

# AN ASYMPTOTIC ANALYSIS OF THE VAN DER POL DELAY DIFFERENTIAL EQUATION

STANCA M. CIUPE

LABORATORY OF COMPUTATIONAL IMMUNOLOGY, DUKE UNIVERSITY MEDICAL  
CENTER, 2424 ERWIN ROAD, SUITE G06, HOCK PLAZA DURHAM, NC, 27705,

STANCA.CIUPE@DUKE.EDU

AND

PATRICK W. NELSON

UNIVERSITY OF MICHIGAN, 525 EAST UNIVERSITY, 2074 EAST HALL, ANN ARBOR,

MICHIGAN, 48109-1109, PWN@UMICH.EDU

ABSTRACT. A nonlinear delay differential equation of van der Pol type is considered. Local stability conditions are derived together with the existence of a sequence of Hopf bifurcations. The direction and stability of the bifurcating periodic solutions is obtained using the center manifold theory. By perturbation analysis techniques we obtain periodic solutions for both a weak and a strong feedback equation. The effect of a delay in the promotion or suppression of limit cycle oscillations is investigated.

## 1. INTRODUCTION

Discovered by the Dutch physicist and radio engineer Balthasar van der Pol in 1926 [23], the van der Pol equation has become a prototype for systems with self-excited limit cycle oscillations. The equation has been studied over wide parameter regimes and has been used by scientists to model a variety of physical and biological

---

*Date:* November 5, 2007.

phenomena. Have been constructed for an electric circuit with a triode valve, the equation has been since used in ecology, biology, aerodynamics, seismology and engineering. The Fitzhugh -Nagumo equation extends the van der Pol equation as a model for action potentials of neurons [7, 14], while Forger, Jewett and Kronauer's analogue of the equation models the human circadian system [9]. In seismology, the van der Pol equation has been used in the development of a model for the interaction of two plates in a geological fault [3].

Time delays have been used by many researchers to account for the the reaction times, as well as complexity of a process. In immunology, time lags have been used at the cellular level to distinguish between an infected and an infectious cell as well as a weak immune response [4, 19]. In epidemiology it is used to describe incubation periods [2], while in population dynamics it describes gestation times [11].

The van der Pol equation has the form

$$(1) \quad \frac{d^2x}{dt^2}(t) + f(x, t) \frac{dx}{dt}(t) + x(t) = g(x, t; \tau).$$

Some studies have considered a constant damping effect  $f(x, t) = a$  [15], while others have considered a non-linear effect  $f(x, t) = \epsilon(x^2(t) - 1)$  [1, 18, 25, 26]. Equation (1), with a non-forcing term  $g = 0$ , is a Liénard type equation [24], known to have an unique stable periodic solution. Equation (1), with  $g(x, t) = ax(t) + bx^3(t)$ , has a stable origin for positive constants,  $a$  and  $b$ , and an unique stable periodic solution for  $a < 0$  and  $b > 0$ . If we add an external excitation,  $c \cos(\omega t)$ , to the function  $g$  we obtain a van der Pol-Duffing equation [6, 12, 18, 26].

Motivated by the need to either create or control motion, this equation has been modified by the addition of either a time delayed position feedback [1, 17, 25, 26],

$$g(x, t; \tau) = ax(t - \tau) + bx^3(t - \tau),$$

or a time delay in both the position and velocity [18],

$$g(x, t; \tau) = ax(t - \tau) + b \frac{dx}{dt}(x - \tau).$$

We investigate the dynamics of van der Pol equation under effect of a linear position feedback,

$$(2) \quad \frac{d^2x}{dt^2}(t) + x(t) = \epsilon(1 - x^2(t)) \frac{dx}{dt}(t) + kx(t - \tau).$$

This equation has been investigated before for positive  $\epsilon$  [1] and a scaling of the feedback parameter  $k = k\epsilon$  [25]. The main goal of this paper is to derive results for the dynamics of (2) in the entire parameter space  $(\epsilon, k)$ , i.e., for  $k = k\epsilon$  and for  $k = \mathcal{O}(1)$ . The paper is structured as follows. In section 2, linear analysis results, the conditions under which the Hopf bifurcations occur, and stability switches of solutions for all  $(\epsilon, k)$  as  $\tau$  varies are presented. In section 3, the direction and stability of Hopf bifurcations are derived by the center manifold theory. In section 4, analytical computations of periodic solutions for  $k = k\epsilon$  and numerical simulations for  $k = \mathcal{O}(1)$  are shown. Conclusions are drawn in section 5.

## 2. LINEAR STABILITY ANALYSIS

We examine the linear stability of the trivial solution  $x(t) \equiv 0$ . Linearizing (1) about the zero equilibrium yields the equation for infinitesimal perturbations,

$$(3) \quad \frac{d^2\tilde{x}}{dt^2}(t) + \tilde{x}(t) = \epsilon \frac{d\tilde{x}}{dt}(t) + k\tilde{x}(t - \tau).$$

Substituting  $\tilde{x}(t) = \exp(\lambda t)$  into (3), we obtain the characteristic equation for eigenmodes of the linear problem,

$$(4) \quad \lambda^2 + 1 = \epsilon\lambda + ke^{-\lambda\tau},$$

where  $\lambda \in \mathcal{C}$ . Equation (4) defines the spectrum of the linearized problem as a function of three parameters  $(k, \tau; \epsilon)$ . The second degree transcendental polynomial (4) has been studied by many researcher [5, 8, 16, 19, 21].

In the absence of delay the origin is stable provided that  $\epsilon$  is negative and  $k < 1$ , and unstable otherwise. We are interested in the existence and stability of periodic solutions bifurcating from zero for different values in our parameter space. For this, we set  $\lambda = i\nu$ , with  $\nu \in \mathbb{R}$ . After separating the real and imaginary parts we obtain

$$(5) \quad \cos(\nu\tau) = \frac{1 - \nu^2}{k}, \quad \sin(\nu\tau) = \frac{\epsilon\nu}{k},$$

for frequencies  $\nu$  and threshold values of the delay parameter  $\tau$ . If we square both equations (5) and add the results we obtain the following relation for  $\nu$

$$(6) \quad \nu^4 + \nu^2(\epsilon^2 - 2) + 1 - k^2 = 0.$$

Equation (6) has two real roots, (see regions II in Figure 1), under the conditions

- i.  $k^2 > 1$  and  $\epsilon^4 - 4\epsilon^2 + 4k^2 > 0$ , or
- ii.  $\epsilon^2 < 2$ , and  $\epsilon^4 - 4\epsilon^2 + 4k^2 = 0$ ,

four real roots, (regions IV in Figure 1), under the conditions

- iii.  $\epsilon^2 < 2$ , ,  $\epsilon^4 - 4\epsilon^2 + 4k^2 > 0$  and  $k^2 < 1$ ,

and no real roots for either one of

- iv.  $\epsilon^4 - 4\epsilon^2 + 4k^2 < 0$ , (region III in Figure 1), or

v.  $\epsilon^4 - 4\epsilon^2 + 4k^2 > 0$ ,  $\epsilon^2 > 2$  and  $k^2 < 1$ , (region I in figure 1).

Without loss of generality we can assume  $\nu$  to be positive, since solutions of equation (6) appear in complex conjugate pairs. Under the above conditions equation (4) has up to four roots on the imaginary axis

$$(7) \quad \begin{aligned} \lambda &= \pm i\nu_1, \nu_1 = \sqrt{\frac{(2 - \epsilon^2) - \sqrt{\epsilon^4 - 4\epsilon^2 + 4k^2}}{2}}, \\ \lambda &= \pm i\nu_2, \nu_2 = \sqrt{\frac{(2 - \epsilon^2) + \sqrt{\epsilon^4 - 4\epsilon^2 + 4k^2}}{2}}. \end{aligned}$$

We present next stability results for the origin in the  $(\epsilon, k)$ -space as the delay  $\tau$  varies.

**Insert FIG 1**

**Lemma 2.1.** *For  $\epsilon < 0$ , system (2) and the corresponding characteristic equation (4), we have*

(1) *if  $k < 1$  and, either ( $\epsilon^2 > 2$  and  $k^2 < 1$ ) or  $\epsilon^4 - 4\epsilon^2 + 4k^2 < 0$  hold, then the roots of the characteristic equation (4) have negative real part for all  $\tau \geq 0$ . Therefore the zero equilibrium of (2) is asymptotically stable for all  $\tau \geq 0$ .*

(2) *if  $k < 1$  and, either ( $k^2 > 1$  and  $\epsilon^4 - 4\epsilon^2 + 4k^2 > 0$ ) or ( $\epsilon^2 < 2$  and  $\epsilon^4 - 4\epsilon^2 + 4k^2 = 0$ ) hold, then the characteristic equation (4) has a pair of purely imaginary roots,  $\pm i\nu_2$ , corresponding to the delay values*

$$\tau_{c,2}(0) < \tau_{c,2}(1) < \tau_{c,2}(2) < \dots < \tau_{c,2}(n) < \dots$$

*Therefore the zero equilibrium of (2) is stable if  $\tau \in [0, \tau_{c,2}(0))$  and unstable if  $\tau > \tau_{c,2}(0)$ . Equation (2) undergoes a Hopf bifurcation at the origin when*

$\tau = \tau_{c,2}(n)$ , for  $n=0,1,\dots$  .

- (3) if  $k^2 < 1$ ,  $\epsilon^2 < 2$  and  $\epsilon^4 - 4\epsilon^2 + 4k^2 > 0$  hold then the characteristic equation (4) has two pairs of purely imaginary roots,  $\pm i\nu_2$  and  $\pm i\nu_1$ , corresponding to the delay values

$$\tau_{c,1}(0) < \tau_{c,1}(1) < \tau_{c,1}(2) < \dots < \tau_{c,1}(n) < \dots,$$

$$\tau_{c,2}(0) < \tau_{c,2}(1) < \tau_{c,2}(2) < \dots < \tau_{c,2}(n) < \dots$$

Moreover, there exists a positive number,  $l$ , such that the origin is asymptotically stable when

$$\tau \in [0, \tau_{c,2}(0)) \cup (\tau_{c,1}(0), \tau_{c,2}(1)) \cup \dots \cup (\tau_{c,1}(l-1), \tau_{c,2}(l)),$$

and unstable when

$$\tau \in (\tau_{c,2}(0), \tau_{c,1}(0)) \cup \dots \cup (\tau_{c,2}(l-1), \tau_{c,1}(l-1)) \text{ and } \tau > \tau_{c,2}(l).$$

where

$$(8) \quad \tau_{c,1}(n) = \begin{cases} \frac{1}{\nu_1} \{ \pi - \sin^{-1}(|\frac{\epsilon}{k}| \nu_1) + 2n\pi \}, & \text{for } k < 0, \\ \frac{1}{\nu_1} \{ 2\pi - \sin^{-1}(|\frac{\epsilon}{k}| \nu_1) + 2n\pi \}, & \text{for } k > 0 \end{cases},$$

and

$$(9) \quad \tau_{c,2}(n) = \begin{cases} \frac{1}{\nu_2} \left\{ \sin^{-1}\left(\left|\frac{\epsilon}{k}\right| \nu_2\right) + 2n\pi \right\}, & \text{for } k < 0, |k| > |\epsilon| \\ \frac{1}{\nu_2} \left\{ \pi - \sin^{-1}\left(\left|\frac{\epsilon}{k}\right| \nu_2\right) + 2n\pi \right\}, & \text{for } k < 0, |k| < |\epsilon| \\ \frac{1}{\nu_2} \left\{ \pi + \sin^{-1}\left(\left|\frac{\epsilon}{k}\right| \nu_2\right) + 2n\pi \right\}, & \text{for } k > 0, k > |\epsilon| \\ \frac{1}{\nu_2} \left\{ 2\pi - \sin^{-1}\left(\left|\frac{\epsilon}{k}\right| \nu_2\right) + 2n\pi \right\}, & \text{for } k > 0, k < |\epsilon| \end{cases},$$

with  $n \in \mathbb{Z}_+$ .

*Proof.* For  $\tau = 0$ , negative  $\epsilon$  and  $k < 1$  the origin is stable. By continuity, we know that the stability of the zero solution remains unchanged until  $\tau > 0$  touches one of the critical values  $\tau_{c,1}$  or  $\tau_{c,2}$  at which the real part of an eigenvalue becomes zero. To study the change in stability we compute

$$(10) \quad \frac{dRe\lambda}{d\tau} = \frac{(2\nu^2 - 2 + \epsilon^2)\nu^2}{(k\tau - \epsilon \cos(\nu\tau) - 2\nu \sin(\tau\nu))^2 + (2\nu \cos(\tau\nu) - \epsilon \sin(\tau\nu))^2},$$

to obtain that  $\frac{dRe\lambda}{d\tau}$  is positive on  $\tau_{c,2}(n)$  and negative on  $\tau_{c,1}(n)$  for all integers  $n$ . This means that as  $\tau$  passes through the critical values  $\tau_{c,1}(n)$  or  $\tau_{c,2}(n)$  a pair of eigenvalues will cross the imaginary axis from right to left or left to right, so the stability of the origin is turned on or off. The only thing left to show is that  $\tau_{c,2}(0) < \tau_{c,1}(0)$ . Using the Taylor expansion of  $\sin^{-1}(x)$  for  $-1 < x < 1$  and the inequality  $\nu_1 < \nu_2$  we obtain the following result for  $k < 0, k > |\epsilon|$ ,

$$\begin{aligned}\tau_{c,1}(0) &= \frac{1}{\nu_1} \left\{ \pi - \sin^{-1} \left( \left| \frac{\epsilon}{k} \right| \nu_1 \right) \right\} = \frac{\pi}{\nu_1} - \left| \frac{\epsilon}{k} \right| - \sum_{n=1}^{\infty} \frac{(2n-1)!!}{(2n+1)(2n)!!} \left| \frac{\epsilon}{k} \right|^{2n+1} \nu_1^{2n} \\ &> \frac{\pi}{\nu_2} - \left| \frac{\epsilon}{k} \right| - \sum_{n=1}^{\infty} \frac{(2n-1)!!}{(2n+1)(2n)!!} \left| \frac{\epsilon}{k} \right|^{2n+1} \nu_2^{2n} = \tau_{c,2}(0).\end{aligned}$$

Here we denote  $(2n)!! = 2 \times 4 \times \dots \times (2n)$  and  $(2n-1)!! = 1 \times 3 \times \dots \times (2n-1)$ .

Similar results follow for the other values of  $k$ .  $\square$

The stability results and the Hopf bifurcation of (2), when  $\epsilon$  is positive are summarized below.

**Lemma 2.2.** *For  $\epsilon > 0$ , equation (2) and the corresponding characteristic equation (4), we have*

(1) *if either ( $\epsilon^2 > 2$  and  $k^2 < 1$ ) or  $\epsilon^4 - 4\epsilon^2 + 4k^2 < 0$  then equation (4) has at least one root with positive real parts for all  $\tau \geq 0$ . This implies that the zero equilibrium of equation (2) is unstable for all  $\tau \geq 0$ .*

(2) *if  $k \neq 1$  and either ( $k^2 > 1$  and  $\epsilon^4 - 4\epsilon^2 + 4k^2 > 0$ ) or ( $\epsilon^2 < 2$  and  $\epsilon^4 - 4\epsilon^2 + 4k^2 = 0$ ) hold then the characteristic equation (4) has a pair of purely imaginary roots,  $\pm i\nu_2$ , corresponding to the delay values*

$$\tau_{c,2}(0) < \tau_{c,2}(1) < \tau_{c,2}(2) < \dots < \tau_{c,2}(n) < \dots$$

*Therefore the zero equilibrium of (2) is unstable for all  $\tau \geq 0$ . Equation (2) undergoes a Hopf bifurcation at the origin when  $\tau = \tau_{c,2}(n)$ , for  $n=0,1,\dots$ .*

(3) *if  $k < 1$ ,  $k^2 < 1$ ,  $\epsilon^2 < 2$  and  $\epsilon^4 - 4\epsilon^2 + 4k^2 > 0$  hold then the characteristic equation (4) has two pairs of purely imaginary roots,  $\pm i\nu_2$  and  $\pm i\nu_1$ ,*

corresponding to the delay values

$$\tau_{c,1}(0) < \tau_{c,1}(1) < \tau_{c,1}(2) < \dots < \tau_{c,1}(n) < \dots,$$

$$\tau_{c,2}(0) < \tau_{c,2}(1) < \tau_{c,2}(2) < \dots < \tau_{c,2}(n) < \dots$$

Equation (2) undergoes a Hopf bifurcation at the origin when  $\tau = \tau_{c,1}(n)$  or  $\tau_{c,2}(n)$  for all  $n=0,1,\dots$ . Moreover, there exists a positive number,  $l$ , such that the origin is asymptotically stable when

$$\tau \in (\tau_{c,1}(0), \tau_{c,2}(0)) \cup (\tau_{c,1}(1), \tau_{c,2}(1)) \cup \dots \cup (\tau_{c,1}(l), \tau_{c,2}(l)),$$

and unstable when

$$\tau \in [0, \tau_{c,1}(0)) \cup \dots \cup (\tau_{c,2}(l-1), \tau_{c,1}(l)) \text{ and } \tau > \tau_{c,2}(l).$$

where

$$(11) \quad \tau_{c,1}(n) = \begin{cases} \frac{1}{\nu_1} \left\{ \pi + \sin^{-1} \left( \frac{\epsilon}{|k|} \nu_1 \right) + 2n\pi \right\}, & \text{for } k < 0 \\ \frac{1}{\nu_1} \left\{ \sin^{-1} \left( \frac{\epsilon}{k} \nu_1 \right) + 2n\pi \right\}, & \text{for } k > 0 \end{cases},$$

and

$$(12) \quad \tau_{c,2}(n) = \begin{cases} \frac{1}{\nu_2} \left\{ \pi + \sin^{-1} \left( \frac{\epsilon}{|k|} \nu_2 \right) + 2n\pi \right\}, & \text{for } k < 0, |k| < \epsilon \\ \frac{1}{\nu_2} \left\{ 2\pi - \sin^{-1} \left( \frac{\epsilon}{|k|} \nu_2 \right) + 2n\pi \right\}, & \text{for } k < 0, |k| > \epsilon \\ \frac{1}{\nu_2} \left\{ \sin^{-1} \left( \frac{\epsilon}{k} \nu_2 \right) + 2n\pi \right\}, & \text{for } k > 0, k < \epsilon \\ \frac{1}{\nu_2} \left\{ \pi - \sin^{-1} \left( \frac{\epsilon}{k} \nu_2 \right) + 2n\pi \right\}, & \text{for } k > 0, k > \epsilon \end{cases},$$

with  $n \in \mathbb{Z}_+$ .

*Proof.* The proof follows easily using the same arguments as in Lemma 2.1.  $\square$

As in [20, 26] we can plot the critical curves in the  $(k, \tau)$ -space for  $\epsilon = -0.5$  (see Fig 2, (a)) and  $\epsilon = 0.5$  (see Fig 2(b)). One can notice that for  $\epsilon = 0.5$  the origin is stable for  $\tau \in (\tau_{c,1}(0), \tau_{c,2}(0))$  and unstable for  $\tau > \tau_{c,2}(0)$  which is consistent to Lemma 2.2 (3) for  $l = 0$ .

### Insert FIG 2

### 3. DIRECTION AND STABILITY OF HOPF BIFURCATION

As seen in the previous section, under certain conditions, the system

$$(13) \quad \begin{aligned} \frac{dx}{dt}(t) &= y(t) \\ \frac{dy}{dt}(t) &= \epsilon(1 - x^2(t))y(t) + kx(t - \tau) - x(t) \end{aligned},$$

undergoes a Hopf bifurcation at the origin, as the delay equals critical values  $\tau_{c,1}$  or  $\tau_{c,2}$ . We will apply the central manifold theory to derive conditions for the direction, stability and period of these periodic solutions [10].

The same approach has been used for the van der Pol equation with  $k = k\epsilon$  [25], the van der Pol equation with distributed delay [17] and for predator-prey systems [22]. We will again consider the general case  $(k, \epsilon)$  for which, under the assumptions of Lemma 2.1 or 2.2, a Hopf bifurcation exists. We first consider the change of variable  $u_1(t) = x(t\tau)$ ,  $u_2(t) = y(t\tau)$ . Also, let  $\tau = \tau_c + \mu$  with  $\mu \in \mathbb{R}$  be a perturbation of the delay from the Hopf bifurcation value. Equation (1) becomes

$$(14) \quad \begin{aligned} \frac{du_1}{dt}(t) &= \tau u_2(t) \\ \frac{du_2}{dt}(t) &= \tau(-u_1(t) + \epsilon(1 - u_1^2(t))u_2(t) + ku_1(t-1)) \end{aligned}$$

To transform system (14) into a functional differential equation, let  $C = \mathbf{C}([-1, 0], \mathbb{R}^2)$  denote the space of continuous vector functions defined on  $[-1, 0]$ , whose domain is independent of the delay,  $\tau$ .

For every  $\phi = (\phi_1, \phi_2) \in C$ , let

$$(15) \quad L_\mu \phi = (\tau_c + \mu) \begin{pmatrix} \phi_2(0) \\ -\phi_1(0) + \epsilon\phi_2(0) + k\phi_1(-1) \end{pmatrix},$$

be a family of linear operators and

$$(16) \quad f(\mu, \phi) = (\tau_c + \mu) \begin{pmatrix} 0 \\ -\epsilon\phi_1^2(0)\phi_2(0) \end{pmatrix},$$

contain the nonlinear terms. Moreover

$$f(\mu, 0) = 0 \text{ and } D_u f(\mu, 0) = 0.$$

By the Riesz representation theorem, there exists a matrix valued function  $\eta(\theta, \mu) : [-1, 0] \rightarrow \mathbb{R}^2$  whose components have bounded variation, such that

$$L_\mu \phi = \int_{-1}^0 d\eta(\theta, \mu)\phi(\theta), \text{ for } \phi \in \mathbf{C}.$$

In our case we can choose  $\eta(\theta, \mu)$  to be

$$(17) \quad \eta(\theta, \mu) = \begin{cases} (\tau_c + \mu) \begin{pmatrix} 0 & 1 \\ -1 & \epsilon \end{pmatrix}, & \text{if } \theta = 0 \\ (\tau_c + \mu) \begin{pmatrix} 0 & 0 \\ -k & 0 \end{pmatrix}, & \text{if } \theta \in [-1, 0) \end{cases} .$$

We make the following assumptions on the spectrum of  $L_\mu$ ,

$$\sigma(\mu) = \{ \lambda \mid \det(\lambda I - L_\mu e^{\lambda \theta} I) = 0 \},$$

- (1) there exists a pair of complex conjugate eigenvalues  $\lambda(\mu)$  and  $\bar{\lambda}(\mu)$  such that

$$\lambda(\mu) = \alpha(\mu) + i\beta(\mu),$$

where  $\alpha$  and  $\beta$  are real and  $\alpha(0) = 0$ ,  $\beta(0) = \tau_c \nu$  and  $\alpha'(0) \neq 0$ ,

- (2) all other elements of  $\sigma(0)$  have negative real parts.

For  $\phi \in (C[-1, 0], \mathbb{R}^2)$  let us define

$$A(\mu)\phi = \begin{cases} \frac{d\phi(\theta)}{d\theta}, & \text{if } \theta \in [-1, 0) \\ \int_{-1}^0 d\eta(\mu, s)\phi(s), & \text{if } \theta = 0 \end{cases} ,$$

and

$$R(\mu)\phi = \begin{cases} 0, & \text{if } \theta \in [-1, 0) \\ f(\mu, \theta), & \text{if } \theta = 0 \end{cases} .$$

Then, since  $\frac{du}{d\theta} = \frac{du}{dt}$ , system (14) becomes

$$(18) \quad \dot{u}_t = A(\mu)u_t + R(\mu)u_t,$$

where  $u = (u_1, u_2)^T$  and  $u_t = u(t + \theta)$ ,  $\theta \in [-1, 0]$ . For  $\mu = 0$  let  $q(\theta) = (q_1, q_2)^T e^{i\nu\tau_c\theta}$  be the eigenvector of  $A(0)$  corresponding to  $\lambda(0)$ , i.e.,

$$A(0)q(\theta) = i\nu\tau_c q(\theta).$$

The adjoint operator  $A^*(0)$  is defined for every  $\psi \in C([0, 1], \mathbb{R}^2)$  by

$$A^*(0)\psi(s) = \begin{cases} -\frac{d\psi(s)}{ds}, & \text{if } s \in (0, 1] \\ \int_{-1}^0 d\eta(t, 0)\psi(-t), & \text{if } s = 0 \end{cases}.$$

For every  $\phi \in C([-1, 0], \mathbb{R}^2)$  and  $\psi \in C([0, 1], \mathbb{R}^2)$  we define a bilinear inner product

$$\langle \psi, \phi \rangle = \bar{\psi}(0)\phi(0) - \int_{-1}^0 \int_{\xi=0}^{\theta} \bar{\psi}(\xi - \theta) d\eta(\theta)\phi(\xi) d\xi,$$

where  $\eta(\theta) = \eta(\theta, 0)$ . Let  $q^*(s) = (q_1^*, q_2^*)^T e^{i\nu\tau_c s}$  be an eigenvector of  $A^*$  corresponding to the eigenvalue  $\bar{\lambda}(0)$ , i.e.,

$$q^*(s)A^* = -i\nu\tau_c q^*(s).$$

We find the eigenvectors  $q$  and  $q^*$  to be

$$q(\theta) = (1, i\nu)^T e^{i\nu\tau_c\theta},$$

$$q^*(s) = B(-\epsilon + i\nu, 1) e^{i\nu\tau_c s},$$

where  $B$  can be found using the normalization formula  $\langle q^*, q \rangle = 1$  to be

$$B = \frac{-\epsilon + 2\nu + \epsilon\nu e^{-i\nu\tau_c}}{\epsilon^2 + 4\nu^2 + \epsilon^2\nu^2 - 2\epsilon^2\tau_c \cos(\nu\tau_c) - 4\nu\tau_c\epsilon \sin(\nu\tau_c)}.$$

Next we compute the coordinates that describe the center manifold  $\mathbf{C}_0$  at  $\mu = 0$ , following the same arguments as in [10]. For  $u_t$ , a solution of (14) at  $\mu = 0$ , we define

$$(19) \quad z(t) = \langle q^*, u_t \rangle \quad \text{and} \quad w(t, \theta) = u_t(\theta) - 2\text{Re}\{z(t)q(\theta)\}.$$

On the manifold  $\mathbf{C}_0$ ,  $w(t, \theta) = w(z(t), \bar{z}(t), \theta)$  where

$$(20) \quad w(z, \bar{z}, \theta) = w_{20}(\theta) \frac{z^2}{2} + w_{11}(\theta) z\bar{z} + w_{02}(\theta) \frac{\bar{z}^2}{2} + \dots,$$

and  $z$  and  $\bar{z}$  are local coordinates for  $\mathbf{C}_0$  in  $\mathbf{C}$  in the directions of  $q^*$  and  $\bar{q}^*$ . Since we are dealing only with real solutions, i.e.,  $u_t$  real, one can notice that  $w$  is real as well.

For solutions  $u_t \in \mathbf{C}_0$  of (14) we have,

$$\langle q^*, \dot{u}_t \rangle = \langle q^*, Au_t + Ru_t \rangle,$$

which, for  $\mu = 0$ , is equivalent with

$$(21) \quad \dot{z}(t) = i\nu\tau_c z + \bar{q}^*(\theta) f(z, \bar{z}, \theta) + 2 \text{Re} \{zq(\theta)\} \equiv i\nu\tau_c z + \bar{q}^*(0)f_0,$$

which we rewrite as

$$(22) \quad \dot{z}(t) = i\nu\tau_c z + g(z, \bar{z}).$$

Note that  $g$  is a function of  $z$  and  $\bar{z}$  that does not depend on  $\theta$ . Let's expand  $g$  in powers of  $z$  and  $\bar{z}$  as follows

$$(23) \quad g(z, \bar{z}) = g_{20} \frac{z^2}{2} + g_{11} z\bar{z} + g_{02} \frac{\bar{z}^2}{2} + g_{21} \frac{z^2\bar{z}}{2} + \dots$$

From (19) it follows that

$$(24) \quad \begin{aligned} u_t(\theta) &= w(t, \theta) + 2 \operatorname{Re} \{z(t)q(\theta)\} \\ &= w_{20}(\theta) \frac{z^2}{2} + w_{11}(\theta) z\bar{z} + w_{02}(\theta) \frac{\bar{z}^2}{2} + (1, i\nu)^T e^{i\nu\tau_c\theta} z + (1, -i\nu)^T e^{-i\nu\tau_c\theta} \bar{z} + \dots \end{aligned}$$

This, together with (16) gives the following formula for  $g$

$$(25) \quad \begin{aligned} g(z, \bar{z}) &= \bar{q}^*(0) f_0(z, \bar{z}) = \bar{q}^*(0) f(0, u_t) \\ &= \bar{q}^*(0) \tau_c \begin{pmatrix} 0 \\ -\epsilon(w^1(0) + z + \bar{z})^2 (w^2(0) + i\nu z - i\nu\bar{z}) \end{pmatrix} \\ &= \bar{B} \tau_c (-\epsilon - i\nu, 1) \begin{pmatrix} 0 \\ -\epsilon(w^1(0) + z + \bar{z})^2 (w^2(0) + i\nu z - i\nu\bar{z}) \end{pmatrix} \\ &= -\epsilon \bar{B} \tau_c (w_{20}^1(0) \frac{z^2}{2} + w_{11}^1(0) z\bar{z} + w_{02}^1(0) \frac{\bar{z}^2}{2} + \dots + z + \bar{z})^2 \\ &\quad (w_{20}^2(0) \frac{z^2}{2} (0) + w_{11}^2(0) z\bar{z} + w_{02}^2(0) \frac{\bar{z}^2}{2} + \dots + i\nu z - i\nu\bar{z}) \\ &= -i \bar{B} \epsilon \tau_c \nu z^2 \bar{z} + O(z^2 \bar{z}^2). \end{aligned}$$

If we equate (25) with (23) we obtain the following identities

$$(26) \quad g_{20} = g_{11} = g_{02} = 0, \quad g_{21} = -2i \bar{B} \epsilon \tau_c \nu,$$

which do not depend on  $w$ . Therefore,

(27)

$$\begin{aligned}
c_1(0) &= \frac{i}{2\nu\tau_c} \left( g_{11}g_{20} - 2|g_{11}|^2 - \frac{|g_{02}|^2}{3} \right) + \frac{g_{21}}{2} = -i\bar{B}\epsilon\tau_c\nu \\
&= \frac{\epsilon\tau_c\nu(-2\nu+\epsilon\tau_c \sin(\nu\tau_c))}{(-\epsilon+\epsilon\tau_c \cos(\nu\tau_c))^2+(2\nu-\epsilon\tau_c \sin(\nu\tau_c))^2} + i \frac{\epsilon^2\tau_c\nu(1-\tau_c \cos(\nu\tau_c))}{(-\epsilon+\epsilon\tau_c \cos(\nu\tau_c))^2+(2\nu-\epsilon\tau_c \sin(\nu\tau_c))^2}, \\
\mu_2 &= -\frac{\operatorname{Re}(c_1(0))}{\operatorname{Re}(\lambda'(\tau_c))} = -\frac{1}{2\operatorname{Re}(\lambda'(\tau_c))} \frac{\epsilon\tau_c\nu(-2\nu+\epsilon\tau_c \sin(\nu\tau_c))}{(-\epsilon+\epsilon\tau_c \cos(\nu\tau_c))^2+(2\nu-\epsilon\tau_c \sin(\nu\tau_c))^2}, \\
\beta_2 &= 2\operatorname{Re}(c_1(0)) = 2 \frac{\epsilon\tau_c\nu(-2\nu+\epsilon\tau_c \sin(\nu\tau_c))}{(-\epsilon+\epsilon\tau_c \cos(\nu\tau_c))^2+(2\nu-\epsilon\tau_c \sin(\nu\tau_c))^2}, \\
T_2 &= -\frac{\operatorname{Im}(c_1(0))+\mu_2 \operatorname{Im}(\lambda'(\tau_c))}{\nu}.
\end{aligned}$$

Thus, the periodic solutions bifurcating from the origin in the center manifold are stable if  $\beta_2 < 0$  and unstable if  $\beta_2 > 0$ . The sign of  $\mu_2$  determines the direction of the bifurcation, i.e., supercritical (subcritical) if  $\mu_2 > 0$  ( $\mu_2 < 0$ ), and the bifurcating solutions exist for  $\tau > \tau_c$  ( $\tau < \tau_c$ ). Furthermore if  $T_2 > 0$  then the period of the bifurcating periodic solution increases, and decreases if  $T_2 < 0$ . The results for equation (2) are summarized below

**Theorem 3.1.** *Suppose that system (2) has a Hopf bifurcation at the origin, then we have*

- (1) *if  $\tau = \tau_{c,1}$  and  $\epsilon\tau_c\nu(-2\nu+\epsilon\tau_c \sin(\nu\tau_c)) > 0$  ( $< 0$  respectively) then the Hopf bifurcation is supercritical (subcritical). Furthermore, the periodic solution is unstable (stable).*

- (2) if  $\tau = \tau_{c,2}$  and  $\epsilon\tau_c\nu(-2\nu + \epsilon\tau_c \sin(\nu\tau_c)) > 0$  ( $< 0$  respectively) then the Hopf bifurcation is subcritical ( supercritical). Furthermore, the periodic solution is unstable (stable).

#### 4. NUMERICAL RESULTS

In this section we will study the stability of the zero solution and the appearance of limit cycles for different values of  $\epsilon$  and  $k$ .

**4.1. Weak feedback, weak positive nonlinearity.** Let us consider the parameter  $k$  to be of same magnitude as  $\epsilon > 0$ , i.e., we rescale the delayed feedback by a factor of  $\epsilon$  to obtain

$$(28) \quad \frac{d^2x}{dt^2} + x = \epsilon(1 - x^2) \frac{dx}{dt} + \epsilon\bar{k}x(t - \tau),$$

where  $\bar{k}$  is real. The existence of periodic stable solutions of this equation was proven by Atay [1] using the method of averaging for delay-differential equations. We use the method of multiple scales [13], to investigate the nature of oscillations and the effect different parameters have on the outcome of the solutions.

Let us consider  $\epsilon$  to be a small positive parameter, i.e.,  $0 < \epsilon \ll 1$ . To apply the method of multiple scales, we begin by considering two time scales  $t$ , and  $T = \epsilon t$ . Regard the solution of (2) as a Taylor series in  $\epsilon$ , for  $\epsilon$  small

$$(29) \quad x(t, T; \epsilon) = x_0(t, T; 0) + \epsilon x_1(t, T; 0) + \epsilon^2 x_2(t, T; 0) + \dots$$

We substitute the expansion into equation (1) to obtain the following relations

(30)

$$\begin{aligned} \frac{d^2 x_0}{dt^2}(t, T; 0) + x_0(t, T; 0) &= 0, \\ \frac{d^2 x_1}{dt^2}(t, T; 0) + x_1(t, T; 0) &= -2 \frac{d^2 x_0}{dt dT}(t, T; 0) + \bar{k} x_0(t - \tau, T; 0) + (1 - x_0^2) \frac{dx_0}{dt}(t, T; 0). \end{aligned}$$

A solution of the first equation has the form  $x_0 = r(T) \cos(t + \theta(T))$  where  $r(T)$  and  $\theta(T)$  are found, after substitution into the equation for  $x_1$ , to satisfy

$$(31) \quad \begin{aligned} \frac{d\theta}{dT}(T) &= -\frac{\bar{k} \cos(\tau)}{2}, \\ \frac{dr}{dT}(T) &= -\frac{1}{2} r(T) \left( \frac{r^2(T)}{4} - 1 + \bar{k} \sin \tau \right). \end{aligned}$$

The solution for the amplitude  $r$  is given by  $r(T) = 2\sqrt{1 - \bar{k} \sin \tau}$ . In the absence of the feedback effect we recover  $2 \cos t$  to be the limit cycle of unforced van der Pol oscillator. As  $\bar{k}$  changes away from zero, and for small  $\epsilon$ , we obtain

$$x(t) = 2\sqrt{1 - \bar{k} \sin \tau} \cos\left(1 - \frac{\epsilon}{2} \bar{k} \cos \tau\right)t + O(\epsilon^2).$$

to be an attracting periodic solution of (2), provided that  $1 - \bar{k} \sin \tau > 0$ . This is consistent with the results obtained in [1] using the method of averaging. If the attracting solution exists, then it exists for all time delay and a change in  $\tau$  only affects the amplitude of the limit cycle.

If  $1 - \bar{k} \sin \tau < 0$  then limit cycle disappears and the zero solution is stable. Numerical example for this case are shown in figure 3.

**Insert FIG 3**

**4.2. Strong feedback, weak positive nonlinearity.** In this section weak nonlinearities will still be consider, i.e.,  $\epsilon \ll 1$ , but unlike [1], we change the feedback effect,  $k$ , to be of magnitude one. In particular we will consider  $k \in (-\infty, -1) \cup (1, \infty)$ .

As in section 4.1 we apply multiple scale analysis to derive  $\epsilon$ -order solutions of (2). For  $x$  of form (29) we obtain the leading and the  $\epsilon$ -order solutions

$$(32) \quad \begin{aligned} \frac{d^2 x_0}{dt^2}(t, T; 0) + x_0(t, T; 0) &= kx_0(t - \tau, T; 0), \\ \frac{d^2 x_1}{dt^2}(t, T; 0) + x_1(t, T; 0) &= -2 \frac{d^2 x_0}{dt dT}(t, T; 0) + kx_1(t - \tau, T; 0) + (1 - x_0^2) \frac{dx_0}{dt}(t, T; 0), \end{aligned}$$

to be delay differential equations. The characteristic equation for leading term  $x_0$  is given by

$$(33) \quad \lambda^2 + 1 = ke^{-\lambda\tau}.$$

In the absence of delay the origin is a saddle if  $k > 1$  and a center if  $k < 1$ . We vary  $\tau$  and look for solutions of (33) of the form  $\lambda = \alpha + i\nu$ , where  $\alpha$  and  $\nu$  are real. Substitute into (33), separate the real and the imaginary parts to obtain

$$(34) \quad \nu^2 - 1 = ke^{-\tau\alpha} \cos(\nu\tau), \quad 2\alpha\nu = -ke^{-\tau\alpha} \sin(\nu\tau).$$

We set  $\alpha = 0$  to obtain pure imaginary roots of (33) in the following cases

- i. If  $k < -1$ ,  $\lambda = \pm i\nu_1$ , for  $\tau = \tau_{c,1}(n)$ ,
- ii. If  $-1 < k < 1$ ,  $\lambda = \pm i\nu_1$ ,  $\lambda = \pm i\nu_2$ , for  $\tau = \tau_{c,1}(n)$ , and  $\tau = \tau_{c,2}$ ,
- iii. If  $k > 1$ ,  $\lambda = \pm i\nu_2$ , for  $\tau = \tau_{c,2}$ ,

where  $\nu_1 = \sqrt{1-k}$ ,  $\nu_2 = \sqrt{1+k}$ ,  $\tau_{c,1}(n) = \frac{(2n+1)\pi}{\sqrt{1-k}}$  and  $\tau_{c,2}(n) = \frac{2n\pi}{\sqrt{1+k}}$  for all integer  $n$ . The origin will change stability if  $\frac{dRe\lambda}{d\tau} < 0$  along any of the critical curves  $\tau_{c,1}(n)$  or  $\tau_{c,2}(n)$ . If we adapt (11) and (12) to this case we obtain

$$(35) \quad \begin{aligned} \operatorname{sgn}\left(\frac{dRe\lambda}{d\tau}\right) &= -\operatorname{sgn}(k) > 0 \text{ on } \tau_{c,1}(n), \\ \operatorname{sgn}\left(\frac{dRe\lambda}{d\tau}\right) &= \operatorname{sgn}(k) > 0 \text{ on } \tau_{c,2}(n), \end{aligned}$$

which shows that the origin stays unstable for all values  $k \in (-\infty, -1) \cup (1, \infty)$ , when the nonlinearity  $\epsilon = 0$ . We now look at the changes in the stability of the zero solution due to the nonlinearity  $\epsilon$ . If  $\epsilon$  is positive, we are in the case (2) of Lemma 2.2 which implies that the origin is unstable for all  $\tau \geq 0$  (see figure 4). If  $\epsilon$  is negative, the origin changes from stable to unstable when the delay parameter crosses the critical value  $\tau_{c,2}(0)$ . Figure 5 displays the numerical solutions of (2), together with phase diagrams, for strong negative feedback and different values of  $\tau$ . The increase in the delay has an effect in the amplitude of the limit cycle.

#### Insert FIG 4 and Fig 5

**4.3. Negative nonlinearity.** In this subsection, we present numerical solutions of (2) for different values of  $\tau$ , negative nonlinearity  $\epsilon$  and  $k < 1$ . In section 3 we studied the direction of Hopf bifurcation and the stability of periodic solutions. If we consider  $\epsilon = -1$  and  $k = 0.9$  we are in the case (3) of Lemma 2.1, i.e., the origin is stable in the absence of the delay and switches stability three times as the delay passes through critical values  $\tau_{c,2}(0) = 5.79$ ,  $\tau_{c,1}(0) = 11.26$ ,  $\tau_{c,2}(1) = 13.07$ ,  $\tau_{c,2}(2) = 20.35$ ,  $\tau_{c,1}(2) = 23.7$  and so on. Moreover since  $\operatorname{Re}(c_1(0)) > 0$  at  $\tau = \tau_{c,2}(0)$  we have that  $\mu_2 < 0$  and  $\beta_2 > 0$ . Thus, the Hopf bifurcation occurring at  $\tau_{c,2}(0)$  is subcritical and the bifurcating periodic solutions are unstable. On the other hand, since  $\operatorname{Re}(c_1(0)) < 0$  at  $\tau = \tau_{c,1}(0)$  we have that  $\mu_2 < 0$  and  $\beta_2 < 0$ .

Thus, the Hopf bifurcation occurring at  $\tau_{c,1}(0)$  is subcritical and the bifurcating periodic solutions are stable. These results are shown in Figure 6, (a)-(f).

**Insert FIG 6**

## 5. DISCUSSION

We have studied the effects of a linear delayed feedback on the dynamics of the van der Pol equation. Using the time delay as a bifurcation parameter, we have proven the existence of Hopf bifurcations. Moreover, we have derived the parameter space where the local stability of the zero solution switches stability as the delay increases. The direction and the stability of the periodic solutions bifurcating from zero were also proven. For different values of the non-linearity parameter  $\epsilon$  we have found stability and instability domains of the origin. We have shown, using multiple scale techniques, that with a small feedback gain the origin is either stable or there exists an attracting periodic solution. Special attention was given to the effects that a strong feedback has on the destabilization of the origin. In this situation the multiple scale techniques no longer apply. We have shown numerically that the origin becomes unstable, as the delay increases. The last section presents a numerical example of the appearance of a subcritical Hopf bifurcation and a change in stability of the solution for system (13) with nonnegative nonlinearity.

An appropriate choice of feedback, damping or time delay parameters for the van der Pol equation leads to rich dynamical behaviors. By presenting conditions in the parameter range that lead to creation of oscillations as well as their suppression, we help understand when such an equation is useful in biological and physical problems.

**Acknowledgements:** The research of P.W.N. and S.C. was supported in part by a Career Award at the Scientific Interface from the Burroughs Wellcome Fund.

## REFERENCES

- [1] F.M. Atay. Van der Pol's oscillator under delayed feedback. *J Sound and Vibration*, 218(2):333–339, 1998.
- [2] M. B. Bonsall. The impact of diseases and pathogens on insect population dynamics. *Physiol Entomol*, 29:223–236, 2004.
- [3] J. Cartwright, V. Eguiluz, E. Hernandez-Garcia, and O. Piro. Dynamics of elastic excitable media. *Internat J Bifur Chaos Appl Sci Engrg*, 17:2197–2202, 1999.
- [4] M.S. Ciupe, B. de Bivort, D.M. Bortz, and P.W. Nelson. Estimates of kinetic parameters from HIV patient data during primary infection through the eyes of three different models. Submitted.
- [5] K. Cooke and Z. Crossman. Discrete delay, distributed delay and stability switches. *J Math Anal Appl*, 86:592–627, 1982.
- [6] W.O. Criminale, T.L. Jackson, and P.W. Nelson. Lymit cycle-strange attractor competition. *Stud Appl Math*, 112:133–160, 2004.
- [7] R. FitzHugh. Impulses and physiological states in models of nerve membrane. *Biophysics J*, 1:445–466, 1961.
- [8] J.E. Forde and P.W. Nelson. Applications of Sturm sequences to bifurcation analysis of DDE models. *J Math Anal Appl*, 300(2):273–284, 2004.
- [9] D. B. Forger, M.E. Jewett, and R.E. Kronauer. A simpler model of the human circadian pacemaker. *J BioRhythms*, 14(6):532–537, 1999.
- [10] B.D. Hassard, N.D. Kazarinoff, and Y.H. Wan. *Theory and applications of Hopf bifurcation*. Cambridge Univ. Press, Cambridge, 1981.
- [11] Chao-Pao Ho and Y.L. Ou. The influence of time delay on local stability for predator-prey system. *Tunghai Sci*, 4:47–62, 2002.
- [12] H. Hu, E.H. Dowell, and L.N. Virgin. Resonance of a harmonically forced Duffing oscillator with time delay state feedback. *Nonlinear Dynam*, 15(4):311–327, 1998.

- [13] J. Kevorkian and J.D. Cole. *Multiple Scales and Singular Perturbation Methods*. Springer-Verlag, New York, 1996.
- [14] C. Koch and I. Segev. *Methods in Neuronal Modeling*. MIT Press, Cambridge, MA, 1998.
- [15] A.Y. Kolesov and N.K. Rozov. The buffer phenomenon in the van der Pol equation with delay. *Differ Equ*, 38:175–186, 2002.
- [16] Y. Kuang. *Delay differential equations and applications in Population Dynamics*. Academic Press, Boston, 1993.
- [17] X. Liao, K.W. Wong, and Z. Wu. Hopf bifurcation and stability of periodic solutions for van der Pol equation with distributed delay. *Nonlinear Dynam*, 26:23–44, 2001.
- [18] A. Maccari. The response of a parametrically excited van der Pol oscillator to a time delay state feedback. *Nonlinear Dynam*, 26:105–119, 2001.
- [19] P. W. Nelson, J. D. Murray, and A. S. Perelson. A model of HIV-1 pathogenesis that includes an intracellular delay. *Math Biosci*, 163:201–215, 2000.
- [20] D.V. Reddy, A. Sen, and G.L. Johnston. Dynamics of limit cycle oscillator under time delayed linear and nonlinear feedbacks. *Phys D*, 144:335–357, 2000.
- [21] S. Ruan. Absolute stability, conditional stability, and bifurcation in Kolmogorov-type predator-prey systems with discrete delays. *Quart Appl Math*, 59:159–173, 2001.
- [22] Y. Song and J. Wei. Local Hopf bifurcation and global periodic solutions in a delayed predator-prey system. *J Math Anal Appl*, 301(1):1–21, 2004.
- [23] B. van der Pol. A theory of the amplitude of free and forced triode vibrations. *Radio Review*, 1:701–710, 754–762, 1920.
- [24] F. Verhulst. *Nonlinear Differential Equations and Dynamical Systems*. Springer-Verlag, Berlin, 1990.
- [25] J. Wei and W. Jiang. Stability and bifurcation analysis in van der pol’s oscillator with delayed feedback. *J Sound Vibration*, 2004. in press.
- [26] J. Xu and K.W. Chung. Effects of time delayed position feedback on a van der Pol-Duffing oscillator. *Phys D*, 80:17–39, 2003.

## 6. FIGURE CAPTIONS

**Figure 1.** Regions in the  $(\epsilon, k)$ -plane where Hopf bifurcations occur: four bifurcation points in regions IV, two in regions II and on the dashed lines, and none in regions I and III .

**Figure 2.** Unstable regions for the zero solution in the  $(k, \tau)$ -space for (a)  $\epsilon = -0.5$ , (b)  $\epsilon = 0.5$ .

**Figure 3.** Solutions of equation (2) for weak feedback  $k = 0.1$ , weak nonlinearity  $\epsilon = 0.1$  and  $\tau = 1$  (dashed line),  $\tau = 5$  (dot line) and  $\tau = 10$  (solid line).

**Figure 4.** Solutions of equation (2) for  $\epsilon = 0.1$  and  $\tau = 1$  and (a)  $k = 3$ , (b)  $k = 5$  and (c)  $k = 9$ .

**Figure 5.** Simulations of the van der Pol equation (2) for  $k=-2$ ,  $\epsilon = 0.1$  and (a)  $\tau = 1$ , (b)  $\tau = 5$  and (c)  $\tau = 10$ .

**Figure 6.** Simulations of the van der Pol equation (2) for  $k=0.9$ ,  $\epsilon = -1$  and (a)-(c)  $\tau = 4.5 < \tau_{c,2}(0)$ ; (b)-(d)  $\tau_{c,2}(0) < \tau = 6.5 < \tau_{c,1}(0)$ , (e)-(f)  $\tau = 12 > \tau_{c,1}(0)$ . At  $\tau = \tau_c$  a Hopf bifurcation occur.

Figure 1

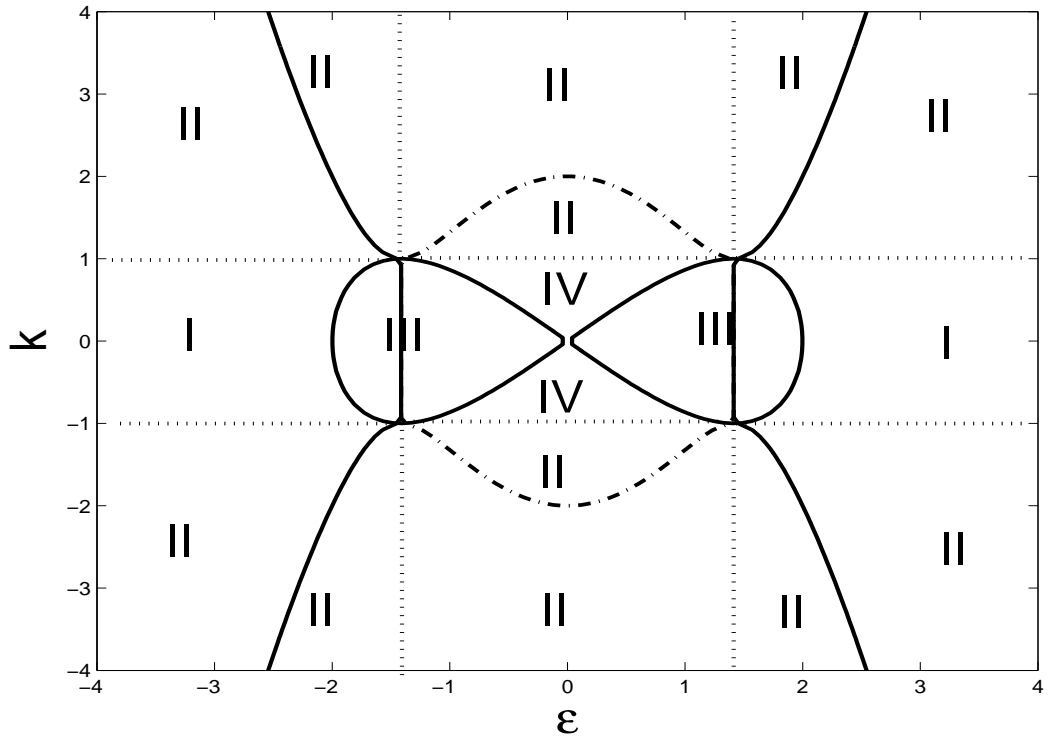


Figure 2

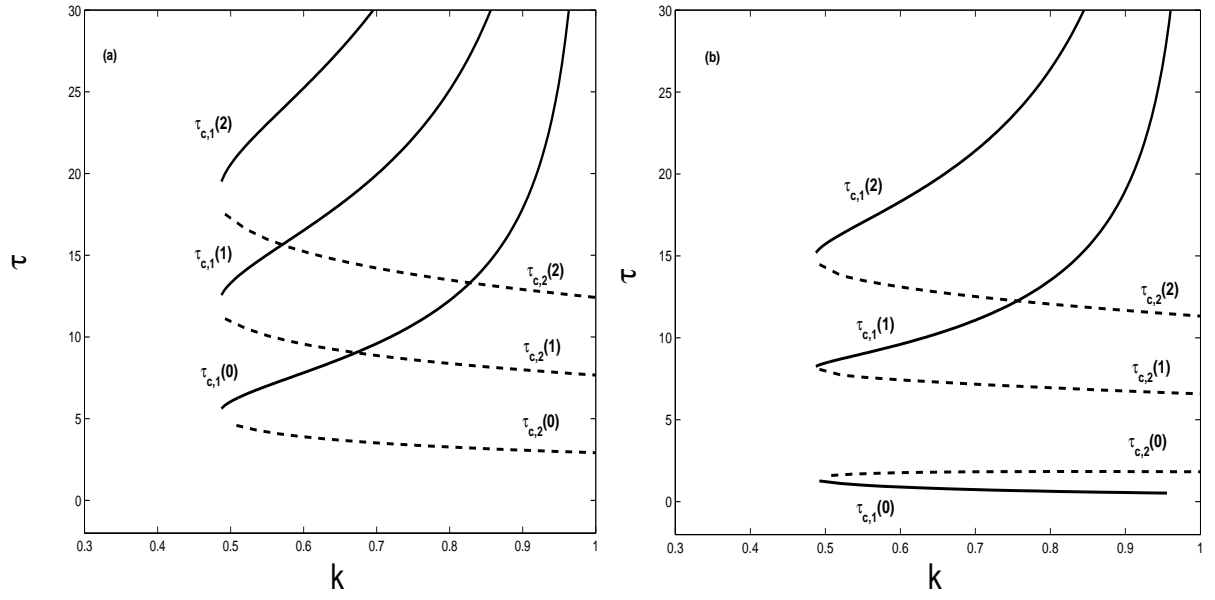
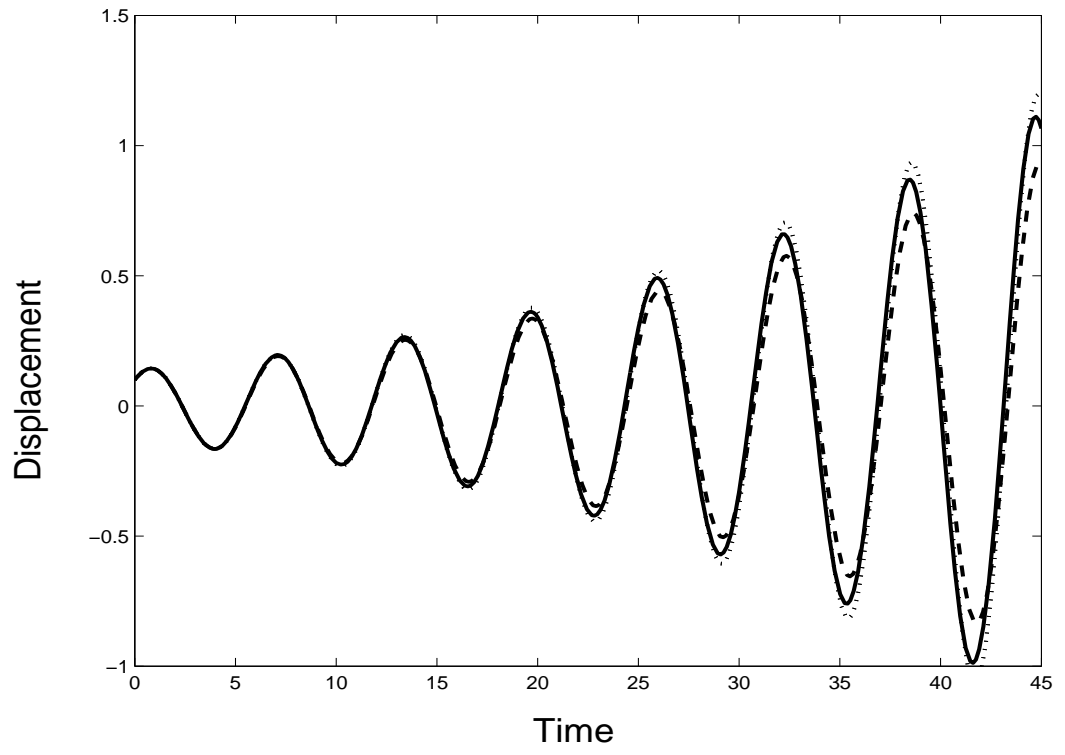


Figure 3



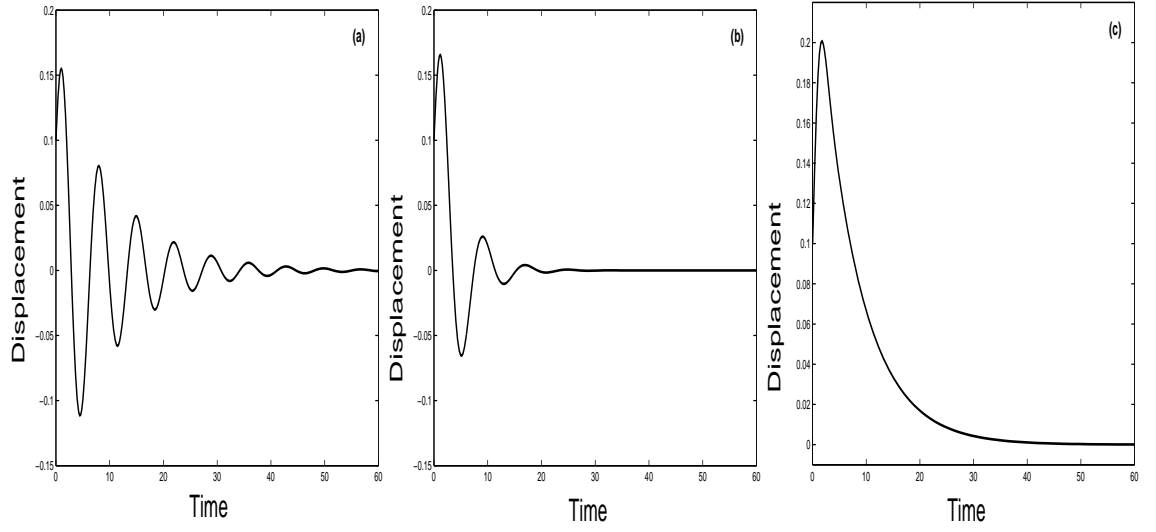
**Figure 4**

Figure 5

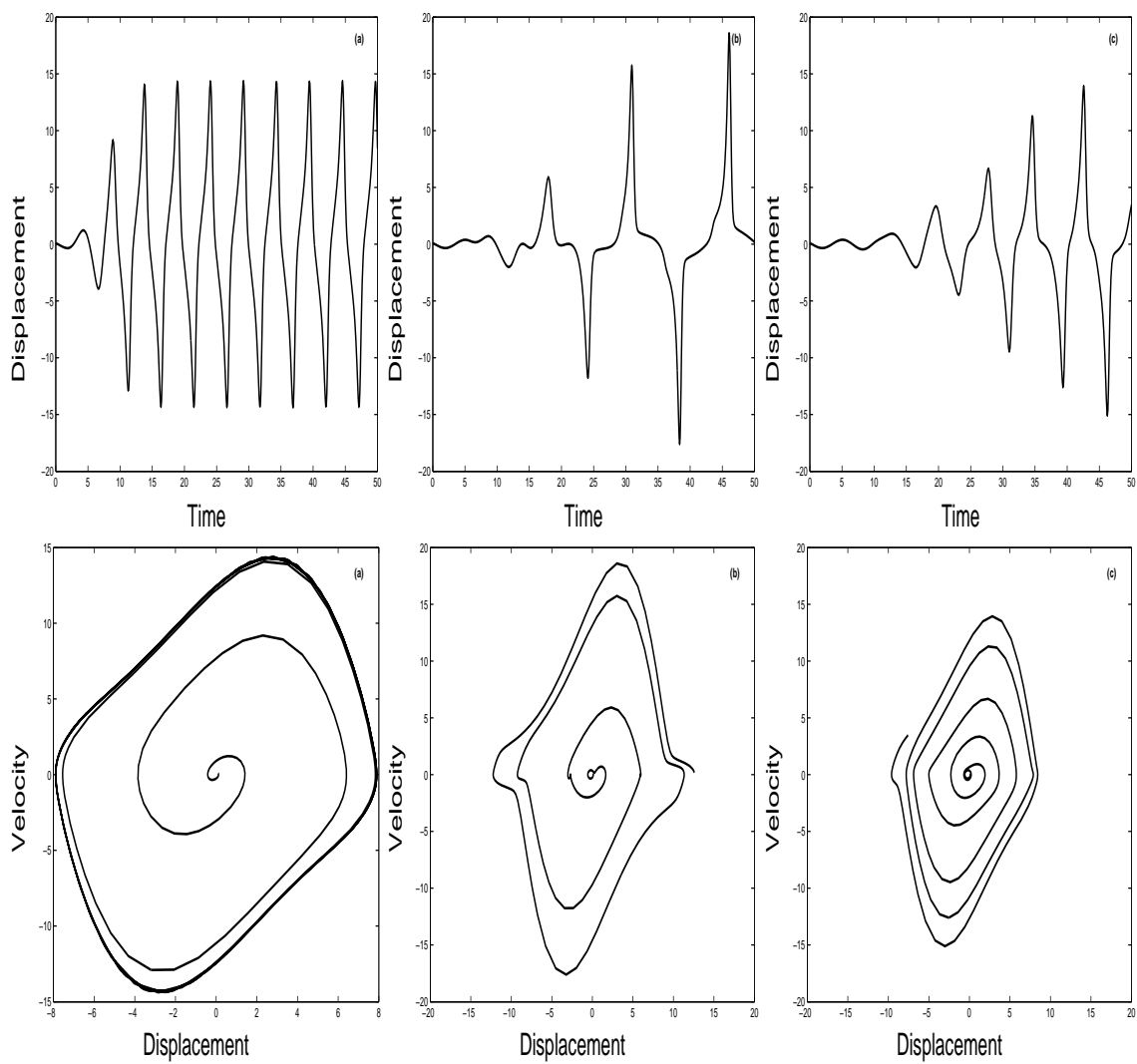


Figure 6

