On non-standard numerical integration methods for biological oscillators

Andrew Hone*

Isaac Newton Institute for Mathematical Sciences,
20 Clarkson Road, Cambridge CB3 0EH, UK.
anwh@kent.ac.uk

Abstract. Mathematical models of biological processes, whether they be the dynamics of populations of individuals, cell populations within an organism, or reactions between different chemical species within a cell, are traditionally formulated in terms of differential equations. For a given model, specified by a system of differential equations, in the generic situation one is unable to solve the equations explicitly, and one must resort to numerical integration methods. There are many standard numerical techniques, both in the literature and in readily available software packages. However, these techniques do not always reproduce the required qualitative features of the solutions, particularly if the system shows regular oscillations and the integration is performed over long time periods. This article highlights some non-standard discretization methods appearing in the work of Kahan, Mickens and others, which have the potential to be extremely useful in modelling biological systems.

1 Introduction

The purpose of this article is to draw attention to some interesting developments in numerical analysis, and more specifically in numerical integration methods for ordinary differential equations, which have taken place over the last twenty years or so, but have only started to filter into the wider scientific community more recently. There is a vast literature on numerical integration, and the standard methods for integrating ordinary differential equations, namely Euler's method, Runge-Kutta methods and their adaptive versions (Runge-Kutta-Fehlberg), and multi-step methods (Adams-Bashforth-Moulton) are described in many introductory texts on differential equations (e.g. [30]) and have been implemented in numerous software packages that are both highly sophisticated and readily available. While the aforementioned techniques are rather successful at dealing with generic differential equations, they can often come unstuck for some particular problems of interest that arise in applications, particularly when such problems exhibit special properties such as symmetries or conservation laws, or when there are solutions with some special structure. Indeed, standard numerical integrators can completely fail to capture the correct qualitative nature of

* On leave from Institute of Mathematics, Statistics & Actuarial Science, University of Kent, Canterbury CT2 7NF, UK.

the solutions of such problems, and can be extremely inefficient at providing accurate results. In contrast, for numerical integration of differential equations that preserve a measure or symplectic structure [29], and those that have conserved quantities [27] or are even completely integrable [28], there are a variety of *ad hoc* methods that give more accurate and qualitatively correct solutions with greater efficiency, because they retain the same features as the original differential equations. A general approach to numerical integration based on incorporating the symmetry structure of a problem into a numerical scheme is known as geometric integration [4]. While symmetries and conservation laws are common in physics, and especially in mechanics, most differential equation models of biological systems do not exhibit any particular symmetry. Nevertheless, these biological models can have particular special solutions (which, most importantly, are often attractors in the space of all solutions) whose features are missed by conventional numerical integrators. For such systems, some relevant techniques for constructing non-standard or unconventional integration methods has been developed in various works by Mickens, Kahan and other researchers. It is the latter set of techniques that are outlined here.

To understand some of the problems that can arise with numerical integration schemes, it is instructive to consider a very simple example, namely the ordinary differential equation describing the logistic growth of a population:

$$\dot{r} = \rho r(1 - r/K). \tag{1}$$

In the above, $r = r(t)$ denotes the size of a population with linear growth rate $\rho > 0$, $\dot{r} = dr/dt$ is the rate of change of the population, and $K > 0$ is the carrying capacity, which is the stable limiting population size as $t \to \infty$. If one performs a numerical integration of this system using the simplest technique available, namely the forward Euler method, then one obtains the logistic difference equation

$$\frac{r_{t+h} - r_t}{h} = \rho r_t(1 - r_t/K), \tag{2}$$

where $r_t \approx r(t)$ denotes the approximation to the solution of the ordinary differential equation at time t. The important thing to notice about (2) is that, while it gives reasonable approximations to the solutions of (1) for small enough h, it also displays behaviour not present in the original model: as h increases the steady state K becomes unstable and goes through an infinite series of period-doubling bifurcations leading to chaos [7]. Although the Euler method is the crudest possible technique for numerical integration, this example illustrates the point that discretization can introduce properties of the solutions that are not present in the original continuous system.

In the next section, to set the scene, Kahan's unconventional discretization [24] of the classic Lotka-Volterra predator-prey model is presented, and the solutions of this discrete model are compared with the results of solving the corresponding ordinary differential equation using a standard numerical package, namely Maple, implementing the Fehlberg fourth-fifth order Runge-Kutta

(RKF45) method. Kahan's general technique for discretizing quadratic vector fields is described, and another non-standard discretization of the same system, due to Mickens, is also mentioned for comparison. The third section is concerned with a model of a trimolecular reaction that exhibits a Hopf bifurcation and a limit cycle (for a suitable range of parameters). By following the guidelines for discretization due to Mickens, a discrete version of this trimolecular reaction model is obtained, and the properties of its solutions are compared with the continuous case. The final section contains some conclusions.

2 Discretization of predator-prey models

The classic Lotka-Volterra model for the interaction between a predator population $P(t)$ and its prey $N(t)$, both specified at time t, has the form

$$\dot{N} = N(a - bP), \qquad \dot{P} = P(cN - d)$$

for positive parameters a, b, c, d. Upon rescaling N, P and t it can be reduced to the dimensionless form

$$\dot{x} = x(1 - y), \qquad \dot{y} = y(x - \alpha), \tag{3}$$

which depends on the single parameter $\alpha > 0$. For the interpretation as a predator-prey model the variables x, y are considered only in the positive quadrant $x \geq 0$, $y \geq 0$. There are two steady states of the system: the fixed point (steady state) at the origin $(0, 0)$ is an unstable saddle point, while linearization around the steady state at $(\alpha, 1)$ gives imaginary eigenvalues and hence a neutrally stable centre. (The reader who is unfamiliar with linear stability analysis should consult the first volume of [18], or [11].)

A complex conjugate pair of imaginary eigenvalues of the Jacobian, at a fixed point in the plane, corresponds to periodic orbits around this point in the linearized system, but then the linear analysis is insufficient to determine the nature of the orbits for the original nonlinear system. However, in this case it turns out that all the non-trivial orbits for the nonlinear system (3) in the interior of the positive quadrant are actually periodic, lying on closed curves $H = H(x, y) =$ constant encircling the point $(\alpha, 1)$, where

$$H = \log(x^\alpha y) - x - y. \tag{4}$$

The shape of twenty of these orbits can be seen in figure 1, in the case $\alpha = 1$. The quantity H is conserved along trajectories, and in fact the system can be written in the non-canonical Hamiltonian form

$$\dot{x} = xy\frac{\partial H}{\partial y}, \qquad \dot{y} = -xy\frac{\partial H}{\partial x},$$

so that (3) is analogous to a conservative system in classical mechanics, with H corresponding to the "energy" (which is neither created nor destroyed). Moreover

the oriented area element (symplectic form)

$$\omega = \frac{1}{xy} dx \wedge dy$$

is preserved by the flow.

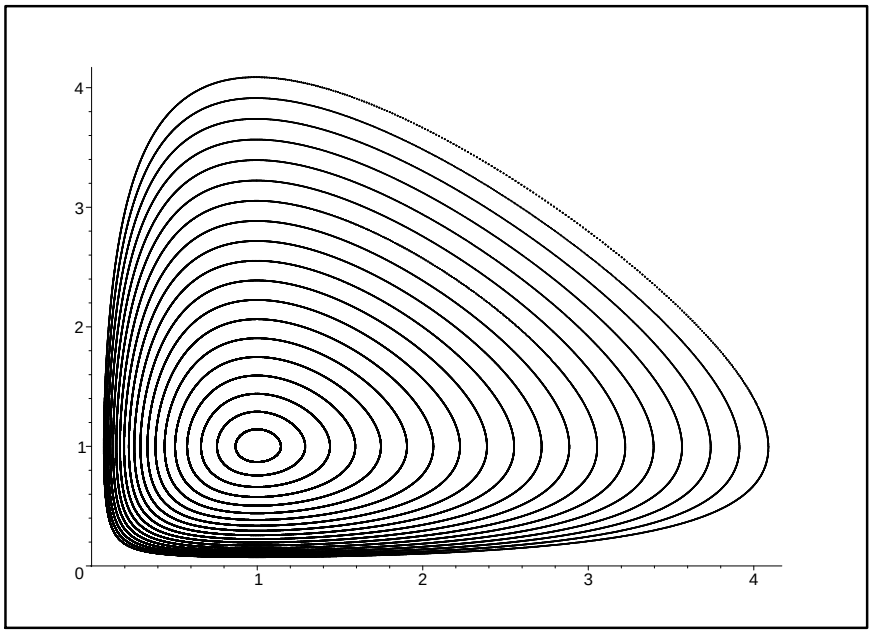

Fig. 1. Twenty orbits of the predator-prey system (3) with $\alpha = 1$, generated with Kahan's discretization (5).

Standard numerical integration schemes reproduce the shape of the orbits of (3) for relatively short times, but a well known problem is that such schemes do not preserve energy, so that over long times the orbits produced numerically either spiral inwards or outwards. To see an example of this, here version 10 of Maple was used to integrate the system for $\alpha = 1$ with the command `dsolve`, which uses the RFK45 method (an adaptive version of the Runge-Kutta method) and the default initial stepsize $h = 10^{-7}$. From a plot of the first part of a single orbit, as in figure 2, one can see that the curve is somewhat thickened compared with the curves in figure 1. The reason for this is that the energy H actually increases monotonically with t when the RFK45 method is applied to the system (3). With $\alpha = 1$ and the initial condition $(x(0), y(0)) = (0.9, 0.8)$, it took Maple 50 seconds on a three-year-old laptop to generate 5000 points $\{(x_t, y_t)\}_{t=0}^{5000}$ of the numerical solution, which produced figure 2. Using these values the energy $H_t = H(x_t, y_t)$ was calculated and found to increase linearly with t, as in figure

3, which shows the energy difference $H_t - H_0$, with the initial energy being $H_0 \approx 2.0285041$. (20-digit floating point numbers have been used to perform all numerical calculations with Maple, set with the `Digits` command.) For longer and longer integration times, the numerically calculated orbit spirals outwards, so that the points (x_t, y_t) lie in an increasingly thick band around the actual solution curve $H = H_0$.

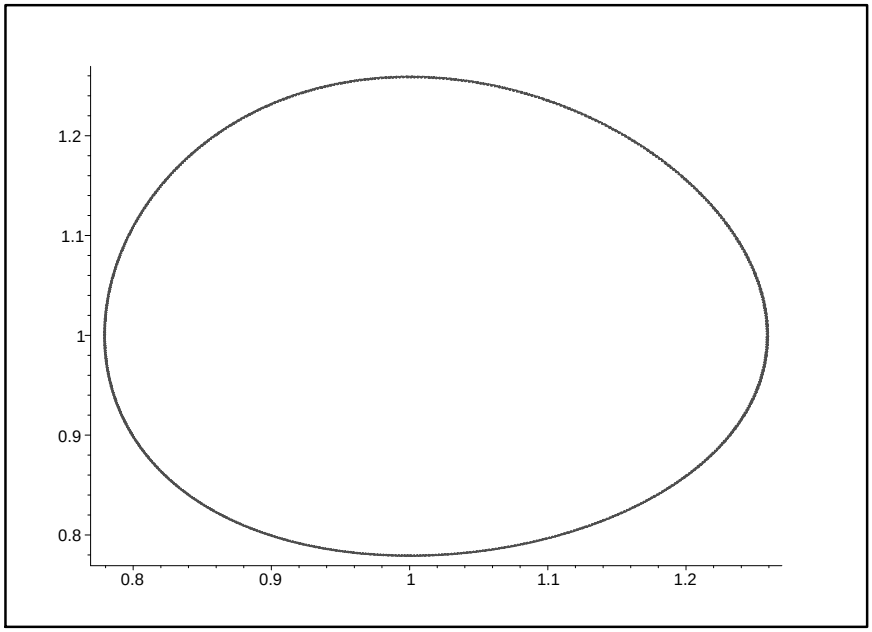

Fig. 2. Numerical integration of the predator-prey system (3) with $\alpha = 1$ and initial point $(0.9, 0.8)$, using the RKF45 method up to $t = 5000$.

To produce the qualitatively more accurate plot of closed orbits shown in figure 1, a discretization of the Lotka-Volterra system due to Kahan was used. This discretization method, which was apparently first presented in some unpublished lectures by Kahan in 1993, is directly applicable to systems of first order ordinary differential equations whose right hand sides are at most quadratic (degree two) in all dependent variables. Each derivative term on the left hand side should be replaced by the standard forward difference (as in the Euler method), so that e.g. $\dot{x}$ becomes $(x_{t+h} - x_t)/h \equiv (\tilde{x} - x)/h$, where the tilde is used to denote the forward time shift $t \to t + h$. Each quadratic term is replaced by an average involving products of variables at time t and those shifted forwards, so e.g. xy on both right hand sides of (3) becomes $\frac{1}{2}(\tilde{x}y + x\tilde{y})$; linear terms are also replaced by an average, so x (on the right hand side of the equation for $\dot{x}$) becomes $\frac{1}{2}(\tilde{x} + x)$ in the discrete version. (There are no purely constant terms in (3), but where such terms appear these should be left as they are.) Apply-

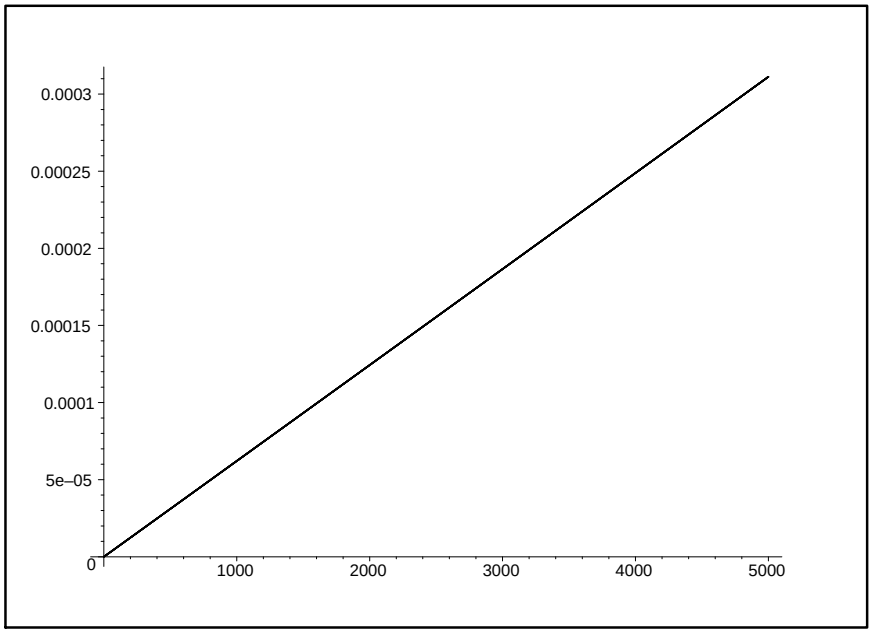

Fig. 3. The energy difference $H_t - H_0$ plotted against t for numerical integration using RKF45 as in figure 2.

ing these rules of discretization to (3) with $\alpha = 1$ produces the system of two difference equations given by

$$\frac{\tilde{x} - x}{h} = \frac{1}{2}\Big(\tilde{x} + x - (\tilde{x}y + x\tilde{y})\Big), \quad \frac{\tilde{y} - y}{h} = \frac{1}{2}\Big(\tilde{x}y + x\tilde{y} - (\tilde{y} + y)\Big). \tag{5}$$

This discretizaton can be said to be nonlocal in time, in the sense that the forward difference of each variable (on the left) is given by a function of both the local variables $(x, y) = (x_t, y_t)$ at time t and the forward shifted variables $(\tilde{x}, \tilde{y}) = (x_{t+h}, y_{t+h})$ (on the right).

The above system clearly reproduces the differential equations (3) in the continuum limit $h \to 0$, and has certain positive features which are immediately obvious, perhaps the first being its inherent simplicity (especially compared with the complexity of Runge-Kutta schemes, for instance). A second important aspect is that the above discretization scheme always has the same fixed points as the original differential equation (these being $(0, 0)$ and $(1, 1)$ in the case at hand) and does not introduce any extra ones. Thirdly, the two equations (5) are both polynomial in $x, y, \tilde{x}, \tilde{y}$, and the system is linear in both pairs of variables $\tilde{x}, \tilde{y}$ and x, y, which means that it can be solved to give the updated $\tilde{x}, \tilde{y}$ as explicit rational functions of x, y, and (vice-versa) the inverse transformation is also given by explicit rational functions, so it constitutes a birational map of the (x, y) plane (also known as a Cremona transformation; see e.g. [3] and

references). Upon solving (5) for $\tilde{x}, \tilde{y}$ the following expressions are obtained:

$$\begin{aligned} \tilde{x} &= \frac{x\Big(4+(4-2x-2y)h+(1-x+y)h^2\Big)}{\Big(4+(2y-2x)h+(x+y-1)h^2\Big)}, \\ \tilde{y} &= \frac{y\Big(4+(2x+2y-4)h+(1+x-y)h^2\Big)}{\Big(4+(2y-2x)h+(x+y-1)h^2\Big)}. \end{aligned} \tag{6}$$

Each of the orbits shown in figure 1 was produced from 10000 iterations of the transformation (6) with timestep $h = 0.1$, by starting with twenty different initial conditions $(x, y) = (x_0, y_0)$. Each orbit appears to lie on a closed curve encircling the fixed point $(1, 1)$, as is required for an accurate representation of the solution of (3).

In order to probe the properties of Kahan's discretization more closely, the same initial condition $(x_0, y_0) = (0.9, 0.8)$ was taken as for the RKF45 method, and then 50000 iterations of (6) were applied with timestep $h = 0.1$ (to give a total time of length 5000 as before). With this much simpler scheme (and relatively large timestep) this took only 22 seconds on the same machine. The energy of the iterates for Kahan's scheme was calculated and the difference $H_t - H_0$ was plotted against time as in figure 4; the results are seen to be quite different. While for the RKF45 method the value of the energy has increased by more than 3×10^{-4} after time 5000 (and carries on increasing linearly), Kahan's method in contrast gives an oscillating energy value that never increases or decreases by more than 10^{-5} within the same length of time. This would be a consequence of the system (6) having closed orbits lying on curves that are close to the original orbits of (3), since in that case the oscillations in energy would be bounded above and below. In [24], Sanz-Serna observed that Kahan's discrete Lotka-Volterra system is also symplectic, in that it preserves the same area form as the original differential equation i.e. $\frac{1}{\tilde{x}\tilde{y}} d\tilde{x} \wedge d\tilde{y} = \frac{1}{xy} dx \wedge dy$ holds. Since the differential equation is Hamiltonian and has one degree of freedom, it is completely integrable, so that (as also mentioned in [1]) one can apply KAM theory in the neighbourhood of the elliptic fixed point at $(1, 1)$. Nevertheless, the stability of Kahan's discretization of the Lotka-Volterra model as a numerical scheme seems quite remarkable.

Kahan's method for discretizing quadratic vector fields is mentioned in some of his published work with Li (see [12], and also [13], where it is described how to turn it into a higher order method). More recently, it has been applied to Lotka-Volterra models with three species [23], and it has been shown that also in that case it correctly reproduces the same qualitative features of the dynamics as are present in the corresponding continuous systems. In fact, Kahan's method for systems with quadratic right hand sides was later rediscovered by Hirota and Kimura in the context of integrable systems in classical mechanics, when they discovered a new completely integrable discretization of the Euler equations for a rigid body rotating about a fixed point [9]. A variety of new discrete integrable mechanical systems have been discovered very recently via this approach [6,

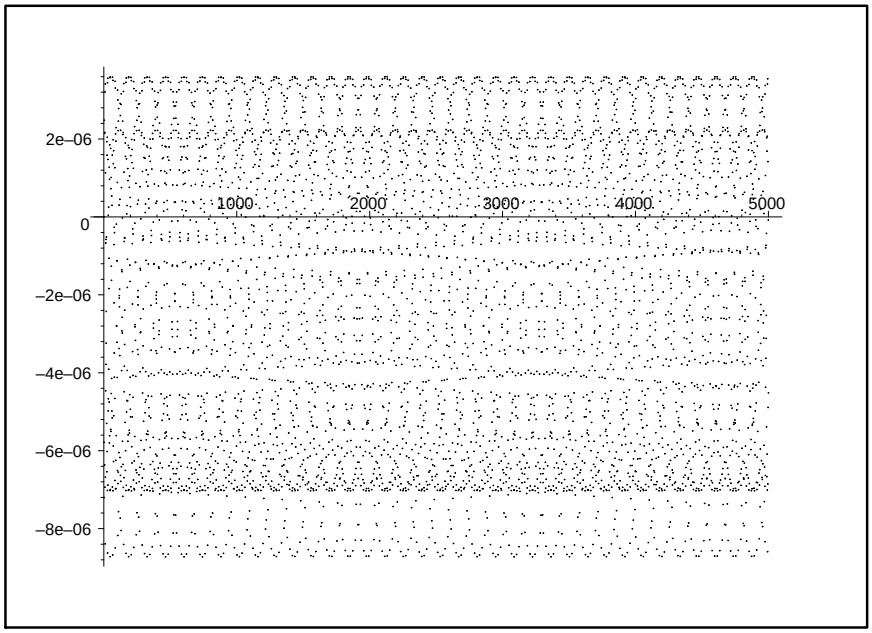

Fig. 4. The energy difference $H_t - H_0$ plotted against t for numerical integration of (3) using Kahan's discretization (5).

10, 21], and the precise properties preserved by Kahan's scheme are currently the subject of theoretical investigation. However, it is fair to say that Kahan's method fits in with a rather broad set of principles for discretizing differential equations that was developed somewhat earlier by Mickens, and is formulated in his book [17]. Mickens has used his approach to study a wide variety of ordinary (and partial) differential equations, and his non-standard methods have been implemented by a number of researchers in different areas of science and engineering; an extensive review can be found in [19].

Mickens has also applied his general guiding principles for discretization to the same predator-prey model (3) in the case $\alpha = 1$ [16]. Rather than just replacing the linear term x by the average $(\tilde{x} + x)/2$, one can consider more general (asymmetric) replacements $x \to A\tilde{x} + (1 - A)x$, and similarly for the quadratic terms. Moreover, in the forward difference Mickens takes a general denominator function $\phi(h) = h + O(h^2)$; while this has little effect for small h, it becomes important as h increases (and for certain systems there are explicit exact discretizations for which the choice of ϕ is crucial). The particular discrete predator-prey system given in [16] has the form

$$\frac{\tilde{x} - x}{\phi} = 2x - \tilde{x} - \tilde{x}y, \qquad \frac{\tilde{y} - y}{\phi} = -\tilde{y} + 2\tilde{x}y - \tilde{x}\tilde{y}. \tag{7}$$

Although the overall system is not linear in $\tilde{x}, \tilde{y}$, the first equation can be solved for $\tilde{x}$ and this can be put back into the second equation to find $\tilde{y}$, so that

this gives another explicit birational map of the plane. Numerical results show that the discrete system (7) also has closed orbits in a large neighbourhood of $(1,1)$ for small values of h. It is straightforward to verify that the map of the plane defined by the above equations for $\tilde{x}, \tilde{y}$ preserves the same symplectic form $\omega = \frac{1}{xy} dx \wedge dy$ as before, which is an indication of why its stability properties appear to be the same as for (6). The application of Mickens' methodology to other Lotka-Volterra systems in the plane is treated in [1] and [5]. For an implicit discretization of the Lotka-Volterra predator-prey model, that conserves energy, see [27].

As already mentioned, models in terms of conservative systems are rather rare in ecology or biochemistry (although enzymatic reactions do involve conservation of total enzyme [26]). The Lotka-Volterra model for predator-prey interaction is somewhat unrealistic, because it predicts that any non-zero pair of populations will go through periodic cycles, and thus always return to their initial values after a fixed time. A more realistic scenario is that there is a single attracting periodic cycle which all solutions approach asymptotically, namely a limit cycle. In the next section, limit cycles in reaction kinetics are considered.

3 Trimolecular reaction model

Biological systems that are close to equilibrium can be modelled extremely effectively by linear differential equations [2]. The disadvantage of using linear models is that a linear differential equation of the form $\dot{\mathbf{x}} = M\mathbf{x}$, with a state vector $\mathbf{x}$ and matrix M, has only a single fixed point at $\mathbf{x} = 0$ (at least generically, when M has no non-trivial kernel). Thus in order to allow the possibility of multiple equilibria, one should use nonlinear systems. For nonlinear systems that are close to an equilibrium of node, spiral or saddle point type, the linearized system provides correct qualitative information about solutions in the neighbourhood of the fixed point [11]. The Euler method is exact for homogeneous autonomous linear systems, so standard numerical integration methods are usually completely adequate for modelling systems close to equilibrium. Therefore in order to see novel phenomena that are inherently nonlinear, and thus more difficult to analyze numerically, one should consider nonlinear models away from equilibrium. In this section we consider the application of nonstandard integration schemes to nonlinear systems with limit cycles.

It is worth emphasizing that quadratically nonlinear systems of differential equations arise immediately when one considers reaction kinetics in chemistry, or biochemistry, where the fundamental processes are all dimolecular, involving reactions of the form $A+B \to C$, $A \to B+C$, or $A+B \to C+D$, where A, B, C, D represent different molecular species. Upon applying the Law of Mass Action to such reaction schemes, the equation for the rate of change of concentration of each reactant is given by a sum of linear and quadratric terms in the concentrations. Thus Kahan's discretization method, making symmetric replacements of variables, that is $x \to (\tilde{x} + x)/2$ for linear terms and $xy \to (\tilde{x}y + x\tilde{y})/2$ for quadratric terms, is ideally suited to numerical integration of reaction kinetics

models (where the variables x, y etc. would correspond to concentrations). For the situation where N, the number of variables, is large, it is no longer practical to solve the system for the upshifted variables explicitly, as was done to obtain (6) from the original form (5) of the discrete system, because this requires inversion of an $N \times N$ matrix whose entries are polynomial in the variables; this becomes an increasingly difficult problem in symbolic algebra as N increases. However, the system for the upshifted variables $\tilde{x}, \tilde{y}, \ldots$ is always linear, so with numerical values of the iterates there are efficient algorithms for solving such systems, which will be stable when h is small, because in that case the $N \times N$ matrix to be inverted (with numerical entries) is a small perturbation of the identity.

In order to illustrate a simple example of a reaction scheme that includes a limit cycle, i.e. an isolated periodic solution corresponding to a closed curve in the phase space, it is not sufficient to consider dimolecular reactions with two reactants, because limit cycles cannot occur. Indeed, one can write down a general two-species reaction model with variables x, y and (by carefully studying all possible quadratic, linear, and even constant terms) check that limit cycles never appear; in [18] the first derivation of this result is attributed to Hanusse [8]. Thus in order to see periodic oscillations (which are not orbits in a conservative system, as for the predator-prey system in the previous prey system) one should either consider three or more species, or allow trimolecular reactions, which can arise by reduction from a system of higher order. Here the latter option is taken, but first it is instructive to use a toy model to illustrate how standard numerical integration methods fare with limit cycle solutions.

A simple toy model of a limit cycle in the plane is provided by the pair of differential equations

$$\dot{r} = r(1-r), \qquad \dot{\theta} = 1 + r^2, \tag{8}$$

which is written in terms of polar coordinates r, θ to represent the evolution of the point $(x, y) = (r\cos\theta, r\sin\theta)$ in the plane. The first equation is just the continuous logistic growth model, and has the explicit general solution

$$r(t) = 1/(1 + ke^{-t}) \to 1 \qquad \text{as} \qquad t \to \infty$$

(with arbitrary constant k). Thus the point $(x(t), y(t))$ approaches the unit circle $r = 1$ as $t \to \infty$, which is the limit cycle given by the exact periodic solution $(x, y) = (\cos(2t), \sin(2t))$. Moreover, trajectories that start inside the cycle remain inside (see figure 5), so $r(t) < 1$ for all t, while those that begin outside approach it with $r(t) > 1$ always. However, upon performing a numerical integration of the system (8) with the RKF45 method in Maple version 10, it is observed that, after an initial period of rapid change (starting from $r_0 = r(0) = 0.8$ in the example illustrated in figure 6), the value of the approximation $r_t \approx r(t)$ oscillates indefinitely between several different values, both above and below $r = 1$. For an iterative integration method with fixed floating point precision, one is dealing with a map in a finite state space, so all iterations must either reach a fixed point or be periodic in the long run [22].

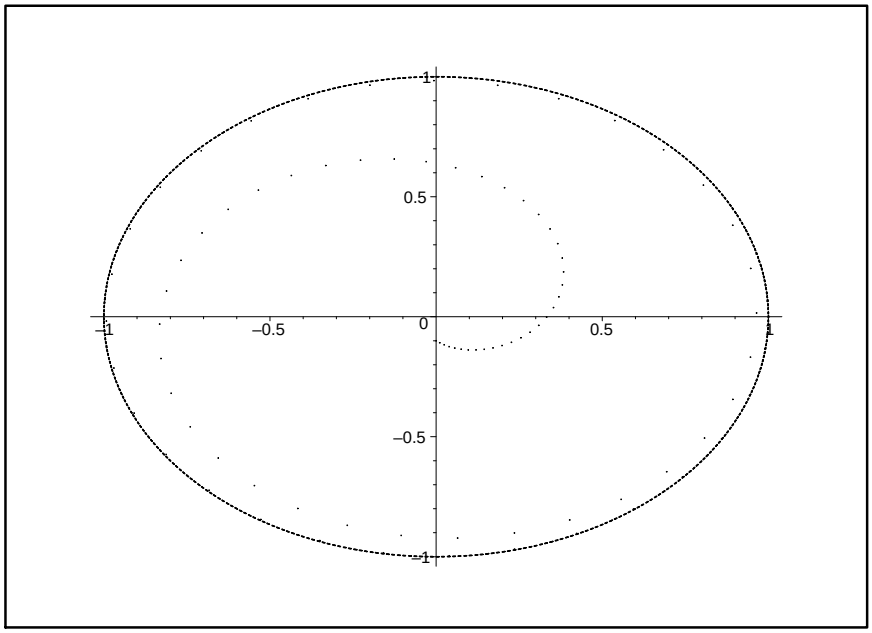

Fig. 5. Numerical integration of (8) using the discretization (9) with stepsize $h = 0.1$ for 2000 iterations starting from $r = 0.1$, $\theta = -\pi/2$ (and plotting $(x, y) = (r\cos\theta, r\sin\theta)$).

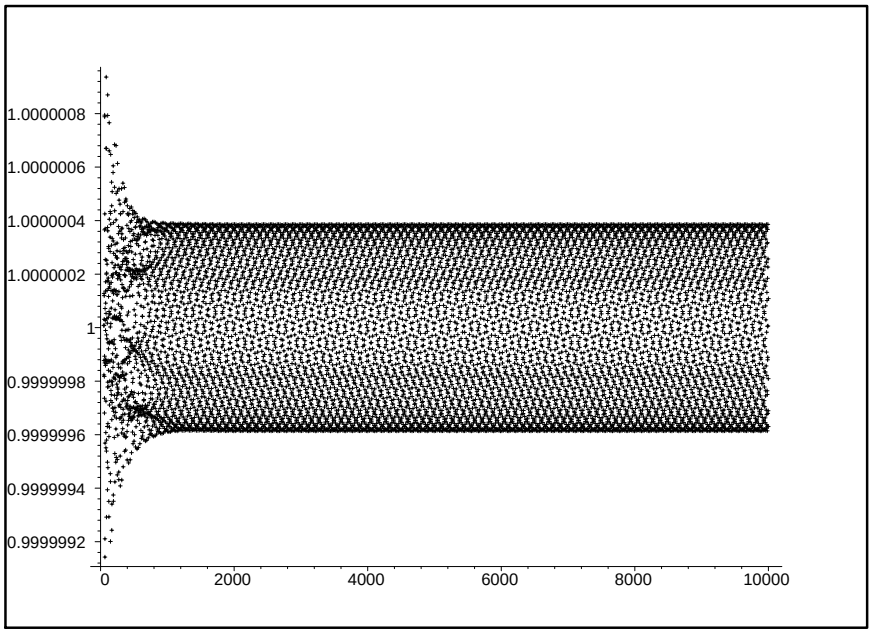

Fig. 6. Plot of r_t against t for $50 \leq t \leq 10000$ from numerical integration of (8) using the RFK45 method.

Alternatively, upon applying Kahan's unconventional discretization method to (8) one obtains the discrete system

$$\frac{\tilde{r}-r}{h} = \frac{\tilde{r}+r}{2} - \tilde{r}r, \qquad \frac{\tilde{\theta}-\theta}{h} = 1 + \tilde{r}r, \tag{9}$$

from which the equation for r decouples as

$$\tilde{r} = \frac{r(2+h)}{2+(2r-1)h}.$$

The latter equation is of discrete Riccati type (it is a Möbius transformation), and has the exact solution

$$r = r_t = \left(1 + k\left(\frac{2-h}{2+h}\right)^t\right)^{-1} \to 1 \quad \text{as} \quad t \to \infty \quad \text{whenever} \quad h > 0.$$

Thus the solutions of the latter discretization have precisely the same qualitative behaviour as those of the original system of differential equations (8). The discrete equation for r has the same fixed points (an unstable one at $r = 0$ and a stable one at $r = 1$) as for $\dot{r} = r(1-r)$, but from a numerical implementation of (9) with timestep $h = 0.1$ and 20-digit precision in Maple 10, using the initial value $r_0 = r(0) = 0.8$ (as for the RKF45 method), one finds that $r_t < 1$ holds for all t but the radius converges prematurely (in just over 400 steps) to the false equilibrium $r_\infty = .99999999999999999952 < 1$. This false value is due to rounding errors, and can clearly be improved by performing the same calculations using floating point numbers with successively more digits.

Having considered a toy model of a limit cycle, we now focus on the following simple reaction scheme, including trimolecular reactions, that was presented by Schnakenberg [25]:

$$X \underset{k_2}{\overset{k_1}{\rightleftarrows}} A, \quad B \overset{k_3}{\to} Y, \quad 2X + Y \overset{k_4}{\to} 3X.$$

In the above there are four molecular species A, B, X, Y and four rate constants k_j for $j = 1, 2, 3, 4$. If it is assumed that the concentrations of A and B are both held constant, then upon applying the Law of Mass Action and rescaling all the variables one obtains the dimensionless differential equations

$$\dot{x} = a - x + x^2 y, \qquad \dot{y} = b - x^2 y \tag{10}$$

for the scaled concentrations of X, Y (denoted x, y respectively) and the constants $a, b > 0$ (corresponding to the fixed concentrations of A, B). The system (10) has limit cycle solutions for the parameter range $b - a > (b + a)^3$ with $0 < b < 1$, giving a closed periodic cycle encircling the fixed point at $(a+b, b/(a+b)^3)$ (see chapter 7 in [18] for details, and see figure 7 for numerical integration of an orbit with parameters in this range).

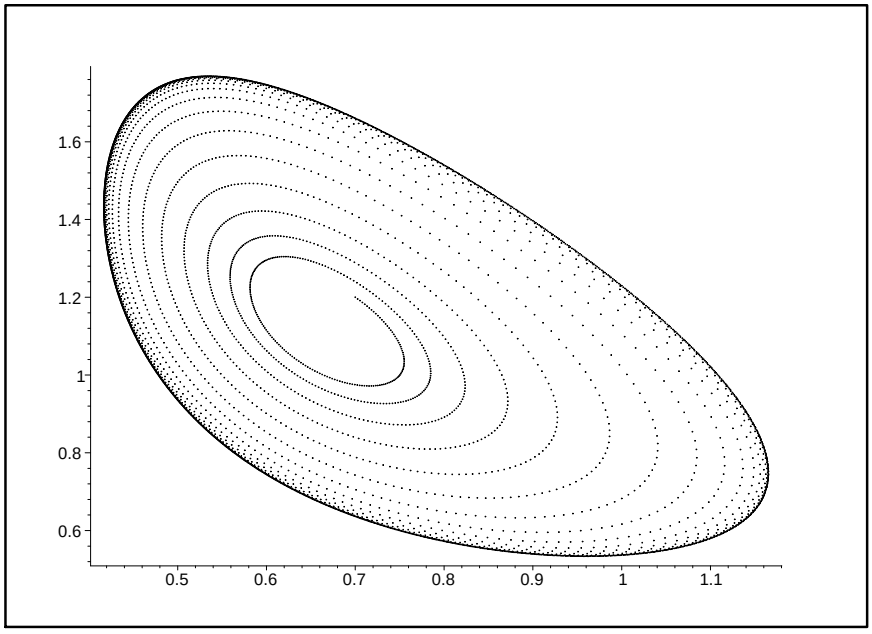

Fig. 7. Numerical integration of (10) with $a = 1/6$, $b = 1/2$ using the birational map φ_h defined by (11), taking the first 5000 points on the orbit of $(0.7, 1.2)$ with $h = 0.05$.

Due to the presence of the cubic (degree 3) terms x^2y on the right hand sides in (10), it is not possible to apply Kahan's scheme for quadratic vector fields. However, we can still obtain a non-standard discretization in the spirit of Mickens' approach. To do so, derivatives are replaced by forward differences, the linear term x in the first equation of (10) is replaced by the symmetric nonlocal expression $(\tilde{x} + x)/2$, and for each cubic term we make a replacement of the general form

$$x^2y \to (cy + d\tilde{y})(ex^2 + fx\tilde{x} + g\tilde{x}^2), \quad c + d = 1, \quad e + f + g = 1,$$

where the constants $c, d = 1 - c, e, f, g = 1 - e - f$ are allowed to be different in each of the two equations. Without any further restrictions on the latter constants, in general one has a multivalued map for $\tilde{x}, \tilde{y}$: in order to find these upshifted variables in terms of x, y one must solve a pair of polynomial equations, which have multiple roots. However, if it is required that the two equations have an unique solution for $\tilde{x}, \tilde{y}$, and furthermore that one can also solve uniquely for x, y, then there are only two possible discretizations, namely

$$\varphi_h : \quad \frac{\tilde{x} - x}{h} = a - \frac{1}{2}(\tilde{x} + x) + x\tilde{x}\tilde{y}, \quad \frac{\tilde{y} - y}{h} = b - x^2\tilde{y}, \tag{11}$$

and

$$\psi_h : \quad \frac{\tilde{x} - x}{h} = a - \frac{1}{2}(\tilde{x} + x) + x\tilde{x}y, \quad \frac{\tilde{y} - y}{h} = b - \tilde{x}^2y. \tag{12}$$

In each case the pair of equations defines a birational map of the plane, $\varphi_h : (x, y) \mapsto (\tilde{x}, \tilde{y})$, given by

$$\tilde{x} = \frac{2x + h(2a - x + 2x^3) + h^2(2ax^2 - x^3)}{2 + h(1 - 2xy + 2x^2) + h^2(x^2 - 2bx)}, \quad \tilde{y} = \frac{y + hb}{1 + hx^2},$$

and similarly for ψ_h. Furthermore, it is not too hard to see from (11) and (12) that these two transformations define each other's inverses, in the sense that $\varphi_h^{-1} = \psi_{-h}$, so henceforth we can concentrate on φ_h.

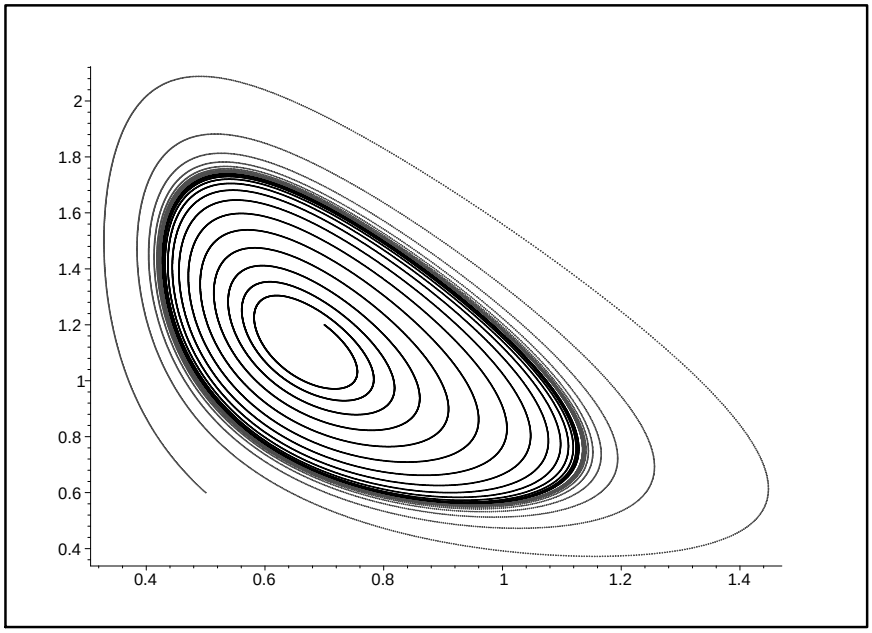

Fig. 8. Two solutions of (10) for $a = 1/6$, $b = 1/2$ integrated numerically using an adaptive modification of the scheme defined by (11), taking variable stepsize $h_{n+1} = h_n d_n / d_{n+1}$ with $h_0 = h_1 = 0.01$ (where d_n is the distance between successive points).

One can perform exact analysis of the Jacobian of the map φ_h at the fixed point $(a + b, b/(a + b)^3)$; this is along the same lines as the analysis for discretizations of Lotka-Volterra models done by Roeger [23]. Such analysis shows that, just as the differential equation (10) undergoes a Hopf bifurcation along the curve $b - a = (b + a)^3$ in the (a, b) parameter space, which produces a limit cycle lying on an invariant curve in the (x, y) plane, for small h the map φ_h similarly undergoes a Neimark-Sacker bifurcation to produce an invariant curve which is at least $O(h)$ close to the limit cycle of the differential equation. (For technical details of Hopf and Neimark-Sacker bifurcations, see [14].) The correct qualitative nature of the orbits of this discretization can be seen from the numerical results. The first plot for (11) is the orbit of the point $(0.7, 1.2)$, shown in

figure 7, for 5000 steps with stepsize $h = 0.05$, which shows convergence towards the attracting invariant curve from the inside. In figure 8, results are shown of applying a simple modification to the method to produce a crude adaptive scheme, by varying the stepsize by a factor proportional to d_n/d_{n+1} at each step, where $d_n = |\mathbf{x}_n - \mathbf{x}_{n-1}|$ is the distance between successive iterates. The latter figure shows the orbit of $(0.5, 0.6)$ spiralling onto the invariant curve from the outside, together with the orbit of $(0.7, 1.2)$, taking 20000 iterations with an initial stepsize $h = 0.01$. The adaptive method shows better resolution than the non-adaptive one in places where the solution of the ordinary differential equation is varying more rapidly.

4 Discussion

For the modelling of biological phenomena in terms of systems of differential equations that exhibit truly nonlinear behaviour, standard techniques for numerical integration can produce solutions which are qualitatively incorrect. However, the non-standard methods developed by Mickens and Kahan (among others) provide simple discretization schemes that manage to incorporate the correct qualitative features of the original continuous system. Thus the unconventional methods outlined above are worthy of consideration by anyone who is interested in modelling with differential equations. Of course, a considerable amount of theoretical work remains to be done in order to understand precisely when and why such methods outperform conventional ones.

When implementing a numerical scheme, one wishes to avoid introducing new properties into the discrete system which were not present in the original continuous one. We have asserted that Kahan's discrete predator-prey system (5) reproduces the closed orbit structure of the differential equations (3), but to be more precise one should qualify this by saying that this structure holds only in a certain neighbourhood of the elliptic fixed point, with this region being large when h is small. An undesirable feature of the scheme is that sufficiently large positive values of x and y, beyond a boundary line, go outside the positive quadrant after iteration, but in fact the Kahan discretization also displays the characteristics of a chaotic map in a fringe region before this boundary is reached, with the size of this "chaotic fringe" increasing as h increases [20]. Of course, for modelling predator-prey systems [15] or interacting populations in other biological scenarios, one can avoid the problem of numerical integration altogether by working directly with discrete models in terms of difference equations or cellular automata [22]. However, in setting up such models one is often guided by intuition based on continuous models in terms of differential equations.

In this paper, we have illustrated how non-standard discretization methods can be used to study the simplest type of nonlinear oscillation that is not exhibited by a linear system, namely a limit cycle. As far as we are aware, the discretization (11) for the simple trimolecular reaction equations (10) is new. Further analysis of this discrete system will be presented elsewhere.

Finally, we should mention that although (due to the Poincaré-Bendixson theorem [11]) only fixed points and limit cycles can arise as attractors in autonomous two-dimensional systems of differential equations, in three or more dimensions there is the possibility of strange attractors, such as the one appearing in the famous Lorenz model. The Lorenz model is defined by a quadratic vector field in three dimensions, and as such can be integrated using Kahan's unconventional scheme. Indeed, the appropriate discretization has been presented as an example in [13], and our own numerical experiments suggest that, for different values of the stepsize h, this discrete system in 3D contains a strange attractor which is qualitatively like the Lorenz attractor, and converges to it as $h \to 0$.

Acknowledgments. The author is grateful to the Isaac Newton Institute, Cambridge for providing him with a Visiting Fellowship during the completion of this work. He also thanks Matteo Petrera, Yuri Suris and Claude Viallet for helpful correspondence and conversations on related matters.

References

1. H. Al-Kahby, F. Dannan and S. Elaydi, Non-Standard Discretization Methods for Some Biological Models, in *Applications of nonstandard finite difference schemes*, R.E. Mickens (Ed.), World Scientific (2000) 155–180.
2. U. Alon, *An Introduction to Systems Biology*, Chapman and Hall/CRC (2007).
3. J. Blanc, *Finite Abelian subgroups of the Cremona group of the plane*, C. R. Acad. Sci. Paris Sr. I Math. **344** (2007) 21–26.
4. C.J. Budd and A. Iserles (Eds.), *Geometric integration: numerical solution of differential equations on manifolds*, Phil. Trans. R. Soc. Lond. A **357** (1999) 943–1133.
5. D. Dimitrov and H.V. Kojouharov, Nonstandard finite-difference schemes for general two-dimensional autonomous dynamical systems, Appl. Math. Lett. **18** (2005) 769–775.
6. V. Dragovic and C. Gajic, Hirota-Kimura type discretization of the classical nonholonomic Suslov problem, Regular and Chaotic Dynamics **13** (2008) 250–256.
7. S.N. Elaydi, *Discrete Chaos*, Boca Raton: Chapman and Hall/CRC (2000).
8. P. Hanusse, De l'existence d'un cycle limite dans l'évolution des systèmes chimiques ouverts, C. R. Acad. Sci. Paris C **274** (1972) 1245–1247.
9. R. Hirota and K. Kimura, Discretization of the Euler top, Jour. Phys. Soc. Jap., **69** (2000), 627–630.
10. A.N.W. Hone and M. Petrera, Three-dimensional discrete systems of Hirota-Kimura type and deformed Lie-Poisson algebras, J. Geom. Mech. **1** (2009) 55–85.
11. D.W. Jordan and P. Smith, *Nonlinear ordinary differential equations*, 3rd edition, Oxford: OUP (1999).
12. W. Kahan and R.-C. Li, Unconventional schemes for a class of ordinary differential equations – with applications to the Korteweg-de Vries equation, J. Comp. Phys., **134** (1997), 316–331.
13. W. Kahan and R.-C. Li, Composition constants for raising the order of unconventional schemes for ordinary differential equations, Math. Comp. **88** (1997) 1089–1099.
14. Y. Kuznetsov, *Elements of Applied Bifurcation Theory*, Springer (1998).

15. R.M. May, M.P. Hassell, R.M. Anderson and D.W. Tonkyn, Density Dependence in Host-Parasitoid Models, J. Animal Ecol. 50 (1981) 855–865.
16. R.E. Mickens, A nonstandard finite-difference scheme for the Lotka-Volterra system, Appl. Num. Math., **45** (2003), 309–314.
17. R.E. Mickens, *Nonstandard finite difference models of differential equations*, World Scientific (1994).
18. J.D. Murray, *Mathematical Biology*, vols. I & II, revised 3rd edition, Berlin: Springer-Verlag (2002).
19. K.C. Patidar, On the use of nonstandard finite difference methods, J. Difference Eq. Appl. 11 (2005) 735–758.
20. M. Petrera and Yu.B. Suris, Hirota-type discretization of 2d Lotka-Volterra system, preprint (2008).
21. M. Petrera, A. Pfadler and Yu.B. Suris, On integrability of Hirota-Kimura type discretizations. Experimental study of the discrete Clebsch system, to appear in Exp. Math., `arxiv:0808.3345[nlin.SI]`.
22. F. Robert, *Les Systèmes Dynamiques Discrets*, Springer (2000).
23. L.W. Roeger, A nonstandard discretization method for Lotka-Volterra models that preserves periodic solutions, J. Diff. Eq. Appl., **11** (2005), 721–733.
24. J.M. Sanz-Serna, An unconventional symplectic integrator of W. Kahan, Appl. Num. Math. **16** (1994) 245–250.
25. J. Schnakenberg, Simple chemical reaction systems with limit cycle behaviour, J. Theor. Biol. **81** (1979) 389–400.
26. L.A. Segel, *Modeling dynamic phenomena in molecular and cell biology*, Cambridge: CUP (1984).
27. B.A. Shadwick, J.C. Bowman, P.J. Morrison, Exactly conservative integrators, SIAM J. Appl. Math. **59** (1998) 1112–1133.
28. Yu.B. Suris, *The problem of integrable discretization: Hamiltonian approach*, Progress in Mathematics **219**, Birkhäuser Verlag, Basel, 2003.
29. H. Yoshida, Construction of higher order symplectic integrators, Phys. Lett. A **150** (1990) 262–268.
30. D.G. Zill and M.R. Cullen, *Differential equations with boundary value problems*, Brooks/Cole - Thomson Learning (2005).