AN UNCERTAINTY QUANTIFICATION APPROACH TO THE STUDY OF GENE EXPRESSION ROBUSTNESS*

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Dedicated to Professor Ling Hsiao's 80th birthday

Abstract. We study a chemical kinetic system with uncertainty modeling a gene regulatory network in biology. Specifically, we consider a system of two equations for the messenger RNA and micro RNA content of a cell. Our target is to provide a simple framework for noise buffering in gene expression through micro RNA production. Here the uncertainty, modeled by random variables, enters the system through the initial data and the source term. We obtain a sharp decay rate of the solution to the steady state, which reveals that the biology system is not sensitive to the initial perturbation around the steady state. The sharp regularity estimate leads to the stability of the generalized Polynomial Chaos stochastic Galerkin (gPC-SG) method. Based on the smoothness of the solution in the random space and the stability of the numerical method, we conclude the gPC-SG method has spectral accuracy. Numerical experiments are conducted to verify the theoretical findings.

Key words. Gene Expression, generalized Polynomial Chaos, sensitivity analysis, spectral accuracy.

Mathematics Subject Classification. 35Q92, 92C37, 65M70, 65M12.

1. Introduction. In this paper, we are interested in a model of a simple gene regulatory network describing the regulation of the transcription of nuclear DNA by microRNAs (further denoted by μRNA). The synthesis of a protein from its DNA sequence involves several steps: the binding of a transcription factor (which can be a protein or another type of molecule) on the gene promotor sequence initiates the transcription of DNA into messenger RNA (further denoted by mRNA). mRNA is later translated into proteins in the ribosomes. Here, we are specifically interested in the first step, i.e. the transcription of DNA into mRNA. This transcription is subject to a high level of noise due for instance to noise in the availability of transcription factors. Yet, cells have to perform functions with a high level of precision and some noise buffering systems must be at play. In recent years, the role of μRNA has attracted focus. μRNAs are very short RNA sequences which are coded by non protein-coding sequences of the nuclear DNA. They seem to have (among other roles) a role in the regulation of transcription. Indeed, in many cases, the transcription factor initiates transcription of DNA into both the mRNA and a regulatory μRNA. The synthetized μRNA binds on the mRNA and prevents its translation into proteins. It has been argued that the main function of this regulation is to reduce the effect of noise in the transcription process (see [2, 3] and the review [10]).

Our model involves a pair of chemical kinetic equations for the mRNA and μRNA content, with source terms modeling the action of the transcription factor. The effect of the noise is taken into account by adding some uncertainty in the noise term and

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the initial data. We are interested in looking at how this uncertainty propagates to the mRNA content and in comparing this uncertainty between situations including μRNA production or not. The uncertainty is modeled by random variables with given probability density functions.

A classical approach to the study of noise in gene regulatory networks is through the chemical master equation [18] which is solved numerically by means of Gillespie's algorithm [9], see e.g. [4, 16]. Here, we use the chemical kinetic approach, which is a valid approximation of the chemical master equation when ther number of molecules is large. However, this approximation is far from being valid in a cell. This is why we mitigate this discrepancy by assuming a random availability of transcription factors. The advantage is a considerably simpler treatment than with the chemical master equation while preserving the important features of the system. An alternate approach presented in [8] considers Brownian perturbations in the chemical kinetic equations. Introducing the joint probability density for mRNA and μRNA leads to a Fokker-Planck equation which can be analytically solved under some time-scale separation hypotheses. Underlying this approach is the idea that random perturbations do not only affect the initial condition and the source term, but are present at all times. In the present work, we restrict to random perturbation of the source term and initial data which allows us to use the simpler framework of uncertainty quantification.

We will mainly focus on two aspects of this problem. First, we study how a random perturbation near the steady state will affect the system by analyzing the long-time behavior of the perturbative solution in the random space in terms of the weighted Sobolev norm H_π^n, where π is the probability density function of the random variable. We also study the stability and the convergence rate of a numerical method to the system with uncertainty, specifically, the generalized Polynomial Chaos approximation based stochastic Galerkin (gPC-SG) method.

There are plenty of developments regarding the sensitivity analysis and convergence analysis in uncertainty quantification. For example, the solution to elliptic equations, parabolic equations, [1, 6, 7], and kinetic equations [11, 14, 13, 12, 17, 15, 21, 20]. To our knowledge, there has been no such analysis done to a system of chemical kinetic equations describing a gene regulatory network.

There are mainly two difficulties in the analysis. The first one is in the sensitivity analysis in the random space. When we do estimates on the Sobolev norm H_π^n, the size of the nonlinear terms will increase to $O(2^n)$. This will result in a strong assumption on the initial data, that is, the initial randomness is required to be as small as $O(1/2^n)$ to get an exponential decay. Similarly, when we do the stability analysis of the gPC-SG method, if we approximate the solution by K-th order polynomial chaos bases, the size of the nonlinear terms in the resulting deterministic system will be $O(K!)$. If we directly do energy estimates on the approximate solution, then we can only prove stability when the initial randomness is as small as $O(1/K!)$. To sum up, how to get a sharp estimate in terms of n and K without strong assumption on the initial data or steady state is the main difficulty in this problem.

In this paper, we obtain a sharp decay of the random perturbation around the steady state in terms of its Sobolev norm H_π^n through a carefully designed weighted energy norm. Under some mild conditions on the initial data that is independent of n, we find that the random perturbation near the steady state will decay exponentially. Our results also reveal that the solution preserves the regularity in the random space. Moreover, with another weighted energy norm, we prove the stability of the K-th order gPC-SG method with an assumption on initial data independent of K. The

smoothness of the solution in the random space and the stability of the gPC-SG method allows us to prove the spectral convergence of the gPC-SG method. When approximating the numerical solution by the K-th order polynomial chaos basis, the error of the approximation solution in H_π^n is $O(K^{-n})$.

This paper is organized as follows. Section 2 gives an introduction to the chemical kinetic system modeling the targeted gene regulatory network and its corresponding steady state. The main result and proof sketch about the sensitivity of the system under random perturbation near steady state is stated in Section 2.1. The proof of this result is in the following Section 3. In Section 4, the gPC-SG method is introduced and the stability and the convergence rate of this method are stated in Section 4.2. The proof of these two results are in Section 5 and 6 respectively. In Section 7 we numerically study how the presence of RNA inuences the noise in the concentration of unbound mRNA.

2. The model. Consider the following model,

$$\begin{cases} \partial_t \tilde\rho = S(z) - a\tilde\rho - c\tilde\rho\tilde m, \\ \partial_t \tilde m = S(z) - b\tilde m - c\tilde\rho\tilde m, \end{cases} \tag{2.1}$$

with initial data $\tilde\rho(0,z), \tilde m(0,z)$. a, b, c are positive constants. Here $\tilde\rho(t,z), \tilde m(t,z)$ respectively stand for the content of unbound mRNA and μRNA of a cell at time t. $S(z)$ is the source term which models the production of mRNA and μRNA through DNA transcription. We assume that a molecule of μRNA is produced each time a molecule of mRNA is produced, hence the same source term arises in the two equations. The production of mRNA and μRNA is subject to the availability of the transcription factor, which is random. We model this randomness by assuming that the source term is a given function of a random variable z (modelling for instance the concentration of transcription factors) with probability density function $\pi(z)$ on a compact set $I_z \subset \mathbb{R}$. The first equation of (2.1) models the decay of unbound mRNA through its binding to an unbound μRNA (the term $-c\tilde\rho\tilde m$) or through other degradation mechanisms (the term $-a\tilde\rho$). The second equation of (2.1) describes the decay of unbound μRNA through its binding to an unbound mRNA (the term $-c\tilde\rho\tilde m$ again) and through other degradation mechanisms (the term $-b\tilde m$). Note that the binding of μRNA to mRNA consumes one molecule of μRNA and one molecule of mRNA at the same time, which explains why the same loss term is involved in the two equations. The remaining unbound mRNA is then supposed to enter the translation process into proteins through the actions of ribosomes. This step is supposed to occur later and is not included in the model.

If one sets $\partial_t \tilde\rho = \partial_t \tilde m = 0$, one can get the steady state $\rho^\infty(z), \tilde m^\infty(z)$,

$$\rho^\infty = br^\infty, \quad \tilde m^\infty = ar^\infty, \quad \text{with } r^\infty(z) = \frac{1}{2c}\left(-1 + \sqrt\Delta\right) > 0,$$
$$\Delta = 1 + \frac{4cS(z)}{ab} > 1. \tag{2.2}$$

Let $(\rho, m) = (\tilde\rho - \rho^\infty, \tilde m - \tilde m^\infty)$ be the random perturbative solution around the steady state, then $(\rho(t,z), m(t,z))$ satisfies

$$\begin{cases} \partial_t \rho = -\left(a + acr^\infty\right)\rho - bcr^\infty m - c\rho m, \\ \partial_t m = -\left(b + bcr^\infty\right)m - acr^\infty \rho - c\rho m, \end{cases} \tag{2.3}$$

with initial data,

$$\rho(0, z) = \tilde{\rho}(0, z) - \rho^\infty(z), \quad m(0, z) = \tilde{m}(0, z) - \tilde{m}^\infty(z).$$

2.1. Main results and proof sketch. We are interested in the estimates for the solution (ρ, m) in the random space using the norm

$$\|\rho(t)\|_{H_\pi^n}^2 = \sum_{i=0}^n \int (\partial_z^i \rho)^2 \pi(z) dz, \quad \|m(t)\|_{H_\pi^n}^2 = \sum_{i=0}^n \int (\partial_z^i m)^2 \pi(z) dz. \tag{2.4}$$

There are two reasons why we are interested in this Sobolev norm. First, by studying this norm, we can understand how sensitive the system with respect to the random perturbation around the steady state is and how this perturbation evolves in time. Second, this norm gives the Sobolev regularity of the solution in the random space. We will approximate the solution by the gPC-SG method in the random space in Section 4. Such regularity allows us to prove the spectral convergence of the method.

The difficulty in the analysis is to get an estimate of $\|\rho\|_{H_\pi^n}^2$, $\|m\|_{H_\pi^n}^2$ that is sharp for large n. For $n = 0$, one can do standard energy estimates on $a\|\rho\|^2 + b\|m\|^2$ to get an exponential decay of the random perturbation in time under a smallness assumption on initial data. We will show the result for $n = 0$ in the following lemma, and explain why it is not trivial to extend it to $n > 0$ after the proof of the lemma.

LEMMA 2.1. *If initially, the random perturbations satisfy*

$$\|\rho(0)\|_\pi^2 \le \frac{b^2}{4c^2}, \quad \|m(0)\|_\pi^2 \le \frac{a^2}{4c^2},$$

then the perturbations $(\|\rho(t)\|_\pi^2, \|m(t)\|_\pi^2)$ decay exponentially in time as follows,

$$\|\rho(t)\|_\pi^2 \le \frac{1}{a}\left(a\|\rho(0)\|_\pi^2 + b\|m(0)\|_\pi^2\right)e^{-at},$$

$$\|m(t)\|_\pi^2 \le \frac{1}{b}\left(a\|\rho(0)\|_\pi^2 + b\|m(0)\|_\pi^2\right)e^{-bt}.$$

Proof. Multiplying $a\rho$ and bm to the two equations in (2.3) respectively, and then adding them together gives,

$$\frac{1}{2}\partial_t\left(a\rho^2 + bm^2\right)$$
$$= -a^2\rho^2 - b^2m^2 \underbrace{-\left(a^2cr^\infty\rho^2 + 2abcr^\infty m\rho + b^2cr^\infty m^2\right)}_{\text{linear part}} \underbrace{-ac\rho^2 m - bcm^2\rho}_{\text{nonlinear part}}$$
$$\le -a^2\rho^2 - b^2m^2 \underbrace{-cr^\infty(a\rho+bm)^2}_{\text{linear part}} \underbrace{+c^2\rho^2m^2 + \frac{a^2}{4}\rho^2 + c^2\rho^2m^2 + \frac{b^2}{4}m^2}_{\text{nonlinear part}} \tag{2.5}$$
$$\le -\left(\frac{3a}{4} - \frac{c^2}{a}m^2\right)a\rho^2 - \left(\frac{3b}{4} - \frac{c^2}{b}\rho^2\right)bm^2,$$

where we apply Young's inequality to the nonlinear part in the first line to obtain the first inequality. Since r^∞ defined in (2.2) is always positive for any $z \in I_z$, this gives $-cr^\infty(a\rho + bm)^2 \le 0$, so we can omit this term in the second inequality.

After we obtain the inequality as in (2.5), the exponential decay of ρ^2, m^2 follows from a smallness assumption on the initial condition. Assume the coefficients of $a\rho^2$ and bm^2 on the RHS of (2.5) are smaller than $-\frac{a}{2}$ and $-\frac{b}{2}$ respectively, which is equivalent to assume

$$m^2(0, z) \leq \frac{a^2}{4c^2}, \quad \rho^2(0, z) \leq \frac{b^2}{4c^2}, \quad \text{for all } z \in I_z, \tag{2.6}$$

then by continuity argument, for all $t > 0$, one has

$$\frac{1}{2}\partial_t \left(a\rho^2 + bm^2 \right) \leq -\frac{a^2}{2}\rho^2 - \frac{b^2}{2}m^2.$$

Integrating the above equation over time, one gets,

$$a\rho^2(t) + bm^2(t) \leq a\rho^2(0) + bm^2(0) - \int_0^t a^2\rho(s)^2 ds - \int_0^t b^2 m(s)^2 ds,$$

which implies

$$a\rho^2(t) \leq a\rho^2(0) + bm^2(0) - a^2 \int_0^t \rho(s)^2 ds,$$

$$bm^2(t) \leq a\rho^2(0) + bm^2(0) - b^2 \int_0^t m(s)^2 ds.$$

By Grownwall's inequality, one can get the exponential decay of ρ^2, m^2 as follows,

$$\rho^2(t, z) \leq \frac{1}{a} \left(a\rho^2(0, z) + bm^2(0, z) \right) e^{-at}, \quad m^2(t, z) \leq \frac{1}{b} \left(a\rho^2(0, z) + bm^2(0, z) \right) e^{-bt}.$$

Finally, one integrates (2.6) and the above estimates over $\pi(z)dz$, one completes the proof of Lemma 2.1. □

The difficulties of extending the results in Lemma 2.1 to $\|\rho\|^2_{H^n_\pi}, \|m\|^2_{H^n_\pi}$ are mainly due to two reasons. First when $n = 0$, the linear part in (2.5) is a negative square without any assumption on r^∞, so we can directly omit these terms in the estimates. However, if we directly do energy estimates on $\|\rho\|^2_{H^n_\pi}, \|m\|^2_{H^n_\pi}$ for $n > 0$, we have to assume $\sum_{i=1}^n |\partial_z^i r^\infty| \leq O(1/n!)$ to make the linear part negative and this assumption is too strong. Second, the nonlinear part will be $O(n(n!)^2)$ if we directly estimate on $\|\rho\|^2_{H^n_\pi}, \|m\|^2_{H^n_\pi}$ for $n > 0$. This implies that one needs to assume the initial data $\|\rho(0)\|^2_{H^n_\pi}, \|m(0)\|^2_{H^n_\pi}$ as small as $O(1/n/(n!)^2)$ to get the exponential decay in time. We will explain it in more details in the following paragraph.

In order to simplify the notation, we set

$$\begin{aligned} \theta &= a\rho + bm; \\ \boldsymbol{\rho}^n &= (\rho, \partial_z \rho, \cdots, \partial_z^n \rho), \quad \text{similar for } \boldsymbol{m}^n, \boldsymbol{\theta}^n, \end{aligned} \tag{2.7}$$

and let $\|\cdot\|^2$ be the regular Euclidean norm,

$$\|\boldsymbol{\rho}^n\|^2 = \sum_{l=0}^n \rho_l^2.$$

If we directly do energy estimates on $a \|\boldsymbol{\rho}^n\|^2 + b \|\boldsymbol{m}^n\|^2$, then we will get the following inequality by taking ∂_z^l ($0 \leq l \leq n$) to (2.3), then multiplying $a\rho_l, bm_l$ respectively and adding all equations together,

$$
\frac{1}{2} \partial_t \left(a \|\boldsymbol{\rho}^n\|^2 + b \|\boldsymbol{m}^n\|^2 \right) = - a^2 \|\boldsymbol{\rho}^n\|^2 - b^2 \|\boldsymbol{m}^n\|^2 + \underbrace{\sum_{l=0}^n \left[-c \partial_z^l \left(r^\infty \theta \right) \right] \theta_l}_{\text{linear part}}
$$

$$
+ \underbrace{\sum_{l=0}^n -ac \partial_z^l (\rho m) \partial_z^l \rho - bc \partial_z^l (\rho m) \partial_z^l m}_{\text{nonlinear part}}
$$

(2.8)

First, for the linear part, when $n = 0$, the linear part is automatically a negative square term, so we do not need to bound this term any more. However, when $n > 0$, since r^∞ in the linear term depends on z, so taking ∂_z^l to the linear terms gives

$$
\text{linear part} = -c \sum_{l=0}^n \partial_z^l \left(r^\infty \theta \right) \theta_l
$$

$$
= -c r^\infty \|\boldsymbol{\theta}^n\|^2 - c \sum_{l=1}^n \sum_{i=1}^l \binom{l}{i} \partial_z^i r^\infty \left(\partial_z^{l-i} \theta \right) \left(\partial_z^l \theta \right).
$$

(2.9)

Since $-\partial_z^i r^\infty(z), i \geq 1$ are not necessarily negative, only the first term in the last equality of the above equation is negative. Therefore, we need to bound all other terms using the first negative term. By applying Young's inequality and Cauchy-Schwatz inequality to all other terms gives,

$$
\left| -c \sum_{l=1}^n \sum_{i=1}^l \binom{l}{i} \partial_z^i r^\infty \left(\partial_z^{l-i} \theta \right) \left(\partial_z^l \theta \right) \right| \leq \frac{c}{2} \sum_{l=1}^n \sum_{i=1}^l \binom{l}{i} |\partial_z^i r^\infty| \left(\left(\partial_z^{l-i} \theta \right)^2 + \left(\partial_z^l \theta \right)^2 \right)
$$

$$
\lesssim \binom{n}{[n/2]} \left(\sum_{i=1}^n |\partial_z^i r^\infty| \right) \|\boldsymbol{\theta}^n\|^2,
$$

where $[n/2]$ represents the smallest integer that is larger than or equal to $n/2$. The coefficient can be upper bounded by

$$
\binom{n}{[n/2]} \leq 2^n,
$$

this implies only when

$$
\sum_{i=1}^n |r_i^\infty| \leq O\left(\frac{r^\infty}{2^n} \right),
$$

(2.10)

the RHS of (2.9) is non-positive. Obviously, the constraint (2.10) on $r^\infty(z)$ is too strong. Only a small set of steady states are included in this analysis. So we will develop another method to avoid that.

Second, for the nonlinear part in (2.8), since the two terms are similar, we only

estimate the first nonlinear term. Applying Young's inequality gives

$$
\begin{aligned}
\left| \sum_{l=0}^{n} ac\partial_z^l (\rho m) \, \partial_z^l \rho \right| &\leq c^2 \sum_{l=0}^{n} \left(\partial_z^l (\rho m) \right)^2 + \frac{a^2}{4} \left\| \boldsymbol{\rho}^n \right\|^2 \\
&= \sum_{l=0}^{n} \left(\sum_{i=0}^{l} \binom{l}{i} \partial_z^i m \partial_z^{l-i} \rho \right)^2 + \frac{a^2}{4} \left\| \boldsymbol{\rho}^n \right\|^2 \\
&\leq \sum_{l=0}^{n} \left(\sum_{i=0}^{l} \binom{l}{i} \left(\partial_z^i m \right)^2 \right) \left(\sum_{i=0}^{l} \binom{l}{i} \left(\partial_z^{l-i} \rho \right)^2 \right) + \frac{a^2}{4} \left\| \boldsymbol{\rho}^n \right\|^2 \\
&\leq \binom{l}{[l/2]}^2 \left\| \boldsymbol{m}^l \right\|^2 \left\| \boldsymbol{\rho}^l \right\|^2 + \frac{a^2}{4} \left\| \boldsymbol{\rho}^n \right\|^2 \\
&\leq c^2 n \binom{n}{[n/2]}^2 \left\| \boldsymbol{m}^n \right\|^2 \left\| \boldsymbol{\rho}^n \right\|^2 + \frac{a^2}{4} \left\| \boldsymbol{\rho}^n \right\|^2 \\
&\leq c^2 n 2^{2n} \left\| \boldsymbol{m}^n \right\|^2 \left\| \boldsymbol{\rho}^n \right\|^2 + \frac{a^2}{4} \left\| \boldsymbol{\rho}^n \right\|^2 ,
\end{aligned}
\tag{2.11}
$$

where the first inequality comes from Cauchy-Schwatz inequality. One can get similar inequality for $\left| \sum_{l=0}^{n} bc\partial_z^l(\rho m)\partial_z^l m \right|$. Therefore, if one ignores the linear terms in (2.8), one ends up with the following estimates,

$$
\begin{aligned}
\frac{1}{2}\partial_t &\left(a \left\| \boldsymbol{\rho}^n \right\|^2 + b \left\| \boldsymbol{m}^n \right\|^2 \right) \\
&\leq -\left(\frac{3a}{4} - \frac{c^2}{a} 2^{2n} n \left\| \boldsymbol{m}^n \right\|^2 \right) a \left\| \boldsymbol{\rho}^n \right\|^2 - \left(\frac{3b}{4} - \frac{c^2}{b} 2^{2n} n \left\| \boldsymbol{\rho}^n \right\|^2 \right) b \left\| \boldsymbol{m}^n \right\|^2 ,
\end{aligned}
$$

which implies that we have to assume

$$
\left\| \boldsymbol{\rho}^n(0) \right\|^2 , \left\| \boldsymbol{m}^n(0) \right\|^2 \leq O\left(\frac{1}{2^{2n}n} \right)
\tag{2.12}
$$

to get an exponential decay as follows

$$
\left\| \boldsymbol{\rho}^n(t) \right\|^2 \leq O(e^{-at}), \quad \left\| \boldsymbol{m}^n(t) \right\|^2 \leq O(e^{-bt}).
$$

If one integrates the above two equations over $\pi(z)dz$, then one will get the corresponding result in the Sobolev space. However, this result is too weak for large n. If the initial perturbation is smooth enough in the random space, then $\left\| \rho(0) \right\|, \left\| m(0) \right\| \in H_\pi^n$ for any large n. However, by the above result, only for the initial random perturbation $\left\| \rho(0) \right\|_{H_z^n}^2, \left\| m(0) \right\|_{H_z^n}^2$ that are as small as $O(1/4^n n)$, then $\left\| \rho(t) \right\|_{H_z^n}^2, \left\| m(t) \right\|_{H_z^n}^2$ will decay exponentially in time.

In our analysis, we overcome the two difficulties mentioned above by adding a weight ω_i^* to ρ_i, m_i. Then we will only have an assumption on the initial data that is independent of n, furthermore, we only require r^∞ to satisfy the following assumption.

ASSUMPTION 2.2. *There exists a constant κ such that, the derivative of r^∞ in the random space can be bounded by*

$$
\sup_{z \in I_z} |(i+1)^2 \partial_z^i r^\infty| \leq \kappa^{i+1} i!,
\tag{2.13}
$$

and it is bounded below and above by r, R respectively,

$$r \leq r^\infty \leq R, \quad \forall z \in I_z. \tag{2.14}$$

This condition is not strict at all. Actually for any analytic function $r^\infty(z)$ in a compact set I_z, there exists a constant C, such that

$$\left|\partial_z^i r^\infty\right| \leq C^{i+1} i!, \quad \text{for } \forall i \geq 0, \quad \forall z \in I_z.$$

Then set

$$\kappa = eC,$$

one can always get

$$\left|(i+1)^2 \partial_z^i r^\infty\right| \leq \kappa^{i+1} i!, \quad \text{for } \forall i \geq 0, \quad \forall z \in I_z.$$

The weight ω_i^* we add to ρ_i, m_i in $\|\boldsymbol{\rho}^n\|^2, \|\boldsymbol{m}^n\|^2$ is

$$\omega_i^* = \frac{L^{n-i}}{\kappa^i} \frac{(i+1)^2}{i!},$$

where κ is the constant in (2.13), L is a constant depending on κ, which we will define later. In this weight, the term $\frac{(i+1)^2}{i!}$ is used to avoid strong assumption on initial data like (2.12). Notice that with $\frac{1}{i!}$, the factorial in (2.11) can be absorbed into the weights, so one can get rid of $O(1/(n!)^2)$ in the initial assumption; while the weight $(i+1)^2$ is used to deal with $O(1/n)$ in the assumption. Another part of the weight $\frac{L^{n-i}}{\kappa^i}$ is used to avoid strong constraint on r^∞ like (2.10). Under Assumption 2.2, the term $\frac{1}{k^i}$ can be used to bound $|r_i^\infty|$. One further notices that when i is smaller, θ_i will be summed for more times, so the term L^{n-i} is used to balance this. Please refer to Lemma 3.1 for details.

The $\frac{(i+1)^2}{i!}$ part of the weight is first introduced in [17]; However, the assumption on r^∞ and its corresponding weight L^{n-i}/κ^i haven't been developed before.

Before we present the main theorems on the sensitivity of the perturbative solution (ρ, m), we first list the frequently used notations here.

  – A, L are constants defined as,

$$A = \sum_{i=1}^\infty \frac{1}{i^2} = \frac{\pi^2}{6}, \tag{2.15}$$

$$L = \sqrt{\frac{16A\kappa^2}{r^2} + 1}, \tag{2.16}$$

where κ is defined in (2.13).

The following Theorem is about the sensitivity of the perturbative solution (ρ, m) in the random space.

THEOREM 2.3. *For $\forall n \geq 0$, under assumption 2.2, in addition, if initially*

$$\|m(0)\|_{H_\pi^n}^2 \leq a^2 C_0, \quad \|\rho(0)\|_{H_\pi^n}^2 \leq b^2 C_0, \tag{2.17}$$

then the perturbative solution to (2.3) satisfies,

$$\|\rho(t)\|_{H_\pi^n}^2 \leq \frac{(5\nu^n n!)^2}{a} E_{H_\pi^n}(0) e^{-at}, \quad \|m(t)\|_{H_\pi^n}^2 \leq \frac{(5\nu^n n!)^2}{b} E_{H_\pi^n}(0) e^{-bt},$$

where $E_{H_\pi^n}(0) = a \, \|\rho(0)\|_{H_\pi^n}^2 + b \, \|m(0)\|_{H_\pi^n}^2$. *Here C_0, ν are constants independent of n, $C_0 = (5^2 2^5 A c^2)^{-1}$, $\nu = \kappa L$ and L, A, κ are constants defined in (2.16), (2.15), (2.13) respectively.*

REMARK 2.4. *The above theorem tells us that as long as the initial random perturbation around the steady state is small enough, then the perturbation will exponentially decay with a rate of e^{-at}, e^{-bt} for ρ, m respectively. We note that this stability result would extend to any regulatory network provided that the dynamics of each chemical species involves a decay term (due to degradation for instance). In the present case, the decay terms are the terms $-a\bar{\rho}$ in the equation for $\partial_t \bar{\rho}$ and $-b\bar{m}$ in the equation for $\partial_t \bar{m}$. More generally, considering a general regulatory network consisting of species $1, \ldots, n$, we can describe its evolution by*

$$\partial_t \rho = S(z) - A\rho + \text{ nonlinear terms },$$

with $\rho = (\rho_1, \cdots, \rho_n)$ being the vector of the densities of the species $1, \ldots, n$, $S = (S_1, \cdots, S_n)$, the corresponding production terms and $A = (A_{ij})_{i,j=1\ldots n}$ the matrix of degradation terms. As long as this system has a unique steady state (or more generally a discrete set of steady states), and A is a uniformly positive definite matrix, then, any perturbation of this steady-state will converge to the steady-state for large times provided the perturbation is small enough.

3. Proof of Theorem 2.3 (The sensitivity analysis around the steady state). In this section, we are going to analyze how $E_{H_\pi^n} = a \, \|\rho\|_{H_\pi^n}^2 + b \, \|m\|_{H_\pi^n}^2$ evolves in time by studying E^n,

$$E^n = a \, \|\boldsymbol{\rho}_\omega^n\|^2 + b \, \|\boldsymbol{m}_\omega^n\|^2 , \qquad (3.1)$$

where $\boldsymbol{\rho}_\omega^n, \boldsymbol{m}_\omega^n, \boldsymbol{\theta}_\omega^n$ are similarly defined as

$$\boldsymbol{\rho}_\omega^n = (\omega_0^* \rho, \omega_1^* \partial_z \rho, \cdots, \omega_n^* \partial_z^n \rho) , \qquad (3.2)$$

for weights ω_i^* defined as,

$$\omega_i = \frac{(i+1)^2}{\kappa^i i!}, \quad \omega_i^* = L^{n-i} \omega_i. \qquad (3.3)$$

After taking the integration of the result for E^n in the random space over $\pi(z)dz$, we can get the results for E_π^n,

$$\|\boldsymbol{\rho}_\omega^n\|_\pi^2 = \int \|\boldsymbol{\rho}_\omega^n\|^2 \, \pi(z)dz, \quad \|\boldsymbol{m}_\omega^n\|_\pi^2 = \int \|\boldsymbol{m}_\omega^n\|_{H_\pi^n}^2 \, \pi(z)dz,$$

$$E_\pi^n = a \, \|\boldsymbol{\rho}_\omega^n\|_\pi^2 + b \, \|\boldsymbol{m}_\omega^n\|_\pi^2 . \qquad (3.4)$$

Using the relationship between E_π^n and $E_{H_\pi^n}(t) = a \, \|\rho(t)\|_{H_\pi^n}^2 + b \, \|m(t)\|_{H_\pi^n}^2$, we can get the exponential decay for $E_{H_\pi^n}$.

The most important part in the proof is stated in the following Lemma 3.1, which will be proved later.

LEMMA 3.1. *For r^∞ under Condition 2.13, and any vector function $\boldsymbol{\rho}^n, \boldsymbol{m}^n, \boldsymbol{\theta}^n$, the following inequalities hold*

$$\sum_{l=0}^n (\omega_l^*)^2 \, \partial_z^l (\rho m) \, \partial_z^l \rho \le \frac{2A}{\gamma L^n} \, \|\boldsymbol{\rho}_\omega^n\|^2 \, \|\boldsymbol{m}_\omega^n\|^2 + \frac{2\gamma}{L^n} \, \|\boldsymbol{\rho}_\omega^n\|^2 , \quad \forall \gamma > 0; \qquad (3.5)$$

$$-\sum_{l=0}^{n}(\omega_l^*)^2\,\partial_z^l\,(r^\infty\theta)\,\partial_z^l\theta \le 0. \tag{3.6}$$

Proof. See Section 3.1. □

If one multiplies ω_l^* to the two equations in (2.8) and adds the two equations together, then sums l from 0 to n, one has,

$$\frac{1}{2}\partial_t E^n = -a^2\,\|\boldsymbol{\rho}_\omega^n\|^2 - b^2\,\|\boldsymbol{m}_\omega^n\|^2 - c\sum_{l=0}^{n}(\omega_l^*)^2\,\partial_z^l\,(r^\infty\theta)\,\partial_z^l\theta$$

$$-c\sum_{l=0}^{n}(\omega_l^*)^2\,\partial_z^l\,(\rho m)\,\partial_z^l\theta. \tag{3.7}$$

Based on (3.6) in Lemma 3.1, one can omit the third term on the RHS of (3.7). Furthermore, by setting $\gamma = \frac{L^n}{8c}$ in (3.5), one can bound the nonlinear terms by

$$\frac{1}{2}\partial_t E^n \le -a^2\,\|\boldsymbol{\rho}_\omega^n\|^2 - b^2\,\|\boldsymbol{m}_\omega^n\|^2 + c^2\frac{16A}{L^{2n}}\,\|\boldsymbol{\rho}_\omega^n\|^2\,\|\boldsymbol{m}_\omega^n\|^2$$

$$+\frac{a^2}{4}\,\|\boldsymbol{\rho}_\omega^n\|^2 + \frac{b^2}{4}\,\|\boldsymbol{m}_\omega^n\|^2 \tag{3.8}$$

$$= -\left(\frac{3a}{4} - \frac{8c^2A}{aL^{2n}}\,\|\boldsymbol{m}_\omega^n\|^2\right)a\,\|\boldsymbol{\rho}_\omega^n\|^2 - \left(\frac{3b}{4} - \frac{8c^2A}{bL^{2n}}\,\|\boldsymbol{\rho}_\omega^n\|^2\right)b\,\|\boldsymbol{m}_\omega^n\|^2.$$

Since (3.8) is similar to (2.5) in the proof of Lemma 2.1, by the continuity arguement, one can conclude that if initially,

$$\frac{8c^2A}{aL^{2n}}\,\|\boldsymbol{m}_\omega^n(0)\|_\pi^2 \le \frac{a}{4}, \quad \frac{8c^2A}{bL^{2n}}\,\|\boldsymbol{\rho}_\omega^n(0)\|_\pi^2 \le \frac{b}{4}, \tag{3.9}$$

$\|\boldsymbol{\rho}_\omega^n(t)\|_\pi^2, \|\boldsymbol{m}_\omega^n(t)\|_\pi^2$ decay as follows,

$$\|\boldsymbol{\rho}_\omega^n(t)\|_\pi^2 \le \frac{E_\pi^n(0)}{a}e^{-at}, \quad \|\boldsymbol{m}_\omega^n(t)\|_\pi^2 \le \frac{E_\pi^n(0)}{b}e^{-bt}. \tag{3.10}$$

Now, we need to transfer (3.9) and (3.10) to the Sobolev norm we want to estimate in the random space $\left(\|\rho\|_{H_\pi^n}^2, \|m\|_{H_\pi^n}^2\right)$. Since

$$\frac{1}{n!} \le \frac{(i+1)^2}{i!} \le 5, \quad \text{for } 0 \le i \le n,$$

so one has

$$\frac{1}{\kappa^n n!} \le \omega_i^* \le 5L^n, \quad \text{for } 0 \le i \le n,$$

which implies that,

$$\left(\frac{1}{\kappa^n n!}\right)^2 \|\rho\|_{H_\pi^n}^2 \le \|\boldsymbol{\rho}_\omega^n(t)\|_\pi^2 \le (5L^n)^2\,\|\rho\|_{H_\pi^n}^2,$$

and similar relationship can be obtained for $\|\boldsymbol{m}_\omega^n(t)\|_\pi^2$ and $\|m\|_{H_\pi^n}^2$. Therefore, the initial requirement (3.9) becomes,

$$\frac{5^2 8c^2A}{a}\,\|m(0)\|_{H_\pi^n}^2 \le \frac{a}{4}, \quad \frac{5^2 8c^2A}{b}\,\|\rho(0)\|_{H_\pi^n}^2 \le \frac{b}{4},$$

then $\left(\|\rho\|_{H^n_\pi}^2, \|m\|_{H^n_\pi}^2 \right)$ will decay as follows,

$$\|\rho(t)\|_{H^n_\pi}^2 \leq (5\kappa^n n! L^n)^2 \frac{E_{H^n_\pi}(0)}{a} e^{-at}, \quad \|m(t)\|_{H^n_\pi}^2 \leq (5\kappa^n n! L^n)^2 \frac{E_{H^n_\pi}(0)}{b} e^{-bt},$$

where $E_{H^n_\pi}(0) = a \|\rho(0)\|_{H^n_\pi}^2 + b \|m(0)\|_{H^n_\pi}^2$ and this is obtained from (3.10). The above two equations give the final results in Theorem 2.3.

3.1. Proof of Lemma 3.1. The following is the proof of Lemma 3.1.

Proof. Expanding $\partial_z^l(\rho m)$ gives,

$$\sum_{l=0}^n (\omega_l^*)^2 \, \partial_z^l (\rho m) \, \partial_z^l \rho = \sum_{l=0}^n \sum_{i=0}^l (\omega_l^*)^2 \binom{l}{i} \partial_z^i \rho \partial_z^{l-i} m \partial_z^l \rho. \tag{3.11}$$

First notice that

$$\left| (\omega_l^*)^2 \binom{l}{i} \partial_z^i \rho \partial_z^{l-i} m \partial_z^l \rho \right| = \left| \frac{(l+1)^2 L^n}{L^i L^{l-i} \kappa^i \kappa^{l-i} l!} \frac{l!}{i!(l-i)!} \partial_z^i \rho \partial_z^{l-i} m \left(\omega_l^* \partial_z^l \rho \right) \right|$$

$$= \left| \frac{(l+1)^2}{(i+1)^2(l-i+1)^2 L^n} \left(\omega_i^* \partial_z^i \rho \right) \left(\omega_{l-i}^* \partial_z^{l-i} m \right) \left(\omega_l^* \partial_z^l \rho \right) \right| \tag{3.12}$$

$$\leq \frac{2}{L^n} \left(\frac{1}{(i+1)^2} + \frac{1}{(l-i+1)^2} \right) \left(\omega_i^* \partial_z^i \rho \right) \left(\omega_{l-i}^* \partial_z^{l-i} m \right) \left(\omega_l^* \partial_z^l \rho \right),$$

where the second inequality is because of

$$(l+1)^2 \leq ((i+1) + (l-i+1))^2 \leq 2(i+1)^2 + 2(l-i+1)^2.$$

If one sums up the first part of (3.12) over i, l, one has,

$$\frac{2}{L^n} \sum_{l=0}^n \sum_{i=0}^l \frac{1}{(i+1)^2} \left(\omega_i^* \partial_z^i \rho \right) \left(\omega_{l-i}^* \partial_z^{l-i} m \right) \left(\omega_l^* \partial_z^l \rho \right)$$

$$\leq \frac{1}{\gamma L^n} \sum_{l=0}^n \left(\sum_{i=0}^l \frac{1}{(i+1)^2} \left(\omega_i^* \partial_z^i \rho \right) \left(\omega_{l-i}^* \partial_z^{l-i} m \right) \right)^2 + \frac{\gamma}{L^n} \sum_{l=0}^n \left(\omega_l^* \partial_z^l \rho \right)^2$$

$$\leq \frac{1}{\gamma L^n} \sum_{l=0}^n \left(\sum_{i=0}^l \frac{1}{(i+1)^2} \right) \left(\sum_{i=0}^l \frac{1}{(i+1)^2} \left(\omega_i^* \partial_z^i \rho \right)^2 \left(\omega_{l-i}^* \partial_z^{l-i} m \right)^2 \right) + \frac{\gamma}{L^n} \|\boldsymbol{\rho}_\omega^n\|^2 \tag{3.13}$$

$$\leq \frac{A}{\gamma L^n} \sum_{i=0}^n \sum_{l=i}^n \frac{1}{(i+1)^2} \left(\omega_i^* \partial_z^i \rho \right)^2 \left(\omega_{l-i}^* \partial_z^{l-i} m \right)^2 + \frac{\gamma}{L^n} \|\boldsymbol{\rho}_\omega^n\|^2$$

$$\leq \frac{A}{\gamma L^n} \sum_{i=0}^n \frac{1}{(i+1)^2} \left(\omega_i^* \partial_z^i \rho \right)^2 \sum_{l-i=0}^n \left(\omega_{l-i}^* \partial_z^{l-i} m \right)^2 + \frac{\gamma}{L^n} \|\boldsymbol{\rho}_\omega^n\|^2$$

$$\leq \frac{A}{\gamma L^n} \|\boldsymbol{\rho}_\omega^n\|^2 \|\boldsymbol{m}_\omega^n\|^2 + \frac{\gamma}{L^n} \|\boldsymbol{\rho}_\omega^n\|^2.$$

The first inequality is obtained by applying Young's inequality, and then applying Cauchy-Schwartz inequality gives the second one. Since $l - i$ and i are symmetric, so the second part of (3.12) can be similarly bounded. Therefore, summing (3.12) over i, l gives an upper bound for the RHS of (3.11). This implies

$$\sum_{l=0}^n (\omega_l^*)^2 \, \partial_z^l (\rho m) \, \rho_l \leq \frac{2A}{\gamma L^n} \|\boldsymbol{\rho}_\omega^n\|^2 \|\boldsymbol{m}_\omega^n\|^2 + \frac{2\gamma}{L^n} \|\boldsymbol{\rho}_\omega^n\|^2.$$

For the second inequality (3.6), one first separates it into two parts,

$$
-\sum_{l=0}^{n} (\omega_l^*)^2 \, \partial_z^l \left(r^\infty \theta \right) \partial_z^l \theta
$$

$$
= -\sum_{l=0}^{n} (\omega_l^*)^2 \, r^\infty \partial_z^l \theta \partial_z^l \theta - \sum_{l=1}^{n} \sum_{i=1}^{l} (\omega_l^*)^2 \binom{l}{i} \partial_z^i r^\infty \partial_z^{l-i} \theta \partial_z^l \theta
$$

$$
= -r^\infty \left\| \boldsymbol{\theta}_\omega^n \right\|^2 - \frac{2}{L^n} \sum_{l=1}^{n} \sum_{i=1}^{l} \left(\frac{1}{(i+1)^2} + \frac{1}{(l-i+1)^2} \right) \left(\omega_i^* \partial_z^i r^\infty \right) \left(\omega_{l-i}^* \partial_z^{l-i} \theta \right) \left(\omega_l^* \partial_z^l \theta \right)
$$

$$
\leq -r^\infty \left\| \boldsymbol{\theta}_\omega^n \right\|^2 + \frac{1}{\gamma L^n} \sum_{l=1}^{n} \left(\sum_{i=1}^{l} \frac{1}{(i+1)^2} \left(\omega_i^* r^\infty \right) \left(\omega_{l-i}^* \theta_{l-i} \right) \right)^2
$$

$$
+ \frac{1}{\gamma L^n} \sum_{l=1}^{n} \left(\sum_{i=1}^{l} \frac{1}{(l-i+1)^2} \left(\omega_i^* r^\infty \right) \left(\omega_{l-i}^* \theta_{l-i} \right) \right)^2 + \frac{2\gamma}{L^n} \sum_{l=0}^{n} \left\| \boldsymbol{\theta}_\omega^n \right\|^2
$$

$$
\leq -\frac{r^\infty}{2} \left\| \boldsymbol{\theta}_\omega^n \right\|^2 + \frac{4}{L^{2n} r^\infty} \sum_{l=1}^{n} \left(\sum_{i=1}^{l} \frac{1}{(i+1)^2} \left(\omega_i^* r^\infty \right) \left(\omega_{l-i}^* \theta_{l-i} \right) \right)^2
$$

$$
+ \frac{4}{L^{2n} r^\infty} \sum_{l=1}^{n} \left(\sum_{i=1}^{l} \frac{1}{(l-i+1)^2} \left(\omega_i^* r^\infty \right) \left(\omega_{l-i}^* \theta_{l-i} \right) \right)^2 , \tag{3.14}
$$

where the second equality is obtained by applying (3.12), then applying Young's inequality gives the first inequality, and setting $\gamma = \frac{L^n r^\infty}{4}$ gives the last inequality. The second and third terms in the last inequality are similar to the first term in the second line of (3.13), so according to the fourth line in (3.13), (3.14) can be further simplified to

$$
-\sum_{l=0}^{n} (\omega_l^*)^2 \, \partial_z^l \left(r^\infty \theta \right) \theta_l
$$

$$
\leq -\frac{r^\infty}{2} \left\| \boldsymbol{\theta}_\omega^n \right\|^2 + \frac{4A}{L^{2n} r^\infty} \sum_{l=1}^{n} \sum_{i=1}^{l} \left(\frac{1}{(i+1)^2} + \frac{1}{(l-i+1)^2} \right) \left(\omega_i^* r_i^\infty \right)^2 \left(\omega_{l-i}^* \theta_{l-i} \right)^2
$$

$$
= -\frac{r^\infty}{2} \left\| \boldsymbol{\theta}_\omega^n \right\|^2 + \frac{4A}{r^\infty} \sum_{l=1}^{n} \sum_{i=1}^{l} \left(\frac{L^{-2i}}{(i+1)^2} + \frac{L^{-2i}}{(l-i+1)^2} \right) \left(\omega_i r_i^\infty \right)^2 \left(\omega_{l-i}^* \theta_{l-i} \right)^2
$$

$$
\leq -\frac{r^\infty}{2} \left\| \boldsymbol{\theta}_\omega^n \right\|^2 + \frac{4A\kappa^2}{r^\infty} \sum_{l=1}^{n} \sum_{i=1}^{l} \left(\frac{L^{-2i}}{(i+1)^2} + \frac{L^{-2i}}{(l-i+1)^2} \right) \left(\omega_{l-i}^* \theta_{l-i} \right)^2
$$

$$
= -\frac{r^\infty}{2} \left\| \boldsymbol{\theta}_\omega^n \right\|^2 + \frac{4A\kappa^2}{r^\infty} \sum_{i=1}^{n} \frac{L^{-2i}}{(i+1)^2} \sum_{l=i}^{n} \left(\omega_{l-i}^* \theta_{l-i} \right)^2
$$

$$
+ \frac{4A\kappa^2}{r^\infty} \sum_{i=1}^{n} L^{-2i} \sum_{l=i}^{n} \frac{\left(\omega_{l-i}^* \theta_{l-i} \right)^2}{(l-i+1)^2} \tag{3.15}
$$

where the first equality comes from the definition of ω_i^* in (3.3), and the second inequality is by Assumption 2.2,

$$
\sup_{z \in I_z} \left(\omega_i \partial_z^i r^\infty \right)^2 \leq \kappa^2.
$$

Furthermore, since

$$\sum_{i=1}^{n} \frac{L^{-2i}}{(i+1)^2} \leq \sum_{i=1}^{n} L^{-2i} \leq \frac{1}{(L^2-1)} \leq \frac{r^2}{16A\kappa^2},$$

by the definition of L in (2.16). Inserting it back to (3.15) gives

$$-\sum_{l=0}^{n} (\omega_l^*)^2 \, \partial_z^l \, (r^\infty \theta) \, \theta_l \leq -\frac{r^\infty}{2} \, \|\boldsymbol{\theta}_\omega^n\|^2 + \frac{r}{4} \, \|\boldsymbol{\theta}_\omega^n\|^2 + \frac{r}{4} \, \|\boldsymbol{\theta}_\omega^n\|^2 \leq 0,$$

which completes the proof for the second inequality (3.6). $\square$

4. The gPC-SG method.

4.1. The numerical method. In this section, we will introduce a numerical method for model (2.1), which enjoys spectral accuracy in the random space.

For random variable z with probability density function $\pi(z)$, there exists a corresponding orthogonal polynomial basis $\{\Phi_i\}_{i=0}^{\infty}$ with respect to the measure $\pi(z)dz$, which is orthonormal to each other in the weighted L_π^2 inner product,

$$\int_{I_z} \Phi_i \Phi_j \pi(z)dz = \delta_{ij}, \tag{4.1}$$

where δ_{ij} is the Kronecker delta function. The K-th order subspace is therefore spanned by $\{\Phi_i\}_{i=0}^{K}$. As a popular numerical method, the generalized Polynomial Chaos stochastic Galarkin (gPC-SG) method is to find the approximate solution in the truncated K-th order subspace. That is, define the approximation solution of the perturbative ρ, m in the form of,

$$\hat{\rho}^K(t,x,z) = \sum_{i=0}^{K} \hat{\rho}_i(t,x)\Phi_i(z), \quad \hat{m}^K(t,x,z) = \sum_{i=0}^{K} \hat{m}_i(t,x)\Phi_i(z), \tag{4.2}$$

then insert $\hat{\rho}^K$, $\hat{m}^K$ into (2.2) and do Galerkin projection, so the approximation solution $\hat{\rho}^K, \hat{m}^K$ satisfies,

$$\begin{cases} \langle \partial_t \hat{\rho}^K, \Phi_j \rangle_\pi = \langle -(a+acr^\infty) \hat{\rho}^K - bcr^\infty \hat{m}^K - c\hat{\rho}^K \hat{m}^K, \Phi_j \rangle_\pi, & 0 \leq j \leq K, \\ \langle \partial_t \hat{m}^K, \Phi_j \rangle_\pi = \langle -(b+bcr^\infty) \hat{m}^K - acr^\infty \hat{\rho}^K - c\hat{\rho}^K \hat{m}^K, \Phi_j \rangle_\pi, & 0 \leq j \leq K. \end{cases} \tag{4.3}$$

Equivalently, (4.3) can be written as a system of the deterministic coefficients of $\hat{\rho}^K$, $\hat{m}^K$, i.e. the vector functions $\hat{\boldsymbol{\rho}}^K(t,x) = (\hat{\rho}_0(t,x), \cdots, \hat{\rho}_K(t,x))^\top$, $\hat{\mathbf{m}}^K(t,x) = (\hat{m}_0(t,x), \cdots, \hat{m}_K(t,x))^\top$ satisfiy,

$$\begin{cases} \partial_t \hat{\boldsymbol{\rho}}^K = -a\hat{\boldsymbol{\rho}}^K - ac\Upsilon\hat{\boldsymbol{\rho}}^K - bc\Upsilon\hat{\mathbf{m}}^K - c \left(\sum_{i,j} \hat{m}_i S_{ij}^l \hat{\rho}_j \right)_{l=0}^{K}, \\ \partial_t \hat{\mathbf{m}}^K = -b\hat{\mathbf{m}}^K - bc\Upsilon\hat{\mathbf{m}}^K - ac\Upsilon\hat{\boldsymbol{\rho}}^K - c \left(\sum_{i,j} \hat{m}_i S_{ij}^l \hat{\rho}_j \right)_{l=0}^{K}, \end{cases} \tag{4.4}$$

with initial data,

$$\hat{\rho}_j(0) = \langle \rho(0,z), \Phi_j \rangle_\pi, \quad \hat{m}_j(0) = \langle m(0,z), \Phi_j \rangle_\pi, \quad 0 \leq j \leq K.$$

Here S^l, Υ are symmetric matrices defined as

$$S_{ij}^l = \int_{I_z} \Phi_i \Phi_j \Phi_l \, \pi(z)dz, \quad \Upsilon_{ij} = \int_{I_z} r^\infty \Phi_i \Phi_j \, \pi(z)dz. \tag{4.5}$$

4.2. Main results and proof sketch. We will prove that the approximate solution obtained by the gPC-SG from solving the deterministic system (4.4) has spectral accuracy. We will decompose the error of the approximate solution into two parts, one is the projection error, another is the Galerkin error. The first part is determined by the regularity of the solution (ρ, m) in the random space, while the second part is determined by the stability of the Galerkin system (4.4).

Define the projection of the analytic perturbative solution (ρ, m) onto the subspace $\{\Phi_i\}_{i=0}^K$ as,

$$\bar{\rho}^K := \left(\int \rho \mathbf{\Phi}^K d\pi(z) \right) \cdot \mathbf{\Phi}^K, \quad \bar{m}^K := \left(\int m \mathbf{\Phi}^K d\pi(\mathbf{z}) \right) \cdot \mathbf{\Phi}^K, \qquad (4.6)$$

where $\mathbf{\Phi}^K(z) = (\Phi_i)_{i=0}^K$ is the vector function that contains all basis functions up to the K-th order. Then we can decompose the error of the approximation solution $(\hat{\rho}^K, \hat{m}^K)$ into two parts,

$$\rho - \hat{\rho}^K = \underbrace{(\rho - \bar{\rho}^K)}_{\varrho_\rho^K} + \underbrace{(\bar{\rho}^K - \hat{\rho}^K)}_{\varepsilon_\rho^K}, \qquad (4.7)$$

$$m - \hat{m}^K = \underbrace{(m - \bar{m}^K)}_{\varrho_m^K} + \underbrace{(\bar{m}^K - \hat{m}^K)}_{\varepsilon_m^K}, \qquad (4.8)$$

where $(\varrho_\rho^K, \varrho_m^K)$ represents for the projection error, $(\varepsilon_\rho^K, \varepsilon_m^K)$ are errors from the stochastic Galerkin. Especially, we set $(\varepsilon_\rho^K, \varepsilon_m^K)$ to be the vector function defined as,

$$\begin{aligned}
\varepsilon_\rho^K = \boldsymbol{\varepsilon}_\rho^K \cdot \mathbf{\Phi}^K &:= \left(\int (\rho - \hat{\rho}^K) \mathbf{\Phi}^K d\pi(z) \right) \cdot \mathbf{\Phi}^K, \\
\varepsilon_m^K = \boldsymbol{\varepsilon}_m^K \cdot \mathbf{\Phi}^K &:= \left(\int (m - \hat{m}^K) \mathbf{\Phi}^K d\pi(z) \right) \cdot \mathbf{\Phi}^K.
\end{aligned} \qquad (4.9)$$

Because of the orthonality of the bases, it is easy to check that

$$\left\| \varepsilon_\rho^K \right\|_\pi^2 = \left\| \boldsymbol{\varepsilon}_\rho^K \right\|^2, \quad \left\| \varepsilon_m^K \right\|_\pi^2 = \left\| \boldsymbol{\varepsilon}_m^K \right\|^2.$$

From Theorem 2.3, one can bound $(\varrho_\rho^K, \varrho_m^K)$ as in the following Corollary.

COROLLARY 4.1. *Under the same initial condition as in Theorem 2.3, the projection error decays in time exponentially according to,*

$$\begin{aligned}
\left\| \varrho_\rho^K \right\|_\pi^2 = \left\| \rho - \bar{\rho}^K \right\|_\pi^2 &\leq \frac{D \left(\nu^n n! \right)^2 E_{H_\pi^n}(0)}{a(K+1)^{2n}} e^{-at}, \\
\left\| \varrho_m^K \right\|_\pi^2 = \left\| m - \bar{m}^K \right\|_\pi^2 &\leq \frac{D \left(\nu^n n! \right)^2 E_{H_\pi^n}(0)}{b(K+1)^{2n}} e^{-bt},
\end{aligned} \qquad (4.10)$$

for some constant D related to the measure $\pi(z)dz$.

Proof. (4.10) comes from the classical approximation theorem of orthogonal basis, one can refer to Theorem 2.1 in [5]. For $\rho \in H_z^n$, there exists a constant D, such that

$$\left\| \rho - \bar{\rho}^K \right\|_\pi^2 \leq D \frac{\|\rho\|_{H_z^n}^2}{(K+1)^{2n}}, \qquad (4.11)$$

then applying the result of Theorem 2.3 directly gives (4.10). □

Since by Corollary 4.1, we already have estimates for the projection error $(\varrho_\rho^K, \varrho_m^K)$, so in order to study the convergence rate of the gPC-SG method, we only need to analyze the Galerkin error $(\varepsilon_\rho^K, \varepsilon_m^K)$. Estimates for $(\varepsilon_\rho^K, \varepsilon_m^K)$ are based on the stability of the gPC-SG method, which is stated in Theorem 4.6. Similar to the analysis we did to get the estimates for $\|\rho\|_{H_\pi^n}$, $\|m\|_{H_\pi^n}$, if one directly does the energy estimates on $\|\hat{\boldsymbol{\rho}}^K\|_\pi$, $\|\hat{\mathbf{m}}^K\|_\pi$, one will end up with a strong assumption on the initial data for large K. In order to avoid that, we add a weight μ_i to $\hat{\rho}_i, \hat{m}_i$, then under Assumptions 4.2 and 4.4, we can get a stability result that is sharp in K.

ASSUMPTION 4.2. *There exists a positive integer p, such that the basis functions $\{\Phi_i(z)\}_{i\geq 0}$ satisfy,*

$$\|\Phi_i(z)\|_{L^\infty} \leq \eta_i = (i+1)^p, \quad \text{for all } i \geq 0. \tag{4.12}$$

REMARK 4.3. *This assumption, first introduced in [17], combined with the weight μ_i defined in (4.16) guarantees that the initial data do not depend on K. For example, the bases of normalized Legendre polynomials, which corresponds to uniform distribution in $[-1, 1]$, satisfy the above condition with $p = 1/2$; The bases of normalized Chebyshev polynomials, which corresponds to the random variable with pdf $\pi(z) = \frac{2}{\pi\sqrt{1-z^2}}$, satisfy this condition with $p = 0$.*

ASSUMPTION 4.4. *Let $r_i^\infty = \langle r^\infty, \Phi_i \rangle_\pi$, we assume*

$$\sum_{j\geq 1}((j+1)^q r_j^\infty)^2 \leq \frac{(r_0^\infty)^2}{2^{2q+3}A}, \tag{4.13}$$

where the constant A is defined in (2.15), $q = p + 2$, with p defined in (4.12); $r_0^\infty = \int_{I_z} r^\infty \pi(z)dz$ is the expectation of r^∞.

REMARK 4.5. *One sufficient condition for r^∞ is,*

$$\left|r_j^\infty\right|^2 \leq \frac{C}{(j+1)^{2q+2}}, \quad \text{for } \forall j \geq 1, \quad C = \frac{(r_0^\infty)^2}{2^{2q+4}AC_S}. \tag{4.14}$$

This implies that the variance of r^∞, which is equal to $\sum_{j\geq 1}\left(r_j^\infty\right)^2$, has to be small enough.

We further define $\hat{\boldsymbol{\rho}}_\mu^K, \hat{\mathbf{m}}_\mu^K$ as weighted approximate solution

$$\hat{\boldsymbol{\rho}}_\mu^K = (\mu_0\hat{\rho}_0, \cdots, \mu_K\hat{\rho}_K), \quad \hat{\mathbf{m}}_\mu^K = (\mu_0\hat{m}_0, \cdots, \mu_K\hat{m}_K) \tag{4.15}$$

where μ_i are weights defined as,

$$\mu_i = (i+1)^q, \quad \text{for} \quad q = p + 2, \tag{4.16}$$

and here p is the positive constant defined in (4.12).

THEOREM 4.6 (Stability of the gPC-SG method). *Under Assumptions 4.2 and 4.4, for the approximate perturbative solution $(\hat{\boldsymbol{\rho}}^K, \hat{\mathbf{m}}^K)$ obtained by the gPC-SG method, if initially*

$$\left\|\hat{\mathbf{m}}_\mu^K(0)\right\|^2 \leq a^2\hat{C}_0, \quad \left\|\hat{\boldsymbol{\rho}}_\mu^K(0)\right\|^2 \leq b^2\hat{C}_0, \tag{4.17}$$

then it decays in time as follows

$$\left\| \hat{\boldsymbol{\rho}}_\mu^K(t) \right\|^2 \leq \frac{1}{a} \hat{E}^K(0) e^{-at}, \quad \left\| \hat{\mathbf{m}}_\mu^K(t) \right\|^2 \leq \frac{1}{b} \hat{E}^K(0) e^{-bt}, \tag{4.18}$$

where $\hat{E}^K = a \left\| \hat{\boldsymbol{\rho}}_\mu^K(t) \right\|^2 + b \left\| \hat{\mathbf{m}}_\mu^K(t) \right\|^2$. Here $\hat{C}_0 = (2^{2q+6}c^2 A)^{-1}$ and A is defined in (2.15).

The above theorem will be proved in Section 5. It tells us that the gPC-SG method is stable under some smallness assumption on the initial data. Based on the above result, we can prove the spectral accuracy of the gPC-SG method, which is stated in Theorem 4.7. Before we state the theorem, we first introduce the Sobolev constant C_S,

$$\|\rho\|_{L_{\mathbf{z}}^\infty}^2 \leq C_S \|\rho\|_{H_{\mathbf{z}}^1}^2, \quad \text{for } \forall \rho \in H_{\mathbf{z}}^1. \tag{4.19}$$

THEOREM 4.7 (Spectral accuracy of the gPC-SG method). *Under Assumptions 2.2, 4.2, 4.4, and in addition, initially the exact solution $(\rho, m) \in H_\pi^n$, and the approximate solution $(\hat{\rho}^K, \hat{m}^K)$ satisfies,*

$$\|m(0)\|_{H_\pi^n}^2 \leq a^2 C_0, \quad \|\rho(0)\|_{H_\pi^n}^2 \leq b^2 C_0, \quad \left\| \hat{\mathbf{m}}_\mu^K(0) \right\|^2 \leq a^2 \hat{C}_0, \quad \left\| \hat{\boldsymbol{\rho}}_\mu^K(0) \right\|^2 \leq b^2 \hat{C}_0,$$

then $(\hat{\rho}^K, \hat{m}^K)$ converges to (ρ, m) according to,

$$\left\| \rho - \hat{\rho}^K \right\|_\pi^2 \leq \frac{C(n)}{a(K+1)^{2n}} e^{-at}, \quad \left\| m - \hat{m}^K \right\|_\pi^2 \leq \frac{C(n)}{b(K+1)^{2n}} e^{-bt},$$

where $C_0 = \frac{b}{a+b}(5^2 2^6 \nu^2 c^2 A C_S)^{-1}, \hat{C}_0 = \frac{a}{a+b}\left(2^{2q+6}c^2 A\right)^{-1}, C(n) = D\left(1 + I_0\right)\nu^{2n}(n!)^2 E_{H_\pi^n}(0), I_0 = \left(32c^2 R^2 + 1\right), A, R, D, C_S$ are constants defined in (2.15), (2.14), (4.10), (4.19) respectively and ν is the same constant as in Theorem 2.3.

5. Proof of Theorem 4.6 (Stability of the gPC-SG method). In this section, we will study the stability of the gPC-SG method for this model. We will use energy estimates to analyze $\hat{E}^K = a \left\| \hat{\boldsymbol{\rho}}_\mu^K(t) \right\|^2 + b \left\| \hat{\mathbf{m}}_\mu^K(t) \right\|^2$. Similar to the proof in the sensitivity analysis in Section 3, the most important part in the proof is how to bound the nonlinear term and the linear term with coefficient $r^\infty(z)$ properly. We use the weight μ_i to make the upper bound of this two terms independent of K, and it is stated in Lemma 5.1, which will be proved in Appendices B.

By multiplying $a(\hat{\boldsymbol{\rho}}^K)^\top U^2$ and $b(\hat{\mathbf{m}}^K)^\top U^2$ with $U = \mathrm{diag}(\mu_0, \cdots, \mu_K)$ to the two systems in (4.4) respectively, one has,

$$\begin{aligned}
\frac{1}{2}\partial_t \hat{E}^K \leq {}& - a^2 \left\| \hat{\boldsymbol{\rho}}_\mu^K \right\| - b^2 \left\| \hat{\mathbf{m}}_\mu^K \right\| - c \left(\hat{\boldsymbol{\theta}}^K\right)^\top U^2 \Upsilon \hat{\boldsymbol{\theta}}^K \\
& - c \sum_{l=0}^n \sum_{i,j} \mu_l^2 \hat{\rho}_i S_{ij}^l \hat{m}_j \hat{\theta}_l,
\end{aligned} \tag{5.1}$$

where $\hat{\theta} = a\hat{\rho}_l + b\hat{m}_l$ and $\hat{\boldsymbol{\theta}}^K = \left(\hat{\theta}_0, \cdots, \hat{\theta}_K\right)$. In the following Lemma 5.1, by (5.4) one can omit the third term on the RHS of the above equation; by (5.3), and setting $\gamma = \frac{1}{2c}$, one can

bound the last term by,

$$
\begin{aligned}
\frac{1}{2}\partial_t \hat{E}^K \leq & -a^2 \left\| \hat{\boldsymbol{\rho}}_\mu^K \right\|^2 - b^2 \left\| \hat{\mathbf{m}}_\mu^K \right\|^2 + 2^{2q+5} c^2 A \left\| \hat{\mathbf{m}}_\mu^K \right\| \left\| \hat{\boldsymbol{\rho}}_\mu^K \right\|^2 \\
& + \frac{a^2}{4} \left\| \hat{\boldsymbol{\rho}}_\mu^K \right\|^2 + \frac{b^2}{4} \left\| \hat{\mathbf{m}}_\mu^K \right\|^2 \\
\leq & - \left(\frac{3a}{4} - \frac{c^2 2^{2q+4} A}{a} \left\| \hat{\mathbf{m}}_\mu^K \right\|^2 \right) a \left\| \hat{\boldsymbol{\rho}}_\mu^K \right\|_{H_x^1}^2 \\
& - \left(\frac{3b}{4} - \frac{c^2 2^{2q+4} A}{b} \left\| \hat{\boldsymbol{\rho}}_\mu^K \right\|^2 \right) b \left\| \hat{\mathbf{m}}_\mu^K \right\|^2 .
\end{aligned}
\tag{5.2}
$$

Since the above inequality is similar to (3.8), by the continuity theorem, one gets similar result for $\left\| \hat{\boldsymbol{\rho}}_\mu^K \right\|^2$, $\left\| \hat{\mathbf{m}}_\mu^K \right\|$, which completes the proof.

LEMMA 5.1. *For S^l defined in (4.5), the following inequality holds,*

$$
\sum_{l=0}^{n} \sum_{i,j} \mu_l^2 \hat{\rho}_i S_{ij}^l \hat{m}_j \hat{\rho}_l \leq \frac{2^{2q+3} A}{\gamma} \left\| \hat{\mathbf{m}}_\mu^K \right\| \left\| \hat{\boldsymbol{\rho}}_\mu^K \right\|^2 + \frac{\gamma}{2} \left\| \hat{\boldsymbol{\rho}}_\mu^K \right\|^2 ,
\tag{5.3}
$$

where q, A are constants defined in (4.16), (2.15).
For Υ defined in (4.5), under Assumption 4.4, the following inequality holds

$$
- \left(\hat{\boldsymbol{\theta}}^K \right)^\top U^2 \Upsilon \hat{\boldsymbol{\theta}}^K \leq 0.
\tag{5.4}
$$

Proof. Similar proof of (5.3) can be found in [21], and based on (5.3) and Assumption 4.4, one can easily get (5.4). Therefore, we put the details of the proof in Appendix B. □

6. Proof of Theorem 4.7 (Spectral accuracy of the gPC-SG method). In this section, we will prove the spectral accuracy of the gPC-SG method based on Theorems 2.3 and 4.6. We will use energy estimates to analyze E_ε^K,

$$
E_\varepsilon^K = a \left\| \boldsymbol{\varepsilon}_\rho^K \right\|^2 + b \left\| \boldsymbol{\varepsilon}_m^K \right\|^2 .
\tag{6.1}
$$

Project (2.3) onto the truncated subspace $\{ \boldsymbol{\Phi}^K \}$, and then subtract the approximate perturbative system (4.3) from it, one has the following system for $(\boldsymbol{\varepsilon}_\rho^K, \boldsymbol{\varepsilon}_m^K)$,

$$
\begin{cases}
\partial_t \boldsymbol{\varepsilon}_\rho^K = -a \boldsymbol{\varepsilon}_\rho^K - ac \Upsilon \boldsymbol{\varepsilon}_\rho^K - bc \Upsilon \boldsymbol{\varepsilon}_m^K - c \int \left(a r^\infty \varrho_\rho^K + b r^\infty \varrho_m^K \right) \boldsymbol{\Phi}^K d\pi(z) \\
\qquad - c \int \left(\rho m - \hat{\rho}^K \hat{m}^K \right) \boldsymbol{\Phi}^K d\pi(z), \\
\partial_t \boldsymbol{\varepsilon}_m^K = -b \boldsymbol{\varepsilon}_m^K - bc \Upsilon \boldsymbol{\varepsilon}_m^K - ac \Upsilon \boldsymbol{\varepsilon}_\rho^K - c \int \left(b r^\infty \varrho_m^K + a r^\infty \varrho_\rho^K \right) \boldsymbol{\Phi}^K d\pi(z) \\
\qquad - c \int \left(\rho m - \hat{\rho}^K \hat{m}^K \right) \boldsymbol{\Phi}^K d\pi(z).
\end{cases}
\tag{6.2}
$$

$$
\tag{6.3}
$$

When one does energy estimates to the above system, the most difficult part lies in how to bound the last nonlinear term. We analyze this term in Lemmas 6.2 and 6.3. For other linear terms, notice that $r \leq r^\infty(z) \leq R$ for all $z \in I_z$, so by Theorem 3.1 in [19], Υ has the following properties. One can also refer to Appendices for the proof.

PROPOSITION 6.1. *For the steady state r^∞ with lower bound and upper bound as in (2.14), the constant matrix Υ defined in (4.5) is a positive definite matrix and for any vector $\boldsymbol{\alpha}$,*

$$
r \left\| \boldsymbol{\alpha} \right\|^2 \leq \boldsymbol{\alpha}^\top \Upsilon \boldsymbol{\alpha} \leq R \left\| \boldsymbol{\alpha} \right\|^2 .
$$

Therefore, if one does dot product of $a\boldsymbol{\varepsilon}_\rho^K, b\boldsymbol{\varepsilon}_m^K$ to the two equations respectively, then add them together, after applying the above Proposition, one has

$$
\begin{aligned}
\partial_t E_\varepsilon^K \\
\leq & -a^2 \left\|\varepsilon_\rho^K\right\|^2 - b^2 \left\|\varepsilon_m^K\right\|^2 - c \left\langle r^\infty \left(a\varrho_\rho^K + b\varrho_m^K\right), a\varepsilon_\rho^K + b\varepsilon_m^K \right\rangle_\pi \\
& \underbrace{-c \left\langle \rho m - \hat\rho^K \hat m^K, a\varepsilon_\rho^K + b\varepsilon_m^K \right\rangle_\pi}_{IV} \\
\leq & -a^2 \left\|\varepsilon_\rho^K\right\|^2 - b^2 \left\|\varepsilon_m^K\right\|^2 + c^2 \|r^\infty\|_{L_z^\infty}^2 \left(8a^2 \left\|\varrho_\rho^K\right\|_\pi^2 + 8b^2 \left\|\varrho_m^K\right\|_\pi^2\right) \\
& + \frac{a^2}{8} \left\|\varepsilon_\rho^K\right\|^2 + \frac{b^2}{8} \left\|\varepsilon_m^K\right\|^2 + \left(16c^2 C_S \|\rho\|_{H_z^1}^2 + \frac{b^2}{8}\right) \left\|\varepsilon_m^K\right\|^2 \\
& + \left(64c^2 A \left\|\hat{\mathbf{m}}_\mu^K\right\|^2 + \frac{a^2}{8}\right) \left\|\varepsilon_\rho^K\right\|^2 \\
& + 16c^2 C_S \|\rho\|_{H_z^1}^2 \left\|\varrho_m^K\right\|_\pi^2 + 64c^2 A \left\|\hat{\mathbf{m}}_\mu^K\right\|^2 \left\|\varrho_\rho^K\right\|_\pi^2 \\
= & -\left(\frac{3a}{4} - \frac{64c^2 A}{a} \left\|\hat{\mathbf{m}}_\mu^K\right\|^2\right) a \left\|\varepsilon_\rho^K\right\|^2 - \left(\frac{3b}{4} - 16c^2 C_S \|\rho\|_{H_z^1}^2\right) b \left\|\varepsilon_m^K\right\|^2 \\
& + \underbrace{\left(8a^2 c^2 R^2 + 64c^2 A \left\|\hat{\mathbf{m}}_\mu^K\right\|^2\right) \left\|\varrho_\rho^K\right\|_\pi^2 + \left(8b^2 c^2 R^2 + 16c^2 C_S \|\rho\|_{H_z^1}^2\right) \left\|\varrho_m^K\right\|_\pi^2}_{J(t)},
\end{aligned}
\tag{6.4}
$$

where Young's inequality and Lemma 6.3 are applied to the second inequality. Based on inequality (6.4), if

$$
64c^2 A \left\|\hat{\mathbf{m}}_\mu^K(t)\right\|^2 \leq \frac{a^2}{4}, \quad 16c^2 C_S \|\rho(t)\|_{H_z^1}^2 \leq \frac{b^2}{4},
\tag{6.5}
$$

then one has

$$
\frac{1}{2}\partial_t E_\varepsilon^K \leq -\frac{a^2}{2} \left\|\varepsilon_\rho^K\right\|^2 - \frac{b^2}{2} \left\|\varepsilon_m^K\right\|^2 + J(t).
\tag{6.6}
$$

If $J(t)$ can be bounded for $\forall t > 0$, then one can have exponential decay of E_ε^K. But first, let us check when assumption (6.5) is satisfied. By Theorems 4.6 and 2.3, one has,

$$
\left\|\hat{\mathbf{m}}_\mu^K\right\|^2 \leq \frac{\hat E^K(0)}{b} \leq a(a+b)\hat C_0, \quad \|\rho\|_{H_\pi^1}^2 \leq \frac{(5\nu)^2 E_{H_\pi^1}(0)}{a} \leq b(a+b)5^2\nu^2 C_0.
$$

Therefore, as long as

$$
\begin{aligned}
\hat C_0 &\leq \min\left\{\frac{a}{(a+b)}\frac{1}{2^8 c^2 A}, \frac{1}{2^{2q+6}c^2 A}\right\} \leq \frac{a}{a+b}\left(2^{2q+6}c^2 A\right)^{-1}, \\
C_0 &\leq \min\left\{\frac{b}{(a+b)}\frac{1}{5^2 2^6 \nu^2 c^2 C_S}, \frac{1}{5^2 2^5 A c^2}\right\} \leq \frac{b}{a+b}(5^2 2^6 \nu^2 c^2 A C_S)^{-1}
\end{aligned}
\tag{6.7}
$$

(6.6) is satisfied, and then the error E_ε^K satisfies (6.6). Integrating (6.6) over t gives,

$$
a \left\|\varepsilon_\rho^K(t)\right\|^2 + b \left\|\varepsilon_m^K(t)\right\|^2 \leq 2\int_0^t J(s)ds - a^2 \left\|\varepsilon_\rho^K\right\|^2 - b^2 \left\|\varepsilon_m^K\right\|^2,
$$

where $E_\varepsilon^K(0) = 0$ is used. Then separate it into two parts, one has

$$
\left\|\varepsilon_\rho^K(t)\right\|^2 \leq \frac{2}{a}\int_0^t J(s)ds - a \left\|\varepsilon_\rho^K\right\|^2, \quad \left\|\varepsilon_m^K(t)\right\|^2 \leq \frac{2}{b}\int_0^t J(s)ds - b \left\|\varepsilon_m^K\right\|^2.
\tag{6.8}
$$

Now we need to bound the term $\int_0^t J(s)ds$. Insert (6.6) and Corollary 4.1 into $J(t)$,

$$J(t) \leq \left(8a^2c^2R^2 + \frac{a^2}{4}\right)\frac{D\left(\nu^n n!\right)^2 E_{H_\pi^n}(0)}{a(K+1)^{2n}}e^{-at}$$
$$+ \left(8b^2c^2R^2 + \frac{b^2}{4}\right)\frac{D\left(\nu^n n!\right)^2 E_{H_\pi^n}(0)}{b(K+1)^{2n}}e^{-bt},$$

which implies that

$$2\int_0^t J(s)ds$$
$$\leq \frac{2}{a}\left(8a^2c^2R^2 + \frac{a^2}{4}\right)\frac{D\left(\nu^n n!\right)^2 E_{H_\pi^n}(0)}{a(K+1)^{2n}} + \frac{2}{b}\left(8b^2c^2R^2 + \frac{b^2}{4}\right)\frac{D\left(\nu^n n!\right)^2 E_{H_\pi^n}(0)}{b(K+1)^{2n}}$$
$$\leq 2\left(16c^2R^2 + \frac{1}{2}\right)\frac{D\left(\nu^n n!\right)^2 E_{H_\pi^n}(0)}{(K+1)^{2n}} \leq \frac{I_0 D\left(\nu^n n!\right)^2 E_{H_\pi^n}(0)}{2(K+1)^{2n}},$$

where $I_0 = 32c^2R^2 + 1$, so (6.8) becomes

$$\left\|\varepsilon_\rho^K(t)\right\|^2 \leq \frac{I_0 D\left(\nu^n n!\right)^2 E_{H_\pi^n}(0)}{a(K+1)^{2n}} - a\left\|\varepsilon_\rho^K\right\|^2,$$
$$\left\|\varepsilon_m^K(t)\right\|^2 \leq \frac{I_0 D\left(\nu^n n!\right)^2 E_{H_\pi^n}(0)}{b(K+1)^{2n}} - b\left\|\varepsilon_m^K\right\|^2. \tag{6.9}$$

Applying Grownwall's inequality gives,

$$\left\|\varepsilon_\rho^K\right\|^2 \leq \frac{I_0 D\left(\nu^n n!\right)^2 E_{H_\pi^n}(0)}{a(K+1)^{2n}}e^{-at}, \quad \left\|\varepsilon_m^K\right\|^2 \leq \frac{I_0 D\left(\nu^n n!\right)^2 E_{H_\pi^n}(0)}{b(K+1)^{2n}}e^{-bt}. \tag{6.10}$$

Therefore, By (4.7),

$$\left\|\rho - \hat{\rho}^K\right\|_\pi^2 \leq \left\|\varrho_\rho^K\right\|_\pi^2 + \left\|\varepsilon_\rho^K\right\|_\pi^2$$

and inserting (4.10), (6.10) gives,

$$\left\|\rho - \hat{\rho}^K\right\|_\pi^2 \leq D(1 + I_0)\frac{\nu^{2n}(n!)^2 E_{H_\pi^n}(0)}{a(K+1)^{2n}}e^{-at}.$$

Similar inequality can be obtained for $\left\|m - \hat{m}^K\right\|_\pi^2$, which completes the proof of Theorem 4.7.

LEMMA 6.2. *For any function*

$$m(z) = \sum_{i=0}^\infty m_i \Phi_i(z), \quad \rho(z) = \sum_{i=0}^\infty \rho_i \Phi_i(z),$$

where $m_i = \int m\Phi d\pi(z)$, $\rho_i = \int \rho\Phi d\pi(z)$, *the following inequality holds,*

$$\sum_{l=0}^K \left(\int \rho m \Phi_l d\pi(z)\right)^2 \leq 4A\sum_{i\geq 0}((i+1)^q \rho_i)^2 \sum_{i\geq 0} m_i^2,$$

where $q = p + 2$ *and* p, A *are constants defined in (4.12), (2.15).*

Proof. First we define a function χ_{ijl} of non-negative integer i, j, l,

$$\chi_{ijl} = \begin{cases} 1, & \text{if } i+j \geq l, \text{or } i+l \geq j, \text{or } j+l \geq i \\ 0, & \text{ortherwise.} \end{cases} \tag{6.11}$$

Then we note that

$$S_{ij}^l = \chi_{ijl} \int \Phi_i \Phi_j \Phi_l \pi(z) dz \le \chi_{ijl}\, \eta_{\min\{i,j,l\}} \left\| \Phi_i \right\|_\pi \left\| \Phi_l \right\|_\pi \le \eta_{\min\{i,j,l\}} \chi_{ijl}, \qquad (6.12)$$

with η_i defined in (4.12). Therefore,

$$\sum_{l=0}^K \left(\int \rho m \Phi_l d\pi(z) \right)^2 = \sum_{l=0}^K \left(\int \left(\sum_{i\ge 0}^\infty \rho_i \Phi_i \right) \left(\sum_{j\ge 0} m_j \Phi_j \right) \Phi_l d\pi(z) \right)^2$$

$$= \sum_{l=0}^K \left(\sum_{i\ge 0}\sum_{j\ge 0} \rho_i m_j S_{ij}^l \right)^2$$

$$\le \sum_{l=0}^K \left(\sum_{i\ge 0}\sum_{j\ge 0} |(i+1)^q \rho_i|\, |m_j|\, \frac{\eta_i}{(i+1)^q} \chi_{ijl} \right)^2$$

$$= \sum_{l=0}^K \left(\sum_{i\ge 0} |(i+1)^q \rho_i|\, \frac{1}{(i+1)^2} \sum_{j\ge 0} |m_j|\, \chi_{ijl} \right)^2$$

$$\le \sum_{l=0}^K \left(\sum_{i\ge 0} \frac{1}{(i+1)^2} \right) \sum_{i\ge 0} \frac{((i+1)^q \rho_i)^2}{(i+1)^2} \left(\sum_{j\ge 0} |m_j|\, \chi_{ijl} \right)^2$$

$$\le A \sum_{l=0}^K \sum_{i\ge 0} \frac{((i+1)^q \rho_i)^2}{(i+1)^2} \sum_{j\ge 0} m_j^2 \chi_{ijl} \sum_{j\ge 0} \chi_{ijl}$$

$$\le A \sum_{l=0}^K \sum_{i\ge 0} \frac{2i+1}{(i+1)^2} ((i+1)^q \rho_i)^2 \sum_{j\ge 0} m_j^2 \chi_{ijl}$$

$$\le A \sum_{i\ge 0} \frac{(2i+1)^2}{(i+1)^2} ((i+1)^q \rho_i)^2 \sum_{j\ge 0} m_j^2$$

$$\le 4A \sum_{i\ge 0} ((i+1)^q \rho_i)^2 \sum_{i\ge 0} m_i^2.$$

In the above estimates, the first inequality is because of (6.12), then the Cauchy-Schwartz inequality is applied in the second and third inequalities. In the fourth inequality, one uses the property of χ_{ijl}, since for fixed i, l, χ_{ijl} is nonzero only if $l - i \le j \le l + i$, which implies that $\sum_{j\ge 0} \chi_{ijl} \le (2i+1)$. Similar property is applied in the fifth inequality for $\sum_l \chi_{ijl}$. The last inequality comes from $(2i + 1)^2 \le 4(i + 1)^2$. □

LEMMA 6.3. *The following inequality holds*

$$\left\langle \rho m - \hat\rho^K \hat m^K, a\varepsilon_\rho^K + b\varepsilon_m^K \right\rangle$$

$$\le \left(16c^2 C_S \left\| \rho \right\|_{H_z^1}^2 + \frac{b^2}{8} \right) \left\| \varepsilon_m^K \right\|^2 + \left(64c^2 A \left\| \hat{\mathbf{m}}_\mu^K \right\|^2 + \frac{a^2}{8} \right) \left\| \varepsilon_\rho^K \right\|^2$$

$$+ 16c^2 C_S \left\| \rho \right\|_{H_z^1}^2 \left\| \varrho_m^K \right\|_\pi^2 + 64c^2 A \left\| \hat{\mathbf{m}}_\mu^K \right\|^2 \left\| \varrho_\rho^K \right\|_\pi^2.$$

Proof. First notice that

$$\rho m - \hat\rho^K \hat m^K = \left(\rho m - \rho \hat m^K \right) + \left(\rho \hat m^K - \hat\rho^K \hat m^K \right) = \underbrace{\rho(\varepsilon_m^K + \varrho_m^K)}_{①} + \underbrace{\hat m^K \left(\varrho_\rho^K + \varepsilon_\rho^K \right)}_{②}.$$

Apply Young's inequality to the first part, one has

$$
\left| -c \left\langle ①, a\varepsilon_\rho^K + b\varepsilon_m^K \right\rangle \right|
$$
$$
\leq 16c^2 C_S \|\rho\|_{H_z^1}^2 \left\| \varepsilon_m^K \right\|^2 + 16c^2 C_S \|\rho\|_{H_z^1}^2 \left\| \varrho_m^K \right\|_\pi^2 + \frac{a^2}{16} \left\| \varepsilon_\rho^K \right\|^2 + \frac{b^2}{16} \left\| \varepsilon_m^K \right\|^2,
$$

(6.13)

where the constant C_S comes from the Sobolev Embedding (4.19). For the second part ②, using Lemma 6.2, one has,

$$
\left| -c \left\langle ②, a\varepsilon_\rho^K + b\varepsilon_m^K \right\rangle_\pi \right| = c \left(\int ② \boldsymbol{\Phi}^K \pi(z) dz \right) \cdot \left(a\varepsilon_\rho^K + b\varepsilon_m^K \right)
$$
$$
\leq 16c^2 \left(\int \hat{m}^K \varrho_\rho^K \boldsymbol{\Phi}^K \pi(z) dz \right)^2 + 16c^2 \left(\int \hat{m}^K \varepsilon_\rho^K \boldsymbol{\Phi}^K \pi(z) dz \right)^2 + \frac{a^2}{16} \left\| \varepsilon_\rho^K \right\|^2 + \frac{b^2}{16} \left\| \varepsilon_m^K \right\|^2
$$
$$
\leq 64c^2 A C_S \left(\sum_{i \geq 0} ((i+1)^q \hat{m}_i)^2 \right) \left(\left\| \varrho_\rho^K \right\|_\pi^2 + \left\| \varepsilon_\rho^K \right\|^2 \right) + \frac{a^2}{16} \left\| \varepsilon_\rho^K \right\|^2 + \frac{b^2}{16} \left\| \varepsilon_m^K \right\|^2
$$
$$
= 64c^2 A C_S \left\| \hat{\mathbf{m}}_\mu^K \right\|^2 \left(\left\| \varepsilon_\rho^K \right\|^2 + \left\| \varrho_\rho^K \right\|_\pi^2 \right) + \frac{a^2}{16} \left\| \varepsilon_\rho^K \right\|^2 + \frac{b^2}{16} \left\| \varepsilon_m^K \right\|^2.
$$

(6.14)

Adding (6.13) and (6.14) together completes the proof. □

7. Numerical examples.

7.1. Coefficient of variation. We want to check how the presence of μRNA influences the noise in the concentration of unbound mRNA. One common way to perform this comparison is to compute the coefficient of variation (CV) of the mRNA content, i.e. the ratio of the standard deviation to the mean. Indeed, we expect the presence of μRNA to reduce the mean in the content of mRNA, simply because binding to μRNA reduces the amount of unbound mRNA. Since we deal with distributions on the positive real line, the reduction of the mean is also likely to reduce the variance. However, we wish to show that the variance reduction obtained by the presence of μRNA is actually bigger than the mere reduction which would be obtained as a consequence of a reduction of the mean. This is the reason of considering the CV. A reduction of the CV by the presence of μRNA shows a reduction of the variance which is larger than the corresponding reduction of the mean. Specifically, we compare the CV on $\rho^\infty(z)$ obtained from system (2.1) which includes μRNA production with the CV on the steady state $\tilde{\rho}^\infty$ of the equation where binding with μRNA is ignored, namely

$$
\partial_t \tilde{\rho} = S(z) - a\tilde{\rho}. \tag{7.1}
$$

We let CV_L be the CV of the steady state obtained from (7.1), i.e. without μRNA, while CV_{NL} is the CV of ρ^∞ obtained from (2.1), i.e. with μRNA ('L' and 'NL' stand for 'linear' and 'nonlinear' as (7.1) is linear while (2.1) is nonlinear).

Figure 1 shows how CV_L - CV_{NL} varies for different random sources. Here we set $a = b = c = 1$, $S(z) = kz + d$, where z follows the uniform distribution in $[-1/2, 1/2]$. The five lines correspond to the choices $d = 1/3, 1/2, 1, 2, 5$. The horizontal axis is the value of $k^2/2$ which is equal to the variance.

Figure 2 displays how CV_L - CV_{NL} depends on the parameters a, b, c. Here we set $S(z) = 2z/3 + 1$, so the mean of the source is 1 and the variance is $1/27$.

From the two plots, one can see that the CV for the steady-state of the nonlinear system is always smaller than that of the linear system. Thus, the influence of μRNAs is always to decrease the uncertainty on the mRNA content. From Fig. 1 we see that the influence of μRNAs increases as the intensity of the source decreases and its variance increases. From Fig. 2 we deduce that the influence of μRNAs increases as their binding rate to mRNA c increases. A larger binding rate means less unbound for mRNAs or μRNAs, which has a similar effect as a reduction of the source intensity. Indeed, the influence of μRNAs increases
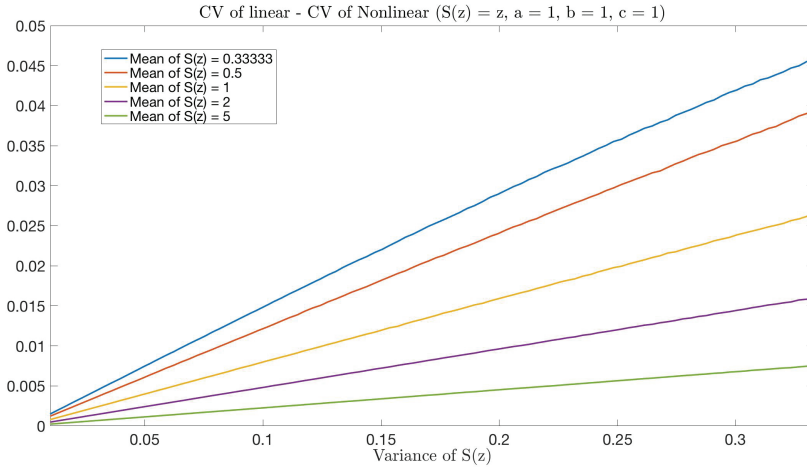
FIG. 1. $CV_L - CV_{NL}$ as a function of the variance of $S(z)$ for different values of the mean of $S(z)$ when $a = b = c = 1$, $S(z) = kz + d$, for $k \in [0, 2]$ and $d = 1/3, 1/2, 1, 2, 5$, where z follows the uniform distribution in $[-1/2, 1/2]$.
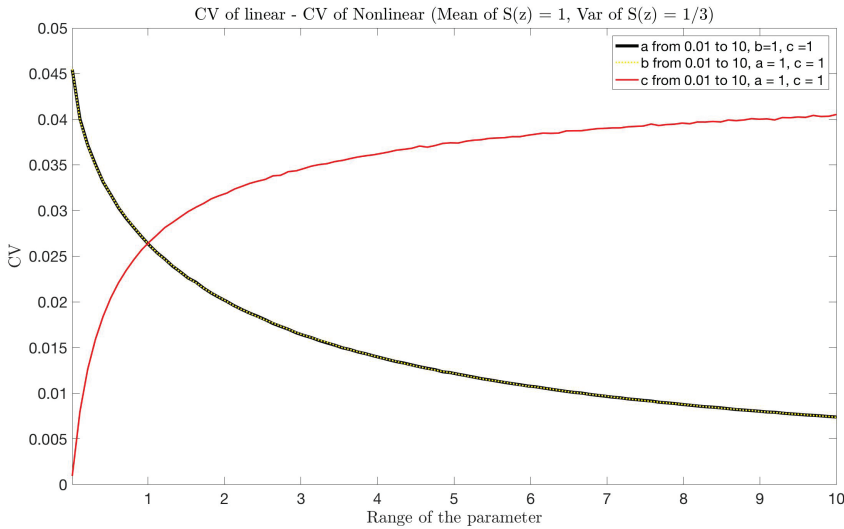

FIG. 2. $CV_L - CV_{NL}$ as a function of a, b, c, where we set $S(z) = 2z/3 + 1$, and z follows the uniform distribution in $[-1/2, 1/2]$.

in both cases. Finally, From Fig. 2, an increase of either the degradation rate a of mRNA or the degradation rate b of μRNA both decrease the influence of μRNAs. In the latter case, this is understandable as the amount of unbound μRNA decreases and less noise reduction occurs. In the former one, this is less intuitive, as an increase of the degradation rate of mRNA should lead to a decrease of mRNA concentration relative to the μRNA concentration and should make the mRNA more sensitive to the presence of μRNA. This shows that nonintuitive

outcome may occur from random perturbation of chemical kinetic systems.

Finally, in spite of repeated attempts, we were not able to show the reduction of the CV in the presence of μRNA analytically. This may be the indication that for some randomness, this reduction does not happen.

Data availability. No new data were collected in the course of this research.

Appendix A. Proof of Proposition 6.1.

Proof. For any $K + 1$-dimensional vector $a \neq 0$,

$$
\begin{aligned}
a^\top F a = \sum_{i,j=1}^{K} a_i F_{ij} a_j &= \sum_{i,j=1}^{K} \int f(z) a_i \Phi_i(z) a_j \Phi_j(z) \pi(z) dz \\
&= \int f(z) \left(\sum_{i=1}^{K} a_i \Phi_i(z) \right) \left(\sum_{j=1}^{K} a_j \Phi_j(z) \right) \pi(z) dz \\
&= \int f(z) \left(\sum_{i=1}^{K} a_i \Phi_i(z) \right)^2 \pi(z) dz \geq C \sum_{i=1}^{K} a_i^2,
\end{aligned}
\tag{A.1}
$$

where the last inequality comes from the orthonormal relationship of Φ_i as shown in (4.1). $\square$

Appendix B. Proof of Lemma 5.1.

Proof. First note that for each l,

$$
\begin{aligned}
\left(\mu_l \sum_{i,j} \hat{m}_i \hat{\rho}_j S_{ij}^l \right) (\mu_l \hat{\rho}_l) &\leq \frac{1}{2\gamma} \left(\mu_l \left(\sum_{i \leq j} + \sum_{i > j} \right) S_{ij}^l \, |\hat{m}_i \hat{\rho}_j| \right)^2 + \frac{\gamma}{2} (\mu_l \hat{\rho}_l)^2 \\
&\leq \frac{\mu_l^2}{\gamma} \left(\sum_{i \leq j} \eta_i \chi_{ijl} \, |\hat{m}_i \hat{\rho}_j| \right)^2 + \frac{\mu_l^2}{\gamma} \left(\sum_{i > j} \eta_j \chi_{ijl} \, |\hat{m}_i \hat{\rho}_j| \right)^2 + \frac{\gamma}{2} (\mu_l \hat{\rho}_l)^2 .
\end{aligned}
\tag{B.1}
$$

The second inequality is because

$$
S_{ij}^l = \chi_{ijl} \int \Phi_i \Phi_j \Phi_l \pi(z) dz \leq \chi_{ijl} \, \eta_{\min\{i,j,l\}} \, \|\Phi_i\|_\pi \, \|\Phi_l\|_\pi \leq \eta_{\min\{i,j,l\}} \chi_{ijl},
\tag{B.2}
$$

where the first equality comes from the orthornality of Φ_i, and η_i defined in (4.12) is the upper bound for Φ_i. We estimate the first part of (B.2) as follows,

$$
\begin{aligned}
\left(\sum_{i \leq j} \eta_i \chi_{ijl} \, |\hat{m}_i \hat{\rho}_j| \right)^2 &= \left(\sum_{i \leq j} \frac{\chi_{ijl}}{(i+1)^2 \mu_j} \, |\mu_i \hat{m}_i \mu_j \hat{\rho}_j| \right)^2 \\
&\leq \left(\sum_i \frac{1}{(i+1)^2} \right) \sum_i \left(\frac{|\mu_i \hat{m}_i|}{i+1} \sum_{j \geq i} \frac{\chi_{ijl} \, |\mu_j \hat{\rho}_j|}{\mu_j} \right)^2 \\
&\leq A \sum_i \left(\frac{\mu_i \hat{m}_i}{i+1} \right)^2 \left(\sum_{j \geq i} \frac{\chi_{ijl} \, |\mu_j \hat{\rho}_j|}{\mu_j} \right)^2 \\
&\leq A \sum_i \frac{|\mu_i \hat{m}_i|^2}{(i+1)^2} \left[\sum_{j \geq i} \left(\frac{1}{\mu_j} \right)^2 \chi_{ijl} \sum_{j \geq i} (\mu_j \hat{\rho}_j)^2 \chi_{ijl} \right].
\end{aligned}
$$

The first equality is because of the definition of μ_i in (4.16), then the Cauchy-Schwarz inequality is applied to the first and the last inequalities, while the second inequality comes from the definition of A in (2.15). Therefore,

$$
\begin{aligned}
\sum_{l=0}^K \mu_l^2 \left(\sum_{i \leq j} \eta_i \chi_{ijl} \, |\hat{m}_i \hat{\rho}_j| \right)^2 &\leq A \sum_{l=0}^K \sum_{i=0}^K \frac{|\mu_i \hat{m}_i|^2}{(i+1)^2} \left[\sum_{j \geq i} \left(\frac{\mu_l}{\mu_j} \right)^2 \chi_{ijl} \sum_{j \geq i} (\mu_j \hat{\rho}_j)^2 \chi_{ijl} \right] \\
&\leq 2^{2q} A \sum_{i=0}^K (2i+1) \frac{|\mu_i \hat{m}_i|^2}{(i+1)^2} \sum_{j \geq i} (\mu_j \hat{\rho}_j)^2 \sum_{l=0}^K \chi_{ijl} \\
&\leq 2^{2q} A \sum_{i=0}^K \frac{(2i+1)^2}{(i+1)^2} (\mu_i \hat{m}_i)^2 \sum_{j \geq i} (\mu_j \hat{\rho}_j)^2 \\
&\leq 2^{2q+2} A \left\| \hat{\mathbf{m}}_\mu^K \right\|^2 \left\| \hat{\boldsymbol{\rho}}_\mu^K \right\|^2.
\end{aligned}
$$

Since χ_{ijl} is nonzero only if when $l \leq i + j$, and for $j \geq i$, this means $l \leq 2j$, so $\left(\frac{\mu_l}{\mu_j} \right)^2 \leq \frac{(2j+1)^{2q}}{(j+1)^{2q}} \leq 2^{2q}$. Furthermore, for fixed i, l, χ_{ijl} is nonzero only when $l - i \leq j \leq l + i$, this means the number of nonzero χ_{ijl} is $(2i+1)$. Therefore,

$$
\sum_{j \geq i} \left(\frac{\mu_l}{\mu_j} \right)^2 \chi_{ijl} \leq \frac{(2j+1)^q}{(j+1)^q} \leq 2^{2q}(2i+1),
$$

which gives the second inequality. Similarly, one can obtain the third inequality. The fourth inequality is because of $(2i+1)^2 \leq 2^2(i+1)^2$.

Since i, j are symmetric, so the second part of (B.1) should have the same bound, hence,

$$
\sum_{l=0}^n \left\langle \mu_l \sum_{i,j} \hat{\rho}_i \hat{m}_j S_{ij}^l, \mu_l \hat{\rho}_l \right\rangle \leq \frac{2^{2q+3} A}{\gamma} \left\| \hat{\mathbf{m}}_\mu^K \right\| \left\| \hat{\boldsymbol{\rho}}_\mu^K \right\|^2 + \frac{\gamma}{2} \left\| \hat{\boldsymbol{\rho}}_\mu^K \right\|^2. \tag{B.3}
$$

For the second inequality (5.4), first notice that,

$$-\sum_{l=0}^{K}\left\langle r^{\infty}\hat{\theta}^K\Phi_l,\,\mu_l^2\hat{\theta}_l\right\rangle_{\pi} = -\sum_{l=0}^{K}\left\langle\left(r_0^{\infty}+\sum_{j\geq 1}r_j^{\infty}\Phi_j\right)\left(\sum_{i=0}^{K}\hat{\theta}_i\Phi_i\right)\Phi_l,\,\mu_l^2\hat{\theta}_l\right\rangle_{\pi}$$

$$= -\left\langle r_0^{\infty},\sum_{l=0}^{K}\sum_{i=0}^{K}\mu_l^2\hat{\theta}_i\hat{\theta}_l\Phi_i\Phi_l\right\rangle_{\pi} - \sum_{l=0}^{K}\sum_{j\geq 1}\sum_{i=0}^{K}\mu_l^2 r_j^{\infty}\hat{\theta}_i S_{ij}^l\hat{\theta}_l$$

$$= -r_0^{\infty}\left\|\hat{\boldsymbol{\theta}}_{\mu}^K\right\|^2 - \sum_{l=0}^{K}\sum_{j\geq 1}\sum_{i=0}^{K}\mu_l^2 r_j^{\infty}\hat{\theta}_i S_{ij}^l\hat{\theta}_l$$

where S_{ij}^l is defined in (4.5). The third equality is because of the orthogonality of $\{\Phi_i\}_{i\geq 0}$. For the last term, using the same technique one uses to get (5.3), then one has

$$-\sum_{l=0}^{K}\left\langle r^{\infty}\hat{\theta}^K\Phi_l,\,\mu_l^2\hat{\theta}_l\right\rangle_{\pi}$$

$$\leq -r_0^{\infty}\left\|\hat{\boldsymbol{\theta}}_{\mu}^K\right\|^2 + \frac{2^{2q+3}A}{\gamma}\left(\sum_{j\geq 1}\left(\mu_j r_j^{\infty}\right)^2\right)\left\|\hat{\boldsymbol{\theta}}_{\mu}^K\right\|^2 + \frac{\gamma}{2}\left\|\hat{\boldsymbol{\theta}}_{\mu}^K\right\|^2.$$

Then set $\gamma = r_0^{\infty}$, and by the condition on $\sum_{j\geq 1}(\mu_j r_j^{\infty})^2 \leq \frac{(r_0^{\infty})^2}{2^{2q+3}A}$, one completes the proof for the second inequality (5.4). □

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