.2.3. Theorem 3.2.1 implies that under certain conditions, Monge problem and Kantorovich problem are equivalent. 2-Wasserstein distance is an effective index

to measure the stability of invariant measures of ODE systems because convergence in 2-Wasserstein metric space is equivalent to the weak* convergence under certain conditions.

The 2-Wasserstein robustness is defined as the reciprocal of metric derivative.

Definition 3.2.2. The 2-Wasserstein robustness R is the following limit

$$R = \liminf_{\epsilon \to 0} \frac{\epsilon}{d_w(\mu_\epsilon, \mu)}$$

where μ_ϵ is the ϵ-invariant measure of stochastic dynamical system

$$\mathrm{d}X_t = f(X_t)\mathrm{d}t + \epsilon dW_t \,.$$

A system is said to be *robust in the 2-Wasserstein sense* if and only if $R \neq 0$. More properties about the 2-Wasserstein robustness will be discussed in the next section.

Remark 3.2.4. 2-Wasserstein robustness is similar as but contains more information than the mean square displacement. That is to say, the attactor must be both strong and stable. To make a system be robust in the 2-Wasserstein sense, the attractor must be a strong attractor. That can be observed easily from the fact that

$$\mathcal{W}^2(\mu_\epsilon, \mu) = \inf_{T\sharp\mu - \nu} \int |x - T(x)|^2 \mathrm{d}x \geq \int \mathrm{dist}^2(x, \mathcal{A})\mathrm{d}x \,.$$

Note that the right term above is the mean square distance between μ_ϵ and μ. Hence bounded 2-Wasserstein robustness implies bounded mean square displacement.

Moreover, the attractor must be stochastically stable. This stochastic stability is not equivalent to the strength of attractor. Intuitively speaking, being stochastic stable means the shapes of ϵ-invariant measures have no significant change when ϵ changes. One counter example is that, as $\epsilon \to 0$, if the family of measure μ_ϵ has two weak limits μ_{01} and μ_{02}, then this attractor is not stable under stochastic perturbation. From the definition, it is not robust in the 2-Wasserstein sense. For more introduction of stochastic stability, see [34].

3.2.2.2 Functional Robustness

The robustness of a biological system could not be completely equivalent to the stability against random perturbation. That's because the performance of a complex biological system could be very complicate. When a complex system deviates from its steady-state due to external perturbation or disfunctions of some components, it is still possible that it could perform normally. According to [42], we can evaluate the performance of a system by the performance function. The performance function is defined on the state space and take maximal value at the steady-state. A system could be robust functionally if the performance has high value even if far away from the steady-state. In this sense, we can describe the robustness of the performance function by the functional robustness.

First we define the performance function:

Definition 3.2.3. The performance function $p(x)$ of the system is a continuous function satisfies following assumptions:

1. $p(x) = 1 \quad \forall x \in \mathcal{A}$
2. $0 < p(x) < 1$ if $x \notin \mathcal{A}$

where $\mathcal{A}$ means the global attractor.

Following Kitano [42], one can define functional robustness $R_f(\epsilon)$ as

$$R_f(\epsilon) = \int \rho_\epsilon(x) p(x) \mathrm{d}x.$$

where $\rho_\epsilon(x)$ is the density function of the ϵ-invariant measure.

Using this notation, the system has the best performance when the perturbation vanishes and robustness is interpreted as the ability to preserve phenotype rather maintaining a fixed steady state. We remark that if a system is robust, and some property of performance function is also known, then some estimate on the functional robustness can be made. The more detailed discussion is provided in Section 3.3.

3.2.3 Algorithms

We will consider the issues of algorithms in this subsection. A good quantitative definition must be practical to compute. Hence some theory about the calculation and estimation of the degeneracy and complexity will be introduced in Section 3.4. However, it is still necessary to study the numerical calculation of these systematic measures. One reason is that some systems may not have fixed point and may be so complex that people don't know the attractor exactly. The other reason is that in the real world one can not expect every system to be well-posed ODE system with known parameters. Some systems behave like black boxes. Hence some knowledge of numerical method is necessary.

It follows from previous discussion that the robustness and 2-Wasserstein robustness requires detailed informations of the dynamics of ODE systems. On the other hand, the functional robustness is more practical to compute. The bottlenecks of computing degeneracy, complexity and functional robustness are the estimation of the probability density function. With the probability density function, all these three measures can be computed by numerical integrations. The probability density function can be obtained by solving Fokker-Planck equation. However, solving high dimensional parabolic equation numerically is very expensive. Especially when the second derivative terms are of $O(\epsilon^2)$ small and the density function looks sharp at the attractors.

An alternative way is the Monte Carlo simulation. One can generate a large sample set by either solving stochastic differential equation or experiment. With a large sample set, the reconstruction of the probability density function can be done by making a histogram. Monte Carlo simulation has lower accuracy, but this can be compensated by large sample set. Moreover, parallel implementation of Monte Carlo simulation is easy and straightforward, which is another advantage of Monte Carlo algorithm.

Of course, the histogram can be computed by the naive equidistant binning estimator, in which the domain is divided into finite number of bins. However, the "curse of dimension" would be inevitable. Even if we only want 100 bins for each variable, about 8TB memory are need to simulate a "small" system with six variables. Even if we do it on distributive computer systems, the amount of message passing in the naive binning estimator is also huge. A much better algorithm is called the k-nearest neighborhood (kNN) method. By using a special data structure called kd-tree, the "curse of dimension" problem can be eased significantly. We only need to store the sample set instead of the high dimension grids. This is especially important when the probability density function concentrates in the vicinity of some low dimension attractors, as we discussed in the previous chapter. For the comparison of mutual information estimators, see [53] for further reference.

3.3 On the properties of robustness

We will consider the properties of robustness in this section, not only in the context of complex biological networks, but also in its mathematical aspect. The properties and calculations of robustness, the issue of ϵ-expansions of ϵ-invariant measures and the connections between robustness in different definitions will be covered.

3.3.1 Discussion of 2-Wasserstein Robustness

We first consider the qualitative and quantitative properties of 2-Wasserstein robustness. The connection between 2-Wasserstein robustness and the ϵ-expansion of invariant measure is particularly addressed. The 2-Wasserstein robustness measures the transportation distance between ϵ-invariant measure and its limit. It measures the robustness in average sense. Further, 2-Wasserstein robustness gives the first order expansion of ϵ-invariant measure in terms of ϵ in the 2-Wasserstein metric spaces. 2-Wasserstein space is the state space of Fokker-Planck equation while the invariant measure plays the role of fixed point, the expansion in term of ϵ is mathematically

nature. Some explicit calculation of 2-Wasserstein robustness will then be presented.

The following theorem shows the finiteness of 2-Wasserstein distance between ϵ invariant measure and its limit. In another word, no matter how strong an attractor is, as long as the vector field is smooth, the effect of stochastic perturbation can not be arbitrarily small. This means the first order term in the ϵ expansion always exists.

Theorem 3.3.1. *The robustness of stochastic dynamical system* (3.2.2) *that satsifies conditions (***H***1) and (***H***5) is finite.*

Proof. It is known from [33] that the limit invariant measure is always supported by the attractor. Hence the ϵ-invariant measure μ_ϵ and the limit invariant measure μ_0 satisfy Theorem 3.2.1. So the 2-Wasserstein distance solves the Monge problem

$$\mathcal{W}^2(\mu_\epsilon, \mu_0) = \inf_{T\sharp\mu_\epsilon - \mu_0} \int |x - T(x)|^2 \mathrm{d}x \,.$$

Since μ_0 is supported by the attractor $\mathcal{K}$, we have

$$|x - T(x)|^2 \geq \mathrm{dist}^2(x, \mathcal{K})$$

for any map $T : \mathbb{R}^n \to \mathcal{K}$. This means the 2-Wasserstein distance is larger than the mean square displacement

$$\mathcal{W}^2(\mu_\epsilon, \mu_0) \geq \int \mathrm{dist}^2(x, \mathcal{K}) \mu_\epsilon(\mathrm{d}x) \,.$$

Implied by Theorem 2.1.21, the mean square displacement is bounded from below by $V_1\epsilon^2$. Hence the 2-Wasserstein robustness is finite by its definition. □

Remark 3.3.2. As the proof indicates, the mean square displacement is always less than the 2-Wasserstein distance between μ_ϵ and μ_0. However, the 2-Wasserstein distance between ϵ-invariant measure and its limit is much more complex than the mean square displacement. Detailed knowledge of the invariant measure is necessary to evaluate this 2-Wasserstein distance. The 2-Wasserstein robustness of general

ODE systems is difficult to calculate. In another word, Theorem 3.3.1 does not mean that uniform robustness implies 2-Wasserstein robustness. If a system does not have unique weak noise limit as ϵ goes to 0, then it is not robust in the 2-Wasserstein sense. Whether this system can be robust in the uniform sense remains open. Further study of 2-Wasserstein robustness and the expansion of ϵ-invariant measure will be included in our future work.

Next we give some quantitative results about 2-Wasserstein robustness for certain ODE systems. Consider an ODE system with a unique stable fixed point x_0.

$$\begin{aligned} \frac{\mathrm{d}x}{\mathrm{d}t} &= f(x) \\ f(x_0) &= 0\,. \end{aligned} \tag{3.3.1}$$

Without loss of generality, assume $x_0 = 0$. According to Section 2.1.2, there exists a quasi-potential function $U(x)$ and a C^2-continuous function $w(x)$ with $w(0) = 1$ such that the density function $u_\epsilon(x)$ of the invariant measure has the form

$$u_\epsilon(x) = \frac{1}{K} e^{-U(x)/\epsilon^2} w(x) + o(\epsilon^2)\,,$$

where the notation $o(\epsilon^2)$ means higher order terms that satisfy

$$\lim_{\epsilon \to 0} \frac{o(\epsilon^2)}{\epsilon^2} = 0\,.$$

Hence the 2-Wasserstein robustness of ODE systems like (3.3.1) can be calculated.

Theorem 3.3.3. *If equation* (3.3.1) *satisfies assumption (***H***1) and the eigenvalues of Jacobian matrix at* $x(0) = 0$ *only have negative real parts, then the 2-Wasserstein robustness* R *of* (3.3.1) *is*

$$R = \frac{\sqrt{2}}{\sqrt{\mathbf{Tr}(S^{-1})}}$$

where S *solves the Lyapunov equation*

$$SB^T + BS^T = Id$$

B *is the Jacobi matrix of* (3.3.1) *at the fixed point.*

Proof. For the system with unique fixed point, the 2-Wasserstein distance between ϵ-invariant measure and the invariant measure is equal to the square root of the mean square displacement

$$d_w^2(u_\epsilon(x), \delta(0)) = \int_{\mathbb{R}^N} x^2 u_\epsilon(x) \mathrm{d}x$$

note that $\delta(0)$ is the limit invariant measure.

The proof only contains some elementary calculus. We will sketch the basic procedures of the proof. First we are going to show the situation of gradient flows. Let $U(x)$ be a potential function of class C_2. To be consistent with the condition (**H**1), we assume there exists constant $a, R > 0$ such that $U(x) > a|x|$ for $|x| > R$.

In the neighborhood of the fixed point, $U(x)$ has the Taylor expansion

$$U(x) = \frac{1}{2} x^T S x + r(x)$$

where $r(x)$ is the reminder that satisfies $|r(x)| \leq b|x|^3$ for some $b > 0$, $\frac{1}{2}S$ is the Hessian matrix of $U(x)$. We write the Hessian as $\frac{1}{2}S$ for simplicity of the further calculation. S is a positive definite symmetric matrix.

It is well known that the invariant measure of

$$\mathrm{d}x = -\nabla U(x)\mathrm{d}x + \epsilon dW_t$$

is the Gibbs density function

$$u_\epsilon = \frac{1}{K} e^{-U(x)/\epsilon^2},$$

where K is a normalizer.

Firstly let us estimate K. Denote $\sigma = \epsilon^{0.9}$ to have

$$\begin{aligned} K &= \int e^{-U(x)/\epsilon^2} \mathrm{d}x && (3.3.2) \\ &= \int_{|x|>R} e^{-U(x)/\epsilon^2} \mathrm{d}x + \int_{\sigma<|x|<R} e^{-U(x)/\epsilon^2} \mathrm{d}x + \int_{|x|<\sigma} e^{-U(x)/\epsilon^2} \mathrm{d}x && (3.3.3) \\ &:= I_1 + I_2 + I_3 \,. && (3.3.4) \end{aligned}$$

In the above equation

$$\begin{aligned} I_1 &\leq \int_{|x|>R} e^{-a|x|/\epsilon^2} \mathrm{d}x \\ &= \int_R^\infty B_n(\rho) e^{-a\rho/\epsilon^2} \mathrm{d}\rho \\ &= P(R,\epsilon) e^{-aR/\epsilon^2}\,, \end{aligned}$$

where $B_n(\rho)$ means the volume of n-sphere with radius ρ, which equals a constant number times ρ^{n-1}. $P(R,\epsilon)$ is a rational function in term of R and ϵ.

For I_2, we can choose small ϵ to make the minimum of $U(x)$ in $\{x|\sigma < |x| < R\}$ be attained on $\{x||x| = \sigma\}$. From the Taylor expansion, there exists β such that $U(x) > \beta|x|^2$ for small $|x|$. Hence

$$I_2 \leq C e^{-\beta\epsilon^{-0.2}}$$

for some constant C.

Then by evaluating I_3, we obtain

$$I_3 = \int_{|x|<\sigma} e^{-x^T Ax/2\epsilon^2} e^{r(x)/\epsilon^2} \mathrm{d}x\,.$$

$|x| < \sigma = \epsilon^{0.9}$ implies $|r(x)/\epsilon^2| < \epsilon^{0.7}$. Taking the limit $\epsilon \to 0$ we have

$$I_3 = (2\pi)^{n/2} \epsilon^n |A^{-1}| (1 + O(\epsilon^{0.7})) := K_0 \epsilon^n + O(\epsilon^n)$$

for some constant K_0. Further, when $\epsilon \to 0$, I_1 and I_2 are all smaller than $O(\epsilon^n)$ for all n. This implies

$$K = K_0 \epsilon^n + O(\epsilon^n)\,.$$

Then by the same approach, one can divide $\mathbb{R}^n$ into $|x| > R$, $\sigma < |x| < R$ and $|x| < \sigma$. Let $U(x) = \frac{1}{2} x^T S x + r(x)$. Some calculation implies that the integral

$$\int \frac{1}{K} x^2 e^{-U(x)/\epsilon^2} \mathrm{d}x$$

converges to

$$\int \frac{1}{K_0 \epsilon^n} e^{-x^T Sx/2\epsilon^2} \mathrm{d}x\,,$$

which is a multivariate normal distribution. Then it follows from the properties of multi-variate normal distribution that

$$\int \frac{1}{K_0\epsilon^n} e^{-x^T Sx/2\epsilon^2} \mathrm{d}x = \mathbf{Tr}(S^{-1})\epsilon^2 + O(\epsilon^2)\,.$$

This implies

$$d_w(u_\epsilon(x), \delta(0)) = \sqrt{\mathbf{Tr}(S^{-1})}\epsilon\,.$$

The above calculation gives the 2-Wasserstein robustness R

$$R = \frac{1}{\sqrt{\mathbf{Tr}(S^{-1})}}\,,$$

where S is 2 times the Hessian matrix of $U(x)$.

We will calculate the 2-Wasserstein robustness of ODE systems with a stable fixed point in a same way. Let $U(x)$ be the quasi-potential function of system (3.3.1). Then it follows from Section 2.1.2 that there exists a small neighborhood of $x_0 = 0$ in which $U(x)$ is smooth. Moreover, the Hessian matrix S of $U(x)$ satisfies the Lyapunov equation

$$SB^T + BS^T = Id\,,$$

where B is the Jacobi matrix of (3.3.1) at $x = 0$. From [30] it is known that S is a symmetric positive definite matrix.

Since the density function of the ϵ-invariant measure has the form

$$u_\epsilon(x) = \frac{1}{K} e^{-U(x)/\epsilon^2} w(x) + O(\epsilon^2)\,,$$

we can evaluate K by dividing $\mathbb{R}^n$ into $|x| > R$, $\sigma < |x| < R$ and $|x| < \sigma$ as what we did above. When $|x| > R$ one can apply the result in Theorem 2.1.17. Let $\sigma = \epsilon^{0.9}$. Note that $w(x) = 1 + O(\sigma)$ when $|x| < \sigma$. After some calculation we can get $K = K_0\epsilon^n + O(\epsilon^n)$.

The integral

$$\int x^2 u_\epsilon(x) \mathrm{d}x$$

can be evaluated in the same way as what we did above by deviding $\mathbb{R}^n$ into $|x| > R$, $\sigma < |x| < R$ and $|x| < \sigma$. After some calculation we obtain

$$\int x^2 u_\epsilon(x) \mathrm{d}x = \frac{1}{2}\mathbf{Tr}(S^{-1})\epsilon^2 + O(\epsilon^2)\,.$$

Hence the 2-Wasserstein robustness is

$$R = \frac{\sqrt{2}}{\sqrt{\mathbf{Tr}(S^{-1})}}\,.$$

This completes the proof. □

Remark 3.3.4. Note that the ϵ-invariant measure of system (3.3.1) has the following expansion under 2-Wasserstein metrics.

$$\mathcal{W}(\mu, \mu_\epsilon) = \frac{1}{R}\epsilon + o(\epsilon^2)\,.$$

Since R has been calculated, the expansion of ϵ-invariant measure now can be explicitly given.

If the system has more than one attractor or the attractor is not a fixed point, then similar approaches are still valid as long as the ϵ-invariant measure has the form

$$u_\epsilon(x) = \frac{1}{K} e^{-U(x)/\epsilon^2} w(x) + o(\epsilon^2) \tag{3.3.5}$$

where $w(x)$ is of C^1 continuous with

$$\int_{\mathcal{K}} w(x) \mathrm{d}x = 1$$

on the global attractor $\mathcal{K}$.

The proof contains just the elementary calculus and is very tedious, so we will not show the detail here. General results of 2-Wasserstein robustness are expected to be done in our future work.

3.3.2 Uniform robustness and 2-Wasserstein robustness imply functional robustness

The connection between robustness in different senses will be studied in this subsection. As in the above section, uniform robustness indicates the strength of attractor in a uniform way, while 2-Wasserstein robustness addresses the ϵ-expansion of ϵ-invariant measures. We will show that both uniform robustness and 2-Wasserstein robustness imply functional robustness.

Proposition 3.3.5. *Assume the performance function $p(x)$ has continuous second derivatives. Then for any system* (3.2.1) *which is robust in the uniform sense or 2-Wasserstein sense, there exists positive constant C, such that*

$$\int u_\epsilon(x)p(x)\mathrm{d}x \geq 1 - C\epsilon^2$$

Proof. Theorem 2.1.21 implies that a robust system has bounded mean square displacement:

$$V_1\epsilon^2 \leq \int u_\epsilon \mathrm{dist}^2(x,\mathcal{K})\mathrm{d}x \leq V_2\epsilon^2\,.$$

Note that 2-Wasserstein robustness also implies the boundedness of the mean square distance. From the proof of Theorem 3.3.3, the 2-Wasserstein distance can be written as

$$\mathcal{W}^2(\mu_\epsilon,\mu_0) = \inf_{T\sharp\mu_\epsilon-\mu_0}\int |x-T(x)|^2\mathrm{d}x\,.$$

Since μ_0 is supported by the attractor $\mathcal{K}$, we have

$$|x-T(x)|^2 \geq \mathrm{dist}^2(x,\mathcal{K})\,,$$

for any map T. This means the 2-Wasserstein distance is larger than the mean square displacement.

$$\mathcal{W}^2(\mu_\epsilon,\mu_0) \geq \int \mathrm{dist}^2(x,\mathcal{K})\mu_\epsilon(\mathrm{d}x)\,.$$

The limit

$$\liminf_{\epsilon\to 0}\frac{\epsilon}{d_w(\mu_\epsilon,\epsilon_0)} = R > 0$$

implies

$$d_w^2(\mu_\epsilon, \epsilon_1) < \frac{2\epsilon^2}{R^2}$$

for all $0 < \epsilon < \epsilon_1$ for some small $\epsilon_1 > 0$. So we obtain

$$\int \text{dist}^2(x, \mathcal{K})\mu_\epsilon(\text{d}x) \leq \frac{2\epsilon^2}{R^2} := V_2\epsilon^2$$

Then it is sufficient to show the statement is true when the mean square distance is bounded by $V_2\epsilon^2$. Since $p(x)$ has second order derivative, there exists a fixed neighborhood N of $\mathcal{K}$ such that $p(x) \geq 1 - M\text{dist}^2(x, \mathcal{K})$ for all $x \in N$. Hence

$$\int u_\epsilon(x)p(x)\text{d}x = \int_N u_\epsilon(x)p(x)\text{d}x + \int_{\mathbb{R}^N \backslash N} u_\epsilon(x)p(x)\text{d}x := I_1 + I_2$$

where $I_2 \geq 0$ and there exists $\beta > 0$ such that

$$\begin{aligned} I_1 &= \mu_\epsilon(N) - M\int_N u_\epsilon(x)\text{dist}^2(x, \mathcal{K})\text{d}x \\ &\geq 1 - M\int u_\epsilon(x)\text{dist}^2(x, \mathcal{K})\text{d}x - \mu_\epsilon(\mathbb{R}^N \backslash N) \\ &\geq 1 - V_2 M\epsilon^2 - e^{-\beta/\epsilon^2}. \end{aligned}$$

According to Theorem 2.1.15, there exists $\epsilon_2 > 0$ such that

$$e^{-\beta/\epsilon^2} < \epsilon^2$$

for all $0 < \epsilon < \epsilon_2$. Let $\epsilon_0 = \min\{\epsilon_1, \epsilon_2\}$ and $C = V_2 M + 1$. Then the proposition follows. □

Remark 3.3.6. Conversely the previous result does not hold. It is known that sometimes an stochastic dynamical system can keep its performance even if it is deviated away from the steady-state. (That's way a performance functions are needed) A function robust system does not have to be robust in either uniform sense of 2-Wasserstein sense.

3.4 Connections between degeneracy, complexity and robustness

As suggested by simulations and experiments, the systematic measures including degeneracy, complexity and robustness are not independent. In this section we develop a variety of results concerning connections among degeneracy, complexity and robustness. Some basic properties of these systematic measure are also covered. In the end, an illustrative example is demonstrated to explain the connection between the topology of networks and their systematic measures.

3.4.1 degeneracy and complexity

It has been observed in neural networks that a degenerate system must have a complex structure [66]. In fact, we can prove that system with high degeneracy always has high complexity. This property is universally valid, no matter in neuron complex network or in complex network described by differential equations.

Theorem 3.4.1. *We have the following inequality*

$$MI(I; I_k; \mathcal{O}) \leq \min\{MI(I; I_k), MI(I_k^c; \mathcal{O}), MI(I; \mathcal{O})\}. \tag{3.4.1}$$

Proof. We can prove equation (3.4.1) in the following way:

$$\begin{aligned} MI(X;Y;Z) &= H(X) + H(Y) + H(Z) - H(X,Y) - H(Y,Z) \\ &\quad -H(X,Z) + H(X,Y,Z) \\ &= H(X) + H(Y) - H(X,Y) \\ &\quad -(H(X,Z) + H(Y,Z) - H(Z) - H(X,Y,Z)) \\ &= MI(X;Y) - MI(X;Y|Z) \end{aligned}$$

Since the l mutual information is nonnegative: $MI(X;Y|Z) \geq 0$, we have $MI(X;Y;Z) \leq MI(X;Y)$.

The nonnegativity of conditional mutual information is a direct corollary of Kullback's inequality. For the complete of this proof, we borrow the proof from [74]: let $P(x, y, z)$ be the density function, then

$$\begin{aligned} MI(X;Y|Z) &= \int P(x,y,z)\log\frac{P(x,y|z)}{P(x|z)P(y|z)}\mathrm{d}x\mathrm{d}y\mathrm{d}z \\ &= \int P(z)\{\int p(x,y|z)\log\frac{P(x,y|z)}{P(x|z)P(y|z)}\mathrm{d}x\mathrm{d}y\}\mathrm{d}z\,. \end{aligned}$$

From Kullback's inequality,

$$\int p(x,y|z)\log\frac{P(x,y|z)}{P(x|z)P(y|z)}\mathrm{d}x\mathrm{d}y \geq 0\,.$$

□

Similarly we can prove $MI(X;Y;Z) \leq MI(X;Z)$ and $MI(X;Y;Z) \leq MI(Y;Z)$, from which (3.4.1) follows. □

If we compare equations (3.2.5) and (3.2.6), by taking the average among all possible subsets I_k, we obtain

$$C(\mathcal{O}) \geq D(\mathcal{O}).$$

because $MI(I; I_k^c; \mathcal{O}) \leq MI(I; I_k^c)$. In other words, with respect to a fixed diffusion matrix, degeneracy implies complexity.

This explains the observation in [19] that biological systems selected for high degeneracy are accompanied by high complexity. Since complexity is always higher than degeneracy, it is sufficient to determine when will a system have high degeneracy. In the next two subsections, we will discuss the system with positive degeneracy.

3.4.2 twisted attractor

We would like to examine the connections between degeneracy and robustness for an ODE system (1.1.1). Robustness alone does not necessarily imply degeneracy of the system; this is because one can certainly have a system with zero complexity which is however robust. By (3.4.1), such a system must be non-degenerate. One example is

the linear system $x_i' = -a_i x_i$ with $1 \leq i \leq N$ with $\sigma(x) = Id$, in which a_i are positive real numbers.

Therefore, for a robust system to be degenerate, the system must be complex and such structural complexity often gives rise to some kind of embedding complexity of the global attractor into the phase space. Roughly speaking, the components of a complex system interact strongly with one another and as a result, the global attractor is twisted in the phase space such that it does not lay in any hyperplane. To characterize the twist property of the global attractor, it is natural to consider its projections on certain hyperplanes and measure the dimensions of the corresponding projections. We note that the attractor as well as its projections may only be fractal sets, hence they should be measured with respect to the Minkowski dimension, also called box counting dimension [54].

For a subspace $\mathcal{V}$ of R^n, we denote by $d_{\mathcal{V}}$ the co-dimension of $\mathcal{A}$ in $\mathcal{V}$, i.e., the dimension of $\mathcal{V}$ subtracts the Minkowski dimension of the projection of $\mathcal{A}$ to $\mathcal{V}$.

The *twisted attractor* is defined as follows.

Definition 3.4.1. The global attractor $\mathcal{A}$ is said to be twisted if there is a linear decomposition $R^n = \mathcal{I} \oplus \mathcal{J} \oplus \mathcal{O}$ such that

$$d_{\mathcal{I}} + d_{\mathcal{J}} + d_{\mathcal{O}} + d_{R^n} < d_{\mathcal{I}\oplus\mathcal{J}} + d_{\mathcal{I}\oplus\mathcal{O}} + d_{\mathcal{J}\oplus\mathcal{O}}.$$

We have the following Theorem for regular attractors.

Theorem 3.4.2. *If the system* (1.1.1) *is robust with a twisted global attractor, and if the ϵ-invariant density function ρ_ϵ is regular for $\mathcal{A}$, then there exists an $\epsilon_0 > 0$, such that $\mathcal{D}_{\epsilon,\sigma} > 0$ for all $0 < \epsilon < \epsilon_0$*

Proof. This Theorem is just a corollary of the Entropy-Dimension identity proved in previous chapter. Under the given conditions, we have

$$\lim_{\epsilon \to 0} \frac{H(\rho_\epsilon(x))}{-\log \epsilon} = N - d \tag{3.4.2}$$

where $H(\rho)$ means the entropy of ρ. Then using the definitions of degeneracy and a twisted attractor, we can prove the positivity of the degeneracy $\mathcal{D}_{\epsilon,\sigma}$. □

Remark 3.4.3. We note that ρ_ϵ is always regular if there exists a quasi-potential function $W(x)$ of $\mathcal{A}$, such that for every $0 < \epsilon < \epsilon^*$, we have

$$\rho_\epsilon(x) = \frac{1}{K} e^{-W(x)/\epsilon^2} + o(\epsilon)$$

where

$$K = \int_{\mathbb{R}^N} e^{-W(x)/\epsilon^2} \mathrm{d}x$$

and $o(\epsilon)$ means high order terms of ϵ.

As reviewed in previous sections, from [48, 15], we can find the desired function $W(x)$ whenever the Freidlin-Wentzell quasi-potential function $W(x)$ has second order derivatives. From [15, 14], we know that the Freidlin-Wentzell quasi-potential function $W(x)$ has high regularity in the neighborhood of stable nodes and limit cycles. So we have the following corollary:

Corollary 3.4.4. *Assume system* (3.2.1) *has a limit cycle that doesn't lie on any subspace spanned by the variable subset, then the limit cycle is a twisted attractor and the system has positive degeneracy for small* ϵ.

Proof. The proof is straight forward. Let the dimension of subspace I, J and $\mathcal{O}$ be i, j and k, then

$$d_I + d_J + d_{\mathcal{O}} + d_{I\oplus J\oplus\mathcal{O}} - d_{I\oplus J} + d_{I\oplus\mathcal{O}} + d_{J\oplus\mathcal{O}} = -1 < 0$$

□

Remark 3.4.5. It follows from the results in section 2.1.3 that the density function concentrates in a small neighborhood of the attractor. Hence the structure and position of the attractor determines the mutual informations between different variable

sets. This means the concentration of noise only depends on the strength of noise. In another word, the degeneracy of system with twisted attractor does not depend on the coefficient matrix $\sigma(x)$ of the white noise. This is different from the degeneracy of systems with stable fixed point.

We provide a three dimensional example to demonstrate the twisted attractor.

Example 3.4.6. *Consider the following competitive Lotka-Volterra system*

$$\begin{aligned}
\dot{x}_1 &= x_1(3 - x_1 - x_2 - x_3) \\
\dot{x}_2 &= x_2(4 - x_1 - x_2 - 2x_3) \\
\dot{x}_3 &= x_3(7.221 - 2.61x_1 - 1.611x_2 - 3x_3).
\end{aligned}$$

This system represents a simple three-species competitive population model. The system has a limit cycle as described previously (Fig. 4) [73]. Using the theory of quasi-potential functions, one can rewrite the vector field as $-\nabla\Psi(x_1, x_2, x_3) + l(x_1, x_2, x_3)$, *where* Ψ *is called a quasi-potential function and* l *is a small perturbation in a definite sense with* $\nabla\Psi \cdot l = 0$. *It is well known that for such a system admitting a limit cycle,* Ψ *is a Lyapunov function which is as regular as the vector field. It then follows from definition that the system is robust. Furthermore, the condition in Theorem 3.4.2 is also satisfied due to the regularity of the quasi-potential function.*

Numerical simulations above show that the limit cycle is not parallel to any coordinate axis. In fact, it follows that $d_x = d_y = d_z = 0$, $d_{xyz} = 2$, $d_{xy} = d_{xz} = d_{yz} = 1$. *Hence the attractor is also twisted. Now applying the theorem on twisted attractors, we conclude that the system is degenerate.*

3.4.3 degeneracy at equilibrium

Degenerate behavior could occur not only at the twisted attractor, but also at certain equilibria, or what a biologist may regard as homeostasis. Here, we introduce another

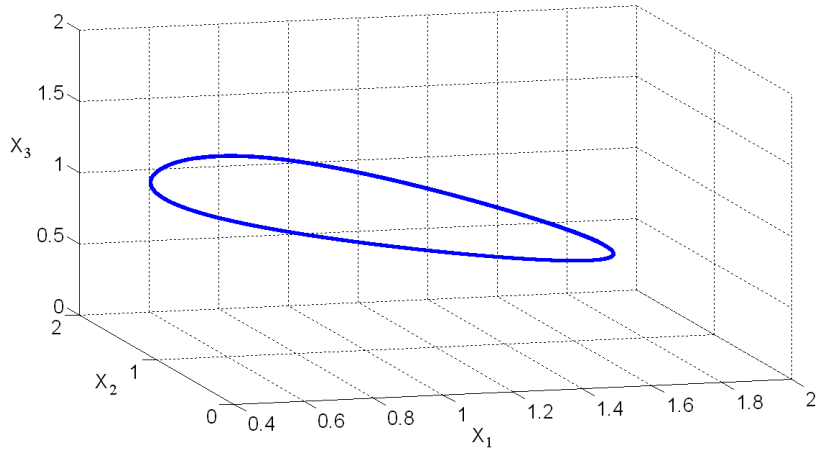

Figure 4: Limit cycle of the Lotka-Volterra system showing a twisted attractor.

theorem on the connection between robustness and degeneracy. If an ODE system has a unique equilibrium point and in the neighborhood of this equilibrium point the reactions to random perturbations have certain level of diversity, then we claim that it is a degenerate system. More precisely, if different directions demonstrate different sensitivities under random perturbation, then it is a degenerate system.

We want to mention that it is known that a large number of chemical reaction networks have unique stable equilibrium points, the degeneracy near equilibrium may be more applicable for biological reaction networks. For more detailed result, see [24, 23, 3].

Assume that system (1.1.1)

$$x' = f(x)$$

satisfies condition (**H**1) and has a unique stable fixed point, say x_0. Let B denote the Jacobian matrix of $f(x)$ at x_0. Since we have assumed the robustness already, it is obvious that the eigenvalues of B only have negative real parts. From Section 2.1.2, one can find the solution to the stationary Fokker-Planck equation (2.1.3):

$$\rho_\epsilon = \frac{1}{K} e^{-V(x)/\epsilon^2} + O(\epsilon^2)$$

where $V(x)$ is the quasi-potential function. Moreover, the Hessian matrix of the

quasi-potential function can be solved by equation (2.1.10). So we get estimation

$$\rho = \frac{1}{K} e^{-z^T S^{-1} z/2\epsilon} + O(|z|^2) + O(\epsilon^2) \tag{3.4.3}$$

where $z = x - x_0$. The symmetric positive definite matrix S solves the Lyapunov equation uniquely:

$$SB^T + BS + A = 0 \tag{3.4.4}$$

where $A = \sigma(x_0)\sigma^T(x_0)$. Then we claim that for weak noise, the matrix S determines the degeneracy. The rigorous proof will be done later.

With the stationary solution ρ, we can find the margins on target subspaces. It is known that the marginal distribution of a normal distribution is also normal, whose covariance matrix is the corresponding sub-matrix of S. More precisely, if $X = \text{span}\{x_{a_1}, \cdots, x_{a_k}\}$ is a subspace, then the sub-matrix $S(a_1, \cdots, a_k; a_1, \cdots, a_k)$ is the covariance matrix of the projection of ρ_ϵ on subspace X. For simplicity, we denote $S(a_1, \cdots, a_k; a_1, \cdots, a_k)$ as $S(X)$.

Then we can compute the degeneracy with split $X = I_1 \oplus I_2 \oplus O$. Since equation (3.4.3) approximates a multivariate normal distribution, calculation of degeneracy yields the following Theorem:

Theorem 3.4.7. *if*

$$\Gamma := \log \frac{|S(I_1)||S(I_2)||S(O)||S(X)|}{|S(I_1, I_2)||S(I_1, O)||S(I_2, O)|} > 0\,. \tag{3.4.5}$$

then the system is degenerate.

Proof. Since $x^T S x$ is the quadratic approximation of $V(x)$, the difference between them is $o(\epsilon^3)$ small. It is sufficient to show that third order difference of the quasi-potential does not generate significant difference of the entropy. To avoid possible confusion, in the proof below, we denote the density function of probability measure μ by $\frac{\mathrm{d}\mu}{\mathrm{d}x}$.

It is known that the quasi-potential function $V(x)$ is smooth in a small neighborhood of x_0, say $B(x_0)$. Hence in $B(x_0)$ there exists

$$\frac{\mathrm{d}\mu_\epsilon}{\mathrm{d}x} = \frac{1}{K} e^{-V(x)/\epsilon}\,.$$

Let ν_ϵ be another measure with density

$$\frac{\mathrm{d}\nu_\epsilon}{\mathrm{d}x} = \frac{1}{L} e^{-x^T S x/\epsilon}\,.$$

Then it is sufficient to show that

$$\lim_{\epsilon\to 0} |\mathrm{Ent}(\mu_\epsilon) - \mathrm{Ent}(\nu_\epsilon)| = 0\,, \tag{3.4.6}$$

where $Ent(\mu)$ is the entropy of μ.

That is because the degeneracy is a linear combination of finite many entropies of marginal probability measures. Note that the degeneracy of ν_ϵ is independent with the value of ϵ. Equality (3.4.6) can implies the same argument of the marginal probability measures. Then the theorem follows.

We will prove equality (3.4.6) in three steps.

Claim 1 We first claim that outside of big ball $B(0, 2R)$, the following two integrals are small:

$$-\int_{|x|>2R} \mu_\epsilon \log \frac{\mathrm{d}\mu_\epsilon}{\mathrm{d}x}\mathrm{d}x$$

and

$$-\int_{|x|>2R} \nu_\epsilon \log \frac{\mathrm{d}\nu_\epsilon}{\mathrm{d}x}\mathrm{d}x$$

It follows from Section 2.1.2 that there exists $\sigma > 0$ such that the quasi-potential is strictly larger than $\sigma(|x| - R)$ for $|x| > R$. Hence the density function of μ_ϵ is less than $e^{-\sigma(|x|-R)/\epsilon}$ for all $\epsilon < \epsilon_1$ for some $\epsilon_1 > 0$. Note that $x \log x$ decreases for small

x. We have

$$\begin{aligned} -\int_{|x|>2R} \mu_\epsilon \log \frac{\mathrm{d}\mu_\epsilon}{\mathrm{d}x}\mathrm{d}x &< \int_{|x|>2R} \sigma(|x|-R)e^{-\sigma(|x|-R)/\epsilon}\mathrm{d}x \\ &= \int_{2R}^{\infty} C(d)\rho^{n-1}\sigma(\rho-R)e^{-\sigma(\rho-R)/\epsilon}\mathrm{d}\rho \\ &< e^{-\sigma R/2\epsilon}\int_{2R}^{\infty} C(d)\rho^{n-1}(\rho-R)e^{-\sigma(\rho-R)/2\epsilon}\mathrm{d}\rho \\ &= Ce^{-\sigma R/2\epsilon} \end{aligned}$$

for some finite C. So the limit of the first integral is 0.

For the second integral, since the quasi-potential function now is replaced by $x^T Sx$ and S is positive definite, there exists some $\alpha > 0$ such that $x^T Sx > \alpha(|x| - R)$ for all $|x| > 2R$. Then by the same reason the limit of the second integral is 0.

Claim 2 Then, we claim that the limit of the entropy intergals of μ_ϵ and ν_ϵ are all 0 in the following area Γ_ϵ.

$$\Gamma_\epsilon = \{x||x| \in B(x_0), d(x, x_0) \geq \epsilon^{2/5}\,.$$

Let $d = \mathrm{dist}(\partial B(x_0, x_0)$ and $\epsilon^2 = d^{5/2}$. For any $\epsilon < \epsilon_2$, the "hole" lies in the set $B(x_0)$ in which $V(x)$ is smooth. Hence $x^T Sx$ is an second order approximation of $V(x)$. This means there exists a constant $\beta > 0$ such that $V(x) > \beta\epsilon^{4/5}$ for all $x \in \Gamma_\epsilon$ and all $0 < \epsilon < \epsilon_2$.

It follows from [26] that

$$\lim_{\epsilon\to 0} \epsilon \log(\frac{\mathrm{d}\mu_\epsilon(x)}{\mathrm{d}x}) \leq -V(x)\,.$$

For sufficient small ϵ, we have

$$\frac{\mathrm{d}\mu_\epsilon}{\mathrm{d}x} \leq e^{-\beta/2\epsilon^{-1/5}}$$

for all $x \in \Gamma_\epsilon$. Combine with the fact that $x \log x$ decreases with small $x > 0$, we have

$$-\int_{\Gamma_\epsilon} \mu_\epsilon \log \frac{\mathrm{d}\mu_\epsilon}{\mathrm{d}x} \leq \int_{\Gamma_\epsilon} \frac{\beta}{2\epsilon} e^{-\beta/2\epsilon^{-1/5}} \leq C_2 e^{-\beta/2\epsilon^{-1/5}}\,.$$

By replacing $V(x)$ by $x^T Sx$, the same argument holds of ν_ϵ. This proves the second claim.

Claim 3 Let $\Delta_\epsilon = \{x | \|x - x_0\| \leq \epsilon^{2/5}\}$. We claim that the following difference converges to 0 as $\epsilon \to 0$.

$$\int_{\Delta_\epsilon} \mu_\epsilon \log \frac{\mathrm{d}\mu_\epsilon}{\mathrm{d}x} - \int_{\Delta_\epsilon} \nu_\epsilon \log \frac{\mathrm{d}\nu_\epsilon}{\mathrm{d}x} \,.$$

In the area Δ_ϵ $V(x)$ is smooth. From Taylor expansion we have

$$|V(x) - x^T Sx| := r(x) \leq C_3 |x|^3$$

for some $C_3 > 0$.

Then we will calculate normalizer K and L where

$$K = \int e^{-V(x)/\epsilon} \mathrm{d}x \,;\, L = \int e^{-x^T Sx/\epsilon} \mathrm{d}x \,.$$

Let

$$\delta(\epsilon) = \int_{x \notin \Delta_\epsilon} e^{-V(x)/\epsilon} \mathrm{d}x + \int_{x \notin \Delta_\epsilon} e^{-x^T Sx/\epsilon} \mathrm{d}x \,.$$

Then from the same argument of Claim 1 and 2, it follows that $\delta(\epsilon)$ is of $e^{-\epsilon^{-1/5}}$ small. Note that $e^{-\epsilon^{-1/5}}$ is smaller than $O(\epsilon^n)$ for any n. This implies

$$\begin{aligned} |K - L| &\leq \int_{\Delta_\epsilon} e^{x^T Sx} C_3 |x|^3 / \epsilon \mathrm{d}x + \delta(\epsilon) && (3.4.7) \\ &\leq C_4 \epsilon^{(N+1)/2} && (3.4.8) \end{aligned}$$

for some $C_4 > 0$, where N is the dimension. Note that the order of K and L are of $\epsilon^{N/2}$. Hence

$$\begin{aligned} & -\int_{\Delta_\epsilon} \frac{1}{K} e^{-V(x)/\epsilon} (-\frac{V(x)}{\epsilon} - \log K) \mathrm{dx} + \int_{\Delta_\epsilon} \frac{1}{K} e^{-x^T Sx/\epsilon} (-\frac{x^T Sx}{\epsilon} - \log K) \mathrm{dx} \\ = & \int_{\Delta_\epsilon} \frac{1}{K} \frac{V(x)}{\epsilon} e^{-V(x)/\epsilon} \mathrm{d}x - \int_{\Delta_\epsilon} \frac{1}{L} \frac{x^T Sx}{\epsilon} e^{-x^T Sx/\epsilon} \mathrm{dx} + (\log K - \log L) \,, \end{aligned}$$

where

$$|\log K - \log L| \leq |log(1 + C_4 \epsilon^{1/2})| \leq C_5 \epsilon^{1/2}$$

for some $C_5 > 0$.

We also have

$$\begin{aligned} & \int_{\Delta_\epsilon} \frac{1}{K} \frac{V(x)}{\epsilon} e^{-V(x)/\epsilon} \mathrm{d}x - \int_{\Delta_\epsilon} \frac{1}{L} \frac{x^T S x}{\epsilon} e^{-x^T S x/\epsilon} \mathrm{d}x \\ = & \int_{\Delta_\epsilon} \frac{1}{K} (\frac{V(x)}{\epsilon} e^{-V(x)/\epsilon} - \frac{x^T S x}{\epsilon} e^{-x^T S x/\epsilon}) \mathrm{d}x + \int_{\Delta_\epsilon} (\frac{1}{K} - \frac{1}{L}) \frac{x^T S x}{\epsilon} e^{-x^T S x/\epsilon} \mathrm{d}x \\ := & \ I_1 + I_2 \,. \end{aligned}$$

The second term satisfies

$$I_2 \leq C_4 \epsilon^{(1-d)/2} \int_{\Delta_\epsilon} \frac{x^T S x}{\epsilon} e^{-x^T S x/\epsilon} \mathrm{d}x \leq C_5 \epsilon^{1/2}$$

for some $C_5 > 0$. That is obvious after letting $u = \epsilon^{-1/2} x$.

The first term I_1 satisfies

$$\begin{aligned} |I_1| \ \leq & \int_{\Delta_\epsilon} \frac{1}{K} \frac{x^T S x}{\epsilon} (1 + C_3 |x|/\epsilon) e^{-x^T S x/\epsilon} e^{r(x)} - \frac{x^T S x}{\epsilon} e^{-x^T S x/\epsilon} \mathrm{d}x \\ \leq & \int_{\Delta_\epsilon} \frac{1}{K} (\frac{x^T S x}{\epsilon} e^{-x^T S x/\epsilon} (1 - e^{-C_3 |x|^3/\epsilon}) + \frac{x^T S x}{\epsilon} e^{-x^T S x/\epsilon} \frac{C_3 |x|^3}{\epsilon} e^{C_3 |x|^3/\epsilon} \mathrm{d}x \\ \leq & \ C_5 \epsilon^{1/2} \end{aligned}$$

for some C_5. This completes Claim 3.

Finally it follows from above calculations that

$$\begin{aligned} \mathrm{Ent}(\mu_\epsilon) - \mathrm{Ent}(\nu_\epsilon) \ = & \int \frac{1}{K} e^{-V(x)/\epsilon} \mathrm{d}x - \int \frac{1}{L} e^{-x^T S x/\epsilon} \mathrm{d}x \\ \leq & \ 2C e^{-\sigma R/2\epsilon} + 2C_2 e^{-\beta \epsilon^{-1/5}} + C_5 \epsilon^{1/2} \,. \end{aligned}$$

By taking the limit $\epsilon \to 0$, we arrive at the desired result

$$\lim_{\epsilon \to 0} |\mathrm{Ent}(\mu_\epsilon) - \mathrm{Ent}(\nu_\epsilon)| = 0 \,.$$

□

In fact, it can be shown that as $\epsilon \to 0$, the degeneracy of ρ_ϵ with respect to decomposition I_1, I_2, O converges to Γ.

We also claim that the degeneracy is persistent with small perturbation of vector fields. Assuming we have two vector fields from two ODEs system

$$\frac{\mathrm{d}X}{\mathrm{d}t} = f(x)$$

and

$$\frac{\mathrm{d}X}{\mathrm{d}t} = \bar{f}(x)$$

where $\bar{f}$ is the small perturbation of f. Since the first system has a stable equilibrium x_0, its dynamics is persistent with small perturbation. Without loss of generality, we denote the Jacobin matrix of the original system at fixed point by B, the Jacobin matrix of the perturbed system at fixed point by $\bar{B}$. And we assume $E := B - \bar{B}$ be a small matrix. Such persistence is proved by the following theorem.

Theorem 3.4.8. *Assume the system with noise is given by*

$$\mathrm{d}X = f(X)\mathrm{d}t + \epsilon\sigma(X)\mathrm{d}W_t$$

Then for any $\epsilon > 0$, we can find some $\delta > 0$, such that $|D - \bar{D}| < \epsilon$ whenever $\|E\|_1 < \delta$. Where D is the degeneracy of the original system with respect to any split, and $\bar{D}$ is the degeneracy of the perturbed system with the same split.

Proof. That's just elementary linear algebra calculation. It is well known that the Lyapunov equation can be rewritten as follows:

$$(I - \mathrm{Kron}(B^T, B^T))\mathrm{vec}(X) = -\mathrm{vec}(A)\,, \tag{3.4.9}$$

where $\mathrm{Kron}(B^T, B^T)$ is the Kronecker product. In the above equation $\mathrm{vec}(A)$ is obtained by stacking the columns of A. The matrix B is the Jacobi matrix of $f(x)$ whose eigenvalues have negative real parts, and $A = \sigma^T(x_0)\sigma(x_0)$. For detail of Kronecker product, see [30].

The linearity of Kronecker product implies

$$\|I - \mathrm{Kron}(B^T, B^T) - (I - \mathrm{Kron}(\bar{B}^T, \bar{B}^T))\|_\infty = \|\mathrm{Kron}(\bar{B}^T, \bar{B}^T) - \mathrm{Kron}(B^T, B^T)\|_\infty\,.$$

Note that the (i,j)-th $n \times n$ block of $\mathrm{Kron}(\bar{B}^T, \bar{B}^T) - \mathrm{Kron}(B^T, B^T$ is $a_{ji}E^T + e_{ji}A^T + e_{ji}E^T$. Let

$$\mathrm{Kron}(\bar{B}^T, \bar{B}^T) - \mathrm{Kron}(B^T, B^T) = C_1 + C_2 + C_3\,,$$

where $C_1 = \mathrm{Kron}(B^T, E^T)$, $C_2 = \mathrm{Kron}(E^T, B^T)$, $C_3 = \mathrm{Kron}(E^T, E^T)$. Then

$$\|C_1\|_\infty = \max_{i,k}(\sum_{j=1}^{n} |b_{ji}| \sum_{l=1}^{n} e_{kl}) = \max_i \sum_{j=1}^{n} |b_{ji}| \|E\|_1 = \|B\|_1 \|E\|_1\,.$$

Similarly we obtain

$$\|C_2\|_\infty = \|B\|_1 \|E\|_1$$

and

$$\|C_3\|_\infty = \|E\|_1^2\,.$$

When $\|E\|_1 < \delta$, the above implies

$$\|\mathrm{Kron}(\bar{B}^T, \bar{B}^T) - \mathrm{Kron}(B^T, B^T)\|_\infty \leq 3\|B\|_1 \|E\|_1 := \alpha\,.$$

Let K be the condition number of matrix $I - \mathrm{Kron}(B^T, B^T)$. It is known that $K < \infty$.

Then it follows from the classical result in matrix analysis [32] that

$$\|\mathrm{vec}(\bar{X}) - \mathrm{vec}(X)\|_\infty \leq \frac{\alpha K \|\mathrm{vec}(X)\|_\infty}{\|B\|_\infty (1 - K\frac{\alpha}{\|B\|_1})} := \beta\,.$$

This means

$$\max_{ij} |(\bar{X} - X)_{ij}| \leq \beta\,.$$

Let $X(I)$ be any submatrix of X with respect to some index set I. Then clearly

$$\max_{ij} |X(I)_{ij}| \leq \max_{ij} |(\bar{X} - X)_{ij}| \leq \beta\,.$$

Note that $\|A\|_2 \leq n\|A\|_{max}$. The following estimation can be obtained from [32]:

$$\begin{aligned} |det(\bar{X}(I)) - det(X(I))| &\leq |det(X(I))| \|\bar{X} - X\|_2 \frac{n\|X^{-1}\|_2}{1 - n\|X^{-1}\|_2 \|\bar{X} - X\|_2} \\ &\leq \frac{n^2 \|X^{-1}\|_2 \beta}{1 - n\|X^{-1}\|_2 \beta} := \gamma\,. \end{aligned}$$

Since $|log(x+y) - log(x)| \leq 2|y|/|x|$, we have

$$|\bar{D} - D| \leq \frac{7}{m}\gamma$$

for small γ, where

$$m = \min\{|X|, |X(I_1)|, |X(I_2)|, |X(O)|, |X(I_1, O)|, |X(I_2, O)|, |X(I_1, I_2)|\}$$

.

The above calculations implies that when

$$\delta < \min\{\frac{2}{3K}, \frac{1}{12Kn\|X^{-1}\|_2}, \frac{\epsilon m}{84n^2\|X^{-1}\|_2}\}\,,$$

the following holds:

$$|\bar{D} - D| < \epsilon\,.$$

Since X, B, K, m are all perdetermined by the unperturbed system, the theorem follows. □

Remark 3.4.9. Different from the twisted attractor, the degeneracy of system with stable fixed point could be changed by changing the coefficient matrix $\sigma(x)$. In another word, if one perturb the differential equation by some correlated random variables, then the correlations in the perturbation term can affect the measured interconnection between components of networks.

The distribution of perturbed system is approximated by the solution of Lyapunov equation (3.4.4). Let

$$\mathcal{L}_B X = -B^T X - XB^T$$

be the Lyapunov operator. Then it follows from [6] that $\mathcal{L}_B$ is an invertible operator in the space of symmetric positive definite matrices as long as matrix B is stable (all eigenvalues of B has negative real parts). This means for any system, we can find some coefficient matrix $\sigma(x)$ such that the system has positive degeneracy in the sense of $D_{\epsilon,\delta}$.

Hence the correlation in the added noise perturbation can disturb the measure of degeneracy of the biological network. In practice, uncorrelated noise is suggested to be used to detect the interconnection of the network. In another word, we usually let $\sigma(x) = Id$.

3.4.4 Continuous Dependency

In this subsection we consider the continuous dependency of degeneracy, complexity and robustness with respect to the vector field. The continuous dependency of robustness is obvious according to its definition, while the continuous dependence of degeneracy and complexity comes from the continuous dependence of invariant measure. Since the projecting and the expression of entropy are all continuous operators, it is sufficient to show that the invariant measure is continuous dependent with the vector field.

This can be easily done if we recall the materials in Section 2.1.2. We can define a family of compact sets Ω_k such that

$$\Omega_1 \subset \cdots \Omega_k \subset \cdots$$

and

$$\lim_{k\to\infty} \Omega_k = \mathbb{R}^N$$

Let $u_k(x)$ be the density of invariant measure μ_k of (3.2.2) on Ω_k. Then it is known that $\mu_k(K) \to \mu(K)$ for any compact set K. Further, the invariant measure μ_k of (3.2.2) satisfies

$$\begin{cases} L^* u_k(x) = 0 & x \in \Omega_k \\ \sum_{i,j=1}^N \partial_i(a_{ij}(x)u_k(x))\nu_j - \sum_{i=1}^N f_i\nu_i u_k(x) := Bu_k = 0 & x \in \partial\Omega_k \end{cases}$$

and $u_k(x)$ is the eigenfunction of the principal eigenvalue of the linear operator L^* on the space $\{f \in W^{2,p}(\Omega_k) | Bf = 0\}$ (see [1, 35]). Since L^* is a linear operator and L^* has continuous dependence on the vector field $f(x)$, we are done.

3.4.5 Systematic Measure and Network Topology

Last but not least, we will discuss the connection between the topological structure of network and the systematic measures by an illustrative example. The complete theory of systematic measure and network topology will be put in a separate paper. In practice, we can not always expect all the parameters (reaction rate, for example) of networks are perfectly measured. That is why it is interesting if some conclusion of the systematic measures can be made without detailed information of the reaction rates.

Example 3.4.10. *Consider the following strong reversible network that has material change with the external environment. Let* A, B, C *be three species,* M*,* a*,* b*,* k_1*,* k_2 *and* 1 *be the reaction rate. Note that without loss of generality, we set the output rate be* 1*. Then we have the following chemical reaction network and the chemical reaction*

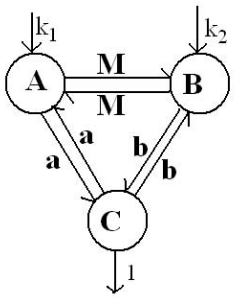

Figure 5: A Network Example

equation

$$\frac{\mathrm{d}X_A}{\mathrm{d}t} = -(M+a)X_A + MX_B + aX_c + k_1 \tag{3.4.10}$$

$$\frac{\mathrm{d}X_B}{\mathrm{d}t} = -(M+b)X_B + MX_A + bX_c + k_2 \tag{3.4.11}$$

$$\frac{\mathrm{d}X_c}{\mathrm{d}t} = -(a+b+1)X_c + aX_A + bX_b \tag{3.4.12}$$

Clearly equation (3.4.10) *has a unique equilibrium with Jacobian matrix* B

$$B = \begin{bmatrix} -(M+a) & M & a \\ M & -(M+b) & b \\ a & b & -(a+b+1) \end{bmatrix}$$

Let $\sigma(x) = Id$*, then the solution of Lyapunov equation is* $S = \frac{1}{2}B^{-1}$*. After some linear algebra calculation, we can find that as* $M \to 0$*, the expression* (3.4.5) *in Theorem 3.4.7 converges to* $\log(1 + \frac{a}{2} + \frac{b}{2})$*:*

$$\lim_{M \to 0} \log \frac{|S(X_A)||S(X_B)||S(X_C)||S(X)|}{|S(X_A, X_B)||S(X_B, X_C)||S(X_A, X_C)|} = \log(1 + \frac{a+b}{2})$$

Since a*,* b *are all positive numbers, above calculation implies that for sufficiently large* M*, the above system has positive degeneracy. This is just a simple example. While numberical stimulations can verify that it is a common phenomenon that strong connection among input variables implies positive degeneracy.*

3.5 Application to JAK-STAT crosstalk network

The purpose of this section is to apply our theory on the JAK-STAT crosstalk network model shown in Figure 6. Using a simplified model of crosstalk in protein signal transduction, we illustrate the calculation of degeneracy using equation (3.4.7) (Note that the model in Figure 6 has deficiency zero hence the fixed point exists). We also demonstrate how certain biological features of the signaling network affect the numerical value of degeneracy.

For illustrative purposes we have chosen the JAK-STAT signaling pathway since it is a relatively simple signaling system. Based on evidence from the literature, this system presents features that are useful for illustrating the concept of degeneracy. The JAK-STAT pathway is a two-step intracellular signaling pathway in which a member of the JAK family of kinases, typically bound to a transmembrane receptor, is activated by phosphorylation following ligation of the receptor with extracellular

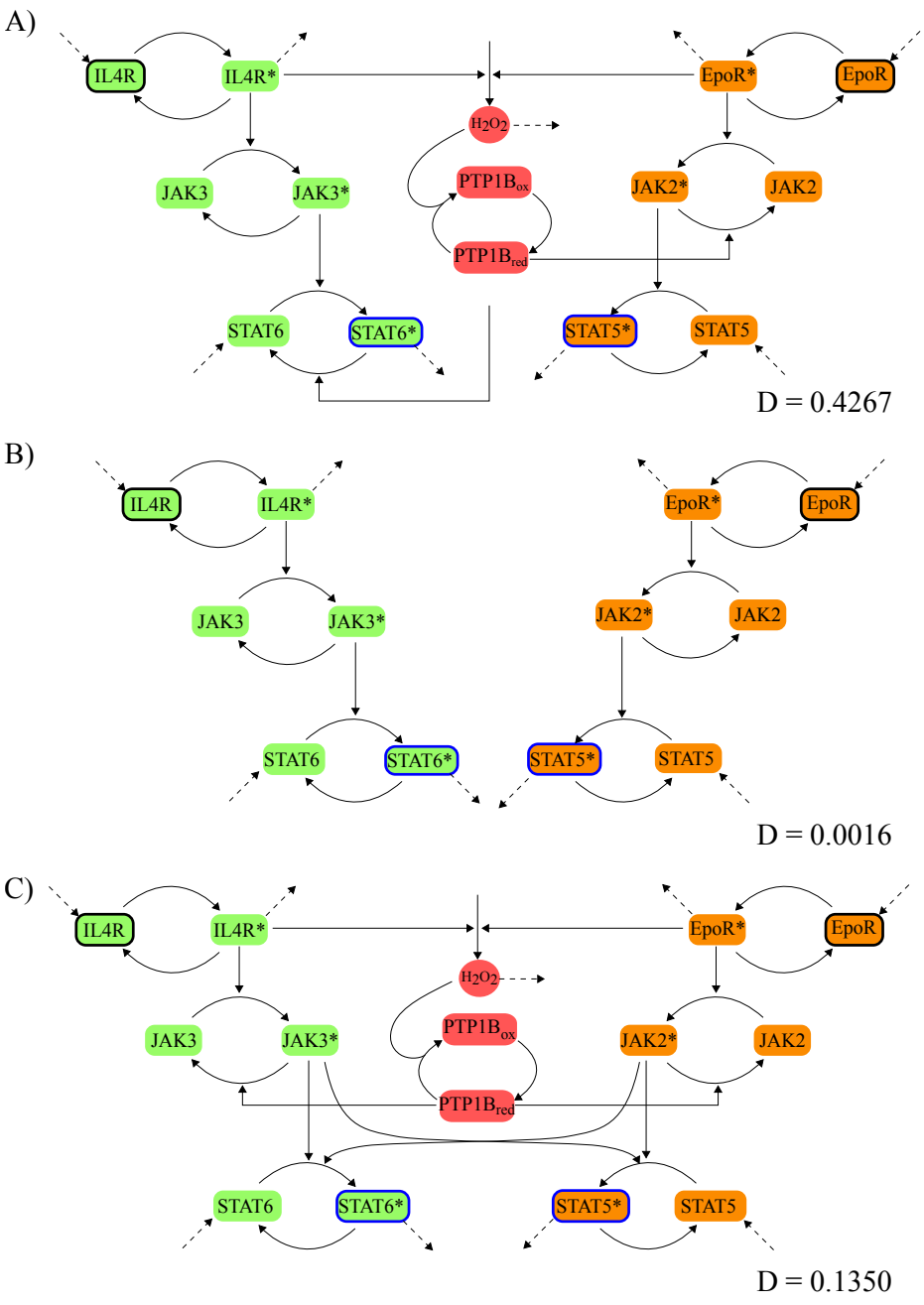

Figure 6: Illustration using IL-4R and EpoR crosstalk model. A) The core JAK-STAT modules of IL-4R and EpoR pathways with crosstalk. Both modules are regulated by PTP1B, both generate ROS which oxidatively inactivates PTP1B. B) Crosstalk enhances degeneracy. The links connecting the two modules were abolished resulting in independent IL-4R and EpoR signaling modules. C) Redundancy vs degeneracy. The edges in panel A were modified to construct a hypothetical signaling system with completely redundant modules with crosstalk. * indicates phosphorylated protein; ox, oxidized; red, reduced; arrows pointing at other edges, catalyzed reactions; dashed arrows entering into species, constant production; dashed arrows exiting species, first order decay; species highlighted in black, inputs; species highlighted in blue, outputs.

cytokine. The activated JAK molecule phosphorylates STAT which can then dimerize and act as a transcription factor. The signaling pathway is regulated by several mediators including phosphatases that dephosphorylate JAK and STAT molecules, thereby inhibiting their catalytic activity [61]. It has been shown previously that cytokine receptor activation can be accompanied by production of reactive oxygen species (ROS) in response to multiple kinds of cytokines [59]. The generated ROS reacts with some phosphatases to oxidize them reversibly, resulting in temporary inactivation of the phosphatases. Phosphatase inactivity results in amplification of STAT phosphorylation. Sharma et al. demonstrated that different cytokines, signaling through their respective receptors, can crosstalk in an ROS-mediated manner to amplify signals coming through other cytokines [59]. This is a result of oxidative inactivation of phosphatases regulating the different JAK-STAT pathways.

Based on this information we have constructed a simplified model of crosstalk between IL-4 and Epo signaling. IL-4 signals through the IL-4 receptor and activates the JAK3/STAT6 pathway [39]. Epo signals through the Epo receptor and activates the JAK2/STAT5 signaling pathway [12]. Multiple phosphatases can regulate these pathways. To illustrate the crosstalk between the pathways we have chosen one phosphatase, PTP1B, which is important in both signaling pathways. In the IL-4 pathway it directly dephosphorylates STAT6 whereas the substrate of PTP1B in the Epo pathway is JAK2 [47, 50]. PTP1B is also susceptible to ROS-mediated oxidative inactivation [59]. This information was compiled to get the IL-4/Epo crosstalk model shown in Fig. 6A. For the sake of parsimony we have treated phosphorylated STAT as the output and ignored phospho-STAT dimerization.

The model we constructed was used to empirically study relationships between the signaling pathway and the computed degeneracy. We chose the receptors (IL-4R and EpoR) as a pair of inputs to the system and activated STAT molecules (STAT5* and STAT6* in Fig. 6A) as the output. By solving the Lyapunov equation, the model

in Fig. 6A was found to be degenerate with a value of D equal to 0.4267. Since our theoretical results relate increased complexity with increased degeneracy, we sought to verify if this was reflected in our model of JAK-STAT crosstalk. The cross-talk between the two linear JAK-STAT pathways is the source of increased complexity of the system. To reduce the complexity of the system, we abrogated all cross-talk by switching off ROS production and regulation by the common phosphatase PTP1B to get the independent signaling systems shown in Fig. 6B. The calculated value of degeneracy decreased by more than 99% for this system as compared to the pathway in Fig. 6A and the value of D was calculated to be 0.0016. This demonstrates that cross-talk between signaling pathways results in increased complexity which could result in increased degeneracy.

Redundancy in signaling systems can also lead to complexity in the pathway, in the sense that there can be significant amount of cross-talk between parallel pathways. However, a redundant system is by definition not degenerate because the redundant modules perform identical functions under any given condition. To test how a redundant system compares with a degenerate system, we modified the pathway in Fig. 6A to that shown in Fig. 6C by inserting some hypothetical connections. This was done to ensure that the two modules were structurally identical and affected the output (STAT5* and STAT6*) identically. The rate parameters were also identical for the two modules resulting in a completely redundant system where EpoR and IL-4R affect STAT5 and STAT6 identically. The redundant system was found to still have a positive D but the magnitude was reduced by more than 68% as compared to the value calculated for the system in Fig. 6A. This agrees with the understanding that redundancy does not lead to degeneracy and our calculation of D successfully reflects this.

3.6 Discussions of Systematic Measures in a Biological Context

As defined in Section 3.2, degeneracy and complexity can be seen as linear combinations of mutual information. To take an example, in the network in Fig. 7, A and B serve as inputs while C is an output. Generally, we expect high degeneracy among the three components if i) both A and B share high mutual information with the output C and ii) the summation of these two mutual information is higher than that between the union of A with B and the output C. The first condition means A and B could perform the same function, while the second condition essentially means that the two modules represented by A and B have different structures. The value $MI(A;C)+MI(B;C)-MI(\{A,B\};C)$, thus measures the degeneracy, or how much more correlation the inputs A and B share with the output C than expected. We can also expect high complexity if the co-dependency in the network appears among different modules rather than the basic elements making up the system. For example, in the context of crosstalk between the IL-4 and Epo pathways, the IL-4 and Epo pathways separately can be thought of as modules while the individual molecules constitute the basic elements of the system. High co-dependency between these modules instead of that between the individual molecules would lead to greater complexity. The co-dependency between modules means that the network is functionally segregated in that the functional modules retain their importance and also functionally integrated because of the co-dependence of the modules.

As is evidenced by the examples above, degeneracy can be generally understood as the ability of structurally distinct components of a system to behave similarly under certain conditions, while the behavior may be different under other conditions. Increasingly large numbers of instances of degeneracy are being found in biological systems at all scales ranging from molecular to animal population levels [19]. Particularly, in the context of cellular signaling networks, there are multiple examples of

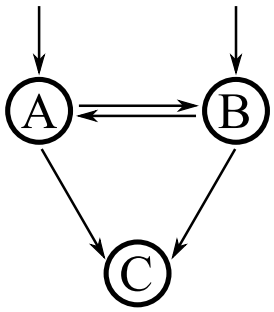

Figure 7: An Example of Modular Biological Network

degenerate behavior. Different members of the interleukin (IL) family can activate the same transcription factor. For instance, IL-2, IL-7 and IL-21 can all activate STAT1 [58]. Growth factors can bind to multiple types of receptors in the EGF receptor family [10]. MAPK signaling induced by growth factors and stress exhibits promiscuous interaction between MEKK and MAPK proteins where multiple types of MEKKs can activate the same MAPK and a single MEKK can activate multiple MAPKs [51]. Recently, experimental studies have indicated that a significant role for genetic buffering by non-homologous genes (i.e. functional redundancy or degeneracy) [69] exists and may confer a selective advantage over paralogs for regulation.

In a more general sense, no signaling pathway operates in isolation because of cross-talk between multiple pathways. Chen et al. showed that the behavior of a signaling pathway in isolation is different from the behavior it exhibits when put in the context of a more complex intracellular environment [10]. Systems biologists are aware that cellular signaling pathways which are classically seen as isolated, and often linear, chains of biochemical modifications rarely operate in this simple fashion. The connections between signaling pathways give rise to networks with much greater complexity. These resulting systems can exhibit degenerate behavior in the sense that one signaling pathway influences another resulting in similar or different outputs depending on conditions. This is important from the point of view of drug targeting. For instance, despite major efforts, very few drugs specifically targeting the PI3K

signaling pathway, which exhibits strong crosstalk with a number of other pathways, make it to the clinical trial stage [31]. The complexity arising from cross-talk is thought to be one reason for the failure of specific inhibitors to work successfully in cells. Determining what points should be targeted in a complex signaling network is a critical question for drug design. It is therefore desirable that the extent of compensation between connected pathways be defined quantitatively. A quantitative measure of degeneracy in the network can be exploited to identify candidate points in the network most suitable for drug intervention. Quantification of degeneracy can also have applications in synthetic biology for designing system modules that are structurally distinct but can be made to perform similar functions when needed.

Despite the existence of multiple instances of degenerate cellular signaling systems and possible applications of estimation of degeneracy, a framework for quantifying degeneracy in such systems has been so far lacking. We have presented in this thesis a theoretical method for calculating the degeneracy of dynamical systems, which include cellular signaling and metabolic networks. Using a model of cross-talk in interleukin signaling we have demonstrated the biological significance of this numerical measure of degeneracy. We found that the IL-4R and EpoR signaling pathways, by virtue of phosphatase and ROS mediated crosstalk, give rise to a degenerate system when the receptors are treated as input and STAT activation as output. By computationally manipulating the signaling pathway we have empirically shown the relationships between degeneracy and some network features. As first shown by Tononi et al. for neural networks, we found that independent signaling modules exhibit very low degeneracy [66]. Reduced connectivity also means that the modules have a reduced ability to influence each other via crosstalk, which our definition of degeneracy is able to reflect. Simply increasing the complexity of the network may not be sufficient to guarantee a degenerate system. For instance, fully redundant signaling modules

with a high degree of crosstalk result in a structurally complex system. In our computational analysis, when the modules were made fully redundant by making them identical in the structure of the network and in the strengths of the internal connections, the calculated degeneracy dropped despite an increase in network edges. This agrees with the notion that redundancy and degeneracy are functionally distinct, and demonstrates that our definition of degeneracy is able to distinguish between a truly degenerate system against one with high complexity but low degeneracy.

We also present a definition of robustness in the context of differential equation models of biological systems. The stability of a differential system can be measured by its robustness under random perturbation. A robust system strongly resists change under fixed random perturbation. Moreover, as suggested by [42], if we know the performance function of a system, we don't have to require that the system offer this resistance everywhere – the system only needs to be stable at places where the performance function decreases dramatically. Biologically, this means that a robust system is not necessarily one that is able to maintain a fixed steady state; instead it is a system that is able to maintain its phenotype in the face of perturbations [42]. We have provided a definition of functional robustness that takes this into account.

While these illustrations with simplistic biological models provide some insight into the significance of our theoretical framework for defining degeneracy, several aspects remain to be explored. For instance, does the calculated degeneracy provide an estimate of the ability of cross-talking pathways to compensate for each other under perturbation? System dynamics are of great importance in understanding cellular signaling networks. Our method for calculating degeneracy takes into account only the fixed points of the differential system. In thinking about the meaning of calculated degeneracy in the context of cell signaling, it is important to keep system dynamics in mind. The outcome of a signaling event is not always dictated by the steady state value, instead instantaneous rates of changes or integrated values of signals may be

of relevance in a given system. For this reason it is important to explore the relationships between system dynamics and degeneracy. Given the "no free lunch" concept in control systems in which operating performance of one control function comes at the cost of fragility elsewhere [43, 18], the consequences of degenerate network properties over redundant components can be explored further. These concepts may be exploited in the design of synthetic biological circuits to ensure a desired functional outcome under a variety of biological contexts. Although several issues remain to be addressed, the methods presented in this thesis are significant in providing a theoretical framework to the concept of degeneracy and functional robustness for the class of systems represented by differential equations.

3.7 Systematic Measures in Discrete Models

This section is dedicated to the systematic measures in discrete settings. The configurations of systematic measures of ODE-modeled complex biological system have been studied in the above sections in detail. In addition, our theoretical frameworks can be extend to the discrete settings. This extension is important because sometimes discrete models make more sense than the ODE-models. For example, in the cell, the number of reacting molecules could be small. In this case, the mass-action model is not suitable any longer. Instead, people model these biochemical reactions by Markov chain networks.

In the discrete setting, same framework can be followed to characterize systematic measures. (1) inject artificial noise, (2) find invariant measure, (3) find the mutual information between components, (4) Calculate degeneracy and complexity. Below, we will particularly study the discrete models of biochemical reaction networks. An illustrative example will also be given.

Consider a biochemical reaction network with N species. Different with the mass-action system, the state space of this network is a graph with vertices set $V =$

$X_1 \times X_2 \times \cdots \times X_N$, where $X_i = \{0, 1, \cdots, K_i\}$, K_i means the maximal possible number of molecules of species i. Then the chemical reaction network can be modeled as a Markov chain on set V. For example, reaction

$$A \to B$$

is represented by edges

$$[mA, (n-1)B] \overset{m\mathrm{P}(mA,(n-1)B)}{\longrightarrow} [(m-1)A, nB]$$

for different m and n. where $\mathrm{P}(A)$ indicates the probability of state $(mA, (n-1)B)$. For detailed explanation, see the reference [55].

Note that this Markovian network is random in nature. In general we do not have to inject external noise to remove the singularity of invariant measure. In case of irreducible Markov chain, injecting artificial noise may be helpful (See subsection 2.2.5). Then we can calculate the marginal distribution of invariant measure by discrete projection. The entropy, mutual information, degeneracy and complexity can be defined in a similiar way as what we did in Section 3.2.

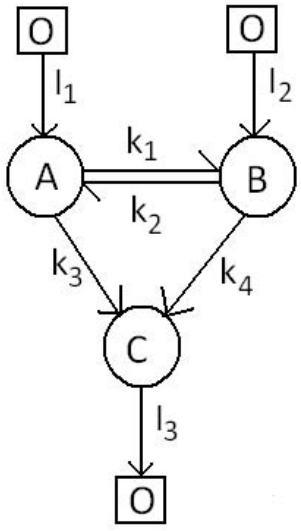

Figure 8: Example of open system

Example 3.7.1. *Consider an open chemical reaction system with material exchange as described in Figure 8. There are three species and* 7 *reactions in this system. O*

means the external environment. k_i and I_i are reaction rate constants. Assume the numbers of molecules of three species A, B and C are all ranged between 0 to 10, then this system can be modeled by Markov chain over a 3-d lattice with 1331 vertices. Let $P(i,j,k,t)$ be the probability of state $A=i, B=j, C=k$ at time t. We obtain the following forward Kolmogorov equation:

$$\begin{aligned}
\frac{\mathrm{d}P(i,j,k,t)}{\mathrm{d}t} &= I_1(P(i-1,j,k,t)-P(i,j,k,t))+I_2(P(i,j-1,k,t)-P(i,j,k,t)) \\
&+ I_3(P(i,j,k+1,t)-P(i,j,k,t)) \\
&+ k_1((i+1)P(i+1,j-1,k,t)-iP(i,j,k,t)) \\
&+ k_2((j+1)P(i-1,j+1,k,t)-jP(i,j,k,t)) \\
&+ k_3((i+1)P(i+1,j,k-1,t)-iP(i,j,k,t)) \\
&+ k_4((j+1)P(i,j+1,k-1,t)-jP(i,j,k,t))
\end{aligned}$$

Note that for the points on the boundary of lattices, the previous equation must be modified with boundary conditions. In this example, we set reaction rates as $k_1=50$, $k_2=50$, $k_3=5$, $k_4=4$, $I_1=6$, $I_2=12$, $I_3=2$.

With the restriction

$$\sum_i \sum_j \sum_j P(i,j,k,t)=1$$

The steady-state shown in figure 9 can be found numerically. The marginal distributions of steady-state follows from the steady-state. Hence one calculate the degeneracy $D=MI(A,B,C)=0.0558$ and the complexity $C=MI(A;B)=4.4461$. This discrete system has positive degeneracy with respect to the decomposition $\mathcal{I}_\infty=\{A\}, \mathcal{I}_2=\{B\}, \mathcal{O}=\{C\}$.

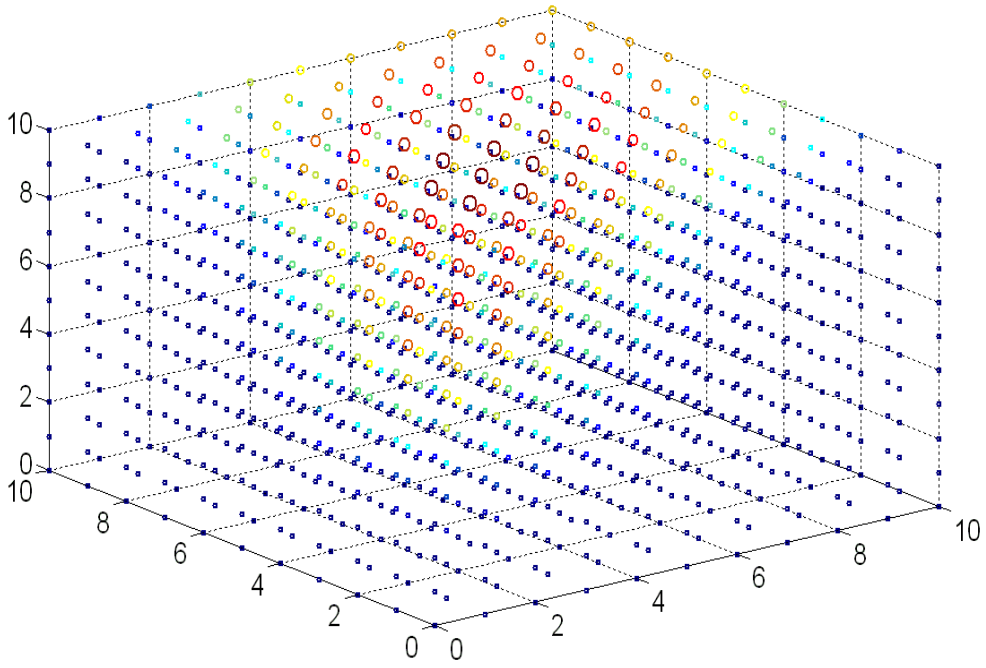

Figure 9: Stationary Probability Distribution. Reder-Larger circle means higher probability

CHAPTER IV

CONCLUSION AND FUTURE WORK

In this thesis, we studied stochastic perturbation of dynamical systems and its application to complex biological network. In the first part, we improved the classical theory of stochastic perturbations of ODE systems. With the help of level set method, more accurate estimation can be given. We also studied stochastic perturbation problem of discrete dynamical systems. The study is motivated by the inconsistency of continuous system and its discretization. A nonlinear scheme is introduced to solve this problem. Further, some geometric properties and exponential convergence rate are proved. Using the stochastic perturbation theory, we studied the systematic measure of complex biological network in the second part of this thesis. Some quantitative characterization of systematic features are given. The robustness of attractors under the stochastic perturbation are particularly discussed. Then we showed that the systematic measures like degeneracy, complexity and robustness have some fundamental connection. Our theory is verified by JAK-STAT crosstalk network.

We would like to say this is the start of our exploration. In this thesis two areas are covered: the stochastic perturbation theory and the application in complex biological network. Some progresses are made; while some problems remain open. In our future study, a more clear landscape of stochastic dynamical systems and its application in complex biological network will be provided.

On one hand, for the stochastic perturbation of dynamical system, the classical large deviation theory provides limit knowledge of perturbed system. People convert problems in stochastic perturbation to problems in Hamilton-Jacob equation, which does not reduce the complexity of problems in general. The level set method in [33]

can provide better estimation. And we believe more results can be carried out by adopting level set method in future. However level set method has its own limitation. The probability distributions on each level set are not studied. Further investigation of stochastic perturbation problems requires a deeper understanding of Fokker-Planck equation as well as the dynamics of unperturbed systems.

On the other hand, the application to complex biological network is even more interesting. In this thesis we introduced some quantitative definitions and proved some of their properties. But the systematic measures are aimed at describing large-scale highly-complex networks, whose parameter may be not explicitly known. An interesting question is: what is the relationship between systematic measures and network structures? This problem will be answered in our future publication. Further, there is the other systematic measure called evolvability. Evidence shows the connection between evolvability and degeneracy. It is also interesting to study complex network under evolutionary pressure in future.

Last but not the least, the systematic measures of complex biological network originally come from the study of neuroscience. Hence it makes a lot of sense to study problems arising in mathematical neuroscience specifically. It would be reasonable to hope a deep study of systematic measures of biological networks can make valuable contributions to the mathematical neuroscience.

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