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The phenomenon of apparent disappearance in the marine bacteriophage dynamics

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THE PHENOMENON OF APPARENT DISAPPEARANCE IN THE MARINE BACTERIOPHAGE DYNAMICS

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Abstract. It was observed, that in aquatic microbial systems, high magnitude variations in abundance, such as sudden blooms alternating with comparatively long periods of very low abundance ("apparent disappearance") are relatively common. In order to explain this phenomenon, in this paper we considered bacteria-phage interaction assuming that the variations in abundance of both, bacteria and phage, are results of phage parasitism on this bacterial species. We construct a simple autonomous mathematical model of a pair "bacteria-phage", which assumes neither seasonal or periodic forcing, nor external factors of another nature. This model exhibits dynamics which is able to explains the phenomenon.

1. Introduction

In marine microbial biosystems, high magnitude variations in abundance and an unstable dynamics, such as sudden planktonic and bacterial blooms alternating with extended periods of low abundances, are quite common. In many cases, such blooms are immediate consequences of seasonal variations in temperature, light and other conditions (spring blooms). However, variations in abundance, which are not directly associated with seasonal forcing, are also common; Anderson and May [2] provided numerous examples of observations, where irregular explosions in abundance of terrestrial insects have clearly non-seasonal nature.

In order to explain this phenomenon, a number of hypotheses was suggested. In particular, Wommack et al. [25] suggested that the dramatic changes in the abundance of a single phage genotype, which they observed, is a consequence of parasitism of the phage on a blooming bacterial strain ("killing the winner population" concept). A certain drawback of this conjecture is that these authors, as well as Thingstad and Lignell [21] earlier, assumed that the bloom of this single bacterial species is triggered by a favorable event, such as the influx of a particular limiting nutrient, which create favorable conditions for growth of this particular species. Thus, this explanation still assumes a sort of external forcing, or an external factor. Furthermore, it is difficult

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to envisage a limiting nutrient, or a limiting factor of another nature, which promotes the growth of a single bacterial species whereas remains neutral for the rest of bacteriaplankton.

Nevertheless, the hypothesis that for aquatic bacteria and phages, the observed high magnitude variations in abundance and comparatively long periods of low abundance ("apparent disappearance") can be a result of phage parasitism on this particular bacterial species, is appealing. This concept was further developed by Hoffmann et al. [15], who suggested that the interaction of a couple "target bacteria-phage" is sufficient for the arising of high-magnitude self-sustained oscillations in abundance of both species, and that no external factor is needed. Unfortunately, this idea was to some extend handicapped by shortcomings of a mathematical model, which Hoffmann et al. designed to illustrate this possibility. This model assumes the unlimited Malthusian growth of bacteria (in this aspect, this model is similar to the first version of the Lotka-Volterra predator-prey model without carrying capacity of the environment), and, as a result, it is structurally unstable (and hence its dynamics should be destroyed by a slight perturbation of the model), and the outcome crucially depends on the initial conditions. (The phase orbits of this model form a one-parameter family of closed curves, and there is a first integral; it is not clear, however, whether Hoffmann et al. recognized this fact.) A few years ago V. Sobolev proposed a purely theoretical hypothesis that in predator-prey type models with slow-fast dynamics the phenomenon of apparent disappearance (by this term we refer to the existence of prolonged periods of very low abundance, when a population sometimes stays below a detection level) does not require seasonal forcing and can be explained with the existence of so-called canard trajectories (see [13, 17] and references therein).

In order to explain irregular variations in abundance of high magnitude in a seemingly regular system and the phenomenon of apparent disappearance, in this paper we considered a simple model of bacteria-phage interaction. The model is autonomous and assumes neither seasonal or periodic forcing, nor external factors of another nature. However, despite its simplicity, this model is capable to produce a result which explains the phenomenon.

Phages (also bacteriophages) are small viruses which infect and kill bacteria, and which were discovered independently by Frederick Twort in 1915 and by Félix d'Herelle in 1917. Phages are one of the most widespread and diverse entities in the biosphere [14]. A phages consists of a protein hull and the enclosed genetic material (which for the majority of the known phages consists of double-stranded DNA). The richest sources of phages, as well as other viruses, is oceans, where about 10 million phages per milliliter found in sea water; this figure grows up to 9×10^8 virions per milliliter found in microbial mats at the surface [24]. As much as 70% of marine bacteria may be infected by phages [24, 19], and it is currently believed that viruses (and in particular phages) is a major cause of bacterial mortality, and that contribution of viral lysis in controlling marine bacterial abundance is at least comparable with protist grazing [5, 22]. It was observed, that bacterial and phages blooms alternate with comparatively long periods of low abundance ("apparent disappearance") at concentrations

several orders of magnitude lower than the bloom concentrations (Wommack et al., 1999; Breitbart et al., 2004; Casas et al., 2006) [6, 7, 25].

According their mode of reproduction, phage can be roughly divided into two major types. The first type, the so-called lytic phages, are highly virulent type. The phage of this type begin reproduction immediately after infecting a bacterium, and after a short time lyse (destroy) the host bacterium, releasing new free phages. Phages of the second type, which are known as the non-lytic, or temperate phages, are either integrating their genetic material into the chromosomal DNA of the host, or establishing themselves as plasmids. These endogenous phages are then copied with every cell division together with the DNA of the host. They do not kill the host cell, until it starts to show signs of stress (meaning it might be about to die soon). At this stage the endogenous phages become active again and start their reproductive cycle, resulting in the lysis of the host cell.

Phage infection of more than one target bacteria occurs in nature (Faruque et al., 1999; Mehrotra et al., 2002) [10, 16]; however, it is generally believed that the most of bacteriaphages are usually specific for target bacteria, thus forming stable phage-bacteria pairs. There is no direct interaction between these pairs, or, where there is some interaction, it is negligibly weak. (However, there is indirect interaction between pairs, because bacteria of different pairs can compete for the same resource. However, for the sake of simplicity, in this paper we disregard this factor.) Following [15], we assume that the dynamics of these pairs are identical in the sense that for all pairs it is governed by the same principles and depends on the same factors, while the current states of these pairs are independent and randomly distributed.

2. Model

In this paper we consider the phages with a lytic reproduction cycle. To describe the interaction of a pair lytic phage-bacteria, we employ a mathematical model of host-microparasite interaction with a free-living infective stage of a parasite; a seminal model of this kind was proposed by R.M. Anderson and R.M. May [2]. Typically, such a model is comprised three populations, namely susceptible hosts (bacteria in our case), infected hosts and free parasites (phage in our case), of sizes or concentrations $x(t)$, $y(t)$ and $v(t)$, respectively, and postulates that the free-living parasites infect the susceptible hosts, that after an instance of infection the infected host moves into the infected class where remains until death, and that the infected hosts produce the free parasites. We assume that the proliferation of bacteria is limited by the carrying capacity of environment K (the original Anderson-May model postulates the unlimited Malthusian growth), and that only uninfected bacteria are able to reproduce. The latter assumption is equivalent to an assumption that parasite's cytopathogenicity is high, and hence the life span of the infected bacteria is low and their contribution to proliferation of the population is negligible, or that the parasite suppresses the reproductive ability of the infected bacteria; the first of these assumptions holds for the lytic phages. All the offspring are assumed to be susceptible. To reduce the

number of debatable assumptions and for the sake of simplicity, we assume that the infective incidence occur according to the law of mass action, and hence the incidence rate is of the standard bilinear form αxv, and that the other functional responses are linear.

Under these assumptions, the model is

$$\begin{aligned} \dot{x} &= ax\left(1-\frac{x+y}{K}\right)-\alpha xv, \\ \dot{y} &= \alpha xv - dy, \\ \dot{v} &= \sigma y - mv. \end{aligned} \tag{2.1}$$

Here, $x(t)$ and $y(t)$ are the concentrations of the susceptible and infected bacteria, and $v(t)$ is the concentration of free phages; a is the per capita bacteria reproduction rate, K is the currying capacity, and $1/d$ and $1/m$ are average life spans of the infected bacteria and the free phage, respectively. The non-negative octant $R^3_{\geq 0} = \{(x,y,v) \in R^3 | x,y,v \geq 0\}$ is a positive invariant set of the model; that is, any solution with initial conditions in $R^3_{\geq 0}$ remains there indefinitely. Indeed, $\dot{x} = 0$ holds at $x = 0$, whereas $\dot{y} \geq 0$ and $\dot{v} \geq 0$ hold at $y = 0$ and $v = 0$, respectively. These relationships imply that there is no phase flow through plane $x = 0$, and that the phase flow through planes $y = 0$ and $v = 0$ is only possible in the positive direction (that is, inside the positive octant). Furthermore, solutions of system (2.1) are bounded. Precisely, there is a region Ω bounded by the coordinate planes and planes $x+y = K$ and $v = \sigma K/m$, which is a positive invariant set of system (2.1) (and hence any solution initiated in the region remains there, while solutions initiated in $R^3_{\geq 0}$ outside of Ω eventually enter this region). Indeed, total bacteria population $x + y$ does not exceed the carrying capacity K, and $\dot{x} + \dot{y} = ax - bx^2 - bxy - dy < 0$ (where $b = a/K$) holds for all $x + y \geq K$. Moreover, in region $\{x, y, v \geq 0; x + y \leq K\}$, inequality $\dot{v} \leq 0$ holds for all $v \geq \sigma K/m$.

The origin $E_0 = (0, 0, 0)$ is an equilibrium state of the model, and it is always a saddle point with two negative and one positive eigenvalues. The yv-plane forms a stable manifold of this three-dimensional saddle which corresponds to two negative eigenvalues, and x-axis is the unstable manifold. The system also has a phage-free equilibrium state $E_K = (K, 0, 0)$. A type of this equilibrium state, as well as the system general global properties, depends on the basic reproduction number

$$R_0 = \frac{\sigma}{d}\frac{\alpha}{m}K.$$

The phage-free equilibrium state E_K is asymptotically stable (at least locally) if $R_0 \leq 1$, and is unstable (a saddle point with two negative and one positive eigenvalues) if $R_0 > 1$. Apart from these two equilibrium states, which always exist, the system can have a positive equilibrium state E^* with coordinates

$$x^* = md/\alpha\sigma, \quad y^* = \frac{am}{\alpha\sigma}\frac{R_0 - 1}{R_0 + a/d}, \quad v^* = \sigma y^*/m,$$

where phage and bacteria coexist. It is easy to see that $R_0 > 1$ is necessary and sufficient for the existence of positive equilibrium state E^*. Further in this paper we assume that $R_0 > 1$ is held, and hence there is a unique positive equilibrium state E^*.

A remarkable property of this model is that it admits a supercritical Andronov-Hopf bifurcation: a decrease of a, d or m, or, alternatively, an increase of α, σ and in particular of carrying capacity K, eventually leads to the loss of stability of the equilibrium state E^* and to the appearance of a stable limit cycle in the system phase space. Appendix A give a formal proof of the Andronov-Hopf bifurcation in system (2.1). In some aspects, this phenomenon is similar to the effect of enrichment (a loss of stability in a two-dimensional predator-prey system via the Andronov-Hopf bifurcation which occurs in response to the growth of a carrying capacity of environment; cf. [20]). However, the principal difference between the loss of stability in system (2.1) and the effect of enrichment is that a nonlinearity of the incidence rate (or the attack rate, in the case of a predator-prey system) with respect to the prey population $x(t)$ is essential for the latter, whereas for this model the Andronov-Hopf bifurcation occurs even for the bilinear incidence rate.

The values of a, d, m, α and σ are specific for a particular phage-bacteria pair, and significant variations of these parameters are unlikely. In contrast, the carrying capacity K can vary (for example, seasonally) to a large extend. Moreover, it is commonly believed that there is no lack of nutrient for bacteria in marine ecosystem, and that food is not a limiting factor for bacterial growth (Alldredge et al., 1986; Azam, 1998; Chin et al., 1998) [1, 3, 8, 15, 24, 25]; these consideration makes K the most important parameter for the page-bacteria system dynamics and indicates that significant changes of this dynamics are possible in response to variations of environmental conditions.

With a further increase of α, σ or, most importantly, K, or with a decrease of a, d or m, the size of this limit cycle grows. The feasible region Ω also expands towards the inner part of the octant $R^3_{\geq 0}$ with the growth of K (the planes $x + y = K$ and $v = \sigma K/m$ are parts of the boundary of the region). However, only these parts of the boundary moves with varying of K, whereas the rest of the boundary is formed by the coordinate planes, and hence is fixed. Moreover, coordinate x^* of the positive equilibrium state E^* does not depend on K. This implies that, as the size of the limit cycle grows, the cycle moves closer and closer to the coordinate planes. In particularly, the cycle approaches the yv-plane, which is a part of the boundary and the stable manifold of the equilibrium state $E_0 = (0, 0, 0)$. As the size of the limit cycle grows with the growth of K, the limit cycle is squeezed to the yv-plane, and, as a result, it unavoidably comes into the vicinity of the origin, where all three populations, as well as their rates of changes, are very low. The larger K becomes, the closer the limit cycle is squeezed to the yv-plane, and hence the closer it comes to and the longer remains in the vicinity of the origin.

This implies that the system dynamics varies to large extends in response to variations (for instance, seasonal) of K. This also implies that this system can exhibit the dynamics with long periods of low abundance, when one or all populations are remaining at very low and probably undetectable levels ("apparent disappearance"), alternating with comparatively short periods of high abundance.

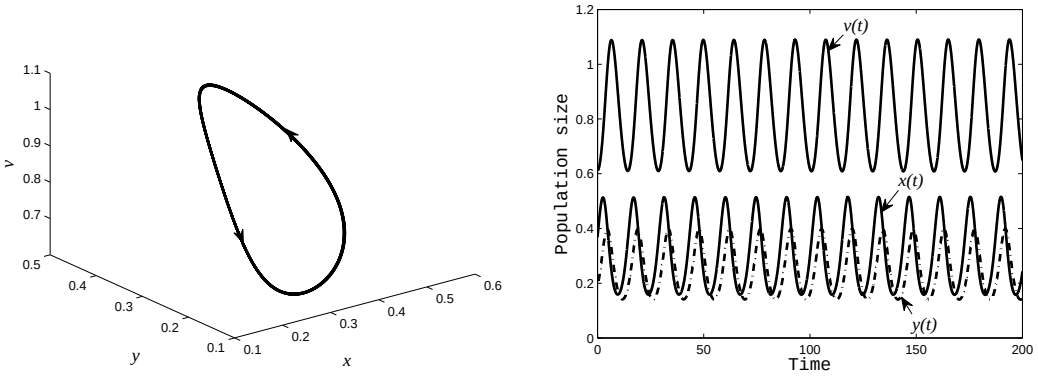

FIGURE 2.1. Appearance of the stable limit cycle; here $a = 1.0$, $\alpha = 1.0$, $d = 1.0$, $\sigma = 1.0$ and $m = 0.3$; $K = 3.33$.

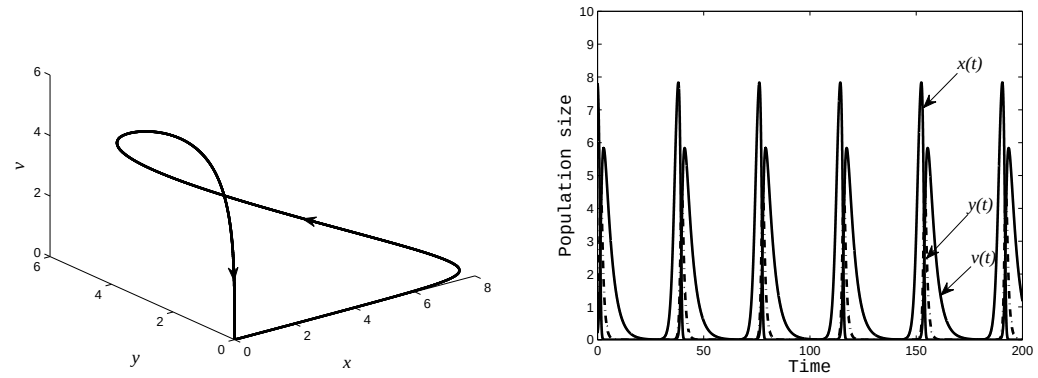

FIGURE 2.2. Further extension of the limit cycle. Here, $K = 10$ (that is, three time larger than K in Fig. 2.1), and the other parameters are the same as in Fig. 2.1.

Figures 2.1–2.3 illustrate appearance and development of the limit cycle, and an arising of the phenomenon of apparent disappearance. In these Figures, $a = 1.0, \alpha = 1.0, d = 1.0, \sigma = 1.0$ and $m = 0.3$; $K = 3.33$ in Fig. 2.1, K =10 in Fig. 2.2 and K =20 in Fig. 2.3. Please note how a comparatively small increase of the carrying capacity (K is three times larger in Fig. 2.2 compared with Fig. 2.1) leads to growth of the limit cycle size and to the squeezing on the cycle, which is clearly seen in Fig.

2.2 and 2.3, to the yv-plane and to the origin. Please note different space scales in these Figures.

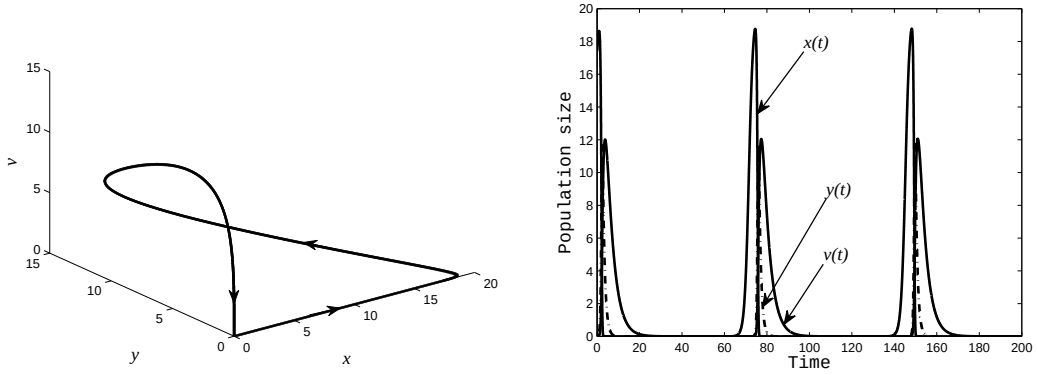

FIGURE 2.3. Further expansion of the limit cycle and arising of apparent disappearance. Here, $K = 20$ (that is, two times larger than in Fig. 2.2), while the other parameters are the same as in Fig. 2.1 and 2.2.

3. Discussion and Conclusion

Significant variations of abundance are common in the population dynamics, and in particular in marine microbial ecosystems. In many cases such variations are caused by seasonal forcing; however, unexpected outbreaks and blooms, which cannot be explained by seasonality, are not unusual either. In some instances, and in particularly for marine microorganisms, comparatively short periods of high abundance alternate with prolonged irregular periods of very low abundance (we refer to these as to "apparent disappearance"). What is more, transitions from high to low abundance and then to the succeeding blooms are in such cases usually very fast. With an aim to demonstrate why and how such irregular variations of abundance can arise in a seemingly regular marine environment, in this paper we considered a simple model of bacteria-phage interaction.

As a basis for this study, we take a host-parasite model with a free living infective stage of the phage, where we postulated the logistic proliferation of the bacteria and bilinear infection rate. Despite its simplicity, this model exhibits a complex dynamics and demonstrates that the behaviour of the system may undergo a radical transformation in response to a variation of the parametrization. In particularly, in response to a growth of the carrying capacity of environment (simply speaking, a concentration of nutrient in sea water), this model admits a supercritical Andronov-Hopf bifurcation leading to a loss of stability and a rise of self-sustained oscillations. In some aspects, this resembles the phenomenon of enrichment in a two-dimensional predator-prey model; a principal difference from the latter is that the phenomenon

of enrichment crucially depends on a nonlinearity of the incidence rate with respect to the prey population, whereas in this model we intentionally avoided any specific assumptions regarding a form of functional responses using the standard bilinear incidence rate. Furthermore, due to a difference in the life cycle time scales of the host bacteria and phage, and to the delay between the instance of infection and the death of infected hosts which is captured to some extend by this model, the loss of stability and the appearance of a limit cycle can eventually lead to the phenomenon of apparent disappearance.

This model allows a simple interpretation for the irregularities in the dynamics and the phenomenon of apparent disappearance. This interpretation is based on a combination of three factors, namely: (i) instability of a positive equilibrium state; (ii) the existence of a stable limit cycle in a bounded feasible region, and (iii) the existence of a saddle type equilibrium state at the origin, with a stable manifold forming a part of the boundary of the feasible region. Under these conditions, as the size of the limit cycle grows, the cycle is squeezed to the boundary of the feasible region and closely approaches the equilibrium state along its stable manifold. In the vicinity of an equilibrium state, the rates of changes for the phase variables are low, and, given that this equilibrium is at the origin, their values are also small. Consequently, as the trajectory is squeezed to the equilibrium state, the system exhibits lengthy periods of very low abundance. The difference in the life cycle time scales makes the change from high abundance to the low abundance very fast.

Moreover, in the vicinity of an equilibrium state the rates of change for the phase variables are proportional to the distance between the current state and the equilibrium, and hence duration of the periods of low abundance (of apparent disappearance) essentially depends on how closely the cycle is pressed to the boundary. This implies that this duration is very sensitive to variations of the system parameters, and in particularly to variations of the carrying capacity of environment K. In marine ecosystems, the carrying capacity can significantly vary (for instance, seasonally), and, as a result, very large variations and irregularities of the dynamics can be typical for marine microbial systems, and in particular for marine bacteria-phages interaction. These results also indicate that the results of isolated tests, and even a sequence of tests taken with too wide intervals, can be misleading.

In this paper, in order to keep the model as simple as possible and reduce the number of assumption to the necessary minimum, we assumed the standard bilinear incidence rate and postulated that the other functional responses are linear. However, there is a number of reasons to believe that for a marine ecosystem the functional responses are nonlinear [12, 15]. The bilinear incidence rate is based on the assumption of a homogeneous distribution of both populations in sea water, whereas in reality in marine environment bacteria form dense colonies on the surface of small particles providing a source of concentrated nutrients for them (Alldredge et al., 1986; Azam, 1998; Chin et al., 1998; Blackburn et al., 1998) [1, 3, 4, 8]. Distribution of phages is also non-homogeneous because they are released as a cohort at the moment of death of their bacterium host; community effects and some form of cooperative effects are

likely to occur for such massive simultaneous releases. In the framework of an ordinary differential equations model, a non-homogeneity of the host distribution and cooperative effects of the phage can be to some extend captured by nonlinearities of functional responses. Specifically, the above mentioned effects can be mimicked by an incidence rate which is concave with respect to the host population and convex with response to the phage population [9]. The non-homogeneity of environment can be also captured by non-linear death/removal rates. It is likely that for a non-linear incidence rate with such properties the phenomenon would be even more intense as, by the analogy with the phenomenon of enrichment, we can expect that for such an incidence rate the Andronov-Hopf bifurcation, which gives the loss of stability and the appearance of the stable limit cycle, occurs at a lower level of K. Furthermore, for an incidence rate of such a form the break up from the canard x-axis would be delayed compared with the bilinear incidence rate, thus giving a sharper and shorter microbial blooms.

In the framework of this model, irregularities in the dynamics can arise due to slow variations of the carrying capacity K, which hardly remains constant in the real aquatic systems. However, apart from this, this model indicates another possibility, which should be taken into account as well. We mentioned above that the bacteria-phage pairs can indirectly interact because the bacterial species in different pairs can compete for the same resource, and, consequently, fast changes of this resource concentrations (and, consequently, of the carrying capacity) caused by blooms of a competing bacterial species are also possible. In a situation where several species compete for the same resource, the most likely outcome of this will be extremely irregular (and probably chaotic) dynamics.

In conclusion, we have to mention that alternations of abundance when fast explosions of a population followed by equally fast declines, as well as the phenomenon of apparent disappearance are not uncommon in the population dynamics in general, including terrestrial ecosystems (and in particularly in invertebrates and microorganisms) and host-parasite systems (cf. [2, 23]). It is likely that in many other cases, where the phenomenon of apparent disappearance cannot be explained by seasonal forcing, the mechanism behind this dynamics is the same as, or similar to that, which we described. An essential element of this dynamics is the existence of a stable trajectory (a stable limit cycle) which passes near a saddle type equilibrium point. It is not necessary for this saddle point to be located at the origin, as it is in model (2.1). However, its stable manifold should be a part of the boundary of the feasible region (to which the trajectory is squeezed), and hence the saddle point should be on the boundary as well.

4. Appendix A: Andronov-Hopf bifurcation in the model

Let assume that $R_0 = \frac{\sigma}{d}\frac{\alpha}{m}K > 1$ holds, and hence the positive equilibrium state E^* exists. A stable limit cycle appears in the system phase space as a result of a supercritical Andronov-Hopf bifurcation, which occurs when a pair of isolated nonzero,

simple complex conjugate eigenvalues of a linearised system crosses the imaginary axis from left to right at a nonzero speed, while the rest of the spectrum (the third eigenvalue) remains in the open left-half plane. For system (2.1), the Jacobian matrix at point E^* is

$$J = \begin{pmatrix} -bx^* & -bx^* & -\alpha x^* \\ \alpha v^* & -d & \alpha x^* \\ 0 & \sigma & -m \end{pmatrix},$$

where $b = a/K$. The corresponding characteristic equation is

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0, \tag{4.1}$$

where

$$a_1 = -\mathrm{tr}\, J = bx^* + d + m > 0,$$

$$a_2 = bx^*(d + m + \alpha v^*) > 0$$

and

$$a_3 = -\det J = \alpha x^* v^*(bm + \sigma\alpha) > 0.$$

By the Routh-Hurwitz criterion, conditions for the Andronov-Hopf bifurcation are satisfied if $a_1, a_2, a_3 > 0$, and $\Delta = a_1a_2 - a_3 = 0$ holds. The first three inequalities, $a_1, a_2, a_3 > 0$, are the Routh-Hurwitz condition for all roots of the characteristic equation to be in the open left-half plane, and the second property, $\Delta = a_1a_2 - a_3 = 0$, together with $a_1, a_2, a_3 > 0$, are sufficient conditions for the existence of one negative real root and a pair of pure imaginary roots [11, pp. 197]. For characteristic equation (4.1),

$$\Delta = x^*\big[b(bx^* + d + m)(d + m) + \alpha v^* b(bx^* + d) - \sigma\alpha^2 v^*\big].$$

That is, equality $\Delta = 0$ holds when

$$m^3\frac{d}{\sigma\alpha}b^3 + m\big[(d+m)^2 + d(m+a)\big]b^2 + \sigma\alpha\big[(d+m)^2 + d(m+a)\big]b - a(\sigma\alpha)^2 = 0.$$

Denoting $\kappa = K^{-1}$ and $M = [(d + m)^2 + d(m + a)]/\sigma\alpha$, and recalling that $b = a/K = a\kappa$, we get the equation

$$P(\kappa) = \frac{a^2}{d^2}(x^*)^3\kappa^3 + \frac{am}{\sigma\alpha}M\kappa^2 + M\kappa - 1 = 0. \tag{4.2}$$

For polynomial $P(\kappa)$, the product of the roots is positive (and equal to $d^2/a^2(x^*)^3$), whereas their sum is negative (and equal to $-Md^2/a^2(x^*)^3$), and hence equation (4.2) always has one positive root $\kappa_{cr} > 0$ such that $\Delta(\kappa_{cr}) = 0$. (Two other roots are in the open left-half of the complex plane.) Furthermore, for $\kappa \to \infty$ (that is, for $K \to 0$), polynomial (4.2) is positive, and hence, by the Routh-Hurwitz criterion, all three root of characteristic equation (4.1) have negative real parts. When $\kappa \to 0$ (that is, for $K \to \infty$), polynomial (4.2) is negative. (Fig. 4.1 shows the graph of polynomial $P(\kappa)$ for the values of parameters which were used in Figures 2.1–2.3.) This implies that if K is not sufficiently large, the equilibrium E^* is asymptotically

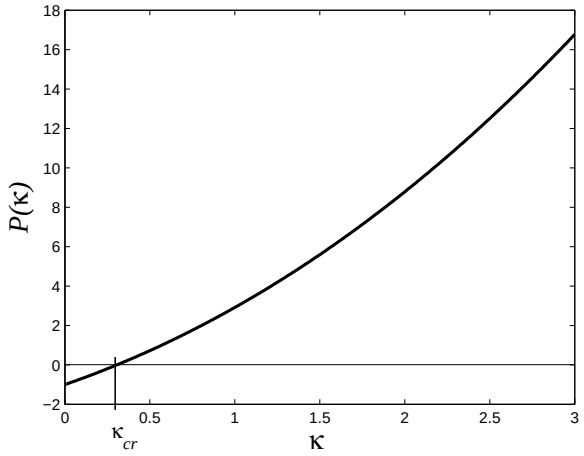

FIGURE 4.1. The graph of polynomial $P(\kappa)$ for the same values of parameters as in Figures 2.1–2.3. Positive equilibrium state E^* is stable for all $\kappa > \kappa_{cr}$, and unstable for $\kappa < \kappa_{cr}$.

stable. However, as K grows, $\Delta(K)$ decreases and eventually crosses zero level at $K = K_{cr} = \kappa_{cr}^{-1}$. At this value of K a supercritical Andronov-Hopf bifurcation occurs, the equilibrium revers its stability, and a stable limit cycle appears. The size of this cycle grows as K further increases.

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