Professor Emeritus Ljiljana Kolar-Anić

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Professor emeritus Ljiljana Kolar-Anić
(22.08.1947-17.06.2023)

Describing the life and works of anyone is fraught with the possibility of objectively making a series of omissions and that something is neglected or insufficiently highlighted. This cannot be avoided. Ljilja's biography is very rich, and, on this occasion, it will be given in an appropriate volume.

Ljiljana was a personality who, whenever she did something, she did it absolutely dedicated, deliberate, systematic and successful, but also with heart, selflessly and responsible, not neglecting her relationship with her relatives, colleagues and friends. Her strong adherence to immutable principles, and determination to stand up to every, even the smallest, injustice was incredible. She could be very harsh, uncompromising, but always constructive.

Ljiljana was born right after the Second World War (1947, Virovitica, Croatia, Yugoslavia), grew up on the ideas of socialism, which she critically accepted, respected and advocated. Thus, in 1967-68, period which is known for the revolt of students all over the world, she participated in the famous June demonstrations, which were raised due to the deviation from the direction of socialism in the development of Yugoslavia. Without a doubt, she deeply believed in and fought for a just society for all, regardless of their ethnic origin, race, religious beliefs. For her, as well as for many like her, "a man is a man", regardless of which social community he belongs to. In her veins flowed the blood of many, Serbs, Croats, Dalmatians, Italians. That is why she felt and declared herself a Yugoslav until the end of her life, despite many who mockingly and condescendingly thought, and many still do today, about Yugoslavs. She had a big handicap because she didn't have the opportunity to meet her paternal grandparents. In the Second World War they, including their immediate and extended family, were executed in the Ustasha camp Jasenovac in the most brutal and cruel way unimaginable to a normal person, as happened to many other Serbs, Jews and Roma. Because of all that, she had a very strong emotional connection with the surviving part of her father's family.

Ljiljana's childhood and youth were filled with many activities. At First Belgrade High School, she was mostly preoccupied with mathematics[1], the drama section and sports. At the same time, she was one of the members of the Sport Club ***Partizan***; her time spent at the club as a member of the national team in athletics was credited towards her pension due to outstanding successes at the Yugoslav level.

She was an excellent housewife: she knew how to cook, bake cakes, sew, embroider. She dressed tastefully and appropriately and did not wear make-up.

Ljiljana was very dedicated to young people as a teacher, colleague, mentor, parent, friend. She wondered and could not understand why young ones do not create families and have children, although it is known that they can do it, that their parents rightly expect it too. What's the matter? Is it conformity, disinterest, indolence, asociality, or is it something else?

EDUCATION

Her original idea was to study technical sciences, but nevertheless, she opted for natural sciences, which occupied her until the end of her life. She came to physical chemistry at the persuasion of her older colleague from the Partizan sports club, who was a student of physical chemistry at the Faculty of Science and Mathematics in Belgrade, but who later never graduated from the same faculty; he remained an eternal senior who needed to pass two exams in order to complete his studies.

In 1966 Ljiljana started to study at the Physical Chemistry Group (now the Faculty of Physical Chemistry) of the Faculty of Science of the University of Belgrade, where she graduated (1970), obtained master's degree (1974), then doctorate (1978), and then got a job and worked continuously until the end of her life. She took the postdoctoral studies (1978-1979), at the Service de Chimie Physique II of Department for Theoretical Physical Chemistry of the Free University of Brussels, headed by Nobel laureate (1977) Ilya Prigogine. Especially at that time, and even later, Prigozhin's department was the world's largest centre that brought together many famous researchers of complex non-equilibrium and non-linear phenomena. (Figure 1) It is widely known that Prigogine's theory of dissipative

[1] Ljiljana Kolar, Decomposed algebraic functions (1966), Graduation Thesis, First Belgrade High School

structure led to pioneering research into self-organized systems. Ljiljana's stay in Brussels during her postdoctoral studies, as well as several stays later, was in the period of the most intensive development of the first personal computers and their applications in computer modelling, especially several well-known chemical oscillators.

Figure 1. Photograph of a scientist from the field of Nonlinear Sciences in Brussels (1987) made during the meeting organized on the 70th birthday of Nobel laureate Ilya Prigogine (first row, five from right to left) under the title *Spatial Inhomogeneities and Transient Behaviour in Chemical Kinetics*. Among them are those with whom Ljiljana will collaborate, get them to be lecturers at the Faculty of Physical Chemistry as well as the Conferences of Physical Chemistry, but also become Honorary Members of the Society of Physical Chemists of Serbia. In the photo you can see, as our Serbian people would say, "leaves of our mountain, forest" young Ljiljana Kolar-Anic (second row, second from left to right) and Slobodan Anić (back row, fourth from left to right).

CEREER – EMPLOYMENT

Ljiljana started (1971) and ended (2012) her official professional career at Physical Chemistry, which transformed over time in terms of organization from the Department of Physical Chemistry of the Faculty of Science and Mathematics to the Faculty of Physical Chemistry of the University of Belgrade (1990). In all the phases of transformations, which were often very stormy, her engagement was significant and successful.

Ljiljana passed through all educative university positions: Assistant (1971-1980), Scientific Associate for the subjects Statistical Thermodynamics and Nonequilibrium Thermodynamics (1980-1984), Docent for the subjects Statistical Thermodynamics and Chemical Reactivity (1984-1991), Associate Professor (1991-1996) and Full professor (1996-2012) for the subjects Statistical Thermodynamics and Nonequilibrium Processes, later Dynamics of Nonlinear Processes (1996-2012). She was elected to position of Emeritus Professor (2017) and also to the position of Full Research Professor (2008) at the Institute of Chemistry, Technology and Metallurgy.

After working at the Faculty of Physical Chemistry, Ljiljana worked for another two years at the University of Belgrade as a Full Research Professor at the Institute of Chemistry, Technology and Metallurgy.

SOME SCIENTIFIC CONTRIBUTIONS

On this occasion, the intention is not to present Liljana's comprehensive and detailed contribution in science, but to mark some of the prominent results which she achieved independently or in collaboration. Those results meant a lot in the further personal and collective scientific development of the researchers in Nonlinear Physical Chemistry and Kinetics.

Heterogeneous processes

She graduated from the field of kinetics of isothermal adsorption on a modified alumina. [1] Also, heterogeneous processes were the subject of a master's study. [2] So, she considers the Weibull function (equations (1) and (2)), as well as the Normal and Gamma functions (but also the connection between mentioned functions) in describing some different heterogeneous processes. [3, 4]

$$F(x) = 1 - e^{-[\frac{x-y}{\eta}]^{\beta}} \quad . \qquad (1)$$

η is the scalar, β is the shape parameter and γ is the location parameter. This distribution is often used in the form

$$F(x) = 1 - e^{-bx^{n}} \quad . \qquad (2)$$

Here $F(x)$ can be the reaction yield at time x i.e. t. Parameters b and n have the same meaning as η and β. The Weibull function will be present in later works as well. [5-9] Likewise, and it was found that they must be considered as time functions when the energies of adsorption centres are not equal and have a random distribution. [10] Also, Ljiljana dealt with the stochastic analysis of the chemical and physicochemical processes. [11, 12] Later, that experience proved valuable for the examinations of the activity of plasmonic sensors in multi-analyte environment. [13-16] Ljiljana successfully incorporated the education in statistical mechanics acquired during her master's studies into her doctoral thesis [17] and a series of notable articles. She calculated the partition function of a real gas in a gravitational field. Then, the partition function of the vapor consisting by molecules grouped into clusters of different sizes was also determined. Furthermore, thermodynamic properties and state functions for real gas and steam in a gravitational field were determined. After that, the basic equations for the sedimentation balance of steam in the gravitational field were found. [18-23]. All this was reflected in the real-world application of the phenomenon of nucleation in the atmosphere. For example, Ljiljana was the project manager related to the research and development of means for artificial influence on the weather and the production of some chemical substances that are included in the composition of these means. [24]. In short, the commercial production of an anti-hail mixture was successfully developed and then established, which contained a significantly less essential substance, and had a markedly higher efficiency than all existing mixtures which were previously used in Yugoslavia. (see more Appendix)

Homogeneous oscillatory reactions

Upon return to Belgrade from Bruxelles (1984) Ljiljana was interested in the research on the Bray-Liebhafsky (BL) homogeneous chemical oscillatory reaction [25,26] which have already been performed at Institute of Physical Chemistry (Faculty of Science, University of

Belgrade-UB) and parallel at the Security Institute (Federal Secretariat of Internal Affairs of Yugoslavia; the first paper officially announced in 1984 (ref)). In fact, in Belgrade, the first research on the BL system was conducted by Professor Slobodanka Veljković. [27] Her research did not last long especially because of her illness and then her death. Her research did not last long especially because of her illness and then her death. The investigations will be continued not only in the Security Institute and the Faculty of Physical Chemistry, but also in Institute of Chemistry, Technology and Metallurgy, Institute for General and Physical Chemistry, VINČA Institute of Nuclear Science, the Faculty of Pharmacy etc. All the researchers of the above-mentioned institutions gathered around the Faculty of Physical Chemistry have been identified in the literature as group [28-32] which have produced notable results in the research of oscillatory reactions and their application. [for example, see references 33-39] Without a doubt, Ljiljana was their leader. The Belgrade Group already exists for 40 years. Its research on the BL reaction [25, 26] is still dominant, but the investigation has expanded, both in the phenomenological and theoretical sense, to the Belousov-Zhabotinsky (BZ) [40] and Briggs-Rauscher (BR) [41] reactions, but also the hypothalamic-pituitary-adrenal (HPA) system and to other oscillatory systems. [32-34]

<u>*Dynamic of BL reaction*</u>

During the experimental investigations of the BL reaction, the knowledge about the existence of regions of regular oscillation (Figure 2 and part of Figure 3) and chaos (Part of figure 3 and Figure 4) was expanded. [33, 34, 42-47]

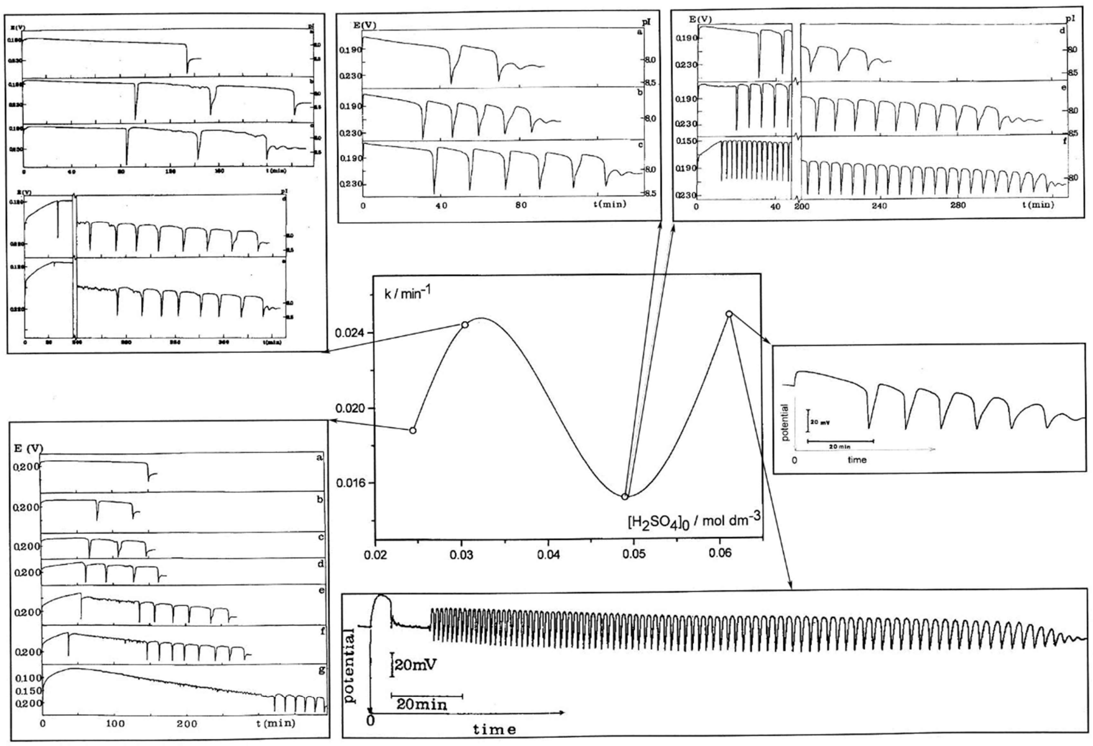

Figure 2. The series of iodide oscillograms, indicated by arrows, with the regular evolutions which have asymmetric relaxing oscillations. In the middle of the picture, it is graph of the dependence of the reaction rate constant ($k=k_D$) of the H_2O_2 decomposition (see below) as a function of acidity. k_D is determining based on the parameters of the given oscillograms (see below). [42]

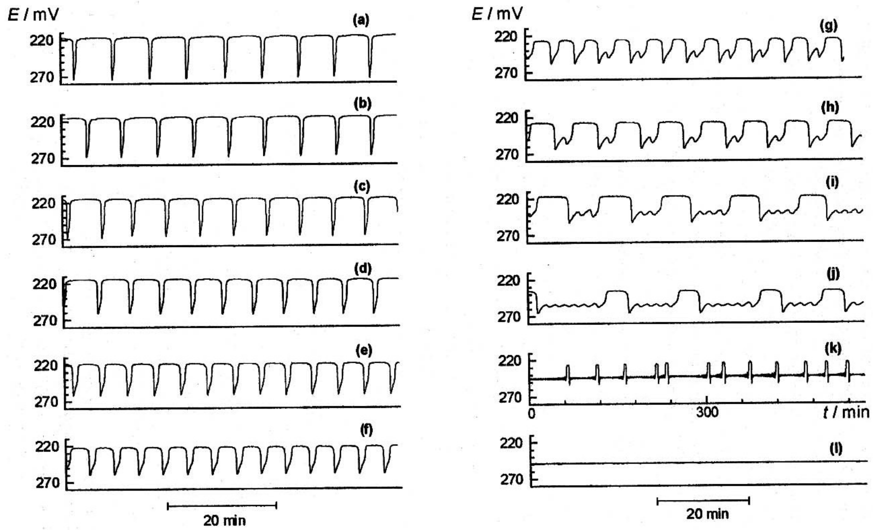

Figure 3. The oscillograms with relax and sinusoidal oscillations of the regular and chaos evolutions of BL systems realized in Continues well Stirred Tank Reactor (CSTR) at temperatures from T=52.8 (a) to T=47.6 ^{o}C (f). The oscillograms recorded by platinum electrode. [43]

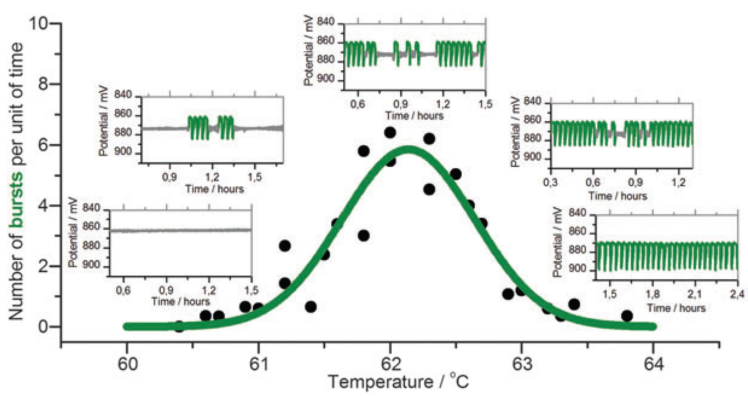

Figure 4. Temperature dependence of number of busters packages which consisted of the relaxation oscillations with large amplitudes realized in CSTR. The oscillograms recorded by platinum electrode. [44]

A few words about deterministic ordered intermittent chaos (IC). The structure of IC is characterized by the stochastic appearing of oscillation packets (busters) that have an irregular duration and number of oscillations but are a deterministic function of the control parameter (temperature, species concentration, specific flow). IC in the BL reaction was first noted by Chopin-Dumas. [48] However, later no one investigated it except the Belgrade Group.

Kinetics of BL reaction

BL reaction [25, 26] realised in mixed water solution of hydrogen peroxide and IO_3^- and H^+ ions as catalysts and it can be represented with overall stochiometric equation

$$2H_2O_2 \xrightarrow{k_D} 2H_2O + O_2 . \qquad \text{(D)}$$

This net reaction is results of the successive, or parallel reaction steps

$$2IO_3^- + 2H^+ + 5H_2O_2 \xrightarrow{k_R} I_2 + 6H_2O + 5O_2 \qquad \text{(R)}$$

$$I_2 + 5H_2O_2 \xrightarrow{k_O} 2IO_3^- + 2H^+ + 4H_2O. \qquad (O)$$

In a closed reactor, based on the empiric parameters of the generated oscillograms and the composition of the BL system (Figure 2), a unique procedure for analysing the kinetics of the reaction (D) was developed. [33, 34, 49-51] It will always be valid if the change in composition, or other control parameters does not affect the qualitative change in the observed kinetics, or in other words, if it does not change the dominant reaction mechanism of reaction (D).

Namely, Figure 5., shows a typical appearance of an oscillogram with one pre-oscillatory period and one oscillatory period with the indicated parameters of the oscillogram.

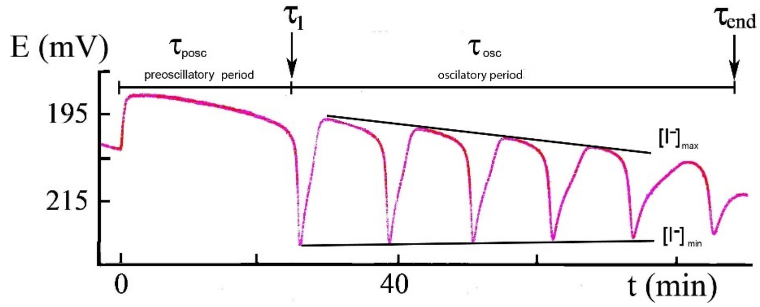

Figure 5. The iodide oscillogram of the regular evolution of the BL reaction generated in an isothermal closed reactor. The slopes of the true maximum (max) and minimum (min) iodide concentrations are constants which the temperature depends can describes with the Arrhenius equation. (see reference 32)

Even earlier, Bray showed [25] that reaction (D) is pseudo-first order with respect to the concentration of hydrogen peroxide. For the oscillatory evolution as it is in Figure 5 defined kinetic equation [49-51]

$$\tau_{end} = -\frac{1}{k_D}\ln[H_2O_2]_{end} + \frac{1}{k_D}\ln[H_2O_2]_0 \qquad (3)$$

where $[H_2O_2]_{end}$ and $[H_2O_2]_0$ denote the concentrations at $t = \tau_{end}$ and $t = 0$ minutes respectively. k_D is a pseudo constant which is a function of the reaction mixture composition.

$$k_D = k[KIO_3]_0^r[H_2SO_4]_0^q. \qquad (4)$$

k is also pseudo a constant; exponents r and q are pseudo-orders of reaction (D).

Obviously, equation (3) was derived under the assumption that the temporal change in H_2O_2 concentration is monotonous, although it is cascaded in oscillatory processes. Second, the fact is that in $t = \tau_{end}$ the bifurcation of the transition from oscillatory to monotonic evolution occurs. It was assumed that the position of the bifurcation point in the concentration phase space is essentially unchanged regardless of the change in H_2O_2 initial concentration. The set assumptions proved to be acceptable because there is satisfactory approximate agreement between the kinetic results obtained based on equation (3) and the data obtained by the process of determining the current concentration of H_2O_2 by direct titration of aliquots of the reaction solution.[52]

What is the significance of equation (3)? First, thanks to equation (3) there is a very simple way to analyse the kinetics of given BL systems without the need for the laborious and time-consuming determination of instantaneous hydrogen peroxide concentrations. Second, the equation (3) is valid and in all cases when the external species added have concentration which does not change the first order kinetic of decomposition in respect to H_2O_2 concentration. This also means that the decomposition of hydrogen peroxide in the BR system can be analysed as well as in the BL system. Likewise, the addition of all external species which do not influence a change in the reaction decomposition kinetics (D) will only affect the change in the reaction rate constant k_D (Equation 4). This means that there is a logarithmic proportionality between the constant k_D and the concentration of the given external species *a*

$$\ln k_D \propto \ln a. \tag{5}$$

The validity of equation (5) can be illustrated by the experimental results obtained by investigating the influence of the cobalt complex on the BL reaction. [53]

Otherwise, equation (3) is valid in the given temperature domain. [54, 55]. Normally, it is also valid in the case of BL equi-concentration systems at different temperatures. Then, the apparent activation energy, not only of reaction (D) but also reactions (R) and (O), can be determined thanks to equation (6) (derived from equation (3)); the analogue of rate constant reactions can be pre-oscillatory period, oscillatory period, oscillogram length, number of oscillations, etc (see Figure 5). [55]

$$\frac{1}{analog} \propto k_D \tag{6}$$

It should be mentioned that, likewise, the same form of equation (3) is valid in the Briggs-Rauscher (BR) [56] and Belousov-Zhabotinsky (BZ) oscillatory reactions. [57]

Modelling the BL and BZ Oscillatory Reaction

Theoretical and computer modelling was always significant part of Ljiljana`s scientific interest. As physical chemist, she followed the general idea that modelling must rely on experimental observation. Hence, she accepted the difficult task to contribute explaining so complex and strange phenomena as chaos and at her forms of emerging behavior generated and observed in non-linear reaction systems far from equilibrium. Oscillatory reactions were appropriate family of systems in physical chemistry, feasible to available techniques in both laboratory and computer experiments. Since there was no experimental technique which would give unambiguous answers to numerous questions about their reaction mechanism, computer modeling was always a necessary component of any research in this field. Theoretical analysis of the reaction mechanism and underlying kinetic models was an intriguing part of research which connects and explains results from laboratory and computer experiments. This was natural environment for Ljiljana`s way of systematic analytical thinking.

Typical examples of oscillatory reactions, which were subject of research in Belgrade Group under the lead of Ljiljana Kolar-Anić, were BL and BZ reactions.

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The dynamics and kinetics of the BL reaction (D) is a consequence of the given reaction mechanism, which is still an unsolved enigma. There will be more work, although much has already been done.

The articles from 1990 are the beginning of the research in Belgrade on uncovering the mechanism of the BL reaction [58-60] and with the article from 1992 [60] is the beginning of a very fruitful, long-time and continuous collaboration with the Professor G. Schmitz from the Free University of Brussels (ULB). It should be known that Professor Schmitz set up a stoichiometric model of the BL reaction (1977) (Figure 6: the reactions from (R1) to (R6) denoted later as model M(1-6). This model already enables simulation of oscillations with properties which structurally resemble the most significant properties of experimental ones, although it does not include explicit step of either autocatalysis or autoinhibition. Only the combination of the given steps can generate a reaction of that type. Namely, until then, each model of the mechanism of a homogeneous reaction which was successful in producing oscillatory behavior, included at least one autocatalytic step. Schmitz's model is the first one capable to generate given oscillatory evolutions that is remarkably consistent with the real one. It was further supplemented with reaction (R7) (reactions from (R1) to (R7) form the model M(1-7), and later (R8) (reactions from (R1) to (R8) form model M(1-8). In both cases, the extended models can successfully additionally describe some more complex dynamic structures, observed in closed reactor. [61]. Figure 2 shows the appearance of the simulated changes in the concentrations of BL system species of the given initial composition.

$IO_3^- + I^- + 2H^+$	$\rightleftarrows$	$HIO + HIO_2$	(R1) (R-1)
$HIO_2 + I^- + H^+$	$\longrightarrow$	$I_2O + H_2O$	(R2)
$I_2O + H_2O$	$\rightleftarrows$	$2HIO$	(R3) (R-3)
$HIO + I^- + H^+$	$\rightleftarrows$	$I_2 + H_2O$	(R4) (R-4)
$HIO + H_2O_2$	$\longrightarrow$	$I^- + H^+ + O_2 + H_2O$	(R5)
$I_2O + H_2O_2$	$\longrightarrow$	$HIO + HIO_2$	(R6)
$HIO_2 + H_2O_2$	$\longrightarrow$	$IO_3^- + H^+ + H_2O$	(R7)
$IO_3^- + H^+ + H_2O_2$	$\longrightarrow$	$HIO_2 + O_2\ H_2O$	(R8)

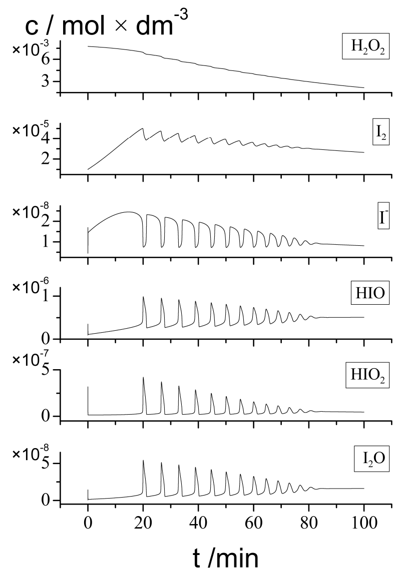

Figure 6. M(1-8) BL system model and numerical simulation of species concentration evolution in it. [34]

Later works were directed toward better understanding of complex forms of dynamical states achieved in experiments using both, closed, and open reactor conditions, including mixed-mode periodic oscillations, chaos and intermittent behaviour of the BL reaction. Much attention was given to identify nature of bifurcations present in both experimental and theoretical model BL systems. It was of tremendous importance for attained results that with Ljiljana`s help and cooperation, several members of Belgrade Group were deeply involved in adoption and further development of so versatile tool as it is the Stoichiometric Network Analysis. This method became one of highlights establishing the Belgrade Group in the sky of few research centres being able to use its advantages for stability analysis. Hence, possibilities were opened for us to investigate systems with more than just few variables.

Although, BL reaction investigation was kind of trademark for Belgrade Group, it was certainly not the only system analysed by engaged researchers, and numerous students passing through the Ljiljana`s school. One of most the significant developments achieved under Ljiljana`s leading role was new variant of the BZ reaction model.

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The overall reaction of decomposition of malonic acid (MK) in the BZ system is most often described by a stoichiometric equation:

$$2BrO_3^- + 3CH_2(COOH)_2 + 2H^+ \xrightarrow{Ce^{3+}/Ce^{4+}} 2BrCH(COOH)_2 + 3CO_2 + 4H_2O \quad (7)$$

The net (overall) reaction (7) is one possible outcome of long sequence of simpler reaction steps. Model version accepted within Belgrade group [57] achieved tremendous level of agreement between experiments and numerical simulations. Part of numerical results are given in Table besides the reaction mechanism which was used to generate oscillations.

$Br^- + HOBr + H^+ \rightarrow Br_2 + H_2O$
$Br_2 + H_2O \rightarrow Br^- + HOBr + H^+$
$HBrO_2 + Br^- + H^+ \rightarrow Br_2O + H_2O$
$Br_2O + H_2O \rightarrow 2HOBr$
$2HOBr \rightarrow Br_2O + H_2O$
$Br^- + BrO_3^- + 2H^+ \rightarrow HOBr + HBrO_2$
$2HBrO_2 \rightarrow BrO_3^- + HOBr + H^+$
$BrO_3^- + HBrO_2 + H^+ \rightarrow 2BrO_2^\bullet + H_2O$
$2BrO_2^\bullet + H_2O \rightarrow BrO_3^- + HBrO_2 + H^+$
$Ce^{3+} + BrO_2^\bullet + H^+ \rightarrow Ce^{4+} + HBrO_2$
$Ce^{4+} + HBrO_2 \rightarrow Ce^{3+} + BrO_2^\bullet + H^+$
$MK + Br_2 \rightarrow BrMK + Br^- + H^+$
$MK + Ce^{4+} \rightarrow Ce^{3+} + P + H^+$
$BrMK + Ce^{4+} \rightarrow Ce^{3+} + Br^- + P$
$MK + Br_2O \rightarrow BrMK + HOBr$
$Br_2\,(rast) \rightarrow Br_2\,(g)$

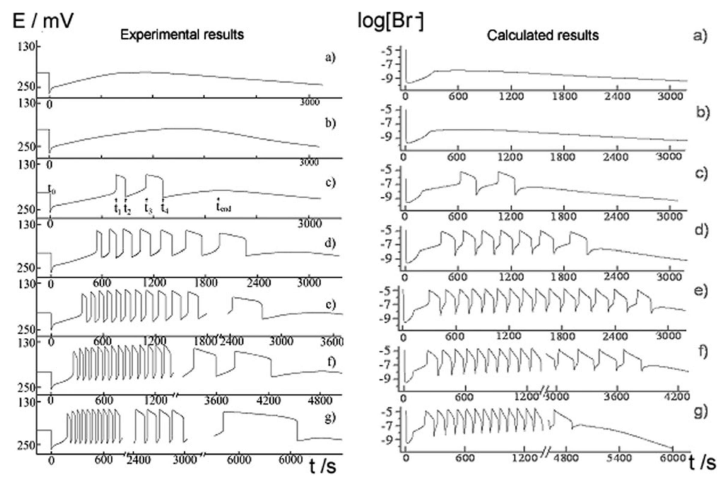

Figure 7. Oscillograms obtained experimentally (left) and by numerical simulation (right) of the BZ reaction at a temperature of 40 °C and an initial concentration of malonic acid (mol dm^{-3}): a) 8.00×10^{-3}; b) 9.00×10^{-3}; c) 1.20×10^{-3}; d) 1.60×10^{-3}; e) 2.20×10^{-3}; f) 3.20×10^{-3}; g) 4.30×10^{-2} .[57d]

Hypothalamo-Pituitary-Adrenal (HPA) system

One of the most important reasons to investigate oscillatory reactions was often its phenomenological analogy with living systems, able to generate spontaneous oscillating behaviour. Therefore, it is not surprising that Ljiljana also used methodology developed in physical chemistry of oscillating reactions, to analyse and to model dynamic phenomena observed in metabolic networks of living organism. [62-76] Most results in this area were done on modelling the *Hypothalamo-Pituitary-Adrenal (HPA) axis.*

Ljiljana guided research in this area as always and developed a specific approach founded on physical chemistry of reaction systems with mass action kinetics. [62] Her approach was particularly convenient for the application of stoichiometric network analysis to estimate numerous unknown parameter values in accordance with instability conditions derived from reaction dynamics equations. [63-68]

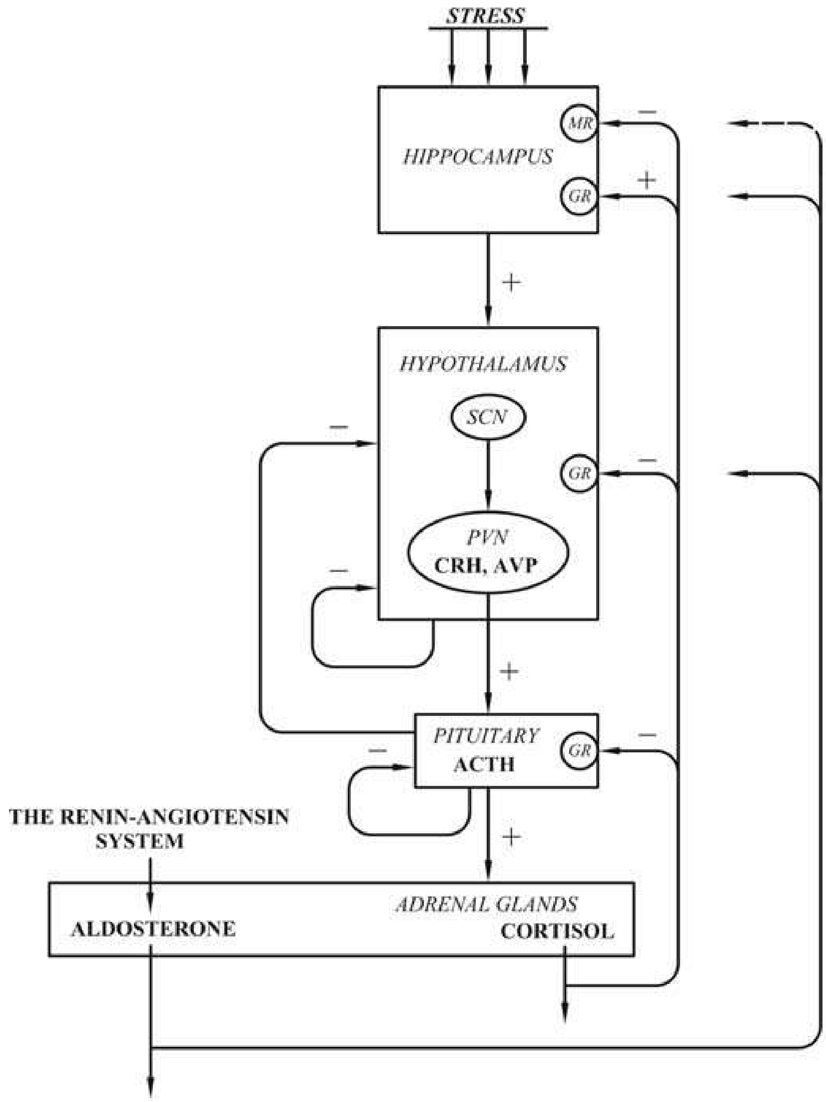

Figure 8. (a) A schematic diagram of the *Hypothalamo-Pituitary-Adrenal (HPA) axis* showing the relationship between key dynamical variables: cholesterol, corticotrophin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH), aldosterone and cortisol. (Reprinted with permission from Ref. [62]

Hence, it was easy to simulate dynamics of the global state of the organism with systems of ordinary differential equations. Although, more detailed description of the HPA system would consider the fact that it includes processes at different (sometimes significantly distant) organs, used approach was in perfect correspondence with usual medical practice relaying on screening the state of the system from instant measurement of hormone concentrations in blood. In the proposed model all signal pathways were incorporated in the reaction network, including both positive and negative feedback. Therefore, it was possible to design a model, simple enough to be analyzed, but rich in nonlinear feedback which makes it applicable to generate complex dynamic phenomena.

Table 1. Model of hypothalamus-pituitary-adrenaline (HPA) system. CRH- cholesterol, corticotrophin-releasing hormone, ALDO- aldosterone, ACTH- adrenocorticotropic

hormone, CORT- cortisol.
$\xrightarrow{k_0} CRH$ $\xrightarrow{k_m} ALDO$ $CRH \xrightarrow{k_1} ACTH$ $ACTH \xrightarrow{k_2} CORT$ $ACTH \xrightarrow{k_3} ALDO$ $ACTH + 2CORT \xrightarrow{k_4} 3CORT$ $ALDO + 2CORT \xrightarrow{k_5} CORT$ $ACTH \xrightarrow{k_6} P_1$ $CORT \xrightarrow{k_7} P_2$

This simple model, forced by circadian rhythm through the rate constant of the process responsible for CRH generation was capable to simulate biorhythmic oscillations of cortisol and other HPA axis hormones (see Figure 9).

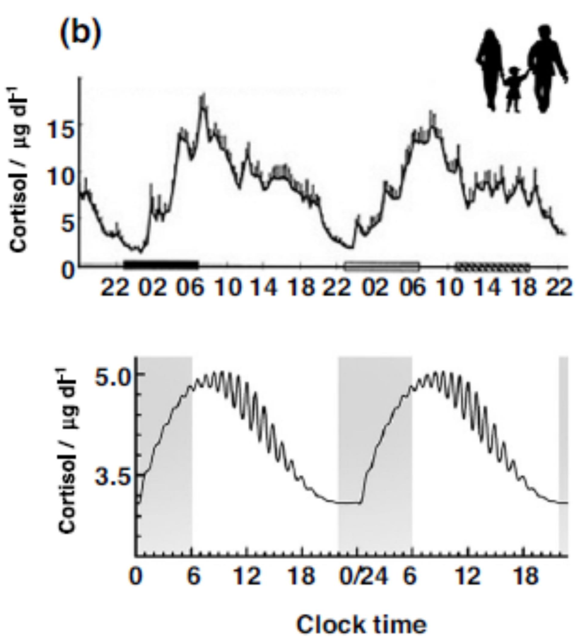

Figure 9. Experimentally determined (top) and numerically simulated (bottom) ultradian and circadian oscillations in cortisol levels in humans [74].

The most important advantage of the proposed modeling approach was adaptability. Thanks to Ljiljana's visionary approach, the proposed model was easily modified to simulate versatile functions of the HPA axis and numerous successful applications extended from this same basic idea.

Moreover, due to inherent ultradian oscillations, the model of the HPA axis has a phase sensitive response on perturbations. This property was crucial for successful simulation of numerous effects which were previously unexplained, like different reaction on the same stress during the night and during the day. [67, 74]

Because of successful application of the Ljiljana's approach to the HPA axis, Belgrade group extended the same approach to the HPT axis too. [76]

In the end, it should be said. Research related to the HPA and HPT systems is certainly very useful for diagnosing the condition of patients during their treatment, primarily in terms of predicting and determining the optimal protocol for the treatment of patients, that is, defining the optimal amount (dose) of drugs and the time of their consumption.

Application of oscillatory reactions

More of the earlier works of the Belgrade group, as said [78, 79], were in focus attention because its were deal with kinetics and mechanisms of analytical interest. Later there will be significant research in the field of application of oscillatory reactions. [53, 81-97], The new analytical methods are developed. Their kinetic meaning is defined based on stoichiometric models of reactions. And finally, such an approach made it possible to successfully simulate the phenomenological results of the research. And the end, such an approach made it possible to successfully simulate the phenomenological results of the research.

Otherwise, the oscillatory reactions with at least two reaction routes and very low concentrations of intermediate species are extremely sensitive on chemical perturbations. [38, 39] Using them, analyte pulse perturbation techniques were developed for determination of paracetamol, ascorbic acid, morphine (Figure 10), 6-monoacetylmorphyne, piroxicam, and for uric acid in human urine and so on. Other substances were recently used for determination its activities, too. [96, 97]

Moreover, perturbations of oscillatory reactions were used to characterize catalytic activity of various heterogeneous materials. [53, 91-95]

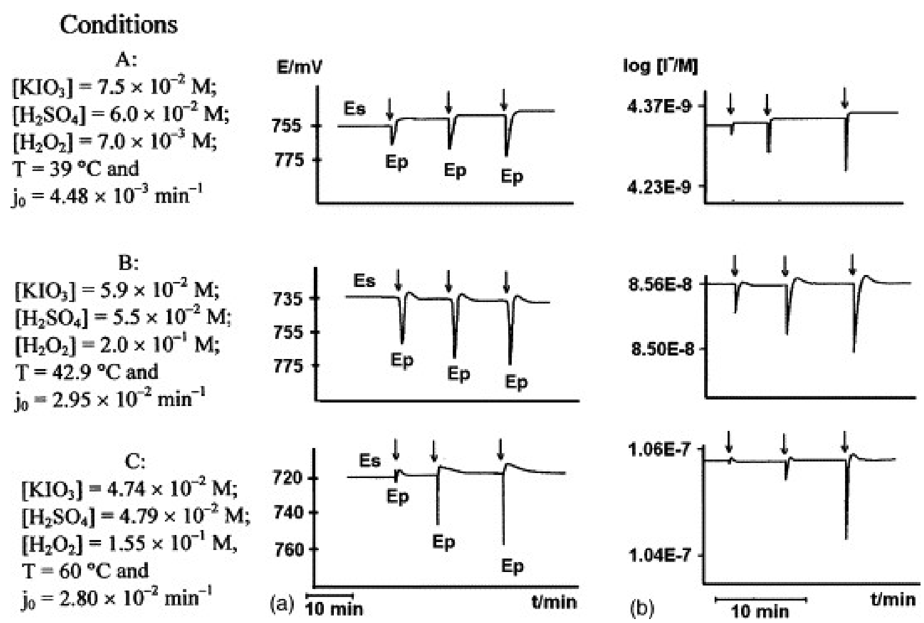

Figure 10. Experimental (a) and simulated (b) responses of BL analytical matrix of different compositions (A-C) realized for given specific flow rates j_0 in CSTR. [85]

Finally, what to say? Ljilja is no more with us, but we know that she was extremely unwaveringly, consistently and responsibly committed to her human and professional goals with all her being and passion, which she always achieved with a smile, with dignity, with love and sincerity that radiated around. She was and will be respected and loved by many. She is one of the jewels of physical chemistry.

Appendix. Part of the text from reference 24

In the official report on the implementation of the Project related to the anti-hail mixture (the so-called reagent), it is said verbatim:

1. This reagent fully meets the technical requirements of the hydrometeorological service of Yugoslavia, because at T= -10 ^{0}C it gives an activity of $7x10^{12}$-$1x10^{13}$ nuclei per gram of reagent. This activity exceeds the activity of all reagents used so far in our anti-hail protection.

2. In the entire temperature interval from -4.5^{0}C to -12^{0}C, the reagent significantly exceeds the activities of all reagents used so far.

3. At the crystallization threshold temperature -50^{0}C, the reagent gives a very high activity - about $1x10^{12}$, which is more than an order of magnitude higher activity than the reagents used so far.

4. The reagent is a fast-acting reagent, because the largest number of millimetre-sized ice crystals is formed 1-2 minutes after scattering.

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