

## Mutually Synchronized Relaxation Oscillators as Prototypes of Oscillating Systems in Biology

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**Summary.** This paper discusses the analogy between phenomena in populations of coupled biological oscillators and the behaviour of systems of synchronized mathematical oscillators. Frequency entrainment in a set of coupled relaxation oscillators is investigated with perturbation methods. This analysis leads to quantitative results for entrainment and explains phenomena such as travelling waves in systems of spatially distributed oscillators.

**Key words:** Frequency entrainment — Asymptotic methods — Van der Pol equation.

### 1. Introduction

Spontaneous periodicity and the phenomenon of synchronization play a role in the temporal organization of life.

Most organisms have some mechanism that synchronizes and adapts internal activities to cyclic changes outside, such as the rhythm of the day or the year. This type of synchronization is called *external synchronization* (see [1], [4] and [30]).

Many types of cells likewise exhibit spontaneous periodic behaviour. In groups of such cells *mutual synchronization* may occur [40]. We mention the following examples: The cells of cardiac pacemakers fire simultaneously [27]. It has been conjectured that the alpha-rhythm of the human brain is caused by interacting oscillators [39]. Under certain circumstances the cells of the heart, the gastrointestinal tract, and the ureter exhibit spontaneous periodicity and synchronization such that waves of activity occur ([3], [22] and [23]). For developing systems models have been proposed in which cells receive positional information from two waves propagating at different velocities [5], [12]. In biochemistry there is a growing interest in periodic reactions, which are often accompanied by wave phenomena ([41], [28], [10], [2] and [8, Ch. VI]).

In this paper we intend to investigate mathematically the phenomenon of synchronization for a particular type of biological oscillations. We shall mainly investigate the mutual synchronization of more or less identical oscillators. We

shall assume that the oscillations and their coupling can be described deterministically with a first order vector differential equation. Attempts to formulate such a model will in general lead to great difficulties. It is often unknown which quantities play a role in the oscillatory process. Moreover it is seldomly possible to follow the quantities that might be of interest for sufficiently long, uninterrupted periods [30]. One thing however, seems to be clear: in most instances an adequate model will consist of a large number of nonlinear differential equations [7]. A general mathematical theory providing a detailed description of the behaviour of the solutions, does not exist for such equations. Consequently, there are biological as well as mathematical reasons to look for simplifications.

A simplification which is implicitly or explicitly present in many studies on periodic processes in biology is the assumption that the state of an oscillator may be approximately characterized by one real variable, which is called, depending on the context, the *phase*, *circadian time* or *subjective time*. The state of the oscillator is periodic with respect to its phase. This means that the state of an oscillator may be represented by a point on a *circle*. Consequently the state of a system of  $n$  oscillators can be represented by a point on an  $n$ -dimensional *torus* (the cartesian product of  $n$  circles). A second simplification which is often encountered in the literature is the assumption that the oscillators are *weakly coupled*. The above assumptions have been made by Winfree [40] in a study on hypothetical oscillators.

It is our purpose to analyse synchronization phenomena for a rather specific class of coupled differential equations. We shall derive the differential equations for the phases, which formed the starting point of Winfree's study. For the description of the isolated oscillators we shall select the simplest possible equations that possess highly stable periodic solutions (the stability is necessary in connection with the first simplifying assumption). Our choice will permit a detailed analysis of interacting systems of such oscillators.

This policy is frequently adopted in applied mathematics. By studying a simple *prototype problem* or *model problem* one hopes to get an impression of the qualitative behaviour of the solutions of a larger class of problems. From the analysis of a prototype problem new concepts may arise that can be helpful in the interpretation of experimental results. One gets an indication about the kind of phenomena that might be explained by certain simple assumptions. Moreover, one may hope that the analytic tools, used to solve a prototype problem, can be adapted to attack more general problems.

For the description of one oscillator only non-linear equations should be taken in consideration, since only these equations can have stable periodic solutions [7]. Moreover, an equation can only possess periodic solutions if there are at least two state variables. Our particular choice will be an oscillator that is described by a differential equation of the form

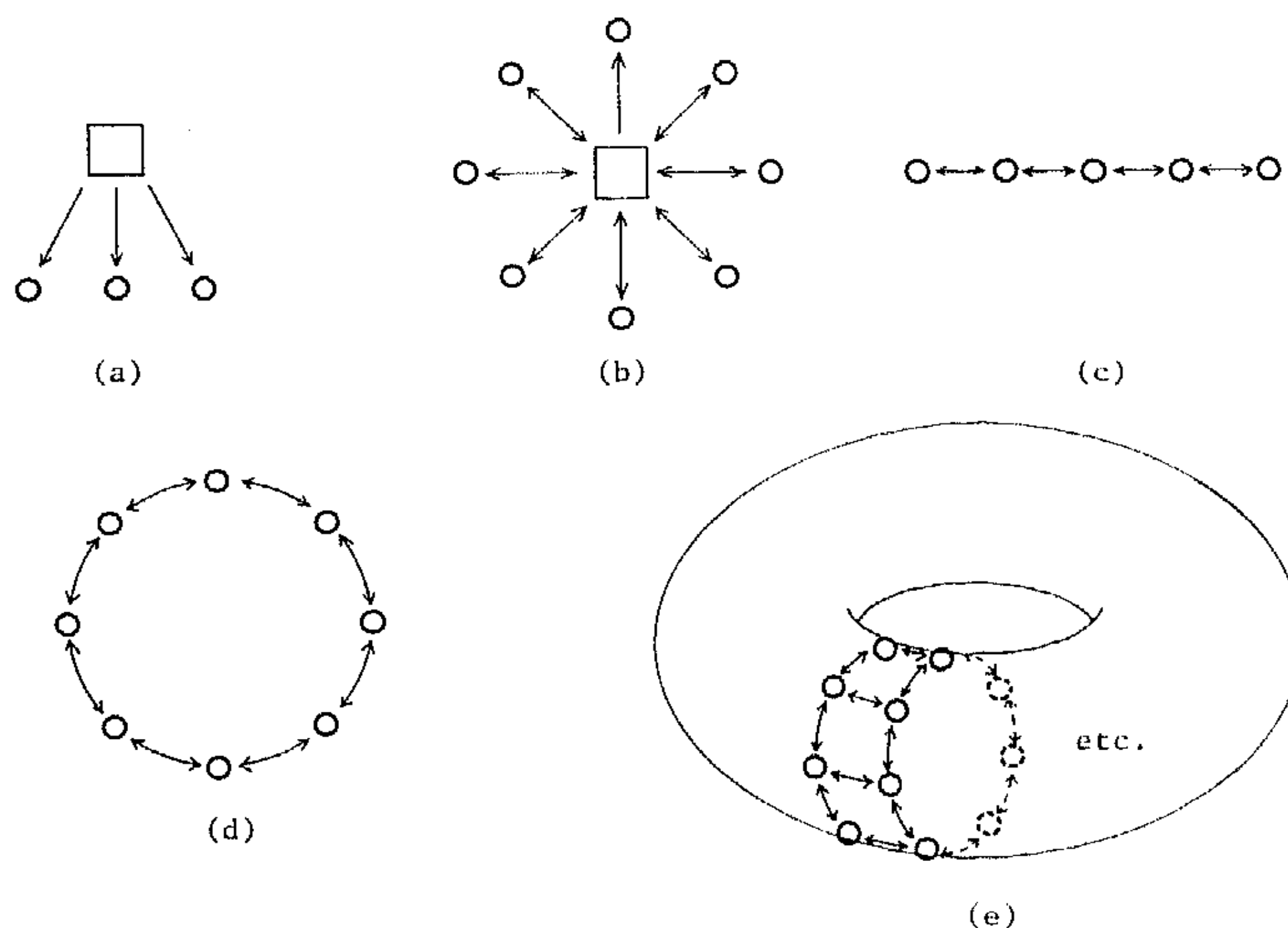
$$\begin{aligned} \dot{x} &= (y - F(x))/\varepsilon, \\ \dot{y} &= -x, \end{aligned} \tag{1.1}$$

in which  $\dot{\phantom{x}} = d/dt$ ;  $x$  and  $y$  real;  $\varepsilon$  small, positive. When  $F(x) = x^3/3 - x$  this

system represents the Van der Pol equation [6]. Under certain conditions for the function  $F$  the above equation has a periodic solution, called a *relaxation oscillation*. One important property of such oscillators is their high orbital stability. When there is weak interaction between two or more of these oscillators, they preserve their orbit almost completely, but they may be accelerated or slowed down on the orbit. Equation (1.1) is a *stiff* equation:  $x$  may change very rapidly (*fast variable*), whereas  $y$  can only change slowly (*slow variable*). The Van der Pol equation was introduced in 1926 as a simple representative of a large class of nonlinear oscillators [32]. Later Fitzhugh [9] proposed an equation of the type (1.1), the Bonhoeffer–Van der Pol equation, as a simplification of the (local) Hodgkin–Huxley equation. More recently Mayeri [24] used a particular form of (1.1) to describe a certain neural oscillator.

We shall mainly investigate systems of oscillators arranged in geometrical structures with *nearest neighbour coupling* (see Fig. 1.1). Such an interaction gives rise to *wave phenomena*. Moreover we also consider oscillators coupled with a *delay*.

Nearest neighbour interaction for nonlinear oscillators has not often been investigated analytically in the biomathematical literature. Only the work of Linkens [22] on linear and circular arrays of regular Van der Pol oscillators is known to us (we investigate singular Van der Pol oscillators). Winfree [40] and Pavlidis [29], for instance, investigate sets of oscillators which are so coupled that all oscillators have equal influence on each other. That is: the oscillators are coupled via a *common medium* (see Fig. 1.1). Othmer [28] and Torre [38] only investigate spatial inhomogeneous states for systems of two oscillators. In contrast many studies deal with digital and electronic simulation of coupled arrays of non-linear oscillators.



**Fig. 1.1.** Different types of coupling: external (a) and mutual (others). Coupling via a (passive) common medium is indicated in (b). In (c), (d) and (e) coupling on a line, circle resp. torus is indicated. Not all elements on the torus have been drawn. The circle and the torus are easier to analyse than the (finite) line which lacks symmetry

The geometrical arrangements of the oscillators will be very simple and symmetrical: line, circle and two-dimensional torus (see Fig. 1.1). A line may be considered as an idealized model of the gastro-intestinal tract or the ureter, see [22]. The circle may be used to model periodic chemical reactions on a ring [2]. One might also devise experiments with ring-shaped, spontaneously active tissue. The torus, however, should only be considered as a prototype for two-dimensional structures: it is hoped that in more complicated structures the waves will show the same local behaviour.

In many instances from biology the autonomous frequency of an oscillator depends on the place in the structure. We mention a simple model for impulse conduction in the human heart by Van der Pol and Van der Mark [33]. This model consists of three oscillators, coupled with delay, representing the sinus, and atria and the ventricles. The autonomous frequency of these parts decreases in the given order. The result is that a contraction of the ventricles is preceded by a contraction of the atria. In order to study effects of this type we shall also consider a line with *place-dependent autonomous frequency*. Brown et al. [3] studied an electronic model of this situation.

In Section 2 the solutions of the isolated oscillator (1.1) are investigated. When  $\varepsilon$  tends to zero the solution tends to a piecewise continuous function, called the *singular solution* or *discontinuous solution*. The behaviour of the singular solution is very simple: on the continuous parts it is governed by one first order differential equation. The Van der Pol oscillator and the piecewise-linear oscillator are treated as examples. By a slight modification of (1.1) the period of the solutions can be altered. At a later stage this will enable us to investigate the synchronization of oscillators with different autonomous frequencies.

In Section 3 the mathematical theory of finite systems of weakly coupled oscillators is considered. The order of magnitude of the coupling is given by a small parameter  $\delta$ . We treat the asymptotic behaviour of such systems for  $\varepsilon$  and  $\delta$  tending to zero. In the singular approximation ( $\varepsilon \rightarrow 0$ ) the state of one oscillator depends on one real variable called the *phase*; the state of an oscillator as a function of the phase is periodic with period  $T_0$ . A differential equation for the phases will be derived. Synchronized solutions are found with the aid of the *Poincaré mapping* of the singular approximation. The asymptotics of the Poincaré mapping are studied for  $\delta$  tending to zero. When the asymptotic solutions are synchronized there also exist synchronized solutions for  $\varepsilon$  and  $\delta$  sufficiently small. The results of this section are based on the theory of relaxation oscillators by Mishchenko and Pontryagin [25], [26], [34]. Two lemma's of Section 3 having rather long and technical proofs are published elsewhere. At the end of the section we formulate some plausible extensions of the main result. It is conjectured that the theory can also be applied to oscillators coupled with delay.

In Section 4 the method of the previous section is applied to two oscillators with different autonomous frequencies, coupled with delay. The coupling in both directions is the same. Synchronization can be investigated by means of a real

valued function  $z(\mu)$ , called the *phase shift function*. This is a continuous,  $T_0$ -periodic function of the phase difference,  $\mu$ , of the oscillators. The derivative of  $z$  is piecewise continuous with jump discontinuities at  $k T_0/2$  ( $k$  integer). The form of the function  $z$  depends in a simple way on the type of coupling and on the singular solution of (1.1). We summarize some results: When  $z'(+0) + z'(-0) < 0$  two oscillators with equal free periods will have a stable synchronized solution with equal phases. This synchronized solution will have a period greater (resp. less) than the free period when  $z(0)$  is negative (resp. positive). Experimental results of this kind were obtained by De Haan and Hilarow [14]. When the oscillators are coupled with a delay  $\rho$  the stable synchronized state  $\mu = 0$  splits up in two stable states  $\mu = \pm \mu_\rho$ , with  $\mu_\rho \rightarrow 0$  as  $\rho \rightarrow 0$ . When the oscillators have unequal free periods, synchronization can only occur if the difference of these periods is within certain bounds. In the synchronized state the quicker oscillator will be ahead in phase.

In Section 5 we investigate a large system of oscillators with different autonomous frequencies, coupled via a common medium. This situation is treated numerically by iteration of the Poincaré mapping (of Section 3) which depends on the phase shift function (of Section 4). With iteration of the Poincaré mapping stable synchronized solutions can be found. Moreover such iterations can be used to follow the system in the course of time. In a numerical experiment it is assumed that the free periods are drawn independently from a Gaussian distribution with a width of the same order of magnitude as the coupling. The initial phases are drawn independently from a homogeneous distribution. In the course of time the mean observed period increases, whereas the width decreases. It may happen that oscillators with relatively long or short free periods do not participate in the common rhythm. This phenomenon is called *partial synchronization*. The synchronized period increases with the number of oscillators involved. Such a phenomenon has been observed in embryonic heart cell cultures by Sachs and De Haan [35]. Similar studies, with similar results, were made by Wiener [39], Winfree [40] and Kuramoto [20], in connection with the alpha-rhythm of the human brain. However these authors do not use the efficient method of iteration of the Poincaré mapping.

In Section 6 we consider nearest-neighbour coupling on a line, a circle and a torus (see Fig. 1.1). The line is used to investigate the effect of place dependent autonomous frequency. It is assumed that the autonomous frequency decreases along the line. This situation is investigated numerically (as in Section 5). The initial phases are assigned randomly. After a certain time a pattern develops with waves running from the quicker oscillators to the slower ones. The average period is increased by the coupling. The fast oscillators are almost completely synchronized, whereas the others are partially synchronized. These results agree with electronic simulations by Brown et al. [3].

Because of the symmetry the synchronized states of identical oscillators on a circle can be investigated analytically. These synchronized states take the form of phase waves; stability is found for several wavelengths. The state in which all oscillators had equal phases was stable but it was destabilized by the introduction of a delay

in the coupling. The qualitative results show some analogy with investigations of Auchmuty and Nicolis [2], on a continuum of chemical oscillators in a ring. In that case the oscillators are coupled by diffusion.

In the last part of Section 6 we investigate a set of identical oscillators arranged on a two-dimensional torus. The synchronization and stability conditions are similar to those for a circle. A numerical experiment was done with random initial phases. After 50 iterations of the Poincaré map the system had not reached a stable waveform. Small waves ran over the torus, breaking down when meeting each other. Wave centres appeared and disappeared spontaneously. The chaotic wave pattern resembles fibrillation of the heart's ventricles, a state in which the coordination of the fibres of the heart muscle decreases very rapidly with increasing distance. Experiments of this type might possibly add to a better understanding of this phenomenon.

The number of stable synchronized wave solutions on the circle and the torus was greater than we had expected. In some physiological systems this might be undesirable. The number of stable wave solutions might be reduced by: shape, boundary condition, unidirectional coupling, place dependence of autonomous frequency (see above), a delay in the transfer of information (see above) and by the shape of the function  $z$ . The effects of place dependent frequency and unidirectional coupling are well known in physiology. The other factors deserve further experimental and mathematical investigation.

## 2. Isolated Relaxation Oscillator

In this section we shall briefly discuss the behaviour of one isolated relaxation oscillator. This will serve as an introduction to Section 3, where the behaviour of coupled oscillators is discussed.

One oscillator shall be described by a real system of two first order equations:

$$\begin{aligned} \dot{x} &= (y - F(x))/\varepsilon, \\ \dot{y} &= -x, \end{aligned} \tag{2.1}$$

where  $\varepsilon$  is a small positive parameter and where  $\dot{\phantom{x}} = d/dt$ . With respect to  $F$  and its derivative  $f$  we assume that

$$\begin{aligned} F(x) &= -F(-x) \quad (x \in \mathbb{R}), \\ f(x) &\text{ is continuous} \quad (x \in \mathbb{R}), \\ F(x) &\rightarrow +\infty \quad (x \rightarrow +\infty). \end{aligned} \tag{2.2a}$$

Moreover, a positive number  $m$  should exist such that

$$\begin{aligned} f(x) &< 0, \quad x \in (0, m), \\ f(x) &> 0, \quad x \in (m, \infty). \end{aligned} \tag{2.2b}$$

Under these conditions (2.1) has a unique periodic solution, which is asymptotically stable [15]. For weaker conditions on the function  $F$  see Lasalle [21].

In order to approximate the solutions of (2.1) we introduce the *reduced system*:

$$y = F(x), \quad (2.3a)$$

$$\dot{y} = -x, \quad (2.3b)$$

which is obtained from (2.1) by substituting  $\varepsilon = 0$ . Note that it follows from (2.3a) and (2.3b) that

$$f(x)\dot{x} + x = 0 \quad (f(x) \neq 0). \quad (2.3c)$$

We also introduce the *fast equation*

$$\dot{x} = (y - F(x))/\varepsilon \quad (y \text{ constant}), \quad (2.4)$$

in which the constant  $y$  can be considered as parameter. With the aid of (2.3) and (2.4) we can define the *singular* or *discontinuous* solution of (2.1), which approximates the solution of (2.1) in a sense that will be made precise later. Let the singular solution start at time zero in the point  $(\tilde{x}, \tilde{y})$ . If  $\tilde{y} \neq F(\tilde{x})$  the singular solution makes an instantaneous jump, along the trajectory of the fast equation until a stable equilibrium  $(x_s, \tilde{y})$ , with  $F(x_s) = \tilde{y}$  and  $f(x_s) > 0$ , is reached. Such a point will be called a *landing point*. From then on the singular solution satisfies the reduced equation (2.3). This part of the singular solution is called *regular*. Along the regular part the absolute value of  $x$  decreases until  $x$  attains a local extremum of  $F(x)$  ( $x = \pm m, f(x) = 0$ ). At that moment  $y = F(x)$  ceases to be a stable equilibrium of (2.4). The point where this happens is called a *leaving point*. It follows from the conditions (2.2) that Equation (2.4) has only one trajectory departing from a leaving point. The singular solution makes an instantaneous jump along this trajectory until a new landing point is reached, after which the reduced equation is satisfied again. Thus the singular solution is described alternately by instantaneous jumps along trajectories of the fast equation and by regular parts satisfying the reduced equation.

The singular solution approximates the exact solution in the following sense: Let  $(x(t), y(t))$  be a solution of (2.1) on a bounded time interval, and let  $(\xi(t), \eta(t))$  be a singular solution of (2.1) starting in the same point. It has been shown that the trajectory of  $(x(t), y(t))$  will tend to that of  $(\xi(t), \eta(t))$  if  $\varepsilon$  tends to zero. The approximation near the regular parts and the jump parts has been studied by Tikhonov [37] and Hoppensteadt [18]. The approximation near the leaving points has been studied by Mishchenko and Pontryagin [25], [34]. In biochemistry a state approximated by the reduced equation is called a pseudo-steady state [16], [11].

From the conditions (2.2) it follows that Equation (2.1) has a unique periodic singular solution, which we shall indicate by  $(x^0(t), y^0(t))$ . The closed trajectory or path  $X_0$  of this solution proceeds along  $ABCD$  as sketched in Figure 2.1. This picture illustrates that after some disturbance the singular solution will instantaneously return to  $X_0$ ; this means that  $X_0$  is a highly stable limit cycle. The arcs  $AB$  and  $CD$  represent the regular parts;  $BC$  and  $DA$  represent the jumps.

Let the periodic singular solution  $(x^0(t), y^0(t))$  start at  $t = 0$  in the point  $A$  (Fig. 2.1). In order to calculate the period  $T_0$  of this solution we remark that on the

regular part  $AB$ , where  $x$  decreases from, say,  $M$  to  $m$ , the time  $t$  is given according to (2.3c) by

$$t = - \int_M^x \frac{f(\xi)}{\xi} d\xi. \quad (2.5)$$

This means that the solution runs through  $AB$  in the time

$$\int_m^M \frac{f(x)}{x} dx.$$

Because of the symmetry of  $F(x)$  the part  $CD$  takes the same time, whereas  $BC$  and  $DA$  represent instantaneous jumps. Consequently the period of the singular solution is given by

$$T_0 = 2 \int_m^M \frac{f(x)}{x} dx. \quad (2.6)$$

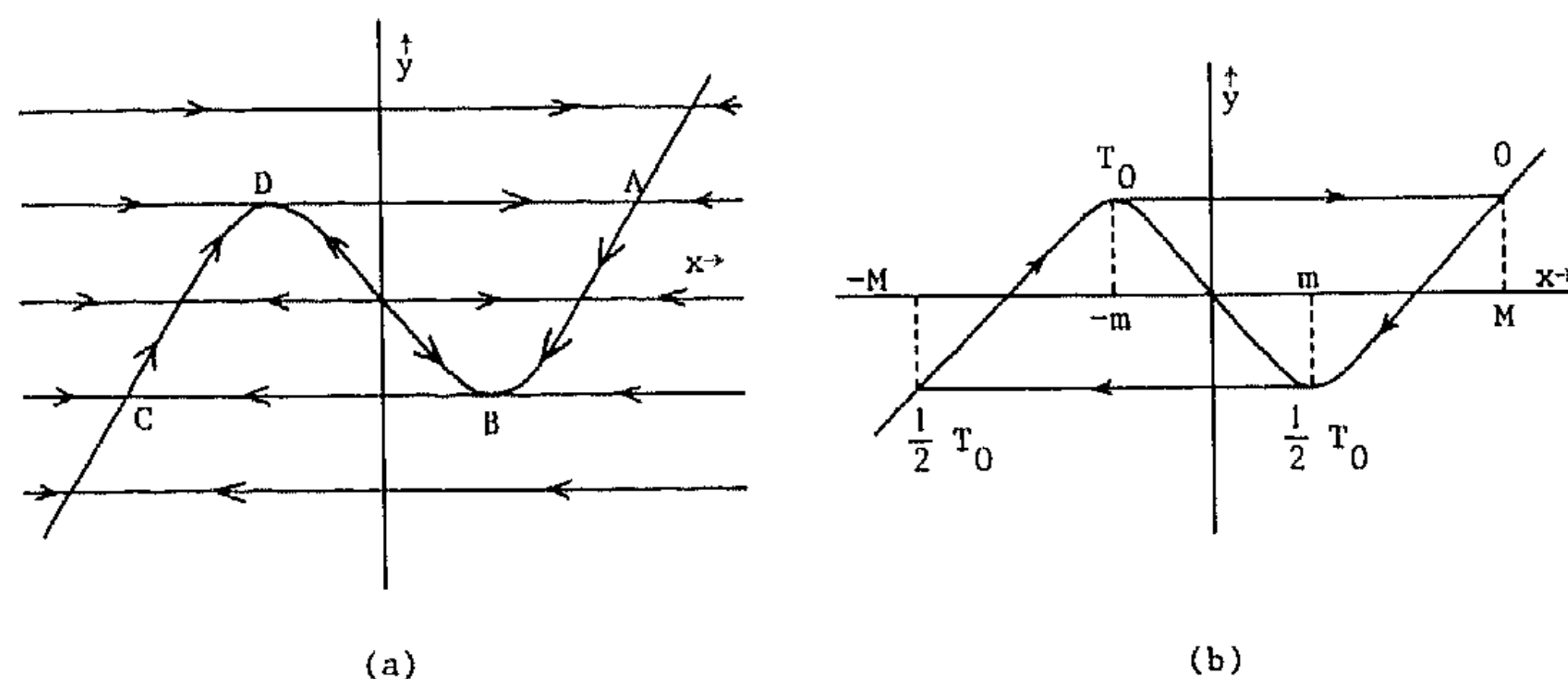


Fig. 2.1. Trajectories of singular solution

In Figure 2.1a the state space of the singular solutions of (2.1) is drawn. The arrows indicate the change of state; horizontal arrows indicate instantaneous changes. The closed trajectory  $X_0 = ABCD$  represents the periodic singular solution. On this trajectory the state of the singular solution can be represented by one real variable, called the phase, which coincides for isolated oscillators with time. The period of the singular solution is denoted by  $T_0$ . In Figure 2.1b the closed trajectory  $X_0$  is drawn. At the points  $A, B, C$  and  $D$  the phases and the values of  $x$  are indicated. In the pictures  $F(x) = x^3/3 - x$  (Van der Pol equation).

The following theorem establishes a relation between the periodic solution of (2.1) for some  $\varepsilon > 0$ , and the singular solution  $(x^0(t), y^0(t))$ . For the proof the reader is referred to Mishchenko and Pontryagin [25], [26], [34].

**Theorem 2.1.** *Let  $F$  satisfy (2.2). Then the period  $T_\varepsilon$  of the asymptotically stable periodic solution of (2.1) satisfies:  $T_\varepsilon = T_0 + o(\varepsilon^{2/3})$  ( $\varepsilon \rightarrow 0$ ). The limit cycle  $X_\varepsilon$  of (2.1) satisfies:  $X_\varepsilon \rightarrow X_0$  ( $\varepsilon \rightarrow 0$ ).*



*Example 2.1.* The Van der Pol oscillator is described by (2.1) with

$$\begin{aligned} f(x) &= x^2 - 1 \\ F(x) &= x^3/3 - x. \end{aligned} \quad (2.7)$$

Denote the abscis of  $A$  by  $M$ , that of  $B$  by  $m$  (see Fig. 2.1); then

$$\begin{aligned} m &= 1, \\ M &= 2. \end{aligned} \quad (2.8)$$

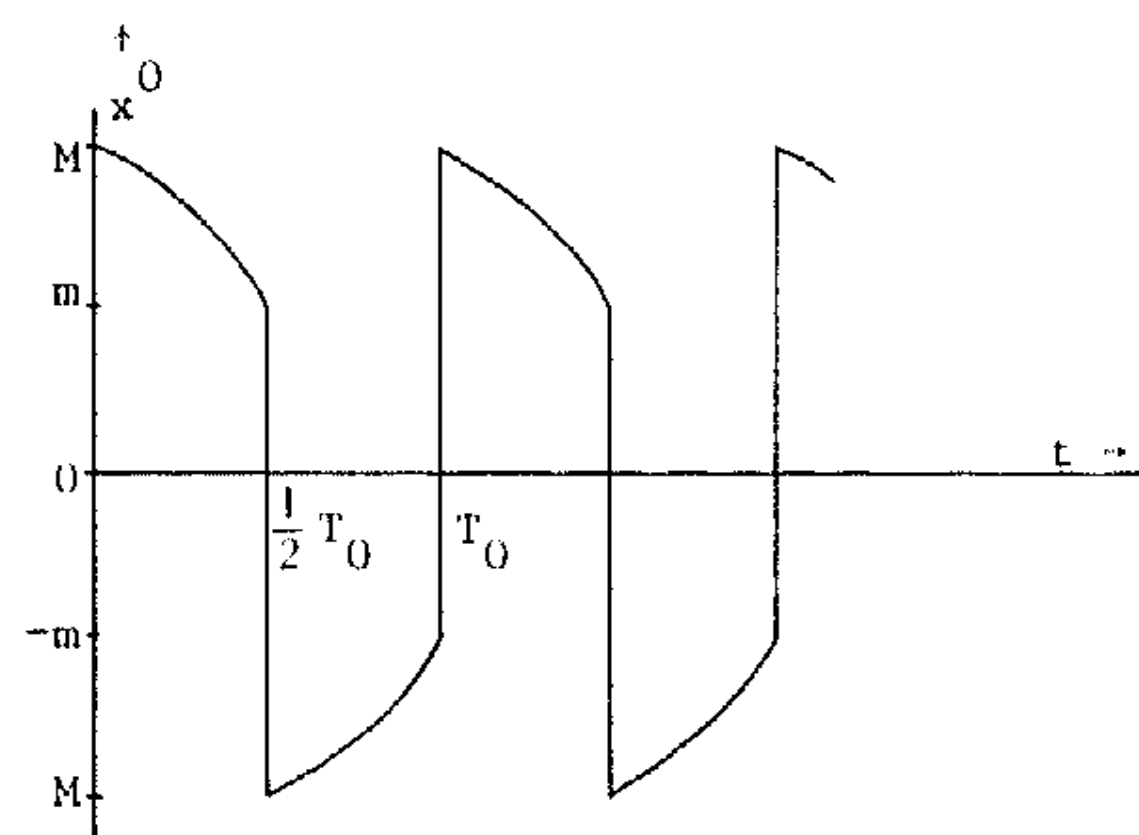
The trajectory of the singular solution  $(x^0(t), y^0(t))$  is drawn in Figure 2.1. The period  $T_0$  is given by (2.6):

$$T_0 = 2 \int_m^M \frac{x^2 - 1}{x} dx = 3 - 2 \ln 2. \quad (2.9)$$

On the interval  $(0, T_0/2)$  the function  $x^0(t)$  is given by the implicit formula (2.5).

$$t = - \int_M^{x^0} \frac{x^2 - 1}{x} = 2 - \ln 2 - \frac{(x^0)^2}{2} + \ln x^0. \quad (2.10)$$

The value of  $x^0(t)$  on  $(T_0/2, T_0)$  is obtained by symmetry;  $x^0(t)$  is drawn in Figure 2.2. The function  $y^0(t)$  follows from  $y^0 = F(x^0)$ .



**Fig. 2.2.** Periodic singular solution of the Van der Pol oscillator. The function  $x^0(t)$  is given implicitly by formula (2.10)

*Example 2.2.* The piecewise linear oscillator is described by (2.1) with

$$f(x) = \begin{cases} 1 & |x| > 1 \\ -1 & |x| \leq 1 \end{cases} \quad (2.11a)$$

$$F(x) = \begin{cases} 2 + x & x < -1 \\ -x & -1 \leq x \leq 1 \\ -2 + x & x > 1 \end{cases} \quad (2.11b)$$

The values of  $m$  and  $M$  are

$$\begin{aligned} m &= 1 \\ M &= 3. \end{aligned} \quad (2.12)$$

The period  $T_0$  of the singular solution is given by

$$T_0 = 2 \int_m^M \frac{dx}{x} = 2 \ln 3. \quad (2.13)$$

Using (2.5) one easily obtains an explicit formula for the singular solution  $x^0$ :

$$x^0(t) = \begin{cases} 3e^{-t} & 0 < t < T_0/2 \\ -3e^{-(t-T_0/2)} & T_0/2 < t < T_0 \end{cases} \quad (2.14)$$

In this case  $f$  is not continuous, so that Theorem 2.1 does not apply. However (2.1) can easily be solved on the intervals where  $F$  is linear. Piecing these parts together, one arrives at the same conclusions as in theorem (2.1), with a sharper estimate for the period:  $T_\varepsilon = T_0 + O(\varepsilon \ln \varepsilon)$  ( $\varepsilon \rightarrow 0$ ) (see Stoker [36]).

In the sequel we investigate synchronization of oscillators with slightly different autonomous periods. Therefore we state:

**Corollary 2.1.** *The differential equation*

$$\begin{aligned} \dot{u} &= (v - F(u))/\varepsilon, \\ \dot{v} &= -(1 - \delta q)u, \end{aligned} \quad (2.15)$$

with  $F$  satisfying (2.2), with  $\varepsilon$  and  $\delta$  sufficiently small, and with  $q$  an arbitrary constant, has an asymptotically stable periodic solution with period  $T_{\varepsilon,q}$  and trajectory  $X_{\varepsilon,q}$  satisfying:  $T_{\varepsilon,q} = T_0 + \delta q T_0 + O(\varepsilon^{2/3}) + O(\delta^2)$ , and  $X_{\varepsilon,q} \rightarrow X_0$  ( $\varepsilon \rightarrow 0$ ).

*Proof.* Introduction of a new time scale  $\tilde{t} = t(1 - \delta q)$  and a small parameter  $\tilde{\varepsilon} = \varepsilon(1 - \delta q)$  transforms (2.15) in an equation of the type (2.1), to which Theorem 2.1 applies.  $\square$

### 3. Theory of Synchronized Relaxation Oscillators

In this section we shall investigate a finite system of coupled relaxation oscillators, described by the following differential equations:

$$\dot{u}_i = (v_i - F(u_i))/\varepsilon \quad (i = 1, 2, \dots, n), \quad (3.1a)$$

$$\dot{v}_i = -(1 - \delta q_i)u_i + \delta h_i(\underline{u}, \underline{v}) \quad (i = 1, 2, \dots, n), \quad (3.1b)$$

where  $n$  denotes the number of oscillators and where  $\underline{u} = (u_1, u_2, \dots, u_n)$ ,  $\underline{v} = (v_1, v_2, \dots, v_n)$ . The parameters  $\varepsilon$  and  $\delta$  are assumed to be small and positive. The functions  $h_i$  represent the coupling between the oscillators. The constants  $q_i$  are arbitrary; they represent the difference of the autonomous periods of the oscillators (see Corollary 2.1). It is assumed that  $F$  satisfies the conditions (2.2). We shall moreover assume that the functions  $F$  and  $h_i$  ( $i = 1, 2, \dots, n$ ) have continuous derivatives of any order. The main results of this section can also be proved when the latter condition is weakened, but this is not necessary for our purposes. Note that the coupling and the differences between the periods have the same order of magnitude,  $O(\delta)$ .

We shall investigate the behaviour of the solutions of (3.1) for  $\varepsilon$  tending to zero. Just as in the previous section we introduce the *reduced system*

$$v_i = F(u_i) \quad (3.2a)$$

$$\dot{v}_i = -(1 - \delta q_i)u_i + \delta h_i(\underline{u}, \underline{v}). \quad (i = 1, 2, \dots, n) \quad (3.2b)$$

Combination of these equations yields a reduced equation for  $\underline{u}$ :

$$f(u_i)u_i = -(1 - q_i)u_i + \delta h_i(\underline{u}, F(\underline{u})), \quad (3.2c)$$

where  $F(\underline{u}) = (F(u_1), F(u_2), \dots, F(u_n))$  and where  $f = F'$ . We also introduce the *fast system*

$$\dot{u}_i = (v_i - F(u_i))/\varepsilon \quad (v_i \text{ constant}), \quad (3.3)$$

in which the constants  $v_i$  can be considered as parameters.

The *singular solution* of (3.1) is defined as follows: When  $(\underline{u}, \underline{v})$  is not a stable equilibrium point of the fast system an instantaneous jump is made along a trajectory of the fast equation until a stable equilibrium of this equation is reached (a landing point). Afterwards the singular solution satisfies the reduced system until one or more of the variables  $u_1, u_2, \dots, u_n$  reaches a local extremum of  $F$  (i.e. a zero,  $\pm m$ , of  $f$ ). At that point (a leaving point) the reduced equation cannot be satisfied any more. Then the singular solution makes an instantaneous jump along the unique trajectory of the fast equation departing from the leaving point, until a new landing point is reached. After the jump the singular solution is described again by the reduced system.

The singular solution approximates the exact solution in the sense indicated in Section 2, that is: the trajectories of the solutions of (3.1) will tend to the trajectories of the singular solution of (3.1) if  $\varepsilon$  tends to zero (for references see Section 2). Moreover system (3.1) has a periodic solution if it has a periodic singular solution satisfying certain conditions. We have to introduce some concepts before formulating a theorem of this kind.

Let the regular parts  $AB$  and  $CD$  of the closed trajectory  $X_0$  of the periodic singular solution of (2.1) be indicated by  $\Omega_0$ . Then we may define the following  $n$ -dimensional surface in the space  $\mathbb{R}^{2n}$ .

$$\Omega_0^n = \{\underline{u}, \underline{v}\} \in \mathbb{R}^{2n} \mid (u_i, v_i) \in \Omega_0 \text{ for } i = 1, 2, \dots, n\}. \quad (3.4)$$

This means that  $(\underline{u}, \underline{v}) \in \Omega_0^n$  when each oscillator  $(u_i, v_i)$  lies on the regular trajectory  $\Omega_0$  of the singular solution of one isolated oscillator. We shall show that for  $\delta$  sufficiently small a singular solution  $(\underline{u}(t), \underline{v}(t))$  will remain in the set  $\Omega_0^n$ , once it has arrived there:

**Lemma 3.1.** *When  $\delta$  is sufficiently small but finite, the set  $\Omega_0^n$  is invariant with respect to singular solutions of (3.1).*

*Proof.* Let  $(\underline{u}, \underline{v}) \in \Omega_0^n$ . We first consider the case when  $f(u_i) \neq 0$  ( $i = 1, 2, \dots, n$ ).

This means that  $f(u_i) > 0$  and that  $|u_i| > m$  (Fig. 2.1). Moreover  $(\underline{u}, \underline{v})$  is bounded. It follows from (3.2) that for  $\delta$  sufficiently small

$$\begin{aligned} v_i &= F(u_i) \\ \text{sign}(\dot{u}_i) &= -\text{sign}(u_i) \quad (i = 1, 2, \dots, n). \end{aligned} \quad (3.5a)$$

From (2.3) we obtain for the isolated oscillator

$$\begin{aligned} y &= F(x) \\ \text{sign}(\dot{x}) &= -\text{sign}(x). \end{aligned} \quad (3.5b)$$

This implies that the coupled oscillators run through the regular parts  $AB$  and  $CD$  in the same direction as the uncoupled oscillator. In the leaving points, where at least one of the functions  $f(u_i)$  is zero, the system makes an instantaneous jump to a new stable equilibrium of (3.3). This is the same for coupled and uncoupled oscillators. Consequently,  $\Omega_0^n$  is invariant.  $\square$

For a concise formulation of a theorem on periodic solutions of (3.1) we will need two definitions:

*Definition 3.1.* Let  $n \geq 2$  and let  $W$  be a smooth  $n - 1$  dimensional surface lying in the  $n$ -dimensional surface  $\Omega_0^n$ . Moreover, let  $W$  be nowhere tangent to the trajectories of the singular solutions of (3.1). Let  $w$  be a point of  $W$  and let a singular solution start in  $w$ . Then it may happen that this singular solution will return in  $W$ . If so, denote the point of first return by  $\mathcal{P}(w)$ . In this way a mapping,  $\mathcal{P}$ , is defined from a part of  $W$  into  $W$ . This mapping is called the *Poincaré map* of  $W$  produced by the singular solution.

The Poincaré map is commonly used to investigate the stability of solutions which are known to be periodic (see for instance Hirsh and Smale [17]). We shall use this mapping also to detect periodic solutions. It is clear that there exists a periodic singular solution if  $\mathcal{P}$  has a *fixed point*, i.e. a point  $w \in W$  such that  $\mathcal{P}(w) = w$ . The closed trajectory of such a periodic solution will be indicated by  $Z_0 \subset \mathbb{R}^{2n}$ , the period by  $P_0$ .

*Definition 3.2.* A periodic singular solution of (3.1) will be called *C-stable* if a surface  $W$  exists as described in Definition 3.1, such that the corresponding Poincaré map,  $\mathcal{P}$ , is *contracting* at the intersection of  $W$  and  $Z_0$ .

The following theorem, proved by Mishchenko [26], permits us to fix our attention to *C-stable* periodic singular solutions of Equation (3.1):

**Theorem 3.1.** *Let  $\delta$  be such that Equation (3.1) has a C-stable periodic singular solution with trajectory  $Z_0$  and period  $P_0$ . Let only one of its components  $u_i(t)$  ( $i = 1, 2, \dots, n$ ) be discontinuous at a time. Then a positive function  $\bar{\varepsilon}(\delta)$  exists such that, for  $0 < \varepsilon \leq \bar{\varepsilon}(\delta)$ , Equation (3.1) has a periodic solution with period  $P_\varepsilon$  and trajectory  $Z_\varepsilon \subset \mathbb{R}^{2n}$  satisfying: (i)  $Z_\varepsilon \rightarrow Z_0$  ( $\varepsilon \rightarrow 0$ ) and (ii)  $P_\varepsilon = P_0 + o(\varepsilon^{2/3})$ .*

We now introduce the *phase-map*

$$\Phi: \mathbb{R}^n \rightarrow \Omega_0^n, \quad (3.6a)$$

defined by

$$\Phi: (\phi_1, \phi_2, \dots, \phi_n) \mapsto (x^0(\phi_1), \dots, x^0(\phi_n), y^0(\phi_1), \dots, y^0(\phi_n)). \quad (3.6b)$$

The point  $\phi_i$  will be called the *phase* of the  $i$ th oscillator (note that the phase is not uniquely defined). It is easy to see that each point of  $\Omega_0^n$  has an original in  $\mathbb{R}^n$ , that is:  $\Phi$  is surjective. The map  $\Phi$  is  $T_0$ -periodic in each of its arguments and it is locally invertible. Moreover it follows from (2.3c) and (2.5) that  $\Phi$  is locally diffeomorphic except at the jump planes  $\phi_i = j_i T_0/2$  ( $j_i$  integer).

**Lemma 3.2.** *A singular solution  $(\underline{u}(t), \underline{v}(t))$  of Equation (3.1), with initial value in  $\Omega_0^n$ , may be represented by*

$$\begin{aligned} u_i(t) &= x^0(\phi_i(t)) \\ v_i(t) &= y^0(\phi_i(t)) \end{aligned} \quad (i = 1, 2, \dots, n), \quad (3.7a)$$

where the functions  $\phi_i(t)$  satisfy the phase equation

$$\dot{\phi}_i = 1 - \delta q_i - \delta k_i(x^0(\underline{\phi}))/x^0(\phi_i), \quad (3.7b)$$

in which

$$k_i(x^0(\underline{\phi})) = h_i(x^0(\phi_1), \dots, x^0(\phi_n), F(x^0(\phi_1)), \dots, F(x^0(\phi_n))). \quad (3.7c)$$

*Proof.* Representation (3.7a) follows from the invariance of  $\Omega_0^n$  and from the surjectivity of  $\Phi$ . Differential Equation (3.7b) is obtained by substituting (3.7a) into (3.2c) and using (2.3c).  $\square$

When the oscillators are uncoupled ( $k_i = 0$ ) and identical ( $q_i = 0$ ) Equation (3.7b) has the form  $\dot{\phi}_i = 1$ ; i.e. phase and time are equal up to an additive constant. This is the reason why the phase of an oscillator is sometimes called, depending on the context, *subjective time* or *circadian time*.

We shall now approximate the solution of (3.7b) in order to investigate the mapping  $\mathcal{P}$ . Since  $\delta$  is a small parameter it is natural to try to solve (3.7b) by iteration. Let  $\underline{\phi}(0) = \underline{\alpha}$ . Then the first and second iterates are

$$\phi_i^{(0)}(t) = \alpha_i + t \quad (3.8a)$$

$$\phi_i^{(1)}(t) = \alpha_i + t - \delta q_i t - \delta \int_0^t \frac{k_i(x^0(\alpha_1 + \tau), \dots, x^0(\alpha_n + \tau))}{x^0(\alpha_i + \tau)} d\tau \quad (3.8b)$$

The integral on the right-hand side of (3.8b) exists since  $x^0$  is bounded away from zero.

We shall frequently need a special condition on the initial value  $\underline{\phi}(0) = \underline{\alpha}$ . Therefore we state:

**Definition 3.3.** A point  $\underline{\alpha} \in \mathbb{R}^n$  will be called *regular* if the functions  $x^0(\alpha_i + t)$  ( $i = 1, 2, \dots, n$ ) are continuous in  $t = 0$  and if they become discontinuous one at a time.

Since  $x^0$  is discontinuous at  $j T_0/2$  ( $j$  integer) the regularity condition implies that  $\alpha_i \neq j T_0/2$  and that no two of the phases  $\alpha_i$  are equal or complementary.

**Lemma 3.3.** *Let  $\underline{\alpha}$  be regular. Then Equation (3.7b) with  $\underline{\phi}(0) = \underline{\alpha}$  has a unique solution  $\underline{\phi}(t)$ . Moreover*

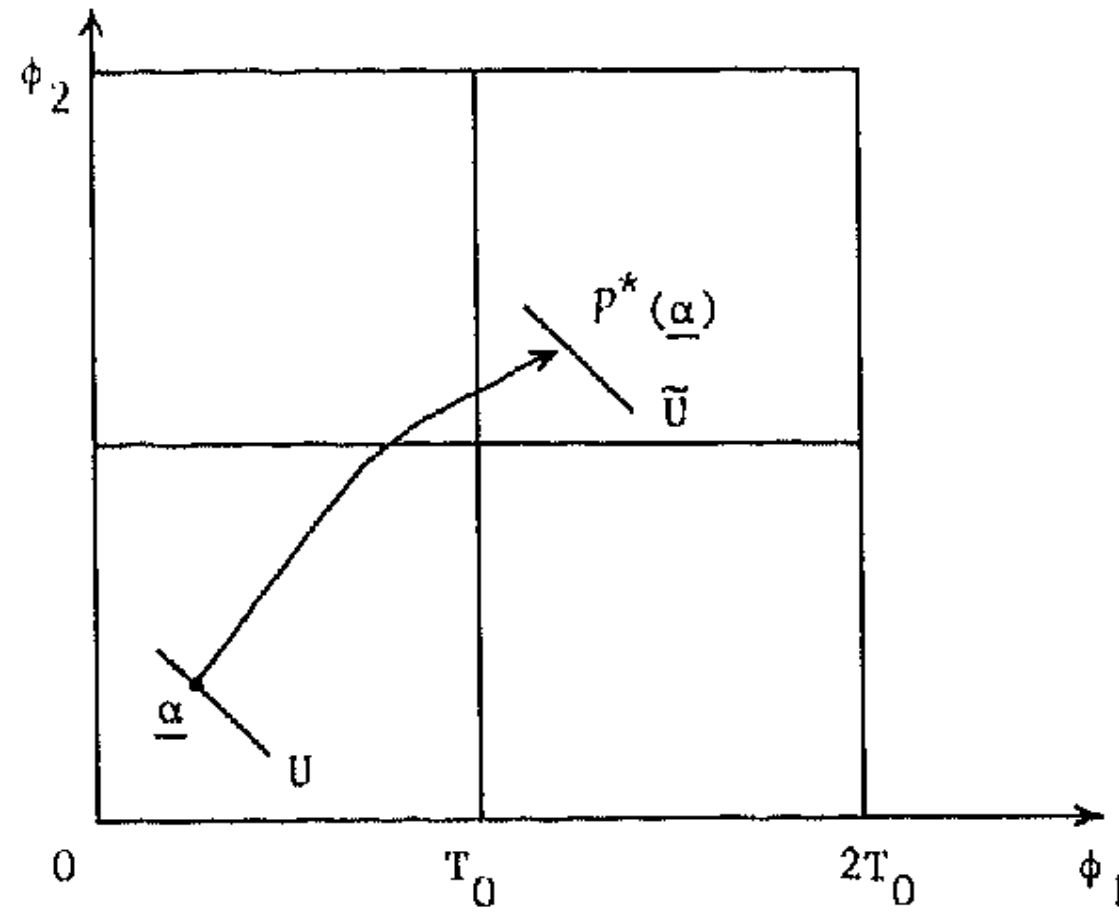
$$\phi_i(t) = \phi_i^{(1)}(t) + O(\delta^{3/2}) \quad (t \text{ bounded}). \quad (3.9)$$

*Proof.* See Jansen [19].

With the aid of approximation (3.9) the Poincaré map  $\mathcal{P}$  of Definition 3.1 can be investigated. Let  $V$  be an  $n - 1$  dimensional plane in  $\mathbb{R}^n$  perpendicular to the vector  $\underline{\ell} = (1, 1, \dots, 1) \in \mathbb{R}^n$ . Let  $\alpha$  be a regular point in  $V$  and let  $U$  be a neighbourhood of  $\alpha$  in  $V$ . Denote by  $\tilde{V}$  and  $\tilde{U}$  the translations of  $V$  and  $U$  along the vector  $T_0 \underline{\ell}$ . And denote by  $W$  the image  $\Phi(U)$  of  $U$  and  $\tilde{U}$ . It is easy to see that  $W$  satisfies the conditions of Definition 3.1. It follows from Lemma 3.2. that the Poincaré map corresponding to  $W$  is given by

$$\mathcal{P} = \Phi \mathcal{P}^* \Phi^{-1}, \tag{3.10}$$

where  $\mathcal{P}^*$  is the mapping from  $U$  into  $\tilde{U}$  produced by following the trajectories of (3.7b) (see Fig. 3.1).



**Fig. 3.1.** The map  $\mathcal{P}^*$  for two oscillators, produced by the trajectories of (3.7b). The Poincaré map is given by  $\mathcal{P} = \Phi \mathcal{P}^* \Phi^{-1}$

**Lemma 3.4.**  $\mathcal{P}$  has a fixed point  $\Phi(\underline{\alpha})$  if there exists a regular point  $\underline{\alpha}$  such that  $\mathcal{P}^*(\underline{\alpha}) = \underline{\alpha} + T_0 \underline{\ell}$ . Moreover  $\mathcal{P}$  is contracting in  $\Phi(\underline{\alpha})$  if the eigenvalues of the derivative of  $\mathcal{P}^*$  in  $\underline{\alpha}$  have absolute values less than one.

*Proof.* The first part of the lemma follows immediately from representation (3.10) and from the fact that  $\Phi$  is  $T_0$  periodic. The second part is proved by defining a distance in  $W \subset \Omega_0^n$  as the corresponding euclidean distance in  $U \subset \mathbb{R}^n$ , produced by the mapping  $\Phi^{-1}$ .  $\square$

Substituting  $t = T_0 + s$  in (3.8b) and using the  $T_0$ -periodicity of  $x^0$  we obtain for  $s = O(\delta)$ :

$$\phi(T_0 + s) = \alpha + T_0 \underline{\ell} + s \underline{\ell} + \delta \underline{G}(\alpha) + O(\delta^{3/2}), \tag{3.11a}$$

where

$$G_i(\alpha) = -q_i T_0 - \int_0^{T_0} \frac{k_i(x^0(\alpha_1 - \alpha_i + \tau), \dots, x^0(\alpha_n - \alpha_i + \tau))}{x^0(\tau)} d\tau. \tag{3.11b}$$

The function  $G(\alpha)$  gives the *phase shift* caused by the coupling. Note that

$$G(\alpha + c \underline{\ell}) = G(\alpha). \tag{3.11c}$$

We shall fix  $s(\alpha)$  so that  $\phi(T_0 + s(\alpha)) \in \tilde{V}$ . This yields

$$s(\alpha) = -\frac{\delta}{n} \sum G_i(\alpha) + O(\delta^{3/2}). \tag{3.12}$$

It follows that  $\alpha \in V$  is mapped by  $\mathcal{P}^*$  on

$$\phi(T_0 + s(\alpha)) = \alpha + T_0 \underline{\ell} + \delta \underline{Q}(\alpha) + O(\delta^{3/2}), \quad (3.13a)$$

where

$$\underline{Q}(\alpha) = \underline{G}(\alpha) - \left( \frac{1}{n} \sum G_i(\alpha) \right) \underline{\ell}. \quad (3.13b)$$

Note that

$$\underline{Q}(\alpha) \perp \underline{\ell}, \quad (3.13c)$$

which implies that

$$\alpha + T_0 \underline{\ell} + \delta \underline{Q}(\alpha) \in \tilde{V}. \quad (3.13d)$$

We may summarize the above calculations by stating:

**Lemma 3.5.** *The mapping  $\mathcal{P}^*$  is approximated with an accuracy  $O(\delta^{3/2})$  by the restriction to the plane  $U$  of the mapping*

$$\Pi(\alpha) = \alpha + T_0 \underline{\ell} + \delta \underline{Q}(\alpha). \quad (3.14)$$

Using this lemma one may prove:

**Lemma 3.6.** *Suppose that*

- (i)  $\underline{\alpha}$  is regular (regularity condition),
- (ii) all eigenvalues, except one, of the derivative of  $\underline{Q}(\alpha)$  in  $\underline{\alpha}$  have negative real parts (stability condition).
- (iii)  $\underline{Q}(\underline{\alpha}) = 0$  (synchronization condition).

*Then a point  $\underline{\beta} = \underline{\alpha} + O(\delta)$  exists such that  $\mathcal{P}^*(\underline{\beta}) = \underline{\beta} + T_0 \underline{\ell}$  and such that the eigenvalues of the derivative of  $\mathcal{P}^*$  in  $\underline{\beta}$  have absolute values less than one.*

*Proof.* See Jansen [19].

At this stage our knowledge of the behaviour of the singular solution is sufficient to return to the original equation (3.1). Putting together the results of this section we obtain:

**Theorem 3.2.** *Suppose that  $\underline{\alpha}$  satisfies the three conditions of Lemma 3.6. Then a positive  $\bar{\delta}$  and a positive function  $\bar{\varepsilon}(\delta)$ , defined on  $(0, \bar{\delta})$  exist such that for  $0 < \delta < \bar{\delta}$  and  $0 < \varepsilon < \bar{\varepsilon}(\delta)$  Equation (3.1) has a periodic solution. This periodic solution has the following properties: (i) Its trajectory  $Z_{\varepsilon, \delta}$  tends to the trajectory of*

$$(x^0(\underline{\alpha}_1 + t), \dots, x^0(\underline{\alpha}_n + t), y^0(\underline{\alpha}_1 + t), \dots, y^0(\underline{\alpha}_n + t))$$

*when  $\varepsilon$  and  $\delta$  tend to zero. (ii) Its period  $P_{\varepsilon, \delta}$  satisfies  $P_{\varepsilon, \delta} = T_0 - (\delta/n) \sum G_i(\underline{\alpha}) + O(\delta^{3/2}) + O(\varepsilon^{2/3})$ .*

**Remarks and Extensions.** The condition that  $\underline{\alpha}$  is regular can be deleted from Theorem 3.2. It should be noted however, that the Poincaré map  $\mathcal{P}^*$  and the function  $Q$  need not be continuously differentiable in irregular points. For stability

one has to require that  $Q$  satisfies stability condition (ii) of Lemma 3.2 separately in each of the sectors where  $\alpha$  is regular.

It seems plausible that the theory of this section can without any changes be applied to systems of the more general form

$$\begin{aligned} \dot{u}_i &= (v_i - F(u_i))/\varepsilon + \delta g_i(\underline{u}, \underline{v}) \\ \dot{v}_i &= -(1 - \delta q_i)u_i + \delta h_i(\underline{u}, \underline{v}) \end{aligned} \quad (i = 1, 2, \dots, n), \quad (3.15)$$

where  $F$ ,  $g_i$  and  $h_i$  have continuous derivatives of all orders. The reduced system of (3.15) is given by (3.2). However the theory of Mishchenko and Pontryagin [25], [26], [34] is not sufficiently general to comprise this situation.

The formalism of this section can be extended to differential equations with a delay  $\rho \geq 0$ :

$$\begin{aligned} \dot{u}_i &= (v_i - F(u_i))/\varepsilon, \\ \dot{v}_i &= -(1 - \delta q_i)u_i + \delta h_i(\hat{u}, \hat{v}) \end{aligned} \quad (i = 1, 2, \dots, n) \quad (3.16a)$$

where

$$\begin{aligned} \hat{u}(t) &= \underline{u}(t - \rho) \\ \hat{v}(t) &= \underline{v}(t - \rho) \end{aligned} \quad (3.16b)$$

For such a system the function  $G_i(\alpha)$  (3.11b) has to be replaced by

$$\hat{G}_i(\alpha) = -q_i T_0 - \int_0^{T_0} \frac{k_i(x^0(\alpha_1 - \alpha_2 - \rho + \tau), \dots, x^0(\alpha_n - \alpha_i - \rho + \tau))}{x^0(\tau)} d\tau, \quad (3.17)$$

and  $\underline{Q}(\alpha)$  (3.13b) has to be replaced by

$$\hat{\underline{Q}}(\alpha) = \underline{G}(\alpha) - \left( \frac{1}{n} \sum \hat{G}_i(\alpha) \right) \underline{e}. \quad (3.18)$$

For a proof of Theorem 3.2 with  $\underline{Q}$  replaced by  $\hat{\underline{Q}}$ , an extension of Theorem 3.1 to systems with delay would be needed.

#### 4. Coupling of Two Oscillators

In this section the theory of the preceding section is applied to the coupling of two oscillators. This subject is interesting in its own right but also for its use in the analysis of larger systems.

Consider a system of two coupled oscillators satisfying the equations

$$\begin{aligned} \dot{u}_1 &= (v_1 - F(u_1))/\varepsilon, \\ \dot{v}_1 &= -(1 - \delta q)u_1 + \delta H(u_2(t - \rho), v_2(t - \rho)), \end{aligned} \quad (4.1a)$$

$$\begin{aligned} \dot{u}_2 &= (v_2 - F(u_2))/\varepsilon, \\ \dot{v}_2 &= -u_2 + \delta H(u_1(t - \rho), v_1(t - \rho)), \end{aligned} \quad (4.1b)$$

with  $\rho \geq 0$ ,  $q$  arbitrary, and with  $F$  and  $H$  satisfying the conditions mentioned in Sections 2 and 3. The coupling, represented by  $H$ , is symmetric. The constant  $\rho$



represents the delay in the coupling. The first oscillator has autonomous period  $T_0 + \delta q T_0 + 0(\delta^2) + 0(\varepsilon^{2/3})$ , whereas the autonomous period of the second oscillator is  $T_0 + 0(\varepsilon^{2/3})$ .

In order to find synchronized solutions we introduce the *phase shift function*

$$z(\nu) = - \int_0^{T_0} \frac{K(x^0(\tau - \nu))}{x^0(\tau)} d\tau, \quad (4.2a)$$

where

$$K(x^0) = H(x^0, y^0) = H(x^0, F(x^0)). \quad (4.2b)$$

It follows from (2.3c) that the derivative of  $z$  has the form

$$z'(\nu) = - \int_0^{T_0} \frac{K'(x^0(\tau - \nu))x^0(\tau - \nu)}{x^0(\tau)f(x^0(\tau - \nu))} d\tau - \frac{K(M) - K(-m) - K(-M) + K(m)}{x^0(\nu)}, \quad (4.2c)$$

where  $f = F'$  and where  $M = x^0(+0)$   $m = -x^0(-0)$ . Because of the discontinuity of  $x^0$ ,  $z'$  is discontinuous in  $kT_0/2$  ( $k$  integer). In most instances  $z(\nu)$  will have to be calculated numerically with  $x^0(t)$  calculated by means of (2.5).

With the aid of the phase shift function we can write for  $\hat{G}$

$$\begin{aligned} \hat{G}_1(\alpha) &= -qT_0 + z(\mu + \rho), \\ \hat{G}_2(\alpha) &= z(-\mu + \rho), \end{aligned} \quad (4.3)$$

where  $\mu$  denotes the phase difference between the two oscillators:

$$\mu = \alpha_1 - \alpha_2. \quad (4.4)$$

For  $\hat{Q}$  we obtain

$$\begin{aligned} \hat{Q}_1 &= \frac{1}{2}\hat{G}_1 - \frac{1}{2}\hat{G}_2 \\ \hat{Q}_2 &= -\hat{Q}_1 = \frac{1}{2}\hat{G}_2 - \frac{1}{2}\hat{G}_1. \end{aligned} \quad (4.5)$$

The synchronization condition of Theorem 3.2 for the point  $\underline{\alpha}$  is  $\hat{Q}(\underline{\alpha}) = \underline{0}$ . With the aid of the function  $S$ , defined by

$$S(\mu; \rho) = [z(\mu + \rho) - z(-\mu + \rho)]/T_0, \quad (4.6)$$

the *synchronization condition* gets the form

$$S(\bar{\mu}; \rho) = q, \quad (4.7a)$$

where  $\bar{\mu} = \bar{\alpha}_1 - \bar{\alpha}_2$ .

For the stability we consider the derivative of  $\hat{Q}$ , which has the form

$$\frac{1}{2}S' \begin{pmatrix} 1 & -1 \\ -1 & 1 \end{pmatrix}$$

where  $S' = [dS(\mu; \rho)/d\mu]$ . The eigenvalues of this matrix are 0 and 2. According to Theorem 3.2 the *stability condition* of the synchronized state is given by

$$S'(\bar{\mu}; \rho) = z'(\bar{\mu} + \rho) + z'(-\bar{\mu} + \rho) < 0. \tag{4.7b}$$

The period of the synchronized solution is given by

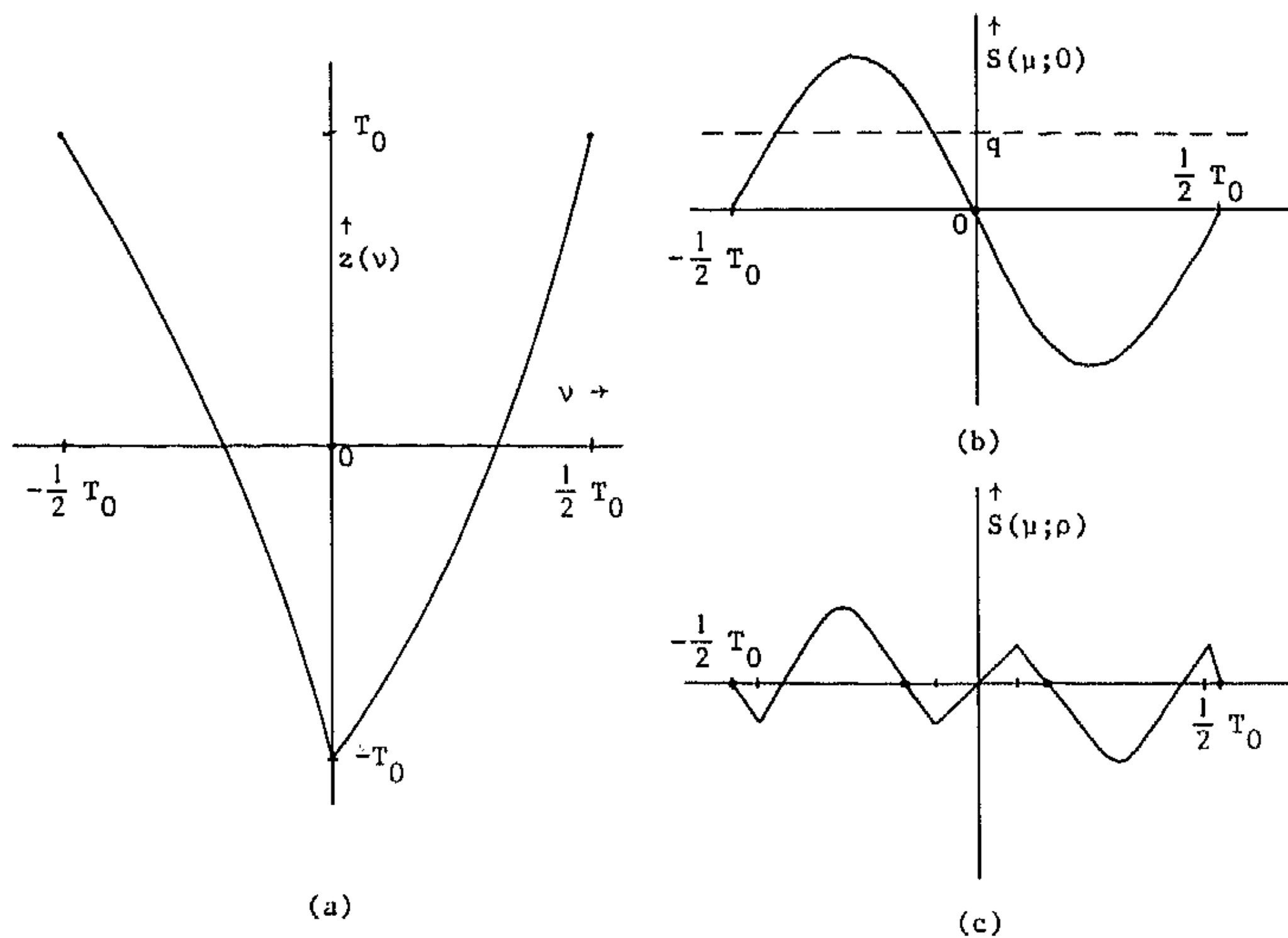
$$P_{\varepsilon, \delta} = T_0 + \delta q T_0 - \delta z(\bar{\mu} + \rho) + O(\delta^{3/2}) + O(\varepsilon^{2/3}). \tag{4.7c}$$

*Example 4.1.* Let  $F$  be given by formula (2.11) (*piecewise linear oscillator*) let  $q$  be arbitrary and let  $H(u, v) = u$ . According to (4.2a) and (2.14) the phase shift function is

$$z(\nu) = \begin{cases} e^{\nu(-T_0 + \frac{8}{3}\nu)} & 0 < \nu < T_0/2 \\ -z(\nu + T_0/2) & -T_0/2 < \nu < 0. \end{cases}$$

In Figure 4.1a  $z(\nu)$  is drawn, in Figure 4.1b  $S(\mu; 0)$  and in Figure 4.1c  $S(\mu; \rho)$  for  $\rho = T_0/10$ . It is seen that for  $q = 0$  (periods equal) Equation (4.7a) has 2 solutions  $\bar{\mu} = 0$  and  $\bar{\mu} = T_0/2$ . According to (4.7b) the solution  $\bar{\mu} = 0$  (equal phases) is stable since  $S'(0, 0) = z'(0) + z'(0)$  is negative. The period of this stable synchronized solution is greater than the period of the autonomous oscillators since  $z(0)$  is negative (4.7c). The solution with complementary phases is unstable. Note that the solution with equal phases is not stable for all types of coupling: if we take  $H(x, y) = -x$  all drawings in Figure 3 have to be mirrored with respect to the  $\mu$ -axis.

When  $|q| < \max S(\mu; 0)$ , that is, when the autonomous periods are not too far apart, Equation (4.7a) has one stable solution in which the faster of the two oscillators is running ahead (Fig. 4.1b).



**Fig. 4.1.** Phase shift function  $z(\nu)$  and the functions  $S(\mu; 0)$  and  $S(\mu; \rho)$ , illustrating Example 4.1

When  $q = 0$ ,  $\rho > 0$  the stable state  $\bar{\mu} = 0$  has been split up in two stable states I and II; the state  $\bar{\mu} = 0$  has become unstable and the state  $\bar{\mu} = T_0/2$  has become stable.

In Grasman and Jansen [13] system (4.1) has been integrated numerically for the case of two Van der Pol oscillators (Example 2.1) with equal periods ( $q = 0$ ) and with coupling given by  $H(x, y) = x$ . The results, for several values of the delay  $\rho$ , agree with asymptotic results derived in this section.

## 5. Coupling Via a Common Medium

In this section we investigate a system of oscillators governed by the equations

$$\begin{aligned} \dot{u}_i &= (v_i - F(u_i))/\varepsilon \\ \dot{v}_i &= -(1 - \delta q_i)u_i + \delta \sum_{j=1}^n H(u_j, v_j) \quad (i = 1, 2, \dots, n), \end{aligned} \quad (5.1)$$

One might describe this type of coupling by saying that the oscillators are coupled via a common medium. The contribution of the  $i$ th oscillator to this medium is given by  $\delta H(u_i, v_i)$  (see Fig. 1.1). The literature about this type of coupling and its applications have been discussed in the introduction (Section 1).

For an initial phase-vector  $\alpha$  the phase shift is given by (3.10b):

$$G_i(\alpha) = -q_i T_0 + \sum_{j=1}^n z(\alpha_i - \alpha_j), \quad (5.2)$$

where  $z$  is the phase shift function defined by (4.2). According to (3.10) and (3.14) the Poincaré map  $\mathcal{P}$  is approximated with inaccuracy  $\delta^{3/2}$  by  $\Phi R \Phi^{-1}$  where

$$R(\alpha) = \alpha + \delta G(\alpha) - \delta \ell \left( \frac{1}{n} \sum G_i(\alpha) \right). \quad (5.3a)$$

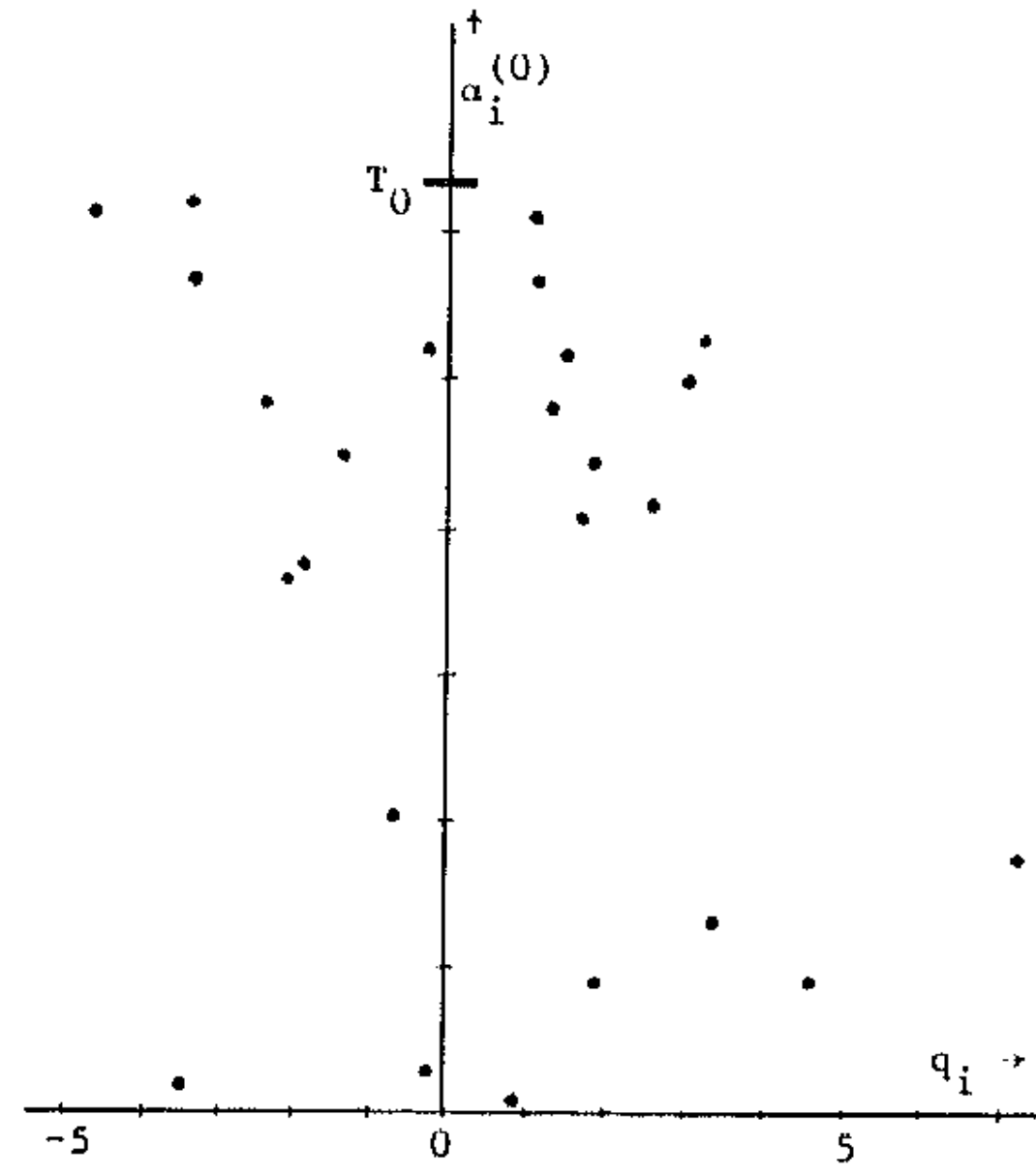
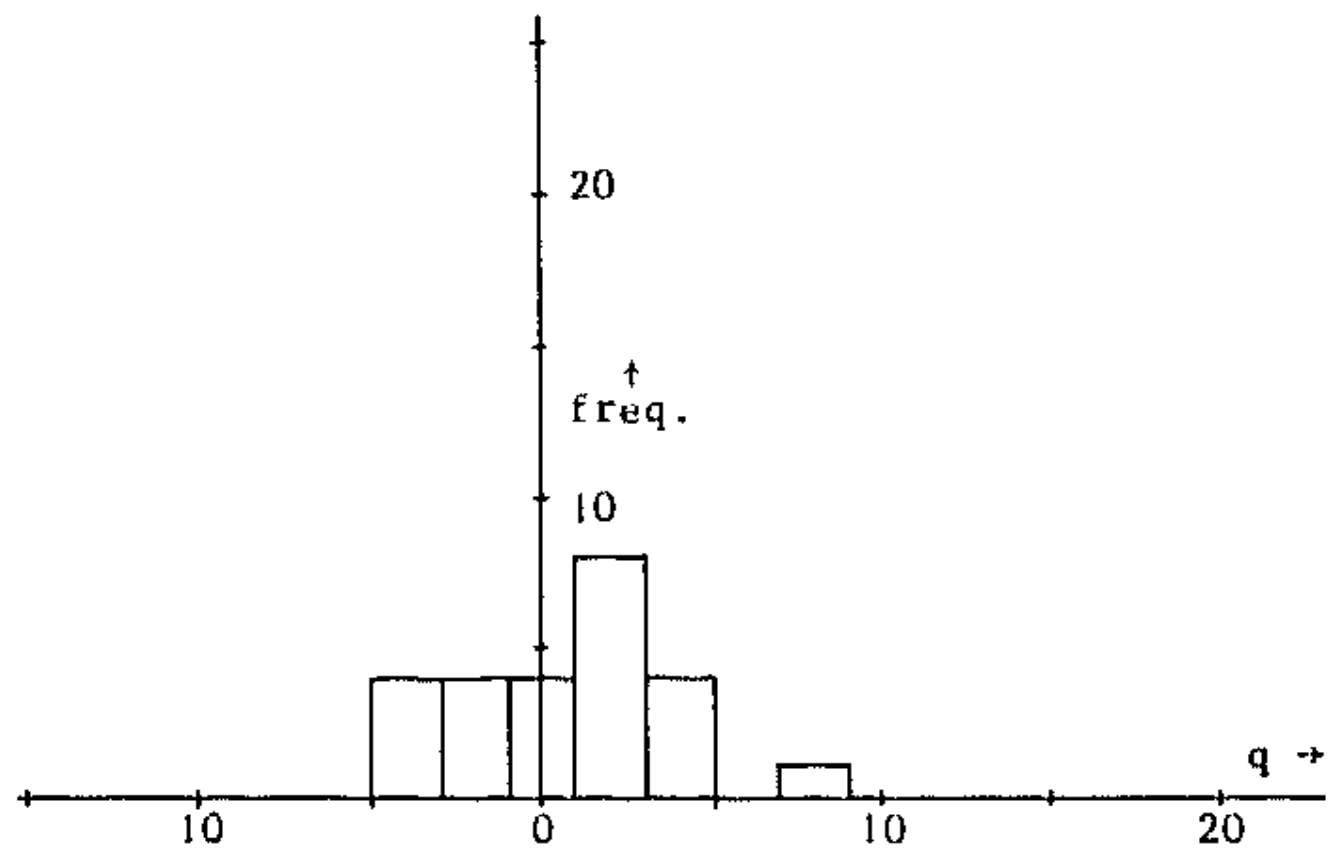
Consequently, synchronized solutions can be found by iteration of the mapping  $R$  with the scheme

$$\begin{aligned} \alpha^{(0)} &= \alpha \\ \alpha^{(k+1)} &= R(\alpha^{(k)}) \quad (k = 0, 1, \dots). \end{aligned} \quad (5.3b)$$

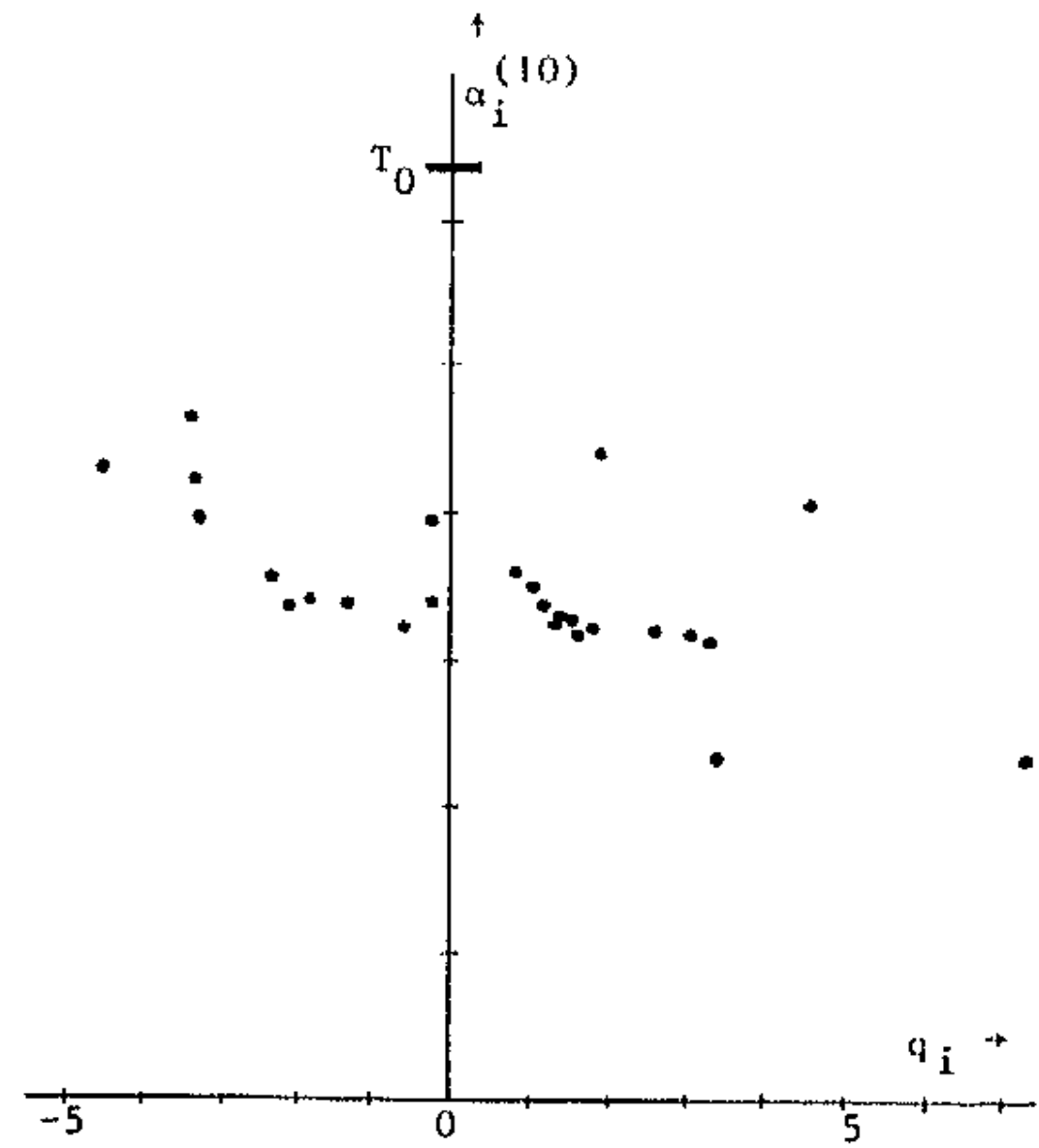
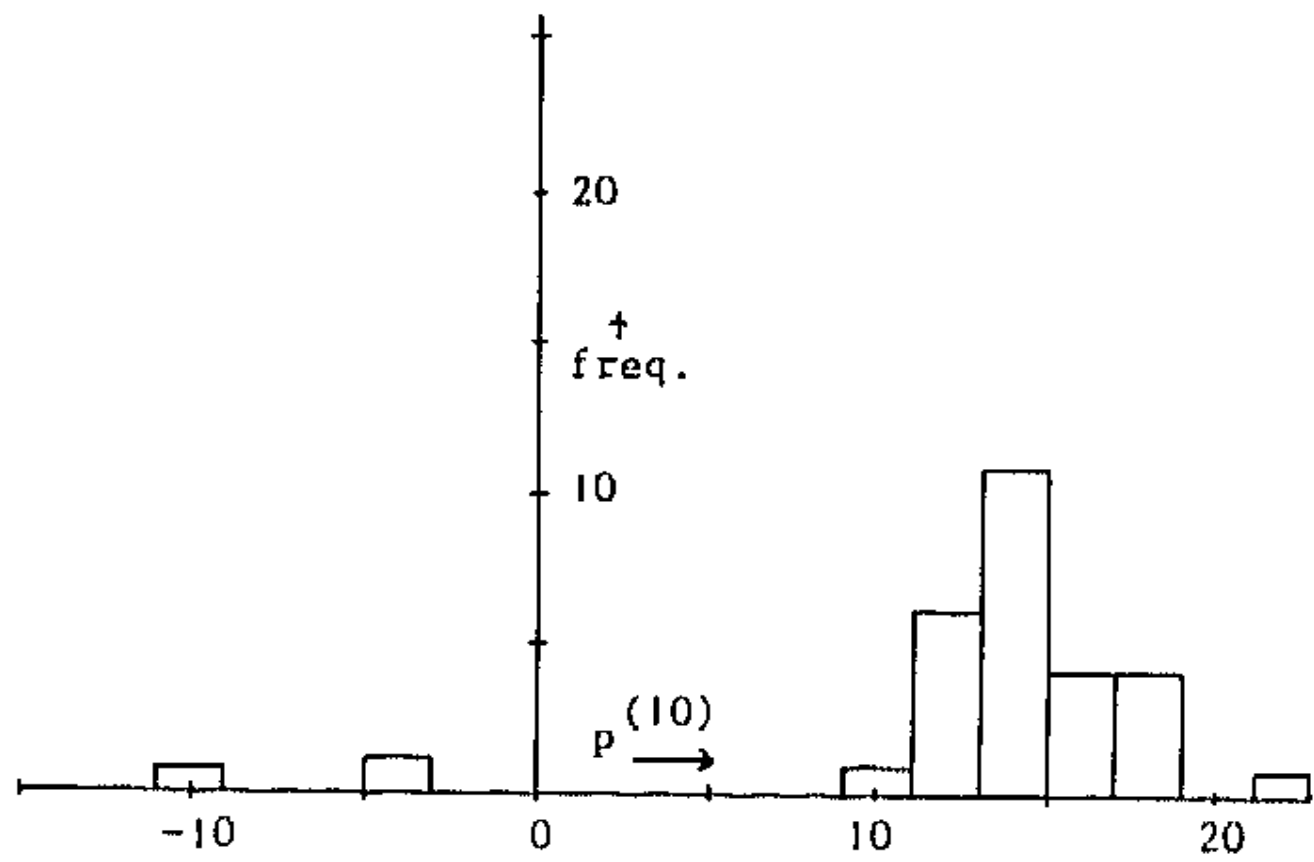
Moreover this iteration scheme can be used to follow the system in the course of time. In that case however the errors can accumulate on long time intervals.

*Numerical experiment.* Using (5.3) we followed the behaviour of 25 piecewise linear oscillators (see Example 2.2) coupled weakly via a common medium, with  $\delta = 0.02$  and  $H(u, v) = u$ . The autonomous period of the  $i$ th oscillator is  $(1 + \delta q_i)T_0$ , where the values of  $q_i$  are drawn independently from a Gaussian distribution with mean zero and standard deviation  $\sigma = 2.5$ . The initial phases were drawn independently from a homogeneous distribution over the interval  $[0, T_0)$ . The actual period of the  $i$ th oscillator at the  $k$ th iteration is given up to  $O(\delta^{3/2})$  by

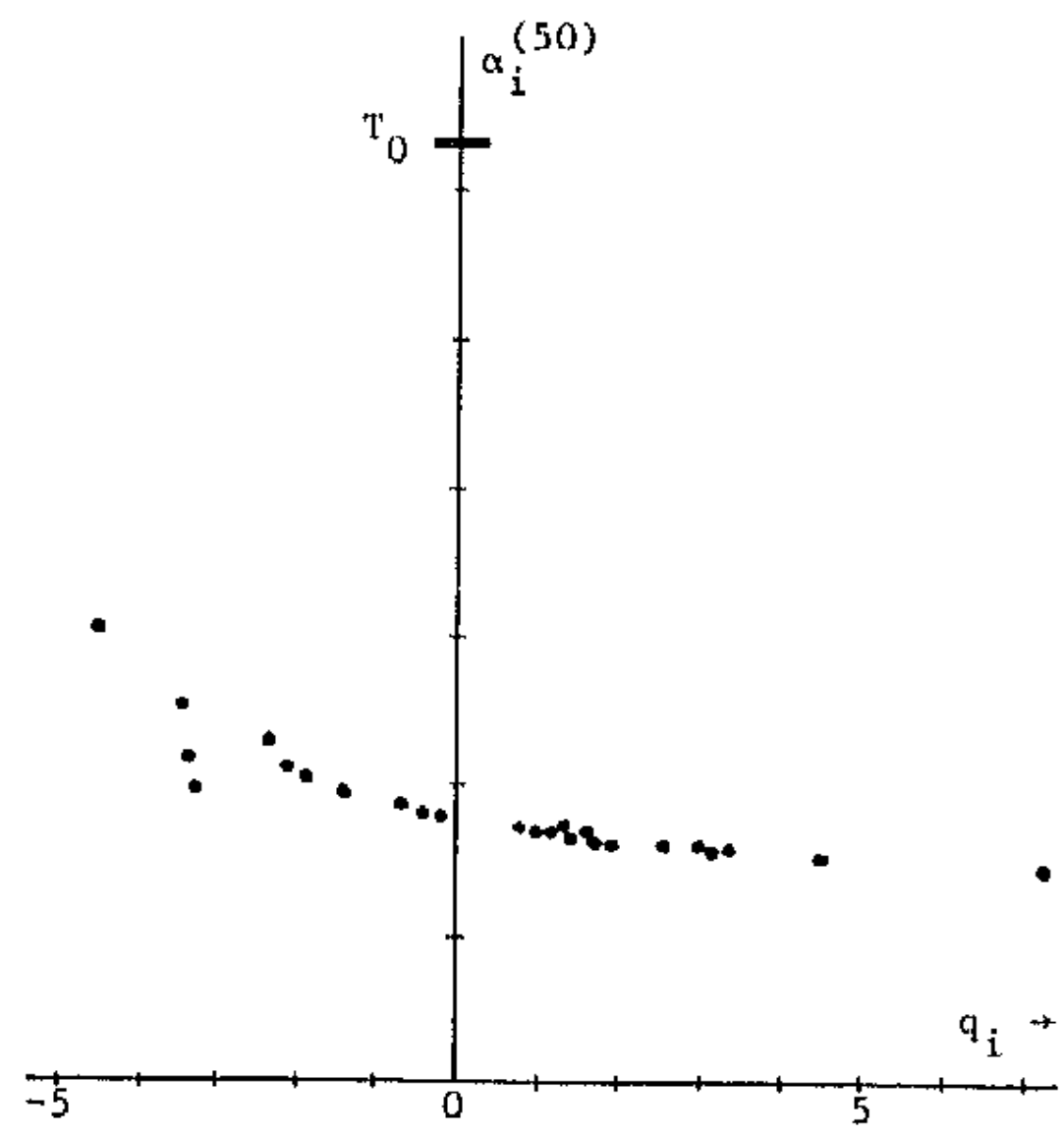
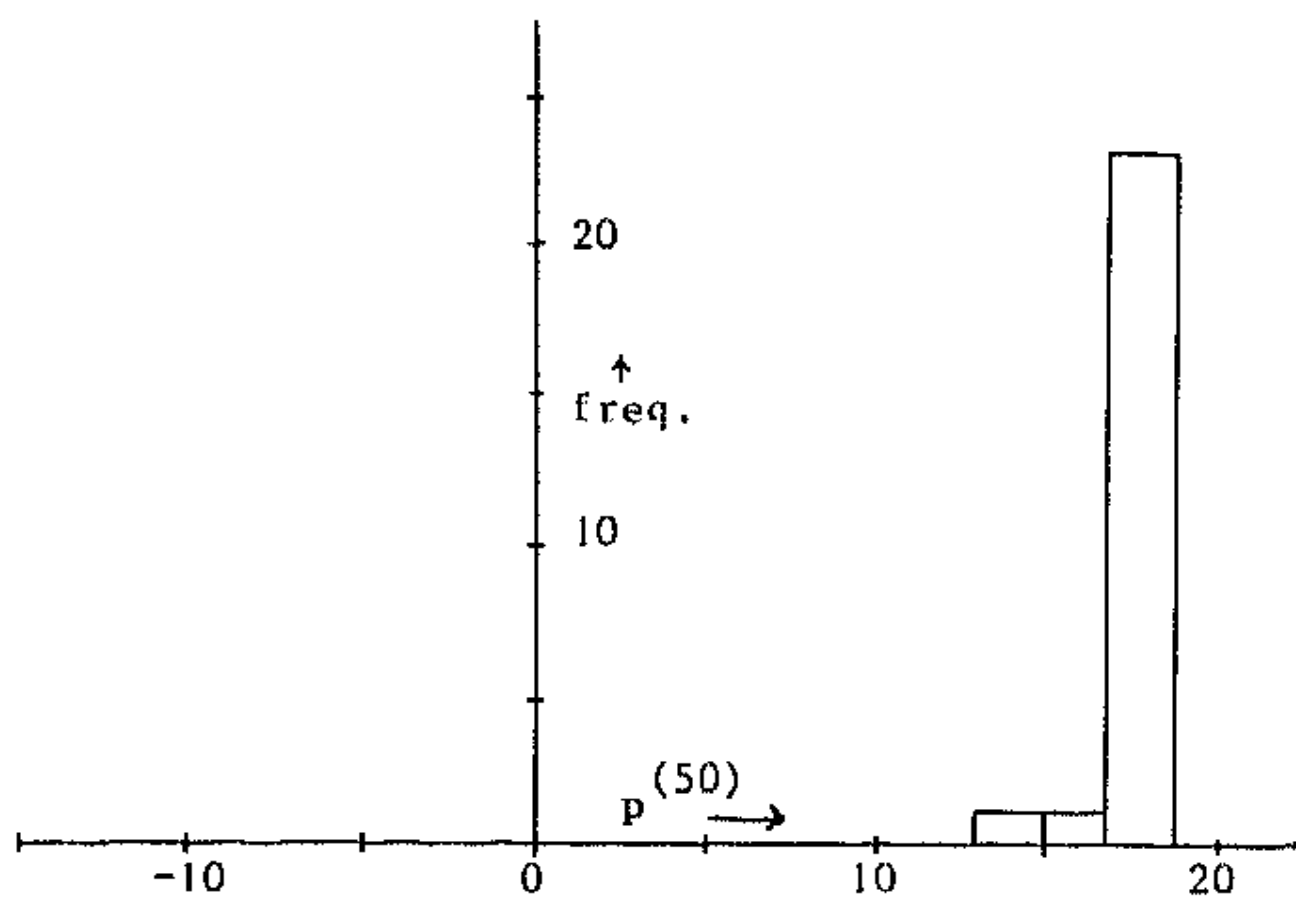
$$T_{(i)}^{(k)} = (1 + \delta p_i^{(k)})T_0 \quad (5.4a)$$



(a)



(b)



(c)

where

$$p_i^{(k)} = -G_i(\alpha_i^{(k)})/T_0. \quad (5.4b)$$

In Figure 5.1 it is shown how the histogram of the actual periods develops in the course of time. It is also shown how the phases  $\alpha_i^{(j)}$  behave as function of  $q_i$ . Some remarks have to be added to the text under this figure. It depends on the size of  $z(0)$  whether the synchronized period is increased or decreased (see previous section). In this example it increases. Moreover the synchronized period increases with increasing number of oscillators. It may even happen that the synchronized period is outside the range of the free periods. When the range of the free periods is too large a fully synchronized state (in which all actual periods are equal) is unattainable. This happened in our experiment. Nevertheless the system arrived in a well organized state of *partial synchronization*, in which only a few outsiders did not participate in the common rhythm.

## 6. Nearest Neighbour Coupling

In this section we investigate nearest neighbour coupling of a finite set of oscillators, arranged on a line, a circle and a torus. The results have been summarized in the introduction (Section 1). Analogous phenomena in biology have also been discussed there.

### 6.1. Oscillators on a Line

Let the position of an oscillator on a line be given by its index  $i$ . Then a system of such oscillators, with symmetrical coupling may be described by the equations

$$\begin{aligned} \dot{u}_i &= (v_i - F(u_i))/\epsilon \\ \dot{v}_i &= -(1 - \delta q_i)u_i + \delta h_i(\underline{u}, \underline{v}) \end{aligned} \quad (i = 1, 2, \dots, n), \quad (6.1a)$$

where

$$h_i(\underline{u}, \underline{v}) = \begin{cases} H(u_2, v_2) & (i = 1) \\ H(u_{i-1}, v_{i-1}) + H(u_{i+1}, v_{i+1}) & (i = 2, \dots, n-1) \\ H(u_{n-1}, v_{n-1}) & (i = n) \end{cases} \quad (6.1b)$$

*Numerical Experiment.* We investigated 51 piecewise linear oscillators (Example 2.2) on a line with  $H(u, v) = u$ ,  $q_i = -1.25 + (i-1)/20$ ,  $\delta = 0.1$ , and with initial phases  $\alpha_i = 0$ . According to Corollary 2.1 the autonomous periods of the

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**Fig. 5.1.** Development of synchronization for 25 piecewise linear oscillators coupled via a common medium (see 'numerical experiment'). (a) describes the situation for the uncoupled oscillators, in (b) and (c) the situation is drawn after 10 resp. 50 iterations of the Poincaré map. On the left the histograms are drawn of the actual periods (formula (5.4)). On the right points  $(q_i, \alpha_i^{(j)})$  are plotted. It can be seen that the mean of the actual periods is increased by the coupling. Moreover the variance of the actual periods decreases. Meanwhile a correlation develops between the free periods and the phases  $\alpha_i^{(j)}$ : the oscillators with the smallest free periods are running ahead in phase

singular approximations increase with increasing  $i$ :  $T_{(i)} = (1 + \delta q_i)T_0 + O(\delta^2)$ . We followed this system in the course of time by iterating the approximate Poincaré map (cf. (5.3)). After 200 iterations the system had arrived in a stable, well-organized state, in which, however, the oscillators were not completely synchronized (partial synchronization). The actual periods of the singular solutions are given by  $(1 + \delta p_i^{(200)})T_0 + O(\delta^{3/2})$  (see (5.4)). It can be seen in Figure 6.1a that the oscillators at the extremities are almost completely synchronized ( $p_i^{(200)}$  almost constant). In the middle of the line the actual periods change more or less continuously. The average period is increased by the interaction as in the previous example with coupling of the type  $H(u, v) = u$ .

Examination of Figure 6.1b and 6.1c shows that a wave pattern has developed although the synchronization is only partial. In a point  $i$  where  $\alpha_i \neq \alpha_{i+1}$  a local wave speed may be defined by  $1/(\alpha_i - \alpha_{i+1})$  (positions per unit of time). Waves are running from the faster oscillators (left) to the slower ones (right). At the right extreme a rudimentary wave is running in the opposite direction.

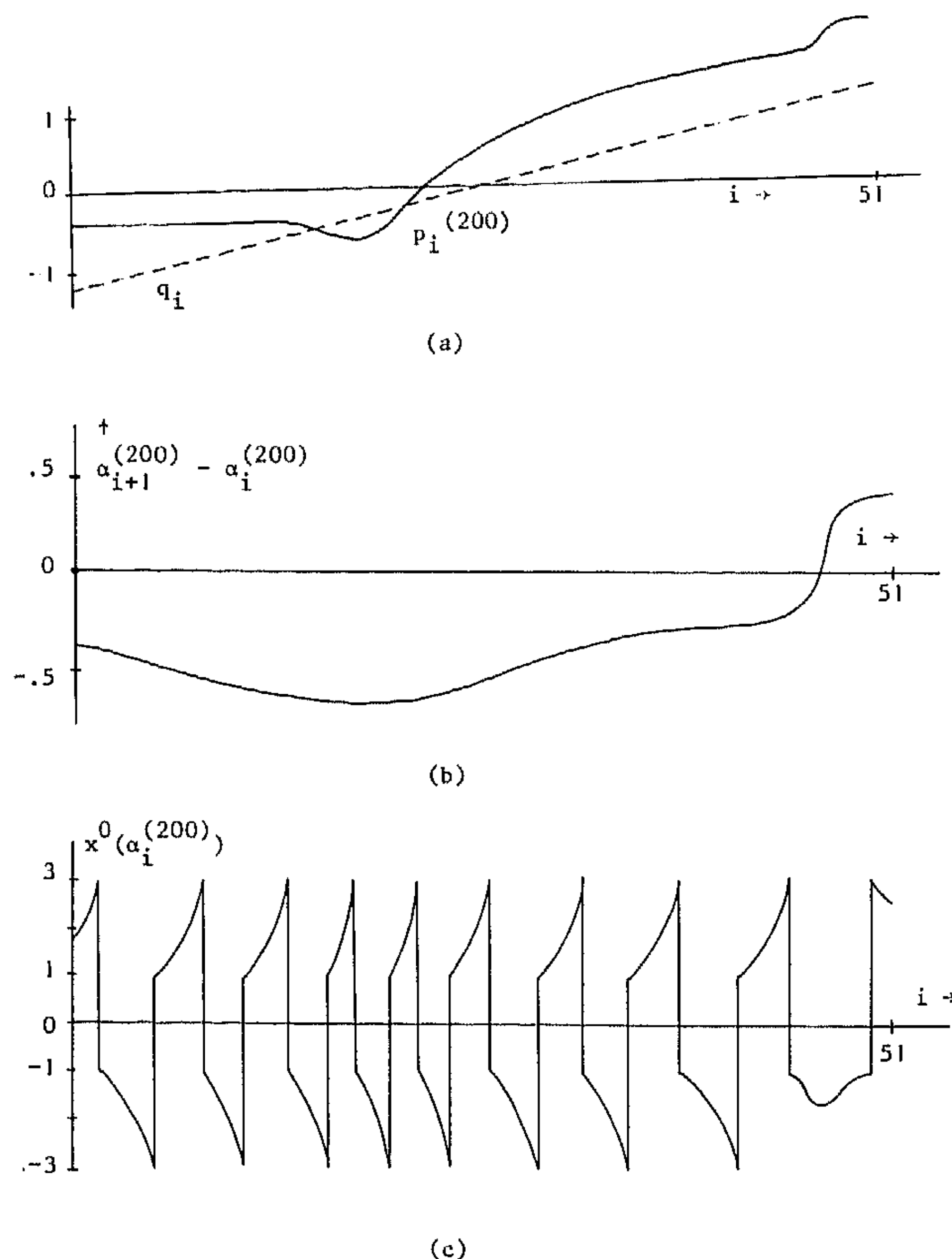


Fig. 6.1. Piecewise linear oscillators on a line (continuous representation)

### 6.2. Oscillators on a Circle

We consider a system of  $N$  identical oscillators on a circle coupled with delay  $\rho$ :

$$\begin{aligned} \dot{u}_j &= (v_j - F(u_j))/\varepsilon \\ \dot{v}_j &= -u_j + \delta h_j(\underline{u}, \underline{v}) \end{aligned} \quad (j = 1, 2, \dots, N), \quad (6.2a)$$

where the coupling is given by

$$h_j(\underline{u}, \underline{v}) = H(\hat{u}_{[j-1]}, \hat{v}_{[j-1]}) + H(\hat{u}_{[j+1]}, \hat{v}_{[j+1]}), \quad (6.2b)$$

with

$$\begin{aligned} \hat{u}_j(t) &= u_j(t - \rho), & \hat{v}_j(t) &= v_j(t - \rho), \\ [j] &= j \pmod{N} = \begin{cases} N & (j = 0) \\ j & (j = 1, 2, \dots, N) \\ 1 & (j = N + 1) \end{cases} \end{aligned} \quad (6.2c)$$

The 1st and  $N$ th oscillators are neighbours. In this way the boundaries, present in the linear arrangement, are removed, which enables us to perform a complete analysis with the methods of Section 3.

Stable synchronized solutions are found by applying Theorem 3.2 to the mapping  $\hat{Q}(\alpha)$  given by (3.17):

$$\hat{Q}(\alpha) = \hat{G}(\alpha) - \left( \frac{1}{N} \sum \hat{G}_j(\alpha) \right) \underline{1}, \quad (6.3a)$$

where  $\hat{G}$  is derived from (6.2), (3.16) and (3.7):

$$\hat{G}_j(\alpha) = z(\alpha_j - \alpha_{[j-1]} + \rho) + z(\alpha_j - \alpha_{[j+1]} + \rho), \quad (6.3b)$$

with  $z$  the phase shift function defined by (4.2).

We shall investigate wave-solutions  $\underline{\alpha}$  for which the phase-difference between neighbouring oscillators is constant:

$$\alpha_j - \alpha_{[j-1]} = \mu \quad (j = 1, 2, \dots, N). \quad (6.4a)$$

Since the wave must fit on the circle, the constant  $\mu$  must satisfy the condition

$$\mu = nT_0/N \quad (n = 0, 1, \dots, N - 1). \quad (6.4b)$$

It follows from (6.3) that for such a wave the function  $G_j(\underline{\alpha})$  is independent of  $j$ , which implies that the *synchronization condition* of Theorem 3.2 is satisfied:  $\hat{Q}(\underline{\alpha}) = \underline{0}$ . The *stability condition* of Theorem 3.2 says that all except one of the eigenvalues of the derivative of  $\hat{Q}$  with respect to  $\alpha$  must have negative real parts. The matrix of the derivative is obtained from (6.3):

$$\frac{\partial \hat{Q}_j}{\partial \alpha_k}(\underline{\alpha}) = (\delta_{j,k} - \delta_{[j-1],k})z'(\mu + \rho) + (\delta_{j,k} - \delta_{[j+1],k})z'(-\mu + \rho), \quad (6.5)$$

where  $\delta_{j,k}$  is Kronecker's symbol. One easily verifies that (6.5) has  $N$  eigenvectors  $c^{(n)}$  ( $n = 0, 1, \dots, N - 1$ ), with components

$$c_k^{(n)} = \exp(ik\gamma^{(n)}) \quad (\gamma^{(n)} = 2\pi n/N), \quad (6.6a)$$

( $i$  is the imaginary unit) and with eigenvalues

$$\begin{aligned} \lambda^{(n)} = & [z'(\mu + \rho) + z'(-\mu + \rho)](1 - \cos \gamma^{(n)}) \\ & + i[z'(\mu + \rho) - z'(-\mu + \rho)] \sin \gamma^{(n)}. \end{aligned} \quad (6.6b)$$

Since  $1 - \cos \gamma^{(n)} > 0$  ( $n = 1, 2, \dots, N - 1$ ), a sufficient condition for stability is

$$z'(\mu + \rho) + z'(-\mu + \rho) < 0. \quad (6.7)$$

Comparison with the stability condition for two oscillators (4.7b) shows that local stability implies global stability. The period of the synchronized solution is given by

$$P_{\varepsilon, \delta} = T_0 - \delta[z(\mu + \rho) + z(-\mu + \rho)] + O(\delta^{3/2}) + O(\varepsilon^{2/3}). \quad (6.8)$$

*Example.* Consider 25 piecewise linear oscillators (Example 2.2) with coupling given by  $H(u, v) = u$  and  $\rho = 0$ . The phase shift function  $z$ , corresponding to this case is given by (4.8) (see also Fig. 4.1a). Stable waves with  $\mu = nT_0/N$  are found for  $n = 1, 2, \dots, 6$ . For  $n = 24, 23, \dots, 19$  stable waves traveling in the opposite direction are obtained. In the case  $n = 0$ , in which all oscillators have equal phases (bulk oscillation), stability condition (6.7) does not apply since  $z(\nu)$  is discontinuous in  $\nu = 0$  (see remarks at the end of Section 3). This case has been investigated numerically by iteration of the approximate Poincaré mapping  $I + \delta Q$ . Experiments showed that the bulk oscillation is stable: in calculations with random initial values the system tended to one of the above stable waves or to the bulk oscillation. It follows from (6.7) that introduction of a delay destabilizes the bulk oscillation (see Fig. 4.1a). This phenomenon was already observed in the case of two oscillators (same stability condition).

### 6.3. Oscillators on a Torus

Let the position of an oscillator on a torus be given by a double index  $i, j$ . Then a system of identical oscillators on a torus with delayed coupling between direct neighbours may be described by

$$\begin{aligned} \dot{u}_{j,k} &= (v_{j,k} - F(u_{j,k}))/\varepsilon \quad (j = 1, 2, \dots, N) \\ \dot{v}_{j,k} &= -u_{j,k} + \delta h_{j,k}(\hat{u}, \hat{v}) \quad (k = 1, 2, \dots, M), \end{aligned} \quad (6.9a)$$

where

$$\begin{aligned} h_{j,k}(\hat{u}, \hat{v}) &= H(\hat{u}_{[j-1,k]}, \hat{v}_{[j-1,k]}) + H(\hat{u}_{[j+1,k]}, \hat{v}_{[j+1,k]}) \\ &+ H(\hat{u}_{[j,k-1]}, \hat{v}_{[j,k-1]}) + H(\hat{u}_{[j,k+1]}, \hat{v}_{[j,k+1]}), \end{aligned} \quad (6.9b)$$

where “ $\hat{\phantom{x}}$ ” denotes the delay  $\rho$  and where

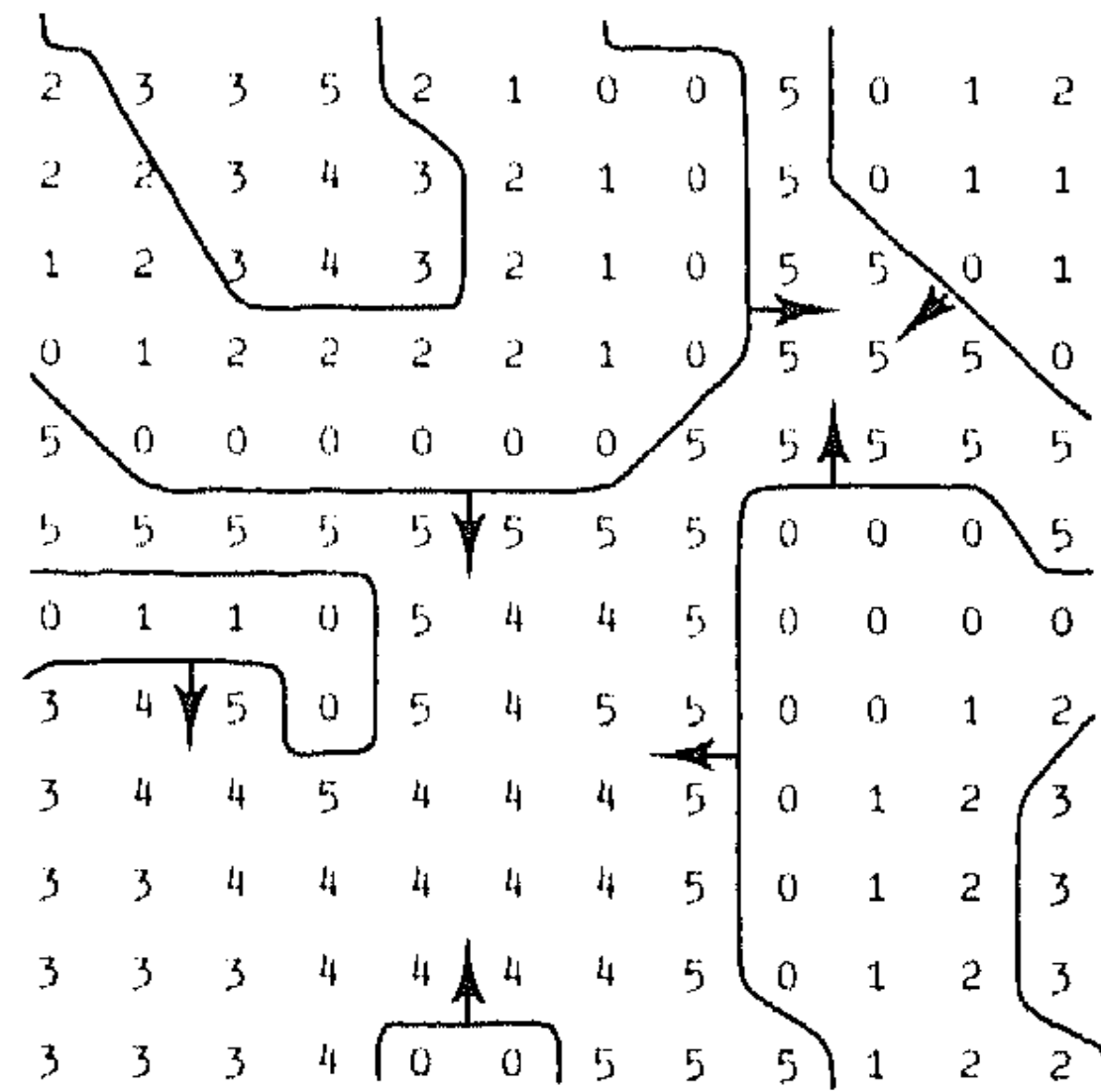
$$[j, k] = j(\text{modulo } N), k(\text{modulo } M), \quad (6.9c)$$

(see (6.2c)).

The torus is a simple two dimensional structure without boundary elements. The synchronization properties can be completely analyzed. The analysis and the results are completely analogous to those for the circle. We restrict ourselves to a statement of the results.



**Fig. 6.2.** Piecewise linear oscillators on a torus, illustrating numerical experiment. The right and left boundaries are connected, as well as the upper and lower boundaries. The phase  $\phi$  of each oscillator is indicated by the rounded off value of  $6\phi/T_0$ . Wave fronts and their direction are indicated by lines and arrows. At the start of the experiment phases were assigned randomly. The figure represents the state after 50 iterations of the Poincaré map



A synchronized wave solution  $\tilde{\alpha}$  satisfies

$$\begin{aligned}\tilde{\alpha}_{[j+1,k]} - \tilde{\alpha}_{[j,k]} &= \nu = nT_0/N \quad (n = 0, 1, \dots, N-1) \\ \tilde{\alpha}_{[j,k+1]} - \tilde{\alpha}_{[j,k]} &= \mu = mT_0/N \quad (m = 0, 1, \dots, M-1).\end{aligned}\tag{6.10}$$

A sufficient condition for stability is

$$\begin{aligned}z'(\mu + \rho) + z'(-\mu + \rho) &< 0 \\ z'(\nu + \rho) + z'(-\nu + \rho) &< 0.\end{aligned}\tag{6.11}$$

This means that the stability condition on a torus can be decomposed in two stability conditions on a circle (6.7). Note that (6.7) is the same as (4.7b) for two oscillators. The period of the wave solution satisfies

$$\begin{aligned}P_{\epsilon,\delta} &= T_0 - \delta[z(\mu + \rho) + z(-\mu + \rho) + z(\nu + \rho) + z(-\nu + \rho)] \\ &\quad + O(\delta^{3/2}) + O(\epsilon^{2/3}).\end{aligned}\tag{6.12}$$

*Numerical Experiment.* We considered 144 piecewise linear oscillators with  $M = N = 12$  and  $\rho = 0.02 T_0$ . The initial phases were drawn independently from a homogeneous distribution on  $[0, T_0)$ . After 50 iterations of  $I + \delta \hat{Q}$  the system had reached a state as sketched in Figure 6.2, instead of one of the stable waveforms described by (6.10) and (6.11). Chaotic waves were running over the torus with wave centres that appeared and disappeared spontaneously. It is not known whether the system would ultimately reach one of the stable waveforms derived above. We only observed that the system persisted in its chaotic state for an extended period of time.

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## References

1. Aschoff, J. (ed.): Circadian clocks. Amsterdam: North-Holland 1965
2. Auchmuty, J. F. G., Nicolis, G.: Bifurcation analysis of reaction diffusion equations—III, chemical oscillations, Bull. Math. Biol. **38**, 325–350 (1976)
3. Brown, B. N., Duthie, H. L., Horn, A. R., Smallwood, R. H.: A linked oscillator model of electrical activity of human small intestine, Am. J. Physiol, **229**, 384–388 (1975)

4. Brown, F. A., Hastings, J. W., Palmer, J. D.: The biological clock: two views. New York: Academic Press 1970
5. Cohen, M. H.: Models of clocks and maps in developing organisms, in: Lectures on mathematics in the life sciences, Vol. 3, American Mathematical Society, Providence, Rhode Island, 1972
6. Cole, J. D.: Perturbation methods in applied mathematics. Blaisdell, Massachusetts: Ginn 1968
7. Cronin, J.: Some mathematics of biological oscillations, *SIAM Review*, **19**, 100–138 (1977)
8. Diekmann, O., Temme, N. M. (eds.): Nonlinear diffusion problems, Amsterdam: Mathematical Centre 1976
9. Fitzhugh, R.: Impulses and physiological states in theoretical models of nerve membranes, *Biophysical J.* **1**, 445–466 (1961)
10. Glansdorff, P., Prigogine, J.: Thermodynamic theory of structure stability and fluctuations. New York: Wiley-Interscience 1971
11. Goebber, F., Seelig, F. F.: Conditions for the application of the steady state approximation to systems of differential equations, *J. Math. Biol.* **2**, 76–86 (1975)
12. Goodwin, B., Cohen, M.: A phase shift model for the spatial and temporal organization of developing systems, *J. Theor. Biol.* **25**, 49–107 (1969)
13. Grasman, J., Jansen, M. J. W.: Mutually synchronized relaxation oscillations. Mathematical Centre, Report TN 82/76 (1976)
14. De Haan, R. L., Hikarow, R.: Synchronization of pulsation rates in isolated cardiac myocytes, *Exp. Cell. Res.* **70**, 214–220 (1972)
15. Hale, J. K.: Ordinary differential equations. New York: Wiley-Interscience 1969
16. Heineken, F. G., Tsuchiya, H. M., Aris, R.: On the mathematical status of the pseudo-steady state hypothesis of biochemical kinetics, *Math. Biosci.* **1**, 95–113 (1967)
17. Hirsch, M. W., Smale, S.: Differential equations, dynamical systems and linear algebra. New York: Academic Press 1974
18. Hoppensteadt, F.: Properties of solutions of ordinary differential equations with small parameters, *Comm. Pure and Appl. Math.*, Vol. 24, 807–840 (1971)
19. Jansen, M. J. W.: Synchronization of weakly coupled relaxation oscillators, *Math. Centre Report*, TW 180/78 (1978)
20. Kuramoto, Y.: Self entrainment of a population of coupled nonlinear oscillators, in: *Int. Symp. on Math. Probl. in theor. physics*, H. Araki (ed.), *Lecture Notes in Physics* **39**, 420–422. Berlin Göttingen, Heidelberg: Springer 1975
21. Lasalle, J.: Relaxation oscillations, *Quart. J. Appl. Math.* 1–19 (1949)
22. Linkens, D. A.: Analytical solution of large numbers of mutually coupled nearly sinusoidal oscillators, *IEEE Trans. Circ. Syst. CAS-21*, 294–300 (1974)
23. Linkens, D. A., Rimmer, S. J., Datardina, S. P.: Spectral analysis of coupled non-linear oscillators under modulation conditions with reference to intestinal modellings, *Comput. Biol. Med.* **8**, 125–137 (1978)
24. Mayeri, E.: A relaxation oscillator description of the burst generating mechanism of the cardiac ganglion of the lobster, *J. Gen. Physiol.* **62**, 473–488 (1973)
25. Mishchenko, E. F., Pontryagin, L. S.: Derivation of some asymptotic estimates for solutions of differential equations with a small parameter in the derivatives (in Russian). *Izv. Akad. Nauk. SSSR, ser. mat.*, **23**, 643–660 (1959)
26. Mishchenko, E. F.: Asymptotic calculation of periodic solutions of systems of differential equations containing small parameters in the derivatives, *Izv. Akad. Nauk SSSR, ser. mat.*, **21** (1957), 627–654. *AMS Translations, series 2, Vol. 18*, 199–230 (1961)
27. Moe, G. K., Rheinboldt, W. C., Abildskov, J. A.: A computer model of atrial fibrillation, *Am. Heart J.* Vol. 67, 200–220 (1964)
28. Othmer, H. G.: Current problems in pattern formation, in: *Lectures on mathematics in the life science*, vol. 9. (American Mathematical Society, Providence, Rhode Island, 1977)
29. Pavlidis, T.: Populations of biochemical oscillators as circadian clocks, *J. Theor. Biol.* **33**, 319–338 (1971)

30. Pavlidis, T.: *Biological oscillators; their mathematical analysis*. New York: Academic Press 1973
31. Peskin, C. S.: *Mathematical aspects of heart physiology* (Courant Institute of Mathematical Sciences, New York University, 1975)
32. Pol, B. van der: On 'relaxation oscillations'. *The London, Edinburgh and Dublin Philosophical Magazine and Journal of Science* (7), 2, 978–992 (1926). Also in: H. Bremmer and C. J. Bouwkamp (eds.), *Balthasar Van der Pol: Selected scientific papers*. Amsterdam: North-Holland pub. cy. 1960
33. Pol, B. van der, Mark, J. van der: The heartbeat considered as a relaxation oscillation and an electrical model of the heart, *Phil. Mag.* Vol. VI, 763–773 (1928), also in: Balthasar Van der Pol selected scientific papers (see [32])
34. Pontryagin, L. S.: Asymptotic behaviour of solutions of systems of differential equations with a small parameter in the higher derivatives, *Izv. Akad. Nauk SSSR, Ser. mat.* 21, 605–626 (1957). *AMS Translations, series 2, Vol. 18*, 295–320 (1961)
35. Sachs, H. G., De Haan, R. L.: Embryonic myocardial cell aggregates: volume and pulsation rate, *Developmental Biology*, 30, 233–240 (1973)
36. Stoker, J. J.: *Nonlinear vibrations*. New York: Interscience 1950
37. Tikhonov, A. N.: Systems of differential equations with small parameters in the derivatives (in Russian), *Mat. Sbornik*, vol. 31, (73), 575–586 (1952)
38. Torre, V.: Synchronization of nonlinear biochemical oscillators coupled by diffusion, *Biol. Cybernetics* 17, 137–144 (1975)
39. Wiener, N.: *Nonlinear problems in random theory*. Cambridge, Mass.: MIT Press 1958
40. Winfree, A. T.: Biological rhythms and the behaviour of populations of coupled oscillators, *J. Theor. Biol.* 16, 15–42 (1967)
41. Zhabotinski, A. M., Zaikin, A. N.: Autowave processes in a distributed chemical system, *J. Theor. Biol.* 40, 45–61 (1973)

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