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Review of the PhD Thesis

State trajectory approach to the interpretation of self-organization in the Belousov-Zhabotinsky reaction

submitted by Anna Zhyrova, MSc

The submitted thesis is a contribution to research aimed at characterizing transitions of complex spatial patterns in time and degree of order in such patterns. As such, it is a cross-disciplinary work ranging from chemistry to biosciences under the unifying umbrella of information sciences. At the current state, this research has distinctly pioneering features, which makes it challenging and requires a great deal of invention.

The specific task of Anna Zhyrova was to apply certain information-theoretic concepts in obtaining, processing and characterizing spatio-temporal patterns in a nonlinear oscillatory chemical system known as the Belousov-Zhabotinsky (BZ) reaction taking place in a thin liquid layer on Petri dish. This system is taken as a simple manifestation of dynamical phenomena occurring in living systems on the hierarchical level of cell assemblages and tissues. Those phenomena include spreading waves of various types (planar, circular, spiral) and their frequently complex interactions. Apart from Introduction and Conclusions, the thesis includes three chapters, proceeding systematically from theoretical overview through experimental methodology to results and discussion. The part containing results and discussion is based on four papers published in journals or in conference proceedings. At the end of each of the four subchapters there is a summary of what has been achieved. This is useful and convenient feature.

The results presented in the thesis are well documented and described. The introductory part (chapter 1) contains basic facts about the BZ reaction, about chemical waves and compares two kinds of modelling approaches to spatio-temporal dynamics: the reaction-diffusion equations (in principle continuous time and space) and the cellular automata modelling (discrete time and space). The outlined overview is supported by an extensive citation of the large body of research done so far. Further, a framework of stochastic systems theory is introduced as a tool for phenomenological analysis based on information-theoretic concepts including Renyi entropy and from it derived entropic quantities suitable for processing and interpretation of experimental measurements.

Chapter 2 on Materials and methods provides details of both experimental and measurement procedures resulting in an innovative approach that includes: i) the processing of the optical signal leading to a time sequence of optimized optical images, ii) application of the entropic quantities to each image, iii) principal component analysis to condense the information and iv)a cluster analysis to identify and quantitatively describe successive phases of the wave patterns.

The third chapter presents four specific applications of the outlined approach resulting in phenomenological analysis of the BZ dynamical patterns.

Overall, the text is readable and documents the author's skills and ability to define, analyze and solve many tasks, problems and challenges that emerged during her work. There are very few typographical errors, the English style is quite smooth, even if not without flaws. Below I present minor technical

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remarks concerning both factual and style issues, followed by queries concerning parts of the text that I was not clear about or aiming at more general formulation of presented results.

Technical remarks:
1) p. 1 - line 11: ...chemical process contradicted the postulates of the second law...
More accurate would be to say: processes seemed to contradict at that time

2) p. 2 - reference to work of Mikhailov and Showalter (2006): the authors certainly know well that chemical waves do not follow Huygen's principle (e.g. they merge rather than interfere), they likely meant just a specific feature of the wave advancing through the maze and splitting at each division.

3) p. 4 - In experiments with vigorous mixing (magnetic mixer)...
I suggest to use the word premixing rather than mixing, otherwise the reader might be mislead that the solution layer on the Petri dish was continually mixed during the experiments.

4) p. 6 - ...hypobromous acid $HBrO_2$,...
Should read bromous acid $HBrO_2$...

5) p. 7 - ...mainly bromine and malonic acid,...
Should read bromate...

6) p. 10 - Reference to Brusselator as a BZ model is incorrect.

7) p. 12 - ...limited cycle...
Should read limit cycle...

8) p. 61 - I counted only 6 phases mentioned in the text in contrast to 7 clusters.

9) p. 121 - ...by the surrounding tissue may change its chemistry....
The word chemistry is misleadingly used in a too broad context than it is normally understood. Standard use of chemistry is the reaction process alone, which is not changed, instead patterns resulting from interaction between chemical and transport processes (such as diffusion, but also convection and migration in electric field) are affected by spatial constraints.

Queries:
1) p. 3 - Can you explain what Winfree turbulence is?

2) p. 5 - Given the complexity of processes that involve ferriin/ferroin, would you consider the measured signal as reflecting the dynamics credibly or could it lead to false conclusions?

3) p. 14 - A reaction-diffusion system is in the text characterized as assuming an almost instantaneous reaction rate compared to a slow diffusion rate. However, chemical reactions in the BZ system (and in general case) occur on various time scales, some are very fast, some are slow, so the RD system still may account for the case when time scales of some reactions is comparable or slower than time scale for diffusion. Could you comment on one versus several reaction time scales?

4) p. 20 - ...It explains the acceleration of fractal fronts phenomena that were observed in BZ reaction wave dynamics...
Assumption of a fractal space in the case of cell assemblages such as a tissue is natural, in the case of a liquid solution layer it is not so obvious. What are the reasons of assuming fractal/segregated nature of a layer of fluid?

5) In dynamical systems theory there is a concept of entropy rate (or Kolmogorov entropy) which expresses degree of (dis)order with respect to time rather than space as used in the thesis. In particular, positive K-entropy implies chaotic dynamics. Could that concept be applied to the time sequence of the images obtained from experiments?

In conclusion, I highly appreciate the multi-faceted work of the author, involving both experimental and theoretical aspects, which has convincingly shown two things: a) the author's skills in handling demanding experimental and theoretical tasks and b) the efficiency of the presented approach in quantitatively describing sequence of patterns that evolve in a reaction-transport system with complex dynamics with potential applications in living systems.

I declare that after reading the work I came to conclusion that the dissertation reflects high standards of scientific work of Anna Zhyrova, conforms with all requirements for a Ph.D. thesis and therefore I recommend it to the defense.

In Prague, November 17, 2017

Igor Schreiber

Anna Zhyrova: State Trajectory Approach to the Interpretation of Self-Organization in the Belousov-Zhabotinmsky Reaction

Some Comments and Questions

In my opinion this is quite an original approach to study the chemical wave activity of the Belousov-Zhabotinsky (BZ) reaction.

As the candidate has rightly pointed out the chemistry of the BZ reaction is quite complex and the application of the Field-Körös-Noyes (FKN) mechanism together with reaction-diffusion conditions are still not understood in their full detail R. M. Noyes once proclaimed that the BZ reaction is apparently the most complicated nonliving chemical reaction!

On page 14 of the thesis the candidate writes "*...if spatial segregation and state quantisation is included, the specific model does not have to be sought –or – in other words – the freedom of choice of available chemical models is much higher.*"

Q.1 Can the candidate comment on this sentence and describe in more detail what is meant by "*... the freedom of choice of available chemical models is much higher.*"

Q.2 In relation to this I also would like to ask the candidate to comment how the state trajectory approach is considered to contribute to our understanding of the generation of the spatial patterns.

One of the problems in studying processes far from equilibrium, at least in semi-closed containers like a petri-dish or a reaction vessel exposed partly to the environment, is that the system eventually reaches equilibrium and dies. This has been shown by a remarkable video by the candidate where equilibrium almost "devours" the non-equilibrium state (Fig. 1).

Fig. 1. The system starts out in a reducing state (left, indicated by and red color of ferroin) and reaches equilibrium in an oxidized state (right, blue color by ferriin)

This problem of having transients leading finally to equilibrium is tried to be overcome by studying such systems in flow reactors, including chemical wave patterns.

Q.3 Since I don't see any explicit comments in the thesis on the different approaches to study chemical waves in open reactors, I would like to ask the candidate whether such an approach has been considered by her or in her group and whether she is aware about such studies. In case the answer is "no", what results would the candidate expect to achieve when applying the state trajectory approach to an open reactor system, for example when stationary (Turing) patterns are observed?

Another aspect to consider is that most chemical waves in the BZ system have been studied as "oxidation waves", i.e., the system starts out in an unstable reduced state (Fig. 1, left picture) and ends up in an oxidized equilibrium state (Fig. 1, right picture). Smoes (1980) was probably the first to publish work on reduction waves/pulses, which was later followed by various researchers including the group (at that times) by Schreiber and Marek (1995). These systems start out in the reduced state showing (excitable) spikes of reduction in agreement with an amplified Oregonator model (Ruoff & Noyes, 1986). There has been little mentioning of these systems in the thesis.

Q4. This question concerns the above-mentioned reduction waves (red reducing wave-fronts traveling on a blue oxidized excitable medium). Would there be a way to predict the path in the three-dimensional trajectory state space (PC-1, PC-2, PC-3)?

In addition, I will have a couple of minor comments on the lay-out/arrangement of the thesis material and the citations.

P. Ruoff
University of Stavanger
November 15, 2017