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MUTUALLY SYNCHRONIZED RELAXATION OSCILLATIONS

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Mutually synchronized relaxation oscillations *)

by

J. Grasman & M.J.W. Jansen

ABSTRACT

This paper deals with a system of two second order differential equations coupled with delay containing two small parameters. In a decoupled state each equation has a periodic solution being a relaxation oscillation. With asymptotic methods it is shown that under certain conditions the coupled system has a periodic solution representing two mutually synchronized oscillations. Biological implications are discussed in relation with a paper of WINFREE [4]. Special attention is given to the phenomenon of pace-maker oscillations and to possible applications to large systems of coupled oscillators.

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*) This paper is not for review; it is meant for publication elsewhere.

1. INTRODUCTION

Most organisms have some mechanism that synchronizes their internal activities with cyclic changes outside, such as the rhythm of the day or the year. It has been conjectured that the observed periodicity of internal processes is completely controlled from the outside. However, even in complete isolation organisms will retain their internal periodicity with possibly a slightly different period. That is why the current viewpoint is that organisms possess some clockwork, consisting of an internal oscillator which can be regulated from the outside. Many types of cells likewise exhibit spontaneous periodic behaviour, synchronized with their environment. For examples of *biological clocks* the reader is referred to PAVLIDIS [3] and WINFREE [4].

In this paper we intend to investigate mathematically some aspects of this type of synchronization. Apart from synchronization with periodic outside stimuli, we will investigate the *mutual synchronization* of more or less identical oscillators.

The state of the organism will be described by an n-dimensional vector $x(t)$; its components are called the state variables. Let the change of the state variables be governed by a differential equation

$$\frac{dx}{dt} = g(x). \tag{1.1}$$

It is supposed that this equation has a periodic solution $p(t)$ with period T:

$$p(t+T) = p(t). \tag{1.2}$$

In the phase space this periodic solution is represented by a closed trajectory X. The influence of the external events will be described by a term $\delta s(t)$ in the differential equation:

$$\frac{dx}{dt} = g(x) + \delta s(t), \tag{1.3}$$

where the scalar δ is supposed to be small.

In physical applications the state variables x_i are usually well-defined and can be measured. In most cases the corresponding differential equations are known. This cannot be said of biological applications, where the investigations are done under quite different circumstances. Besides these difficulties, one may expect that a mathematical model of a relevant biological problem consists of a large number of highly nonlinear differential equations. The mathematical analysis of periodic solutions of such systems can be extremely complicated. Thus, there are mathematical as well as biological excuses to look for simplifications.

WINFREE [4] approached this problem as follows.
Without using the specific form of g(x) he derives an approximate expression for the behaviour of the forced oscillations of (1.3), and assumes that the oscillator (1.1) is orbitally very stable, so that independent of the forcing term the solution of (1.3) follows the orbit X of the autonomous oscillation (1.1). The solution of (1.3) is then approximated by

$$(1.4) \qquad x(t) = p(\phi(t)),$$

where for δ sufficiently small ϕ satisfies

$$(1.5) \qquad \frac{d\phi}{dt} = 1 + \delta z(\phi) \,.\, s(t).$$

Formula (1.4) implies that x(t) depends only on one variable the "phase" ϕ. The function $z(\phi)$ is called the "sensitivity function" of the oscillator; $z(\phi)$ has period T. When s(t) is periodic with a period T_s close to T, the phenomenon of *frequency entrainment* or *synchronization* may occur. The oscillator will then be forced to take over the rhythm of s(t). With the method described above Winfree derived some valuable results. He was able to find relations for the phase differences between synchronized oscillators and to derive conditions for the existence of synchronized solutions. These results agree with observations of physical and biological systems. For example, a set of oscillators can only synchronize completely if their autonomous periods are sufficiently close to each other. In the synchronized state the inherently faster oscillators (with smaller autonomous period) will be ahead in phase. In his paper Winfree gives many examples of biological oscillators exhibiting this behaviour.

It is our purpose to analyse synchronized oscillations by considering a specific system of differential equations of the type (1.1) and (1.3). We will derive equation (1.5) which was the starting point of Winfree's study. For an appropriate model of a biological system, the dimension of x has to be taken large and the function g(x) may become rather complicated. However, our main goal is to analyse the mechanism of synchronization. Therefore, we avoid complicated computations and select a simple oscillator for which mutual coupling leads to synchronized oscillations with neglectable disturbance of the orbit X. We are not concerned about the agreement of such oscillator with some specific biological system. Thus we work with a model-problem, not with a model. In our case the system

$$\frac{dx}{dt} = (-F(x)+z)/\varepsilon \qquad (1.6)$$

$$\frac{dz}{dt} = -x$$

is a prototype for autonomous oscillations of a biological system. For $F(x) = x^3/3 - x$ this system represents the well-known Van der Pol equation. Periodic solutions of this strongly nonlinear system are called *relaxation oscillations*. One important property of this oscillator is its high stability on the orbit. When there is small interaction between two or more of these oscillators, they preserve their orbit almost completely, but they are easily accelerated or slowed down on the orbit.

The method we apply to analyse the oscillations is based on the work of LIÉNARD [1] and gives a first order asymptotic approximation for $\varepsilon \to 0$, see section 2. When we consider coupled oscillators a second small parameter δ is introduced. The interactions are assumed to be of $O(\delta)$. Their influence on the solution is also found by asymptotic approximation. In section 3, the influence of one oscillator upon another is investigated. In section 4, two oscillators influence each other with a delay $\rho(\geq 0)$. In the sections 3 and 4 we deal with two classes of examples; one, the *piece-wise linear oscillator*, for which the influence of the interactions can be given in an analytical expression and the other, the *Van der Pol oscillator*, which is treated numerically. In section 5 the mechanism of *pace-maker oscillations* is investigated. Finally, in section 6 extensions to systems of more than 2 oscillators are discussed.

2. AUTONOMOUS OSCILLATIONS

Let us first investigate periodic solutions of the differential equation

$$\varepsilon \frac{d^2x}{dt^2} + f(x) \frac{dx}{dt} + x = 0, \qquad 0 < \varepsilon << 1, \tag{2.1}$$

where f(x) satisfies

$$f(x) = f(-x) \tag{2.2a}$$

$$f(x) > 0, \qquad |x| > a > 0 \tag{2.2b}$$

$$f(x) < 0, \qquad |x| < a. \tag{2.2c}$$

We will apply Liénard's method [1] to approximate the solutions of (2.1). By the introduction of

$$F(x) = \int_0^x f(s)ds,$$

and

$$z = \varepsilon \frac{dx}{dt} + F(x),$$

we obtain a system of the type (1.1)

$$\frac{dx}{dt} = (-F(x)+z)/\varepsilon, \tag{2.3a}$$

$$\frac{dz}{dt} = -x. \tag{2.3b}$$

In the phase plane (the x,z-plane) the trajectories satisfy

$$(F(x)-z) \frac{dz}{dx} = \varepsilon x. \tag{2.4}$$

For x bounded, the left-hand side of this equation will be $O(\varepsilon)$.

We will now consider the limit case where $\varepsilon \to 0$. In that case the trajectories tend to either $z = F(x)$ or to $z = c$ (constant). In this way one finds a closed trajectory X_0 along ABCD as sketched in figure 1. It is easily seen that after some disturbance the solution always returns to this trajectory, which, therefore, is an asymptotically stable *limit cycle*.

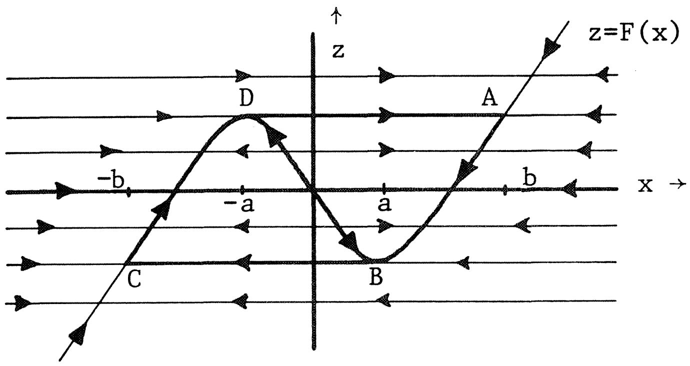

Fig.1 Phase plane of (2.3) for $\varepsilon \to 0$. The closed trajectory ABCD represents the periodic solution.

The intervals AB and CD are called the regular intervals, while BC and DA are the singular intervals of the limit cycle. On the regular intervals the periodic solution approximately satisfies

$$z = F(x)$$

$$\frac{dz}{dt} = -x.$$

From this one obtains

$$f(x) \frac{dx}{dt} = -x, \tag{2.5}$$

where, according to (2.2b) f(x) is positive.

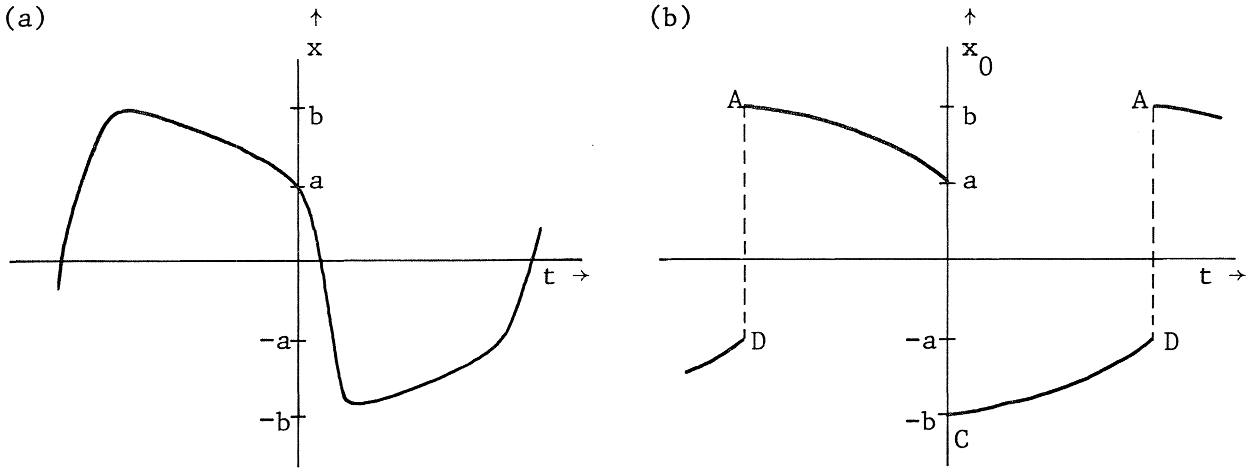

Fig.2 Periodic solution of (2.1) and its approximation.

In figure 2a the periodic solution of (2.1) with some $\varepsilon > 0$ is sketched. The corresponding closed trajectory X_ε lies near X_0 in the phase plane. For $\varepsilon \to 0$ X_ε tends to X_0. We distinguish two types of behaviour $x'(t) = O(1)$ on the regular intervals and $x'(t) = O(\varepsilon^{-1})$ on the singular intervals. In figure 2b a first order approximation of this periodic solution is constructed. On the regular interval AB the solution is approximated by $x = x_0(t)$ satisfying (2.3) with $\varepsilon = 0$ so

$$(2.6) \qquad t = -\int_a^{x_0} \frac{f(x)}{x}\,dx, \qquad t < 0.$$

On the singular intervals the solution is approximated by the trajectories BC and DA of figure 1, denoting jumps in x from $\pm a$ to $\mp b$. From (2.3b) we deduce that the period can be written as the integral

$$T = \oint_{\substack{\text{limit}\\\text{cycle}}} -\frac{dz}{x},$$

which is approximated by the contributions from the regular intervals.

$$(2.7) \qquad T_0 = 2 \int_a^b \frac{f(x)}{x}\, dx.$$

Let the difference between T and T_0 be denoted by $R(\varepsilon)$. It can be proved that $R(\varepsilon) \to 0$ as $\varepsilon \to 0$.
When in the sequel, we refer to the approximate solution of the autonomous problem (2.1) we mean the discontinuous periodic solution $x_0(t)$ with period T_0, defined by (2.6) for $-\frac{1}{2}T_0 < t < 0$ and by the relation $x_0(t) = - x_0(t-\frac{1}{2}T_0)$.

3. FORCED OSCILLATIONS

In a next step, we consider a system of two equations of the type (2.1) with coupling in one direction. It is assumed that the difference of the autonomous frequencies is of the same order as the coupling, which is supposed to be small;

$$(3.1a) \qquad \varepsilon \frac{d^2y}{dt^2} + f(y)\frac{dy}{dt} + y = (py+v)\delta,$$

$$(3.1b) \qquad \varepsilon \frac{d^2v}{dt^2} + f(v)\frac{dv}{dt} + v = 0,$$

where p is an arbitrary constant and δ satisfies

$$0 < \varepsilon << \delta << 1.$$

In the foregoing section we approximated the solution of (3.1b). Let us call this approximation $v_0(t)$. The autonomous equation corresponding to (3.1a):

$$\varepsilon \frac{d^2y}{dt^2} + f(y)\frac{dy}{dt} + y = p\delta y,$$

has, according to the theory of section 1, a periodic solution with period

$$T_y = T_0(1+p\delta) + O(\delta^2) + O(R(\varepsilon)).$$

We will demonstrate that because of the forcing term there exists a synchronized periodic solution of (3.1a) for p sufficiently small; it will have the same period as $v(t)$. To be more precise: We will construct synchronous asymptotic approximations for $y(t)$ and $v(t)$.

We start with writing (3.1) as a first order system if the type (2.3)

(3.2a) $$\varepsilon \frac{dy}{dt} = - F(y) + u,$$

(3.2b) $$\frac{du}{dt} = - y + \delta py + \delta v,$$

(3.2c) $$\varepsilon \frac{dv}{dt} = - F(v) + w,$$

(3.2d) $$\frac{dw}{dt} = - v,$$

and construct a first order approximation of this system with respect to ε. Elimination of t yields

(3.3a) $$(F(y)-u) \frac{du}{dy} = \varepsilon(y-\delta py-\delta v)$$

(3.3b) $$(F(v)-w) \frac{dw}{dv} = \varepsilon v.$$

As with (2.4) we see that for $\varepsilon \to 0$ the trajectories of the first equation tend to either $u = F(y)$ or to $u = c$ (constant) regardless of the order δ change of the equation. Therefore, as $\varepsilon \to 0$ y runs through the same limit cycle X_0 as in the unperturbed case, however its velocity is slightly different. From (3.2) it follows that on the regular interval $u = F(y)$ one has

(3.4) $$f(y_0) \frac{dy_0}{dt} = - y_0 + \delta py_0 + \delta v.$$

Consequently, for δ sufficiently small $\left(\frac{dy_0}{dt}\right)_{x=b} < 0$ and $\left(\frac{dy_0}{dt}\right)_{x=-b} > 0$

(see fig.3).

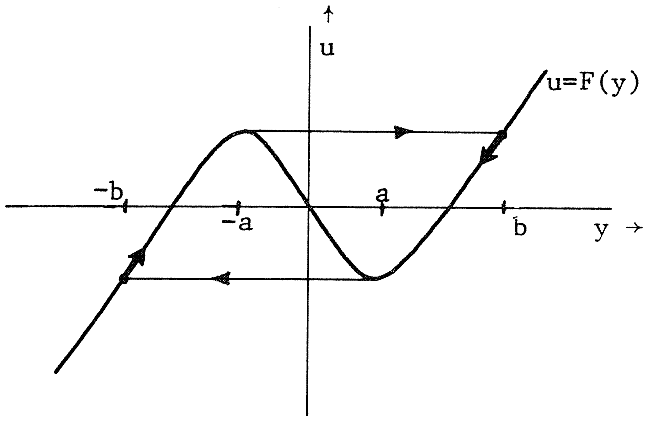

Fig.3 Phase plane of (3.2ab) for $\varepsilon \to 0$ and δ sufficiently small.

From this it follows that $y_0(t)$ can be written as

(3.5a) $$y_0(t) = x_0(\phi_y(t)),$$

for some time-dependent function $\phi_y(t)$, which is called the phase of $y_0(t)$. Substitution of (3.5a) into (3.4) yields, with the aid of (2.5) a differential equation for the phase of y,

(3.5b) $$\frac{d\phi_y}{dt} = 1 - \delta p - \delta \frac{v(t)}{y_0(t)} .$$

It is evident that the first order approximation with respect to ε of (3.1b) can be represented by

(3.6a) $$v_0(t) = x_0(\phi_v(t))$$

where ϕ_v satisfies

(3.6b) $$\frac{d\phi_v}{dt} = 1.$$

We take $\phi_y(0) = \alpha_y$, $\phi_v(0) = \alpha_v$ and denote the difference by $\beta = \alpha_y - \alpha_v$. For ϕ_v we obtain

(3.7) $$\phi_v(t) = \alpha_v + t.$$

After a period T_0 the v oscillation will return to its original state

$$(3.8) \qquad \phi_v(T_0) = \alpha_v (\text{mod } T_0).$$

A synchronized periodic solution occurs if the y oscillation will also return to its former state in the same time:

$$(3.9) \qquad \phi_y(T_0) = \alpha_y (\text{mod } T_0).$$

The solution of (3.5) will be approximated by iteration. The first approximation is

$$\phi_y^{(0)}(t) = \alpha_y + t.$$

A second iteration yields

$$(3.10) \qquad \phi_y^{(1)}(t) = \alpha_y + t - \delta pt - \delta \int_0^t \frac{x_0(\alpha_v+\tau)}{x_0(\alpha_y+\tau)} d\tau.$$

It can be shown that

$$(3.11) \qquad \phi_y^{(1)}(t) - \phi_y(t) = 0(\delta^2)$$

Applying condition (3.9) to the approximation (3.10) of $\phi_y(T_0)$ we obtain

$$(3.12) \qquad \alpha_y + T_0 - \delta p T_0 - \delta \int_0^{T_0} \frac{x_0(\alpha_v+\tau)}{x_0(\alpha_y+\tau)} d\tau = \alpha_y \ (\text{mod } T_0).$$

Since x_0 has period T_0, the integral in (3.12) depends only on $\beta = \alpha_y - \alpha_v$. Introducing the *asymptotic influence function*

$$(3.13) \qquad \Psi(\beta) = \frac{1}{T_0} \int_0^{T_0} \frac{x_0(\tau)}{x_0(\tau+\beta)} d\tau,$$

one can write the condition (3.12) as

(3.14) $\qquad \Psi(\beta) = -\, p.$

From this equation it can be seen that synchronization is possible only when $|p|$ is sufficiently small: the difference in natural frequencies should not be too large.

In order to study the *stability* of a synchronized solution with $\beta = \bar{\beta}$ satisfying $\Psi(\bar{\beta}) = -\, p$, we define the mapping g that assigns to a given phase difference β_0 at a time t_0 a phase difference β_1 at a time $t_0 + T_0$. This mapping is based on formula's (3.7) and (3.10) and has the form

(3.15a) $\qquad \beta_1 = g(\beta_0)$

with

(3.15b) $\qquad g(\beta) = \beta - p\delta T_0 - T_0\delta\Psi(\beta).$

This synchronized state is asymptotically stable if for β_0 in a certain neighbourhood of $\bar{\beta}$ we have $|\beta_1 - \bar{\beta}| \leq k|\beta_0 - \bar{\beta}|$ for $0 \leq k < 1$. If g is differentiable in $\bar{\beta}$ this amounts to $|g'(\bar{\beta})| < 1$. Since δ is small, this stability condition is equivalent to

(3.16) $\qquad \Psi'(\bar{\beta}) > 0.$

The asymptotic influence function has the following properties

(3.17ab) $\qquad \Psi(\beta + \tfrac{1}{2}T_0) = -\, \Psi(\beta), \qquad \Psi(0) = 1,$

(3.18a) $\qquad \lim\limits_{\beta \downarrow 0} \Psi'(\beta) = -\frac{2}{T_0}\left(1 + \frac{a}{b} - \log\frac{b}{a}\right),$

(3.18b) $\qquad \lim\limits_{\beta \uparrow 0} \Psi'(\beta) = \frac{2}{T_0}\left(1 + \frac{b}{a} + \log\frac{b}{a}\right);$

where a and b are given in figure 1.

EXAMPLE 1

The oscillator (2.1) with $f(x) = \operatorname{sign}(x^2-1)$ is called the *piecewise linear oscillator*. This oscillator has the nice property that the asymptotic approximation of its solution has a simple form. For $\varepsilon \to 0$ the solution tends to $x_0(t)$, with period $T_0 = 2 \log 3$:

$$x_0(t) = e^{-t} \qquad \text{for } -\frac{T_0}{2} < t < 0$$

$$x_0(t) = -3e^{-t} \qquad \text{for } 0 < t < \frac{T_0}{2} .$$

Consequently the asymptotic influence function can be easily calculated. Substitution of x_0 in (3.13) yields:

$$(3.19) \qquad \Psi(\beta) = \left(1+\frac{4\beta}{\log 3}\right) e^{\beta}, \qquad -\frac{T_0}{2} < \beta \leq 0,$$

which together with $\Psi(\beta+\frac{T_0}{2}) = -\Psi(\beta)$ defines Ψ.

Note that the amplitude of $\Psi(\beta)$ is 1. Thus a synchronized solution exists if $|p| \leq 1$.

For p on the interval $(-1,1)$ the equation $\Psi(\beta) = -p$ has two roots in $\left(-\frac{T_0}{2}, \frac{T_0}{2}\right)$. The root β_s on $(-\frac{T_0}{2},0)$ corresponds to a stable synchronized solution, the root β_u in $(0,\frac{T_0}{2})$ corresponds to an unstable synchronized solution.

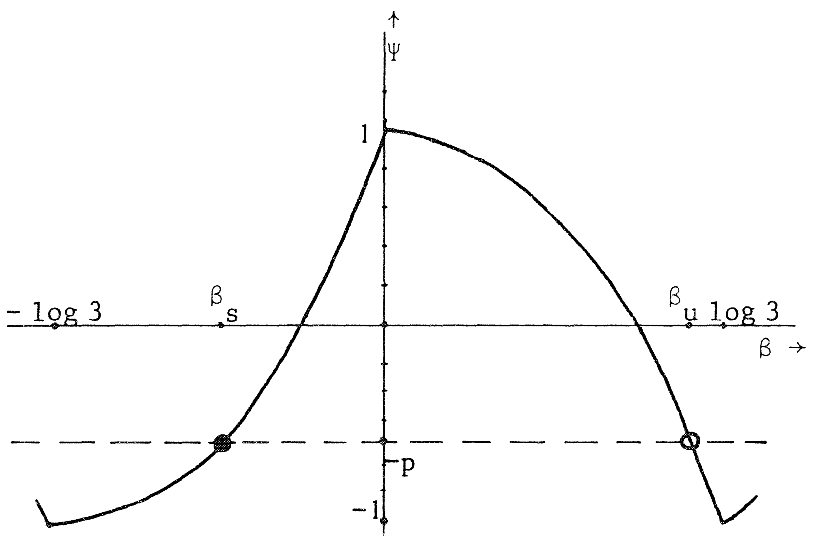

Fig.4 Asymptotic influence function $\Psi(\beta)$ for the piece-wise linear oscillator.

In this section synchronous asymptotic solutions of (3.2) were found. In order to compare these solutions with numerical solutions, we define a phase Φ for (3.2ab) or (3.2cd) in a neighbourhood of the limit cycle X_ε of (2.3). On the limit cycle X_ε a phase Φ is defined by

(3.20) $$\Phi(x(t),z(t)) = t \pmod T.$$

When $0 < \delta << 1$ the point $(y(t),u(t))$ of (3.2) will stay in a neighbourhood Ω of the limit cycle X_ε. We will extend Φ to the ring-shaped domain Ω. Let $(y,u) \in \Omega$. The form of X_ε is such that there exists a unique point $(y',u') = (\lambda y,\lambda u)$, $\lambda > 0$ with $(y',u') \in X_\varepsilon$. For $(y,u) \in \Omega$ we define

$$\Phi(y,u) = \Phi(y',u').$$

The initial values for (3.2) are taken on X_ε,

$$y(0) = x(\alpha_y), \qquad u(0) = z(\alpha_y),$$

$$v(0) = x(\alpha_v), \qquad w(0) = z(\alpha_v),$$

so $\Phi(y(0), u(0)) = \alpha_y$, $\Phi(v(0),w(0)) = \alpha_v$.
We will denote the phase difference by $\beta(t)$;

(3.21) $$\beta(t) = \Phi(y(t),u(t)) - \Phi(v(t),w(t)).$$

Let a function S be defined by

$$S(\alpha_y,\alpha_v) = -\frac{\beta(T) - \beta(0)}{\delta T}.$$

For $\varepsilon \to 0$ we have

$$(y(t),u(t)) \to (x_0(\phi_y(t)),z_0(\phi_y(t))),$$

$$(v(t),w(t)) \to (x_0(\phi_v(t)),z_0(\phi_v(t))),$$

and because of the continuity of Φ near X_ε,

$$\Phi(y(t),u(t)) \to \phi_y(t),$$

$$\Phi(v(t),w(t)) \to \phi_v(t).$$

Using (3.5), (3.6) and (3.7) we find the following limit behaviour for S

$$\lim_{\varepsilon \to 0} S(\alpha_y,\alpha_v) = \Psi(\alpha_y - \alpha_v) + O(\delta),$$

where Ψ satisfies (3.13).

Note that in the first order asymptotic approximation in δ of S only the phase difference $\alpha_y - \alpha_v$ occurs.

EXAMPLE 2

For coupled oscillators (3.1) with $f(x) = x^2 - 1$ (Van der Pol oscillators), the function $S(\beta,0)$ has been approximated numerically for $\varepsilon = \frac{1}{400}$ and $\delta = \frac{1}{20}$. The autonomous period is $T = 1.72$ for this value of ε. Note that $T_0 = 3 - 2\log 2 = 1.61$. For the numerical integration of (3.2) the procedure Multistep of the library NUMAL [2] was used. In figure 5, $S(\beta,0)$ is compared with $\Psi(\beta)$.It is noted that the two functions indeed agree up to $O(\delta)$ and that a maximum influence is obtained when the two oscillators are in the same phase. Obviously, it is advantageous to start with oscillator (3.1a) slightly ahead, so that during the following period when this oscillator slows down the point is passed where the oscillators have equal phases. This adjustment is found in $S(\beta,0)$, where the maximum value is obtained for $\beta_m > 0$.

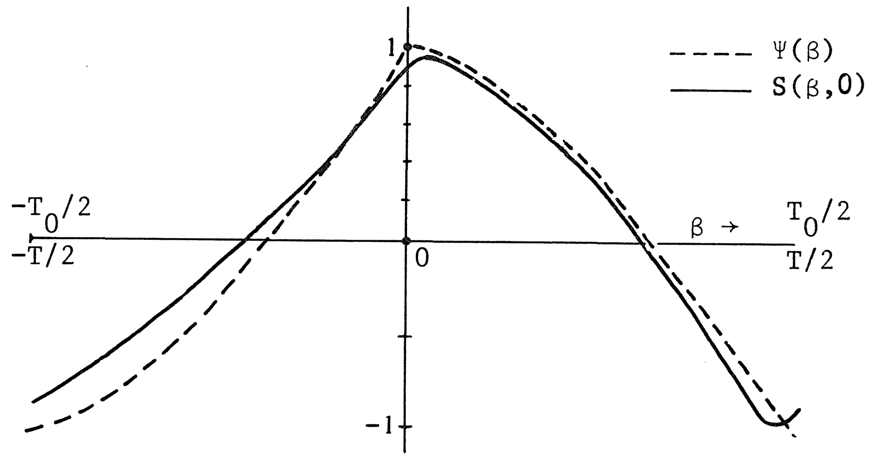

Fig.5 Comparison of the asymptotic influence function $\Psi(\beta)$ with a numerical approximation of $S(\beta,0)$ for the Van der Pol oscillator.

4. MUTUAL SYNCHRONIZATION OF TWO OSCILLATORS COUPLED WITH DELAY

In this section we consider a system of two equations of the type (2.1) coupled with delay $\rho \geq 0$:

$$\varepsilon \frac{d^2y}{dt^2} + f(y) \frac{dy}{dt} + y = \delta\{py(t) + v(t-\rho)\}, \tag{4.1a}$$

$$\frac{d^2v}{dt^2} + f(v) \frac{dv}{dt} + v = \delta\, q\, y(t-\rho), \tag{4.1b}$$

where $0 < \varepsilon << \delta << 1$, $q > 0$ and p arbitrary. In order to analyse the *mutual influence* of y and v we apply the same method as in section 3. For ε tending to zero and δ sufficiently small the solutions tend to $y_0(t)$ and $v_0(t)$:

$$(4.2a)\qquad y_0(t) = x_0(\phi_y(t)),$$

$$(4.2b)\qquad v_0(t) = x_0(\phi_v(t)),$$

where ϕ_y and ϕ_v satisfy

$$(4.2c)\qquad \frac{d\phi_y}{dt} = 1 - \delta p - \delta \frac{v_0(t-\rho)}{y_0(t)} ,$$

$$(4.2d)\qquad \frac{d\phi_v}{dt} = 1 - \delta q \frac{y_0(t-\rho)}{v_0(t)} .$$

Let

$$(4.3)\qquad \phi_y(0) = \alpha_y, \qquad \phi_v(0) = \alpha_v, \qquad \beta = \alpha_y - \alpha_v.$$

Synchronization will occur if a T^* exists such that

$$(4.4a)\qquad \phi_y(T^*) = \alpha_y (\mathrm{mod}\ T_0),$$

$$(4.4b)\qquad \phi_v(T^*) = \alpha_v (\mathrm{mod}\ T_0).$$

We write for T^*

$$(4.5)\qquad T^* = T_0(1+\gamma\delta)$$

and solve (4.2) by iteration. The first approximation is

$$(4.6a)\qquad \phi_y^{(0)}(t) = \alpha_y + t$$

$$(4.6b)\qquad \phi_v^{(0)}(t) = \alpha_v + t.$$

Iteration yields

$$(4.7a)\qquad \phi_y^{(1)}(t) = \alpha_y + t - \delta pt - \delta \int_0^t \frac{x_0(\alpha_v+\tau-\rho)}{x_0(\alpha_y+\tau)}\, d\tau$$

(4.7b) $$\phi_v^{(1)}(t) = \alpha_v + t - \delta q \int_0^t \frac{x_0(\alpha_y+\tau-\rho)}{x_0(\alpha_v+\tau)}\, d\tau$$

It can be shown that

(4.8a) $$\phi_y^{(1)}(t) - \phi_y(t) = 0(\delta^2)$$

(4.8b) $$\phi_v^{(1)}(t) - \phi_v(t) = 0(\delta^2)$$

Applying the conditions (4.4) to the approximation (4.7) we obtain

(4.9) $$T^* = T_0 + \delta q T_0 \Psi(-\beta+\rho)$$

(4.10) $$-\chi^{(\rho)}(\beta,q) = p$$

where Ψ is given by (3.11) and $\chi^{(\rho)}$ satisfies

(4.11) $$\chi^{(\rho)}(\beta,q) = \Psi(\beta+\rho) - q\ \Psi(-\beta+\rho).$$

In order to study the stability of a synchronized solution with $\beta = \overline{\beta}$ satisfying (4.10) we define the mapping that assigns to a given phase difference β_0 at time t_0 a phase difference β_1 at time $t_0 + T^*$. This mapping is based on (4.7) and has the form

(4.12a) $$\beta_1 = h(\beta_0)$$

(4.12b) $$\text{with } h(\beta) = \beta - p\delta T_0 + \chi^{(\rho)}(\beta,q)\ T_0\delta$$

This synchronized state is asymptotically stable if for β_0 in a certain neighbourhood of $\overline{\beta}$

$$|\beta_1-\overline{\beta}| \le k|\beta_0-\overline{\beta}|$$

for $0 \le k < 1$. If h is differentiable in $\overline{\beta}$ we must have $|h'(\overline{\beta})| < 1$.

Since δ is small this condition is equivalent to

$$\frac{\partial}{\partial\beta}\chi^{(\rho)}(\beta;q)\Big|_{\beta=\beta_0} > 0. \tag{4.13}$$

The function $\chi^{(\rho)}(\beta,q)$ has the following symmetry property

$$\chi^{(\rho)}(\beta+\tfrac{1}{2}T_0;q) = -\chi^{(\rho)}(\beta,q). \tag{4.14}$$

According to (3.18) one has for $q = 1$ and $0 < \rho, |\beta| \ll 1$,

$$\chi^{(\rho)}(\beta;1) \approx c\beta - d\rho \qquad \beta > \rho \tag{4.15a}$$

$$\chi^{(\rho)}(\beta;1) \approx -2e\beta \qquad |\beta| < \rho \tag{4.15b}$$

$$\chi^{(\rho)}(\beta;1) \approx c\beta + d\rho \qquad \beta < -\rho \tag{4.15c}$$

with

$$c = \frac{2}{T_0}\left(\frac{b}{a} - \frac{a}{b} + 2\log\frac{b}{a}\right), \qquad d = \frac{2}{T_0}\left(2 + \frac{a}{b} + \frac{b}{a}\right)$$

and

$$e = \frac{2}{T_0}\left(1 + \frac{a}{b} - \log\frac{b}{a}\right).$$

In the figures 6a and 6b we give the behaviour of $\chi^{(\rho)}(\beta;1)$ near $\beta = 0$ for $\rho = 0$ and $\rho > 0$. We see that for $p = 0$, $q = 1$ and $0 < \rho, |\beta| \ll 1$ two stable synchronized solutions exist with phase differences $\beta_s \approx \pm (d/c)\rho$. In figure 6c the phase differences for stable synchronized solutions are given as a function of ρ; ρ can be considered as a bifurcation parameter.

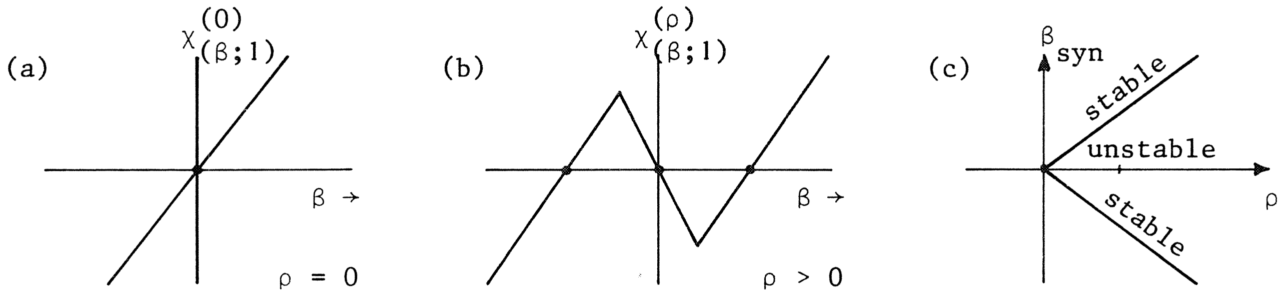

Fig.6 Behaviour of $\chi^{(\rho)}(\beta;1)$ for different values of ρ naar $\beta = 0$ and the stability of the synchronized solution for $p = 0$.

EXAMPLE 3

For the system (4.1) with f(z) sign (z^2-1) and $\rho = 0.1 \log 3$ (piece-wise linear oscillator with delay $\rho = .005\ T_0$) the asymptotic mutual influence function $\chi^{(\rho)}(\beta;1)$ is given in figure 7. Note that for $p = 0$, $q = 1$ and ρ sufficiently small and positive three stable synchronized states are possible: S_+, S_- and C.

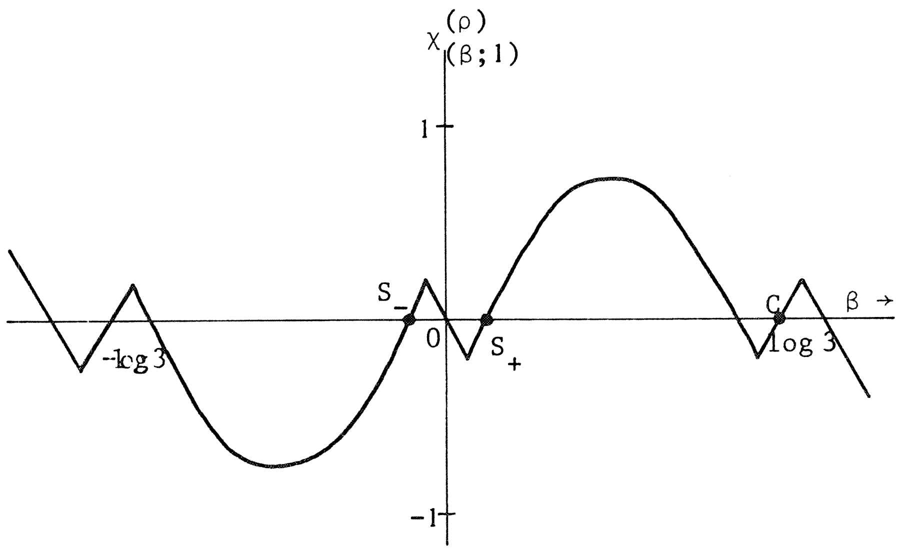

Fig.7 The function $\chi^{(\rho)}(\beta;1)$ for the piece-wise linear oscillator with $\rho > 0$.

Let us consider the system (4.1) with $q = 1$ in the vector form

$$(4.16a) \qquad \varepsilon \frac{dy}{dt} = -F(y) + u,$$

$$(4.16b) \qquad \frac{du}{dt} = -y + \delta py + \delta v(t-\rho),$$

$$(4.16c) \qquad \varepsilon \frac{dv}{dt} = -F(v) + w,$$

$$(4.16d) \qquad \frac{dw}{dt} = -v + \delta y(t-\rho),$$

satisfying the initial conditions

$$(4.17ab) \qquad y(\tau) = x(\alpha_y+\tau), \qquad v(\tau) = x(\alpha_v+\tau),$$

$$(4.17cd) \qquad u(\tau) = z(\alpha_y+\tau), \qquad w(\tau) = z(\alpha_v+\tau),$$

where $(x(\alpha),z(\alpha)) \in X_\varepsilon$ and $\tau \in (-\rho,0]$. Similar to (3.21), the phase difference between $(y(t),u(t))$ and $(v(t),w(t))$ is denoted by

$$\beta(t) = \Phi(y(t),u(t)) - \Phi(v(t),w(t)),$$

if these points are sufficiently close to X_ε. Further, we define the function

$$(4.18) \qquad M(\alpha_y,\alpha_v) = -\frac{\beta(T)-\beta(0)}{\delta T}.$$

Using (4.7), (4.8) and (4.11), we find that

$$(4.19) \qquad \lim_{\varepsilon\to 0} M(\alpha_y,\alpha_v) = \chi^{(\rho)}(\alpha_y-\alpha_v) + O(\delta).$$

EXAMPLE 4

The function $M(\beta,0)$ has been approximated by numerical integration of (4.16), (4.17) with $f(x) = x^2 - 1$, $\varepsilon = \frac{1}{400}$ and $\delta = \frac{1}{20}$. As in example 2 the integration was carried out with the procedure Multistep. Because of the delay ρ a memory was used. It is noticed that near $\beta = 0$, the behaviour of

$M(\beta,0)$ for $\rho = 0$ differs qualitatively from $\chi^{(0)}(\beta;1)$, see figure 6a. The fact that according to formula (4.11) the function $\chi^{(0)}(\beta;1)$ is not differentiable in $\beta = 0$ may be responsible for this discrepancy between the numerical result for some $\varepsilon > 0$ and the asymptotic result for $\varepsilon = 0$. It is emphasized that the difference lies within the accuracy claimed in formula (4.9).

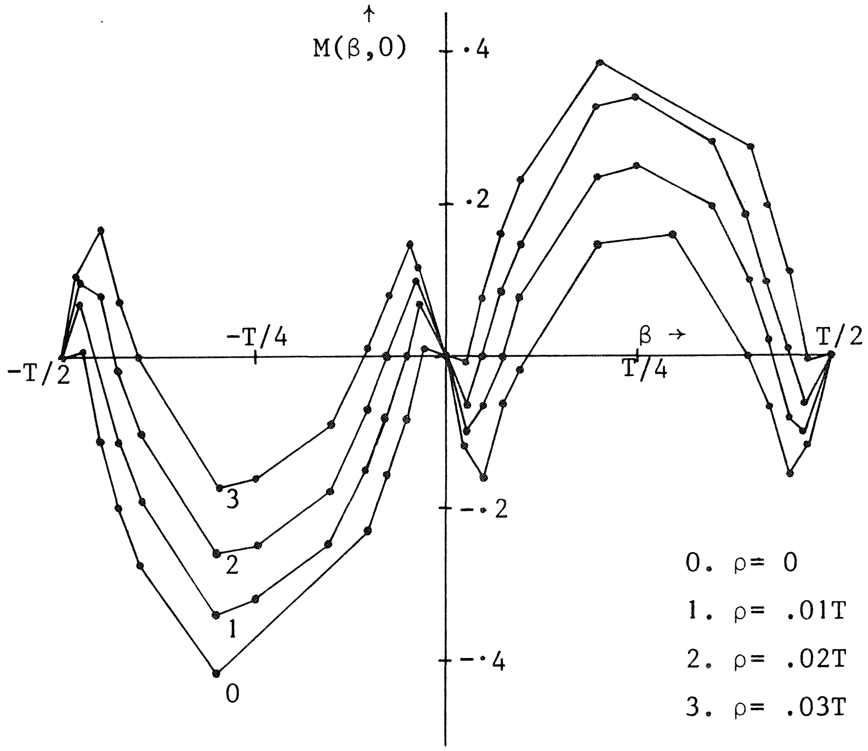

Fig.8 The function $M(\beta,0)$ for two Van der Pol oscillators coupled with delay ρ.

5. THE PACE-MAKER

In a population of biological oscillators there usually exists an oscillator or a set of oscillators which directs the rhythm of the population. It is observed that such oscillators, called *pace-makers*, are ahead in phase. Usually their autonomous frequency is higher. Also the coupling itself can be the source of the pace-maker oscillations. In that case, the pace-maker oscillator forces the other oscillators stronger than it is forced. Let us illustrate the above behaviour by considering two coupled identical piece-wise-linear oscillators ($p=0, q=1, \rho\geq 0$). By a small disturbance of the parameters p and/or q, we want one of the two oscillators to turn into a pace-maker. In the figures 9a and 9b we sketch two possibilities. In figure 9a $p > 0$, so that $y(t)$ is inherently faster and in figure 9b $q < 1$, so that $y(t)$ forces $x(t)$ stronger. In both cases the oscillator $y(t)$ will run ahead with phase difference $\bar{\beta}$.

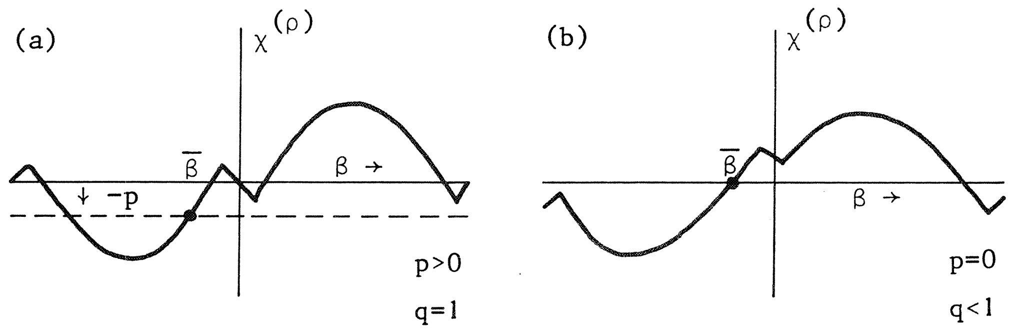

Fig.9 Two possibilities of coupled, almost identical oscillators with one stable synchronized state.

In most studies, the pace-maker is seen as an inherently faster oscillator. For example, ZHABOTINSKY and ZAIKIN [5] consider a spatially distributed system of chemical oscillators in which spontaneously oscillators start to function as pace-makers. Considering the phase of an oscillator as a function of time and position, one observes, after some time, waves with circular wavefronts travelling away from the pace-makers (the wave-centers). Indeed in most cases these wave-centers have a higher autonomous frequency. According to our above model of a pace-maker the wave phenomenon can also be found in a perfectly mixed chemical system. Initially, the phases of the oscillators are distributed randomly. In a large population of oscillators one always finds a small group of oscillators running for some time in about the same phase. Together they are strong enough to force their direct neighbours and as the synchronization proceeds, a wave arises with the small group of oscillators as wave-center. We conclude from this that wave-centers may arise spontaneously and that in nonhomogeneous media it is more likely that they occur at points where the oscillators have a higher autonomous frequency. However, the higher autonomous frequency is not the driving mechanism. If it were, one should also expect circular waves travelling towards a center with a lower autonomous frequency. This has not been observed so far.

6. LARGE SYSTEMS OF OSCILLATORS

Without meeting any essential difficulties one may extend the method of section 4 to systems of three or more oscillators coupled with delay. For n oscillators there are n-1 phase differences. The synchronization condition gives n-1 nonlinear algebraic equations for the phase differences. It might be difficult to find all solutions of these equations, but sometimes particular solutions can be obtained by trial and error. In this way one may investigate the behaviour of oscillators arranged in various geometries, e.g. a system of oscillators on a ring. Also the question of stability of synchronized solutions can be answered. If the n-1 equations do not have a solution, there still exists the possibility of *partial synchronization*. In that case subsets of oscillators take a common rhythm, while others with fairly different autonomous frequencies persist in their own rhythm. WINFREE [4] gives a descriptive analysis of partial synchronization. We believe that a systematic study of this problem will lead to substantial difficulties. On the other hand, it is very well possible to simulate the synchronization process for any system of oscillators of the type

$$(6.1) \qquad \varepsilon \frac{d^2x_i}{dt^2} + f(x_i)\frac{dx_i}{dt} + (1-p_i\delta)x_i = \delta \sum_{\substack{k=1\\k\neq i}}^{n} a_{ik}x_k(t-\rho_{ik}), \qquad i = 1,2,\ldots n,$$

with $\rho_{ik} \geq 0$ and with $f(x)$ satisfying (2.2). Let $\alpha_i^{(j)}$, $i = 1,2,\ldots,n$ be the phases of the n oscillators at time $t = jT_0$ with T_0 given by (2.7), then using (4.7) we will have

$$(6.2) \qquad \alpha_i^{(j+1)} = \alpha_i^{(j)} - \delta\left\{p_i + \sum_{\substack{k=1\\k\neq i}}^{n} a_{ik}\Psi(\alpha_i^{(j)}-\alpha_k^{(j)}+\rho_{ik})\right\}T_0 \qquad i = 1,2,\ldots,n,$$

where $\Psi(\beta)$ is given by (3.13).

Formula (6.2) opens the possibility of computer simulations for large systems of oscillators with different structures in coupling a_{ik} and delay ρ_{ik}.

The process of synchronization can then be followed over a large number of periods.

7. CONCLUDING REMARKS

Comparing our computations with those of WINFREE [4], we observe that quantities, defined in Winfree's paper, such as stimulus function and sensitivity function, easily can be traced in this study. But, whereas Winfree works with hypothetical oscillators, we obtain equivalent results by applying asymptotic methods to a specific system of differential equations.

In this paper we investigated *coupled, highly nonlinear oscillations* governed by a specific system of differential equations with the objective to verify whether or not such a system has the properties which are usually assigned to hypothetical oscillators. Using Liénard's method we were able to find approximations for such oscillations. Most of the results of this paper confirm our ideas about synchronized oscillations. For example, synchronization only occurs when the autonomous frequencies are sufficiently close. Moreover, it is observed that in the synchronized state the inherently faster oscillators will be ahead in phase.

On the other hand, this study has called the attention to some other interesting properties of interacting highly nonlinear oscillations. It is noted from figure 7 that for two identical oscillators coupled with small delay three stable synchronized states exist. In two of these cases one of the two oscillators is slightly ahead in phase; in the third case the two oscillators are exactly in complementary phases. From (4.9) we learn that in the synchronized state the period of the system is not necessarily some average of the autonomous periods of the oscillators. It may happen that in the synchronized state all oscillators slow down or speed up. Moreover, in section 5 it is emphasized that a pace-maker is not necessarily an oscillator with a higher autonomous frequency. Finally, in section 6 we indicated how our method can be applied to large systems of oscillators. The results of such a study will be given in a subsequent paper.

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