

Oscillations and Multiscale Dynamics in a Closed Chemical Reaction System: Second Law of Thermodynamics and Temporal Complexity

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We investigate the oscillatory reaction dynamics in a closed isothermal chemical system: the reversible Lotka-Volterra model. The Second Law of Thermodynamics dictates that the system ultimately reach an equilibrium. Quasi-stationary oscillations are analyzed while free energy of the system serves as a global Lyapunov function of the dissipative dynamics. A natural distinction between regions near and far from equilibrium in terms of the free energy can be established. The dynamics is analogous to a mechanical system with time-dependent increasing damping. Near equilibrium, no oscillation is possible as dictated by Onsager's reciprocal symmetry relation. We observe that while free energy decreases in the closed system's dynamics, it does not follow the steepest descending path.

1. INTRODUCTION

Chemical and biochemical oscillations are one of the most important aspects of nonlinear dynamics of living cellular systems¹⁻³. Since the discovery of the Belousov-Zhabotinsky (BZ) reaction and the "Oregonator" mechanism⁴⁻⁶, chemical oscillations are considered one of the best examples of systems far from equilibrium that exhibit complex temporal self-organization⁷⁻⁹. The BZ reaction and its colorful dynamical change are now one of the great demonstration tools in modern chemistry classrooms¹⁰.

In reality, there are two fundamentally different types of systems in which chemical oscillations can occur. The first type is a *closed* chemical system, such as a graduated cylinder that contains a mix of molecules and then is left alone. Such systems, according to the Second Law of Thermodynamics, will ultimately tend to a chemical and dynamical equilibrium. However, the relaxation process can be very slow. Hence it is possible for the system to exhibit quasi-stationary chemical oscillations. For classroom demonstrations, this usually is sufficient.

The second type is an *open* chemical system which has a constant exchange of molecules with a source(s) and a sink(s). The best example of such a chemical system is a cell culture in a Petri dish in which cells are immersed in a chemical fluid, the medium, that contains a high level of nutrients and low level of wastes. Of course, the medium is regularly changed anew¹¹. In a laboratory, an open chemical system can be achieved by a constant monitoring of the level of source and sink molecules, and a feedback system that controls their levels. For example a chemostat is a biochemical reaction system which one keeps at a constant chemical environment by continually adding nutrients and removing a mix-

ture of waste products. Also in single-molecule studies of motor proteins, recycling adenosine diphosphate (ADP) and orthophosphate (Pi) to adenosine triphosphate (ATP) is now routinely done via regenerating systems.

From a theoretical chemistry point of view, the above two types of systems lead to two different kinds of mathematical formulations for modeling chemical dynamics. Almost all currently existing models for chemical reaction dynamics that exhibit oscillatory behavior, with the exception¹², assume constant sources and sinks, i.e., the second type. There is a great advantage of this type of mathematical models since the long-time behavior of a system can be mathematically defined rigorously^{6,13} and obtained relatively easily. Prigogine and his Brussels school have championed this perspective, in particular its thermodynamics^{7,14}.

The statistical thermodynamics of open chemical systems, however, is not without controversy; physicists have been skeptical about its value¹⁵. On the other hand, studying chemical oscillations via mathematical models for closed chemical systems means one deals with a quasi-stationary phenomenon, which is often much more difficult to define with rigorous mathematics. Dynamics in such a system is complex with multiple time scales¹⁶. But there is a theoretical advantage of studying such models: The thermodynamics of such systems is well understood. By the Law of Mass Action kinetics¹⁷, there is a free energy functional that serves as the Lyapunov function for the nonlinear dynamics³.

We have carried out a detailed nonlinear mathematical analysis on one of such systems: the reversible Lotka-Volterra (LV) reaction to be introduced below. We employed methods from nonlinear dynamical system analysis developed for perturbed Hamiltonian systems^{18,19}. We show that the multiscale dynamics can be nicely separated into *near* and *far from* equilibrium. In the region near equilibrium, Onsager's reciprocal relations dictate a certain sym-

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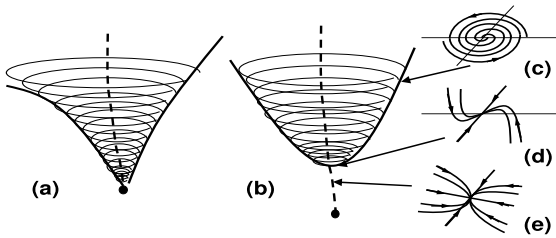


FIG. 1: Schematic comparison of qualitative dynamics between standard damped oscillation (a) and reversible LV (b). The filled dots in (a) and (b) represent the equilibrium point of the system. The reversible LV system is three dimensional(3d) (Eq. 2), with the vertical direction along the axis of the cone (w) being intimately related to the total free energy of the system. The dynamics has two regimes: When far from equilibrium, chemical oscillations occur in the xy plane approximately perpendicular to the w . The motion is oscillatory, with a pair of complex eigenvalues with its real part greater than the third real eigenvalue (c). When near the equilibrium, the motion is a monotonic, exponential relaxation with two real eigenvalues (e). The switch occurs when the two eigenvalues are equal and real (d). System in (b) has been termed quasi-planar oscillation in contrast to the “corkscrew oscillations”¹².

metry which implies mathematically that the relaxation dynamics has only real eigenvalues. There can be no trace of oscillation near the equilibrium²⁰.

The system’s total free energy continuously decreases toward its minimum. However, in the region where it is sufficiently far from its minimum, complex eigenvalues for relaxation kinetics appear. If the damping is sufficiently small, i.e., the free energy dissipation is sufficiently slow, then a quasi-stationary oscillation appears. In our mathematical model, this quasi-stationary dynamics is precisely the periodic oscillation of the standard LV system which can be found in any elementary nonlinear dynamics text².

In this communication, we report the main findings from the analysis of the reversible LV reaction in a closed system¹⁹. The main dynamical features of the system can be summarized in a schematic shown in Fig. 1(b-e). An analogue can be made to a mechanical system: a harmonic oscillator with a dynamic damping that increases with time²¹. The underdamped region corresponds to the far from equilibrium, and the overdamped region corresponds to the near equilibrium.

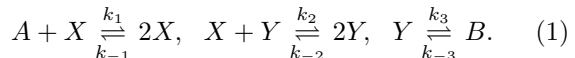
The study of chemical oscillations in a closed system also led us to a surprising observation: The Second Law of Thermodynamics states that the free energy of a closed isothermal system decreases until it reaches its minimum which corresponds to the equilibrium state of the system. However, it is imperative that the dynamic *does not* follow the steepest descent of the free energy function (i.e., not a gradient system). In fact, no such function should exist since if that were the case, then there would be no chemical oscillations, even transient ones, or any other complex temporal behavior, in any graduated cylinder. Recall that thermodynamics is an emergent theory of a system of a large number of Newtonian particles. It remains a puzzle, therefore, why

free energy dissipation does not follow its negative gradient; and whether there could be an explanation based on Newtonian mechanics.

2. REVERSIBLE LOTKA-VOLTERRA REACTION SYSTEM

Lotka-Volterra reaction systems consist of four chemical species. In the traditional treatment, the chemical species A and B are considered “fixed” while species X and Y are dynamical. This leads to a system of two ordinary differential equations (ODEs). A simple mathematical analysis can show that the system has sustained periodic oscillation. However, it depends on the initial amount of X and Y , the amplitude of the oscillations can be different. In mathematical terms, the system has a center. The chemical dynamics is very much like a harmonic oscillation with conserved total mechanical energy (Hamiltonian system).

In reality, if all the four types of molecules, A , B , X and Y are sealed in a graduated cylinder as a closed chemical system, then the concentrations of A and B can not be absolutely constant, no matter how slowly they change. The chemical potential differences across each and every reaction diminishes according to the Law of Thermodynamics. The *reversible Lotka-Volterra system* is:



The system contains autocatalytic reactions like $A + X \rightleftharpoons 2X$ and $X + Y \rightleftharpoons 2Y$, which are widely present in biochemical reaction systems. To study biochemical reaction networks both in terms of kinetics and nonequilibrium thermodynamics, it is essential that no reaction is assumed irreversible since free energy of any physical system has to be finite³.

Following the Law of Mass Action, the complete dynamic equations for (1) in a closed system is

$$\begin{cases} \frac{dx}{dt} = k_1wx - k_2xy - \varepsilon_1 \{k_{-1}x^2 - k_{-2}y^2\}, \\ \frac{dy}{dt} = k_2xy - k_3y - \varepsilon_1 \{k_{-2}y^2 - k_{-3}(c_t - x - y - \frac{w}{\varepsilon_2})\}, \\ \frac{dw}{dt} = -\varepsilon_2 \{k_1wx - \varepsilon_1 k_{-1}x^2\}, \end{cases} \quad (2)$$

in which x , y and w are the concentrations of X , Y , and A , respectively. c_t is the total concentration of all molecules: $c_t = c_A + c_B + c_X + c_Y$ which is conserved in the closed reaction system.

Parameter ε_1 in Eq. (2) represents the ratio of time scales of the set of rate constants k_1, k_2, k_3 and the set k_{-1}, k_{-2}, k_{-3} . For example, the former is on the order of (second)⁻¹ while the latter is on the order of (hour)⁻¹. In this case, $\varepsilon_1 = 1/3600$ is a small number. Parameter ε_2 represents the ratio of concentration scales for X and Y , say in millimolar, and A , say in molar. (Note that the second-order rate constant k_1 is in units of $s^{-1}M^{-1}$ while all other rate constants are in millimolar.) Hence, $\varepsilon_2 = 10^{-3}$. For small ε_1 and ε_2 , the chemical reaction system exhibits quasi-stationary oscillation. Mathematically, system (2) can be treated as the perturbation of the system with $\varepsilon_1 = \varepsilon_2 = 0$ (see Eq. 3 below).

When $\epsilon_2 = 0$, $w = w_0$ is a constant and Eq. (2) is then reduced from a 3d to a 2d system, which oscillates. For a very small ϵ_2 , the dynamics along w direction causes a slow relaxation of the oscillation toward the globally stable equilibrium.

2.1. Standard Lotka-Volterra system

The standard Lotka-Volterra (LV) system is a model for an open system in which the concentrations of A and B in (1) are kept constant by an experimenter (see Sec. 2.3 for more discussion). We see that in this case if one eliminates the intermediate X and Y , the net chemical reaction of the system is $A \rightleftharpoons B$. In other words, A is a source and B is a sink if the chemical potential of A is greater than that of B , and vice versa.

For completeness, we provide some of the well known results^{1,2,6,7,22}. More specifically, standard LV reaction assumes $k_{-1} = k_{-2} = 0$ and $c_B = 0$. Then the ordinary differential equation (ODE) for the chemical reaction system in (1) is

$$\begin{cases} \frac{dx}{dt} = \widehat{k}_1 x - k_2 xy \\ \frac{dy}{dt} = k_2 xy - k_3 y \end{cases} \quad (3)$$

where $\widehat{k}_1 = k_1 w_0$. This is a special case of LV system. In the more general LV system, the two $k_2 xy$ terms need not have same coefficient. Analysis of this system can be found in many texts². We see that Eq. (3) is the *unperturbed system* of Eq. (2).

We now introduce some thermodynamics. The chemical potential of a species Z is defined, in units of $k_B T$, as $\mu_Z = \mu_Z^o + \ln c_Z$, where c_Z is its concentration, and μ_Z^o is the internal energy of the molecule²³. For simplicity, we assume the chemical solution is dilute, hence concentration is the same as activity. Applying this formula to the species Y and B of the third reaction in (1), we have $\mu_B - \mu_Y = \mu_B^o - \mu_Y^o + \ln(c_B/c_Y)$. For an isolated chemical reaction in its dynamical and chemical equilibrium, one has $k_3 c_Y = k_{-3} c_B$ and $\mu_B = \mu_Y$. Combining these two results, we have

$$\mu_B^o - \mu_Y^o = \ln \left(\frac{k_{-3}}{k_3} \right). \quad (4)$$

And similarly, we have for the other two reactions

$$\mu_X^o - \mu_A^o = \ln \left(\frac{k_{-1}}{k_1} \right), \quad \mu_Y^o - \mu_X^o = \ln \left(\frac{k_{-2}}{k_2} \right). \quad (5)$$

The total free energy of the chemical reaction system with concentrations c_A , c_B , c_X , and c_Y is

$$L[c_A, c_B, c_X, c_Y] = \sum_{Z=A,B,X,Y} c_Z \mu_Z = \sum_Z c_Z \mu_Z^o + \sum_Z c_Z \ln c_Z. \quad (6)$$

where $\sum_Z c_Z \mu_Z^o$ is known in statistical thermodynamics as mean internal energy, and $\sum_Z c_Z \ln c_Z$ the negative of entropy: free energy = Internal energy – entropy.

2.2. Quasi-steady oscillation in a closed chemical reaction system

The detailed dynamics of the reversible LV system (2) can be summarized as follows:

(i) The temporal-organization of the system, more specifically chemical oscillations, can only arise when the system is sufficiently far from equilibrium. When the system is perturbed away from its equilibrium, if the perturbation is small, then the relaxation is strictly exponential and monotonic. However, if a perturbation is greater than a threshold, then the relaxation proceeds via a damped oscillation. The latter shares similarity with that of excitable systems with threshold phenomenon^{2,6}. Figs. 2 and 3 show examples of the dynamics with $c_t = 500$ and $c_t = 10$, respectively. The frequency of the oscillation increases with the c_t .

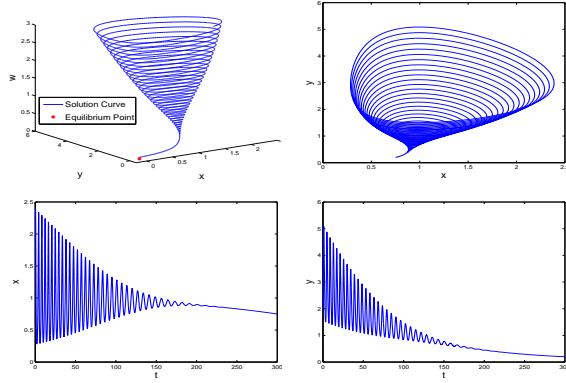


FIG. 2: Dynamics of reversible LV system (2) with a large total concentration of all molecules $c_t = 500$. Parameter used in the calculations: $\epsilon_1 = \epsilon_2^2 = 0.0001$, $k_1 = k_2 = k_{-2} = k_3 = k_{-3} = 1$, $k_{-1} = 0.01$. Initial value $(x, y, w)_0 = (2, 2, 3)$, total run time $t = 500$. The “cone-shaped” dynamics is obligatory for quasi-planar oscillation in which the radial relaxation is faster than the vertical relaxation.

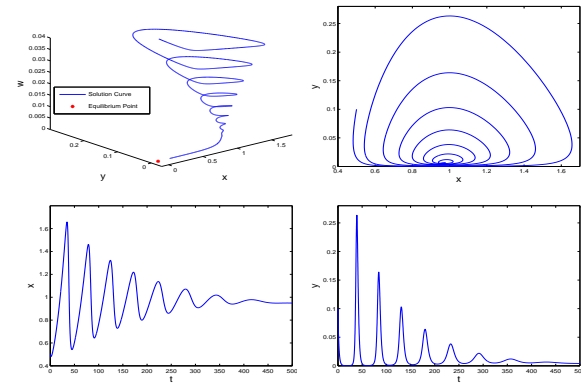


FIG. 3: Dynamics of reversible LV system (2) with a small total concentration of all molecules $c_t = 10$. Parameters used in the calculations: $k_{-1} = 0.005$, $\epsilon_1 = \epsilon_2^2 = 0.000025$, initial values $(x, y, w)_0 = (0.5, 0.1, 0.045)$. All other parameters used are the same as in Fig. 2.

(ii) There is a unique 1d invariant curve in the 3d space, represented by the axis of the cone in Fig. 2(a). The curve can be obtained approximately from the equilibrium point of the unperturbed system in

(3). Note that \hat{k}_1 is a function of w . Hence the equilibrium point of (3), as a function of w , consists the invariant curve in the 3d system. If the system's initial concentrations are located on the line, then the dynamic of the system is contained along the curve, with only slow relaxation to its equilibrium without any oscillation. In reality, if the initial concentration is near the curve, there will be no observable chemical oscillation. See Fig. 4.

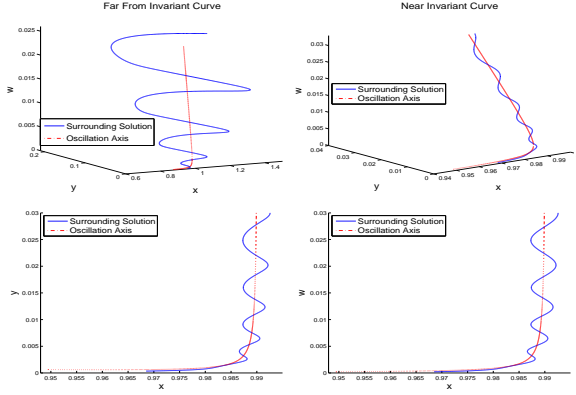


FIG. 4: Oscillation around the invariant curve(dashed). (a) is for initial point far from the invariant curve, $(x, y, w)_0 = (1.3, 0.1, 0.25)$. (b) is for initial point near the invariant curve, $(x, y, w)_0 = (0.993, 0.03, 0.03)$ which is much closer to the invariant curve. (c) and (d) are the projections of the 3d trajectory in (b) onto xy and xw planes. Parameters used in the simulations are $k_{-1} = 0.01$, $\epsilon_1 = \epsilon_2^3 = 10^{-6}$, $c_t = 10$.

(iii) The 1d curve in (ii) corresponds to the free energy of the system, decreasing when approaching to the equilibrium. The chemical oscillations occur in planes with approximately equal free energy; the oscillation is fast while the free energy dissipation is slow. See Fig. 5. The Fig. 5b clearly show that the dynamics is not in the direction of the gradient of the free energy. Rather, for quasi-planar oscillation it is almost following the constant energy level curves.

(iv) There is a dynamic transition from oscillation to non-oscillation, which can be understood from a driven chemical reaction system parametrized by the driving force $\Delta\mu_{AB} = \mu_A - \mu_B \neq 0$, (see Sec. 2.3 and Appendix). It can also be observed in Figs. 2, 3, and 4 in which the solution oscillates around an invariant curve and then proceeds along a certain direction when w falls into a low level.

(v) The reversible LV system has a semi-quantitative mechanical analogue²¹:

$$\begin{cases} \ddot{x} = -\eta(z)\dot{x} - x, & \eta(z) = \frac{4}{1+z}, \\ \dot{z} = -\varepsilon z. \end{cases} \quad (7)$$

The damped oscillation has a dynamic damping. As $\eta < 2$, the system is under-damped and the equilibrium is a spiral; and as $\eta > 2$, the system is over-damped and the equilibrium is a node. When $z(t) = z(0)e^{-\varepsilon t}$ slowly decreases toward zero, the dynamics switches from underdamped motion to damped motion at the threshold $z = 1$. But if the dynamics is fast, then oscillation can disappear when z significantly greater than 1, as shown in Fig. 6.

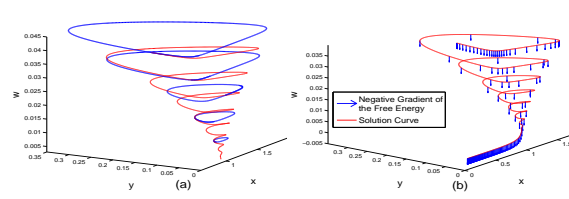


FIG. 5: (a) Perturbed system(solid line) versus unperturbed system(dot lines). For the perturbed system, all the parameters used are the same as in Fig. 3, with initial point $(0.5, 0.1, 0.045)$. The five closed orbits for the unperturbed system, from top to bottom, are with $w_0 = 0.045, 0.0361, 0.027, 0.0186$ and 0.0105 , respectively. (b) Chemical dynamics in a closed system does not follow the negative gradient of the free energy of the system. On the solution curve, all the arrows represent the direction of the negative gradient of the free energy. Note that the directions of the free energy gradient in (b), which should be perpendicular to the constant energy level curves, are approximately perpendicular to the closed orbits in (a).

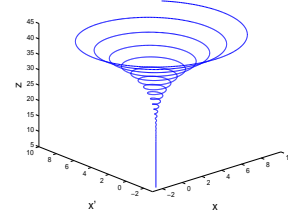


FIG. 6: Mechanical analog model according to Eq. (7) with $\varepsilon = 0.01$ and the initial values $(5, 5, 45)$. This figure should be compared with Figs. 2(a) and 3(a).

2.3. Driven reversible Lotka-Volterra reactions in an open chemical system

If the species A and B in the system (1) are being controlled by an experimenter at constant level of c_A and c_B , then only the concentrations of species X and Y are dynamic, following the ODEs

$$\begin{cases} \frac{dx}{dt} = k_1 c_A x - k_{-1} x^2 - k_2 x y + k_{-2} y^2, \\ \frac{dy}{dt} = k_2 x y - k_{-2} y^2 - k_3 y + k_{-3} c_B. \end{cases} \quad (8)$$

If the experimenter is constantly providing chemical energy to the system, the reaction is called *driven*. The amount of energy for every A molecule becoming B molecule is the difference between μ_A and μ_B :

$$\Delta\mu_{AB} = \mu_A - \mu_B = \ln \left(\frac{k_1 k_2 k_3 c_A}{k_{-1} k_{-2} k_{-3} c_B} \right). \quad (9)$$

It can be shown that this 2d system in (8) has a unique positive steady state. For a wide range of parameters, the steady state goes through a switching from a node (Fig. 1e) to a focus (Fig. 1c) with increasing $\Delta\mu_{AB}$. The critical switching point (Fig. 1d) for $\Delta\mu_{AB}$ is discussed in the Appendix.

3. DISCUSSION

Nonlinear chemical dynamics is a foundation for quantitatively understanding cellular biochemical systems^{1,6,23,24}. Complex dynamical behavior arises in chemical and biochemical systems far from equilibrium⁷. While both nonlinearity and nonequilibrium natures of chemical and biochemical complexity are well appreciated, a theoretical approach to chemical dynamics that integrates nonlinear mathematics and nonequilibrium physics has not been fully developed (see²⁵ for a general discussion).

In the present paper, we have studied a simple model for an isothermal chemical reaction system in a closed vessel. We consider its nonlinear dynamics according to the Law of Mass Action as well as the implication from the Second Law of Thermodynamics in terms of a free energy function. We found that the dynamics can indeed be divided naturally into near equilibrium and far from equilibrium regions in terms of the free energy function. In the near equilibrium region, dynamics are strictly monotonic, i.e., the system still preserves all real eigenvalues as required by Onsager's reciprocal symmetry in the linear region. In the far from equilibrium region, dynamics can exhibit oscillations: a transition from real to complex eigenvalues might occur. Away from chemical equilibrium, the system's dynamics exhibits a threshold; it is analogous to a mechanical oscillator with time-dependent, increasing damping.

Finally, we observe that the existence of complex dynamic behavior in chemical reaction systems indicates that while free energy decreases in a closed system, as dictated by the Second Law of Thermodynamics, the descending path of a system does not follow the gradient of the free energy function. If that were the case, then there would be no complex behavior whatsoever in this world. The Newtonian or quantum mechanical basis of this observation remains to be elucidated.

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APPENDIX

The reversible, driven LV system in Eq. (8) behaves significantly different from the traditional LV system. Here we provide a complete mathematical analysis. Under the following transformation

$$u = \frac{k_2}{k_3}x, \quad v = \frac{k_2}{k_3}y, \quad \tau = \frac{1}{k_3}t, \\ w = \frac{k_1}{k_3}c_A, \quad \varepsilon = \frac{k_{-2}}{k_2}, \quad \delta = \frac{k_{-1}}{k_2}, \quad \beta = \frac{k_2k_{-3}}{k_3^2}c_B,$$

system (8) is in the following dimensionless form

$$\begin{cases} \dot{u} = u(w - v) - \delta u^2 + \varepsilon v^2, \\ \dot{v} = v(u - 1) - \varepsilon v^2 + \beta, \end{cases} \quad (10)$$

and the driving force for the system becomes

$$\gamma = e^{\Delta\mu_{AB}} = \frac{k_1k_2k_3c_A}{k_{-1}k_{-2}k_{-3}c_B} = \frac{w}{\varepsilon\delta\beta}. \quad (11)$$

System (10) has a unique positive equilibrium (\bar{u}, \bar{v}) where its Jacobian matrix

$$J = \begin{pmatrix} -\delta\bar{u} - \frac{\varepsilon\bar{v}^2}{\bar{u}} & 2\varepsilon\bar{v} - \bar{u} \\ \bar{v} & -\varepsilon\bar{v} - \frac{\beta}{\bar{v}} \end{pmatrix}.$$

have negative trace $\text{tr}(J)$ and positive determinant $\det(J)$. Therefore the equilibrium (\bar{u}, \bar{v}) must be stable, and it is a stable node if the discriminant $\Delta(J) = \text{tr}^2(J) - 4\det(J) > 0$ and a stable focus if $\Delta(J) < 0$. And $\Delta(J) = 0$ provides the critical values for transition from a node to a focus.

Define $\Omega_{(\beta,w)} = \{(\beta, w), \beta, w > 0, \Delta(\beta, w) \leq 0\}$. Then $\Omega_{(\beta,w)}$ is bounded. Moreover, if $w \leq \varepsilon\delta\beta$, then $\Delta > 0$. Thus

$$\gamma_c = \inf_{(\beta,w) \in \Omega} \left\{ \frac{w}{\varepsilon\delta\beta} \right\} > 1$$

is well defined. And if we replace β by $\frac{w}{\varepsilon\delta\gamma}$ and consider the critical discriminant against (γ, w) , then $\Omega_{(\gamma,w)}$ is unbounded, see Fig. 7.

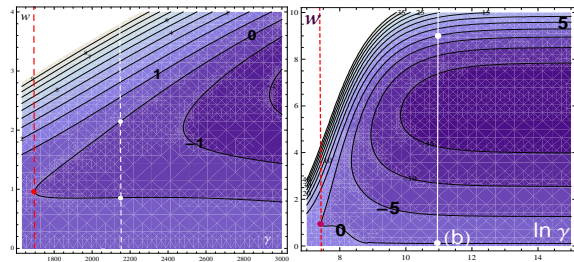


FIG. 7: Contour Plots of Δ with $\varepsilon = \sigma^2 = 0.04$ and $\delta = \sigma\varepsilon = 0.008$. (a) is drawn against (γ, w) and (b) against $(\ln \gamma, w)$. And in both panels, the dashed lines indicate the critical driving force γ_c and its logarithm; and solid lines are the counterparts for $\gamma > \gamma_c$.

In Fig. 7, we observe that when $\gamma < \gamma_c$, for any w , no point meets the zero isocline of Δ , thus Δ remains positive, (\bar{u}, \bar{v}) is a stable node and no oscillation occurs. While if $\gamma > \gamma_c$, the solid line intersects the isocline $\Delta = 0$ at two points, which implies that when w decreases, with $\gamma > \gamma_c$ fixed, down through these two intersection points, (\bar{u}, \bar{v}) starts as a stable node, transits to a focus and then changes back to a node. And precisely $\gamma_c \sim \frac{1}{2\varepsilon\delta}$.

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 - ¹⁸ W. Liu, D. Xiao, and Y. Yi, *J. Diff. Equ.* **188**, 306 (2003).
 - ¹⁹ In current mathematical literature, the perturbation theory in Hamiltonian systems have been established within Hamiltonian framework, i.e., the perturbed system remains Hamiltonian. In the present model, the perturbation is dissipative. As far as we know, no previous study has investigated such a problem rigorously. The mathematical analysis of the present model by the authors will be published elsewhere.
 - ²⁰ See D. Walz, and S.R. Caplan, *S.R. Biophys. J.* **69**, 1698 (1995). In this paper, the authors have shown that a chemical reaction system with every individual reaction being reversible can exhibit oscillatory dynamics. This is in complete agreement with the present study. However, the previous authors identified reversible system with “near equilibrium”. Even though it is mainly semantics, we believe their terminology is misleading. As we have shown in the present paper, a reversible system can be either near or far from equilibrium, depending on how severe the chemical driving force is.
 - ²¹ Strictly speaking, the reversible LV system is an anharmonic oscillation since the frequencies of different periodic orbits vary in the system. In mechanics, harmonic oscillators are usually referred to linear oscillation whose frequencies are the same irrespective of the amplitudes of the oscillation. In reversible LV system, not only the amplitudes of oscillations change but also their frequencies. The unperturbed Hamiltonian is nonlinear and frequencies for periodic orbits lying in different energy levels are not the same.
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