Report by Dr. Massimiliano Esposito on the PhD thesis of Mr. Gabriel Morgado:

"Organization and fluctuations in living systems"

Nonlinear chemical kinetic can produce a rich variety of complex phenomena such as Turing structures and chemical waves. The role of noise can also dramatically modify these phenomena. The present thesis considers interesting new problems in this context often motivated by biology.

Chapter 1 provides an introduction to the basic tools to study the deterministic dynamics and stability of chemical reactions, without and with diffusion. The stochastic description in terms of the chemical Langevin equation and the chemical master equation are also presented. Beside this introductory material, two methodologies that are used in the later chapters of the thesis are briefly presented: how to model the effects of highly concentrated reactants that react with the solvent and how to model reaction diffusion using the Direct Simulation Monte Carlo method. Overall this chapter is well written and serves its purpose.

Chapter 2 studies the important problem of eliminating fast variables in a specific nonlinear chemical kinetics model. While this problem is well understood at the deterministic level, the stochastic description is a notoriously difficult problem. An important observation of the study is that methods based on the chemical Langevin equation fails to correctly reproduce fluctuations. Using a chemical master equation for the reduced model is also shown to lead to poor results.

Chapter 3 considers the problem of controlling the shape of Turing patterns. The motivation comes from morphogenesis where the reaction-diffusion paradigm is still debated based on the argument that Turing patterns lack controllability. Indeed their wavelength only depends on transport coefficients and not on boundary conditions. Two aspects of that problem are investigated. First, by considering a simple kinetic scheme producing Turing patterns and analyzing the parameter dependence of stability analysis, it is shown that by varying the concentration of one of the reservoir in space, the amplitude and wavelength at the end of the pattern can decrease as should be the case to describe the vertebra of an embryo. Second, a previous finding by the group showing that concentrated reactants which react with the solvent can be used to control the wavelength of the pattern, is verified by adapting the direct simulation Monte Carlo method to concentrated solutions.

Chapter 4 studies the Fisher-Kolmogorov-Petrovsky-Piskunov model of chemical waves by considering two novel aspects of the problem. First the effect of different diffusion coefficients between the two species is investigated. Differences in concentration profile are observed and proposed as a possible way to detect diffusion perturbations. Second, this problem is treated by including fluctuations. The wave front is shown to propagate much slower than expected (deterministically) under certain conditions. The effect of cross-diffusion on the wave front is also analyzed.

Conclusions start by summarizing the results, then briefly discuss these results from an historical perspective and end with considerations comparing holistic and reductionist approaches placing the mesoscopic approaches used in this thesis in between the two.

Overall this thesis presents timely and good quality research combining analytical and numerical work which meets international standards. I found the thesis well written and the quality of the presentation very good. I believe therefore that the quality of the work and the five papers published as first author by Gabriel Morgado are more than sufficient to award him the title of doctor.

Comments and questions:

- I.38 I think the +1 -1 should have the opposite sign

- I.44 I would rather write: $A \rightarrow S$ rather then $A \rightarrow 2S$

- Above I.47, is it appropriate to speak of center of mass when reaction-diffusion is an overdamped theory where mass never enters into play? Can one not simply introduce a relative motion of the solvent with respect to the reference frame. Or is there a way to justify this terminology based on kinetic theory, in which case a link to I.4.2 could be helpful?

- I.49-I.52 u should be defined and I failed to derive I.51-I.52 with the information given.

Chapter III:

- The result that doubling the solute concentration decreases the wavelength of the pattern by two is model specific or broader generality can be argued?

- How realistic is it biologically to assume that water is significantly affected by reactions with the reactants?

Chapter IV:

- I would be nice to elaborate a bit more on how the waves could be used as concentration sensors.

Luxembourg, June 29, 2021.

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