2.1 Some elements of dynamic simulation

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2.1.1 Introduction

When analysing systems, one is usually interested in the status of the system at a given moment and in its behaviour as a function of time. A system, which can be defined as a limited part of reality that contains interrelated elements, may be too complex to study directly. However, a model, which can be defined as a simplified representation of a system that contains the elements and their relations that are considered to be of major importance for the system's behaviour, may be easier to study. The design of such models and the study of the model properties in relation to those of the system is called simulation; if these models change with time they are called dynamic simulation models.

Dynamic simulation models are based on the assumption that the state of each system – at any given moment – can be quantified, and that changes in the state can be described by mathematical equations: rate or differential equations. This leads to models in which state, rate, and driving variables can be distinguished.

The purpose of this Section is to introduce the method of constructing models according to the state variable approach by using the very elementary system units described in Subsection 2.1.2. Subsection 2.1.3 shows how the appropriate differential equations may be integrated analytically to obtain the state variables as a function of time in these simple system units. The concept of feedback, and the possibility of visualizing the available knowledge of a system by means of relational diagrams, will be discussed in Subsection 2.1.4. Slight changes in differential equations make analytical solutions impossible, so solutions must be obtained by numerical integration methods. These solutions are based on the assumption that the rate of change is constant over a short period of time, Δt. The principle of numerical integration, the relation between the time interval of integration, Δt, and the time coefficient of an equation, are discussed in Subsection 2.1.5. Some numerical integration methods are presented in Subsection 2.1.6. During a time interval of integration, rates will usually change, so numerical integration methods introduce errors in the solution of differential equations. This will be demonstrated in Subsection 2.1.7, and relations between these errors and the time coefficient of the system will also be discussed. Finally, in Subsection 2.1.8 a more complex system is analysed using the methods presented.

2.1.2 State variables, rate variables and driving variables

To introduce the method of constructing models according to the state-variable approach, the following elementary system units are used (Figure 4):

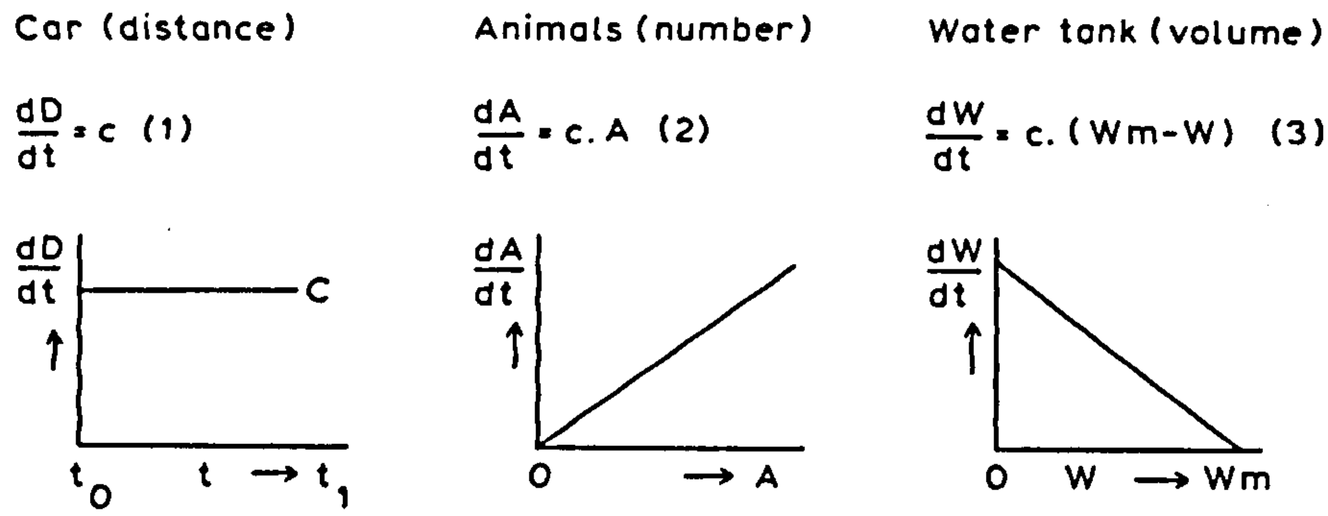


Figure 4. Rate or differential equations (Equations 1, 2 and 3), and their graphs, for three elementary system units. D, A and W stand for the state variables, t for time and c is a constant that may be different in each equation. Wm is the maximum water level that can be reached.

1. A car driving at a constant speed;
2. A number of animals that increases every year by a certain fraction;
3. A tank which is filled by a flow of water through an adjustable valve until a certain water level is reached.

The state variables in these examples are the distance covered by the car, the number of animals, and the amount of water in the tank, respectively. Generally, state variables have dimensions of length, number, volume, weight, energy or temperature. Such quantities can be measured directly.

The ultimate status of a system is not the only feature of interest; we are also concerned with its behaviour in time. Thus, the rate of change of the state variables in time, as well as the direction of change must be known. If these rates have a clear pattern, they may be formalized by means of rate equations or differential equations. The rate equations and their graphical representation for the three elementary system units are given in Figure 4. Rate variables, on the left hand sides of Equations 1, 2 and 3, have the dimension of a state variable per time, i.e. length $time^{-1}$, number $time^{-1}$ and volume $time^{-1}$, respectively. These variables cannot be measured directly and are usually calculated from state variables. For instance, when both the distance covered by the car and the time are measured, the (average) speed is given by their ratio. In Equations 2 and 3 the rate variables are functions of the state variables, A and W, respectively, whereas in Equation 1 the state has no effect on the rate. The influence of a state on its rate of change is called feedback and will be discussed in Subsection 2.1.4. The proportionality coefficients, c, in Equations 2 and 3 are important with regard to the behaviour of the state variables and are often given special names. In biological systems c is called the relative growth rate; in technical systems the inverse of c is used, and is called the time coefficient. Time coefficients and their effect on numerical integration are crucial in dynamic simulation, which is discussed in Subsection 2.1.5. The constant c in Equation 1 is a driving variable with the dimension for speed. Driving variables, or forcing functions, characterize the effect of outside conditions on a system at its limits or boundaries, and their value must be monitored continuously. Driving variables may have the dimension of rate variables, as in Equation 1, or of state variables, depending on their nature. When the driving variable is temperature, e.g. when the fraction by which the number of animals increases each year depends on temperature, it has the dimension of a state variable. It is good practice to check the dimensions of all variables in a particular model.

Exercise 1

a. What are the dimensions of c in Equations 1, 2 and 3 in Figure 4?
b. Which general rules form the basis of dimensional analysis?

2.1.3 Analytical integration and system behaviour in time

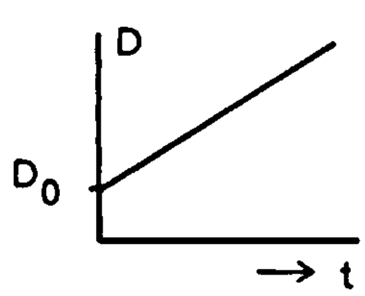
Differential equations summarize the existing knowledge of a system, i.e. they relate rate variables to state variables, driving variables and parameters. Hence, they form a model for that system. When the differential equations are formulated, and when the state of the model at a certain moment is known, then its future state can be calculated. For this purpose, the differential equation must be solved with respect to its state variable. This process of integration can be visualized for the simplest case of Equation 1 by determining the distance covered by the car after a certain period of time when its speed is constant and known. Here, the speed is multiplied by the time. Thus, the value of the state variable equals the area (Figure 4) delimited by the time axis, the line parallel to this time axis at the value c on the rate axis, and the two lines, parallel to the rate axis, at two points of time, t_0 and t_1, indicating the period. This does not apply to Equations 2 and 3 as the rate variables depend on the state; they are not expressed as functions of time. The formal process to obtain the state variable as a function of time must be applied. This is shown in Figure 5 for all three models. Integration of Equation 2 produces the familiar exponential growth curve (Equation 5). The relationship between the rate variable, dA/dt, and time is obtained by differentiating Equation 5 with respect to time. This yields Equation 2a, which has the same form as Equation 5. The graph depicting Equation 2a may be used to obtain the state variable. It may seem trivial to state this, since the analytical solution is already available in the form of Equation 5. The graph may, however, be used to illustrate the errors introduced by numerical integration methods when these are used to solve differential equations (Subsection 2.1.7).

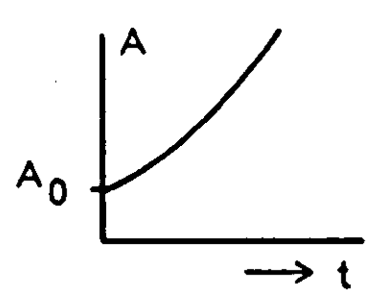
In the case of the water tank, it is assumed that the rate of water inflow decreases linearly with the difference between a known maximum water level, Wm, and the actual water level, W (Equation 3). Integration yields Equation 6, which shows that the amount of water in the tank approaches Wm exponentially.

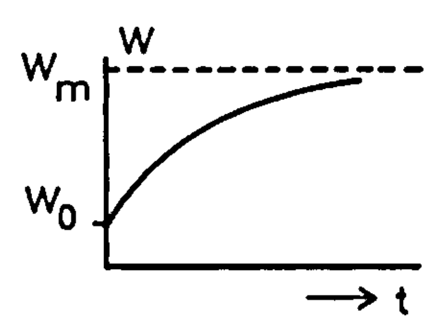
Car	Animals	Water tank
		$\frac{dW}{dt} = -c.(W - Wm)$
		$\frac{d(W-Wm)}{dt} = -c.(W-Wm)$
$\int dD = c. \int dt$	$\int \frac{dA}{A} = c \int dt$	$\int \frac{d(W-Wm)}{W-Wm} = -c \int dt$
$D = c.t + Q$	$\ln A = c.t + Q$	$\ln(W - Wm) = -c.t + Q$

initial value of the state variable at t = 0:

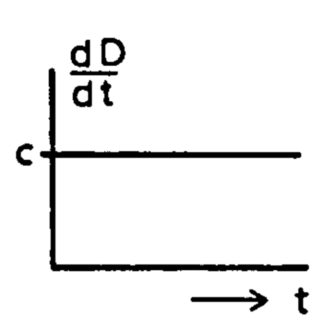
$D = D_0$ so $Q = D_0$	$A = A_0$ so $Q = \ln A_0$	$W = W_0$ so $Q = \ln(W_0 - Wm)$
	$\ln \frac{A}{A_0} = c.t$	$\ln\left(\frac{W-Wm}{W_0-Wm}\right) = -c.t$
$D = c.t + D_0$ (4)	$A = A_0\, e^{c.t}$ (5)	$W = Wm - (Wm - W_0).e^{-c.t}$ (6)

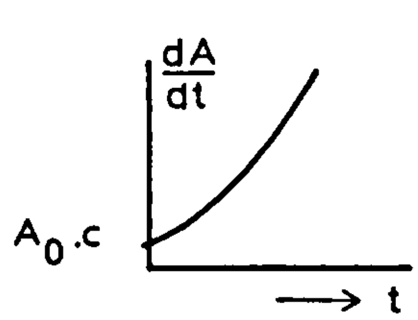






$\frac{dD}{dt} = c$ (1)	$\frac{dA}{dt} = A_0\, c.e^{c.t}$ (2a)	$\frac{dW}{dt} = (Wm - W_0)c.e^{-c.t}$ (3a)





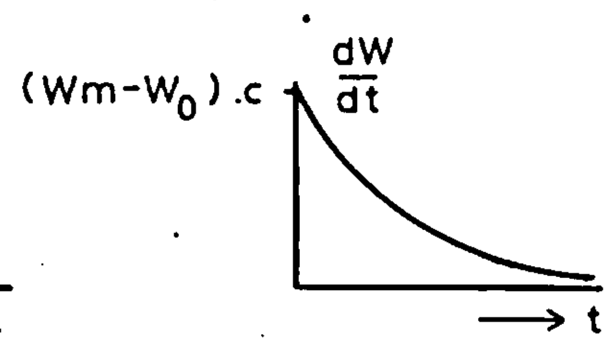


Figure 5. Upper half: analytical solutions (Equations 4, 5 and 6) to differential Equations 1, 2 and 3, respectively, and their graphs.
Lower half: rate variables (Equations 1, 2a and 3a) as a function of time, derived from Equations 4, 5 and 6, respectively, and their graphs. For an explanation of variables see Figure 4. Q stands for a general integration constant, and D_0, A_0 and W_0 are the initial values of the state variables in the particular models.

Equation 3a, obtained by differentiating Equation 6, shows that the rate of inflow decreases exponentially.

Exercise 2

Consider the graphs depicting Equations 4, 5 and 6 in Figure 5.

a. What do the slopes of the different lines represent?
b. What is the dimension of the slope in each case?
c. How do the numerical values of the slopes change as a function of time?
d. Are your findings in accordance with the graphs depicting Equations 1, 2a and 3a?

As long as differential equations are simple, they may be solved analytically to study the behaviour of the models. Slight changes in these equations, e.g. if c in Equation 2 is a function of temperature, make analytical solutions impossible. The equations should then be solved numerically. Before the principle of numerical integration is discussed (Subsection 2.1.5), and some integration methods presented (Subsection 2.1.6), the concept of feedback and the possibility of representing state, rate and driving variables in the form of relational diagrams is considered.

2.1.4 Feedback and relational diagrams

The rate variables in Equations 2 and 3 (Figure 4) are, respectively, a function of the state variables A and W, whereas the rate in Equation 1 is independent of the distance covered. When a rate variable, dX/dt, of a differential equation depends on the state variable X, there is a feedback loop, i.e. the state of the variable determines the degree of action or rate of change of this state. This process takes place in a continuously circulating loop. There are two types of feedback loops.

In a negative feedback loop, the rate may be either positive or negative, but will decrease as a function of the state variable. For instance, in the case of the water tank, Equation 3, the rate is positive, but decreases linearly with the increasing volume of water in the tank. An example of a negative rate which decreases the state variable, and vice versa, is obtained when the sign of the coefficient c in Equation 2 is made negative. Then, the number of animals decreases each year by a certain fraction. This denotes exponential mortality. A negative feedback loop can be recognized in a differential equation when the rate of change of the state variable is negatively related to that state variable (Equation 3). Negative feedback causes the system to approach equilibrium. Such an equilibrium state is stable: if the system is perturbed it returns to its equilibrium state. In the case of the water tank, the equilibrium state is the maximum level of water, Wm, whereas in the case of exponential mortality the state variable approaches zero.

In a positive feedback loop, the rate enhances the state, and vice versa, so that both become greater and greater. The exponential growth of the animals that is described by Equations 2 and 5 is an example of positive feedback. In nature, however, there are limits to growth. For instance, there may be a shortage of food. Then, the simple Equations 2 and 5 no longer describe the system and the model needs revision. A positive feedback loop can be recognized in a differential equation when the rate of change of the state variable is positively related to that state variable (Equation 2).

Relational diagrams are used to visualize feedback loops, rate and state variables and, more generally, the available knowledge about a system. They depict the most important elements and relationships of a system and form qualitative models of systems. Relational diagrams may be especially helpful at the start of the research in order to simplify the formulation of rate and state variables. They also make the content and characteristics of a model easily accessible. Relational diagrams for the three systems are given in Figure 6. They are drawn according to Forrester (1961), as shown in Figure 7. Figure 6 shows that feedback is absent in the case of the car, and that there is positive and negative feedback in the case of the animals and the water tank, respectively. When a parameter turns out to be variable, it must be replaced by a table or by an auxiliary equation. For instance, if the coefficient c, in the relational diagram for the animals, is temperature dependent, it can be replaced by a so-called auxiliary variable which contains information concerning this temperature dependence, and from which information flows to the rate variable.

Relational diagrams of more complex models may often be analysed in terms of the elementary units of Figure 6.

2.1.5 Numerical integration and the time coefficient

The differential equations considered so far can be solved analytically in order to study the state variable as a function of time. When model computations do not agree with the behaviour of the system, more complex (sub-)models are needed, based on new knowledge of the system. The resulting set of differential equations cannot be integrated analytically; instead, numerical integration methods must be used.

In numerical integration the assumption is made that the rate of change of a state variable is constant over a short period of time, Δt. To calculate the state of a model after that short period, one must know the state of the system at time t, $state_t$, and the value of the rate variable, $rate_t$, calculated from the differential equation. By multiplying the $rate_t$ by Δt, and adding this product to the value of the state variable according to

$$state_{t+\Delta t} = state_t + \Delta t \cdot rate_t \qquad \text{Equation 7}$$

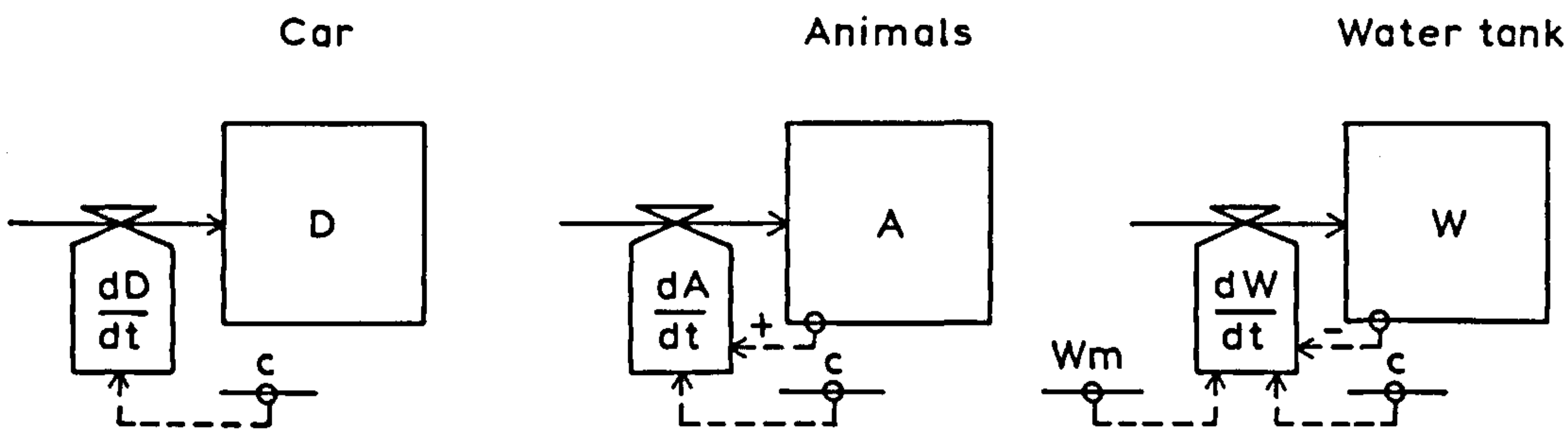
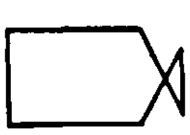


Figure 6. Relational diagrams for three elementary systems. Variables and symbols are explained in Figures 4 and 7, respectively.

A state variable, or integral of the flow; the final result of what has happened.

Flow and direction of an action by which an amount, or state variable, is changed. These flows always begin or end at a state variable, and may connect two state variables.

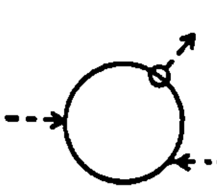
Flow and direction of information derived from the state of the system. Dotted arrows always point to rate variables, never to state variables. The use of information does not affect the information source itself. Information may be delayed and as such be a part of a process itself.



Valve in a flow, indicating that calculation of a rate variable is taking place; the lines of incoming information indicate the factors upon which the rate depends.

Source and sink of quantities, the content of which is considered to be unimportant. This symbol is often omitted.

A constant or parameter.



Auxiliary or intermediate variable in the flow of information.

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Sometimes placed next to a flow of information to indicate whether a loop involves a positive or negative feedback.

Figure 7. Basic elements of relational diagrams. Abbreviated names of variables represented by these elements are usually written inside the symbols. Note that driving variables are often underlined or placed in parenthesis. Intermediate variables are often characterized by circles.

the new state, $state_{t+\Delta t}$, of the system is determined. From this new state, a new rate is calculated which holds for the next interval Δt, and so on. Much can be said about the 'short period', Δt, especially in the context of its relation to the time coefficient of a particular model (see below), and with respect to errors introduced by numerical integration methods (see Subsection 2.1.7). The calculation of $rate_t$ will be discussed further in Subsection 2.1.6.

Numerical integration is first applied to the example of the water tank, Equation 3. Assume that there is no water in the tank at $t = 0\,s$, so $W_0 = 0\,l$; coefficient c equals $\frac{1}{4}\,s^{-1}$, and the maximum water level $Wm = 16\,l$. The rate at which water flows into the tank at $t = 0$ is calculated from the rate equation

$$(dW/dt)_t = c \cdot (Wm - W_t) \qquad \text{Equation 8}$$

as $4\,l\,s^{-1}$. If the time interval Δt, or the 'short period' equals $2\,s$, the volume of water at time $t + \Delta t$ is obtained from the state equation

$$W_{t+\Delta t} = W_t + \Delta t \cdot (dW/dt)_t \qquad \text{Equation 9}$$

as $8\,l$. During the following time interval of $2\,s$, the rate is: $\frac{1}{4} \cdot (16 - 8) = 2\,l\,s^{-1}$. Thus, during this time interval, $4\,l$ of water will flow into the tank and the total quantity of water after $4\,s$ equals $8 + 4 = 12\,l$. The calculations thus proceed according to Equations 8 and 9, and can be facilitated by the following diagram:

times	s	0	$\leftarrow \Delta t \rightarrow$	2	4	6	8	10
W	l	0	$\rightarrow$	8				
		$\downarrow$						
dW/dt	$l\,s^{-1}$	4		2				

Exercise 3

Complete the calculation and plot the amount of water in the tank against time. Calculate the amount of water in the tank using Equation 6 and the same parameters, and plot the results in the same graph.

a. What do you notice about the difference between the numerical and analytical solution?

b. When is the rate of inflow zero?

c. What happens if coefficient c is 1/8 instead of 1/4?

In the case of the water tank the rate of filling decreases (see Figure 5 depicting Equation 3a), so that the numerical integration, where the rate variable is kept constant during the time interval Δt, overestimates the amount of water in the tank compared to the analytical solution (see also Exercise 3). The difference between the value of the state variable obtained by the numerical method, and the analytical value, will be smaller when Δt is smaller. The lower limit of Δt is set by the technical (rounding errors) possibilities of performing the calculations over large time spans.

Exercise 4

The parameters in Equations 8 and 9 are:

$W_0 = 0\,l$; $Wm = 16\,l$; $c = \frac{1}{4}s^{-1}$.

a. Perform numerical integration up to about 30 s for the filling of the water tank using the following time intervals:
$\Delta t = 1 \cdot c^{-1}$; $\Delta t = 1\frac{1}{2} \cdot c^{-1}$; $\Delta t = 2 \cdot c^{-1}$; $\Delta t = 2\frac{1}{2} \cdot c^{-1}$.
b. Plot your results in the graph of Exercise 3.
c. What can you say about the ratio of the time interval and the value of c^{-1}?
d. What upper limit would you set to this ratio? (Also consider your calculations for Exercise 3.)

The upper limit to Δt is determined by the inverse of coefficient c in the differential equation. The inverse of c is called the time coefficient, τ, which has the dimension of time. It is a measure of the reaction rate of a model. In models containing more than one time coefficient, a first approximation to the time interval is obtained by taking Δt smaller than one-tenth of the smallest τ in that model. The time coefficient appears equal to the time that would be needed by the model to reach the equilibrium state, if the rate of change were fixed. This applies to any point on the integrated function, as shown in Figure 8.

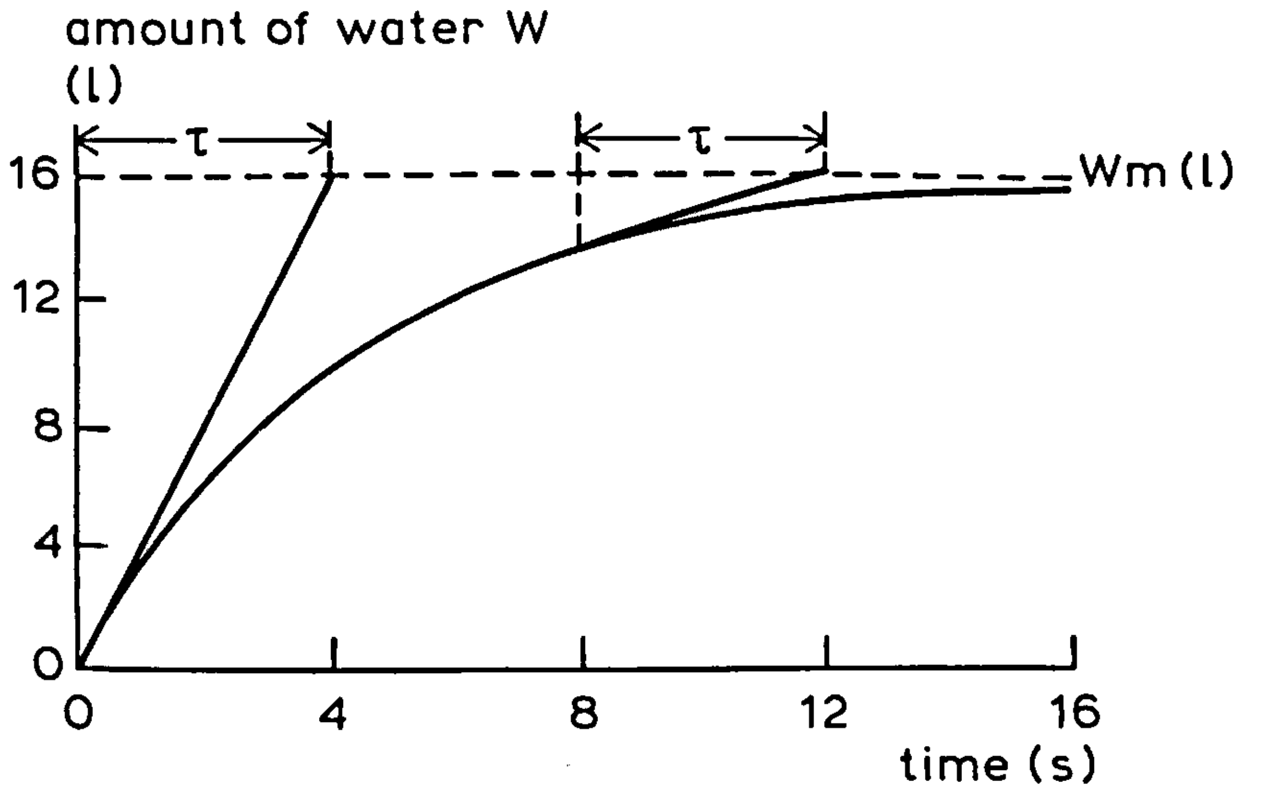

Figure 8. The amount of water as a function of time, according to Equation 6, with $W_0 = 0$ l, $Wm = 16$ l and $c^{-1} = \tau = 4$ s, yields $W = Wm \cdot (1 - e^{-t/\tau})$. The time interval over which the tangent must be extended to intercept the line of equilibrium is the time coefficient, τ.

Exercise 5

a. Prove this last statement by using Equation 8 for the water tank case.
b. This is also correct for a positive feedback loop, but the formulation is different. Explain this for the case of exponential growth.

Biological models are often characterized by a relative growth rate (rgr), i.e. coefficient c in Equation 2, with dimension t^{-1}. This name is clarified by writing c explicitly: $c = (dA/dt)/A$.

Exercise 6

a. Calculate the time coefficients when the relative growth rates are 1.5, 0.2, and 0.05 per year.
b. What time intervals would you use for numerical integration in these cases? Also take into account the practical aspect of numerical calculations.
c. Compute the number of animals after 5 years, when $c = 0.2$, $A_0 = 100$, by using
   1. The analytical solution to the problem, Equation 5;
   2. The numerical solution to the problem, using Equation 2 and $\Delta t = c^{-1}/10$.
d. Plot your results on graph paper.
e. Explain the underestimate of the numerical solution compared with the analytical one.

A note of caution may be appropriate here. The time coefficient is defined as the inverse of the relative growth rate (see also Exercise 6). The growth percentage (i.e. the relative increase in the number of animals after one year, or annual relative increase) is often used to calculate τ, but this gives incorrect results. A growth rate of, for example, 20% per year is not equivalent to an rgr of 0.2 per year. The relative growth rate is less: when $A_0 = 100$, A equals 120 after one year and Equation 5 can be used to calculate the relative growth rate as follows: $A = 120 = 100 \cdot e^{rgr \cdot 1}$, so $rgr = \ln 1.2 = 0.182\,yr^{-1}$ and $\tau = 5.48\,yr$ instead of $1/0.2 = 5\,yr$. The relative growth rate (rgr) may be expressed in the annual relative increase (ari) as: $A_0 + A_0 \cdot ari = A_0 \cdot e^{rgr \cdot 1}$ or $rgr = \ln(1 + ari)$. For an exponential decline, one can derive $rdr = -\ln(1 - ard)$, rdr and ard being the relative death rate and the annual relative decrease, respectively. The differences between ari and rgr, or that between ard and rdr, will be substantial when the annual relative increase or decrease is large.

Other names for the time coefficient and related concepts are time constant, transmission time (in control-system theory), average residence time, delay time, extinction time and relaxation time; this indicates the significance of the time coefficient in various sciences. Doubling time, the time needed to double an amount, is sometimes used to characterize a system but it is not synonymous with the time coefficient.

Exercise 7
The relationship between doubling time, t(2), and the time coefficient in exponential growth is $t(2) \cong 0.7 \cdot \tau$. Why?

Relaxation time, a term often used in physics, is the time needed in exponential increase to change the state by a factor e, or in exponential decrease, to change the state by a factor 1/e: it is equivalent to the time coefficient. For an example of average residence time, consider an exponentially decreasing population of animals without the effects of birth or migration. Then, the average residence time equals the time coefficient.

Exercise 8
Prove this last statement mathematically by using the definition of the average residence time:

$$-\frac{1}{A_0}\int_0^\infty t \cdot \frac{dA}{dt} \cdot dt = \frac{1}{A_0}\int_0^{A_0} t \cdot dA = \frac{1}{A_0}\int_0^\infty A \cdot dt,$$

and the analytical equation describing exponential decrease: $A = A_0 \cdot e^{-t/\tau}$.

In nature many processes occur simultaneously. Calculations in simulation models of such processes, however, take place one after another. But since dynamic simulation is based on the principle that rates of change are mutually independent (i.e. they depend individually on state variables and driving variables), all rates applicable to any one moment can be calculated in series; they can then be integrated (in series) to obtain the values of the state variables a moment (Δt) later. In this way the model operates in a semi-parallel fashion, and simulates simultaneously occurring processes. It is convenient to use special simulation languages to describe parallel processes in a semi-parallel fashion. If other computer languages are used, this requirement should still be met.

2.1.6 *Some numerical integration methods*

The principle of numerical integration was illustrated using the simplest and most straightforward, rectangular integration method of Euler. Rectangular integration gives the poorest agreement with an analytical solution (if available). Other, more sophisticated methods, e.g. the trapezoidal method and the Runge-Kutta method, are more accurate, but cannot always be used. These two sophisticated methods will now be considered in more detail. Their computation schemes are given in Table 1. The example of the water tank will be used to illustrate the trapezoidal integration method. A first estimate of the rate variable, R1, and the state variable, A1, is calculated using the rectangular integration method, yielding (for a 2 s time step): R1 $= (dW/dt)_{t=0} = 4\,l\,s^{-1}$ and A1 $= W_{t=2} = 8$ l. The estimated final state, A1, is used to calculate a second rate, R2, pertaining to t = 2 s: R2 $= (dW/dt)_{t=2} = \frac{1}{4} \cdot (16 - 8) = 2\,l\,s^{-1}$. The rate which is integrated is the arithmetic average of R1 and R2; thus, the final amount of water, after 2 seconds, is: $0 + 2 \cdot ((4 + 2)/2) = 6$ l. The following diagram clarifies the calculations:

time	s	$0 \longleftarrow$	$\Delta t \longrightarrow 2$	4	6	8
W_{final}	l	0 $\downarrow$ a	$\xrightarrow{e}$ 6	9.75		
$(dW/dt)_{1st\,est.}$	$l\,s^{-1}$	4 b	2.5			
$W_{1st\,est.}$	l	8 $\downarrow$ c	11			
$(dW/dt)_{2nd\,est.}$	$l\,s^{-1}$	2 d	1.25			
$(dW/dt)_{final}$	$l\,s^{-1}$	3	1.875			

where the sequence, a to e, indicates the computational sequence. At a and c, the rate equation is used (Equation 3 from Figure 4); at b and e, integration takes place and, at d, the arithmetic average is calculated; est. stands for estimate.

Exercise 9

Complete the calculation above and plot the amount of water in the tank against time on the graph from Exercise 3.

a. What do you notice about the difference between the numerical and analytical solutions?

b. Show graphically that thc trapezoidal integration method underestimates the analytical solution, and explain why; make use of the graph depicting Equation 3a, and the appropriate numerical values.

In this method, the differential equation had to be evaluated twice to obtain the state of the model after one time interval. The larger computation effort is more than compensated for by the larger ratio of $\Delta t/\tau$ that can be taken to reach the same accuracy as in the rectangular method (see Subsection 2.1.7). This is even more so for the Runge-Kutta integration method. This method will not be

Table 1. Summary of the rectangular, trapezoidal and Runge-Kutta integration methods; t stands for time, R for rate and A for state. The equals sign is not used here algebraically but as an assignment.

Euler's rectangular method

$R = f(A_t, t)$

$A_{t+\Delta t} = A_t + \Delta t \cdot R$

$t = t + \Delta t$

Trapezoidal method

$R1 = f(A_t, t)$

$A1 = A_t + \Delta t \cdot R1$

$R2 = f(A1, t + \Delta t)$

$A_{t+\Delta t} = A_t + \Delta t \cdot (R1 + R2)/2$

$t = t + \Delta t$

Runge-Kutta method

$R1 = f(A_t, t)$

$A1 = A_t + \Delta t \cdot R1 \cdot 0.5$

$R2 = f(A1, t + 0.5 \cdot \Delta t)$

$A2 = A_t + \Delta t \cdot R2 \cdot 0.5$

$R3 = f(A2, t + 0.5 \cdot \Delta t)$

$A3 = A_t + \Delta t \cdot R3$

$R4 = f(A3, t + \Delta t)$

$A_{t+\Delta t} = A_t + \Delta t \cdot (R1 + 2 \cdot R2 + 2 \cdot R3 + R4)/6$

$t = t + \Delta t$

explained in detail, but its scheme, given in Table 1, shows that four estimates are necessary to calculate the final rate.

Exercise 10
Calculate the amount of water in the tank after a time interval of 2 s using the numerical integration scheme of Runge-Kutta. Use the numerical values from Exercises 3 and 9.

So far, the integration routines have had a fixed time interval, which was set arbitrarily to one-tenth of the time coefficient of the model. If the time coefficient changes during simulation, and its smallest value is known, one can fix the time interval to one-tenth of that value. This, however, implies that during periods with large τ values, the accuracy of integration would be greater than that during periods with small τ values. In models intended to quantify natural systems, it is preferable to preset the accuracy of integration and to vary the time interval to meet this accuracy. This is done by combining the integration methods of Runge-Kutta and Simpson. (The Simpson method, the accuracy of which lies somewhere between that of the trapezoidal and the Runge-Kutta methods, is discussed in detail in IBM, 1975.) Two integration routines, Runge-Kutta's and Simpson's are applied to integrate the differential equations. Their results are compared and, if they differ by more than a preset error, the time interval of integration, Δt, is halved. If the deviation is much smaller than required, Δt is doubled for the next time step. Because of the constancy of the integration error, this method is to be recommended as standard.

Exercise 11
The principle of the combined Runge-Kutta and Simpson methods is demonstrated in the program given in Figure 9, for the example of exponential population growth (for numerical constants see Exercise 6c). For simplicity, the Runge-Kutta and Simpson methods are replaced by the trapezoidal and rectangular methods, respectively. Also, Δt (DELT) is doubled at the beginning of each new time interval. The program is written in FORTRAN and the results given in Table 2.

a. Draw a flow diagram of the program listed in Figure 9, indicating decisions by ◇ and calculations, etc., by ▭

Note that the purposes and symbols of a flow diagram are completely different from those of the relational diagram. The first is a technical scheme of how calculations are arranged, whereas the second expresses the conceptualization of the system.

Figure 9. Program demonstrating the principle of an integration method that adapts its time interval to meet a pre-set error criterion, using the rectangular and the trapezoidal integration methods.

```
C Demonstration program of a variable time-step integration method
C         using the rectangular- and trapezoidal methods.
C Timer variables 1) DELT should not become smaller than a certain small
C                    value (DELMIN) or larger than the print interval (PRDEL)
C                 2) timer variables have been set double precision to
C                    avoid rounding errors on the PRDEL-timings.
C INITIAL PART.
      DOUBLE PRECISION TIME,PRDEL,FINTIM,DELT,DELMIN,DELTIM,COUNT3
      TIME  =0.D00
      FINTIM=5.D00
      PRDEL =5.D00
      DELMIN=1.D-5
      DELT  =5.D00
      ERROR =1.E-5
C Relative growth rate and initial amount.
      A     =100.
      RGR   =0.2
C Counter one gives number of times that algorithm has been executed.
C Counter two gives number of times final integration has been performed.
C Counter trhee gives the number of times that output has been written.
      COUNT1=0.
      COUNT2=0.
      COUNT3=0.D00
C DYNAMIC PART.
5     IF(TIME.EQ.COUNT3*PRDEL) GOTO 10
      IF(TIME.GT.FINTIM) STOP 'FINTIM'
      DELT  =2.D00*DELT
      DELTIM=COUNT3*PRDEL-TIME
      IF(DELT.GT.DELTIM) DELT=DELTIM
C Remember current amount 'A' in memory 'B'.
15    B     =A
      GR1   =RGR*A
      A1    =A+DELT*GR1
      GR2   =RGR*A1
      A     =A+((GR1+GR2)/2.)*DELT
C RELERR=ABSolute value of (A(RECT)-A(TRAPZ))/A(TRAPZ)
      RELERR=ABS((A1-A)/A)
      COUNT1=COUNT1+1.
      IF(RELERR.GT.ERROR) GOTO 20
      TIME  =TIME+DELT
      COUNT2=COUNT2+1.
      GOTO 5
20    CONTINUE
C Restore current amount 'A' again in memory A, because
C calculation is not accurate enough and should be done again
C starting with the previous final amount and a halved DELT.
      A     =B
      DELT  =DELT/2.
      IF(DELT.LT.DELMIN) STOP 'DELMIN'
      GOTO 15
C PRINT PART.
10    WRITE(21,25)TIME,A,A1,RELERR,DELT,COUNT3,COUNT1,COUNT2
25    FORMAT(/10H  TIME    =D12.7,10H   A      =F12.5,10H   A1     =F12.5/
     $10H  RELERR =E12.7,10H   DELT  =D12.7,10H   COUNT3=F9.2/
     $10H  COUNT1 =F8.2,14H        COUNT2=F8.2)
      COUNT3=COUNT3+1.
      GOTO 5
      END
```

Table 2. Results of the program shown in Figure 9.

Symbols mean:

A, A1	: Results of integration by the trapezoidal and the rectangular methods, respectively.
RELERR	: Absolute value of the relative error between methods.
DELT	: Δt.
COUNT1, 2 and 3:	See Comments in Figure 9 (lines starting with C in first column).

TIME	=	.0000000D+00	A	=	100.00000	A1	=	0.00000
RELERR	=	.0000000E+00	DELT	=	.5000000D+01	COUNT3	=	0.0
COUNT1	=	0.00	COUNT2	=	0.00			
TIME	=	.5000000D+01	A	=	271.82767	A1	=	271.82559
RELERR	=	.7634231E−05	DELT	=	.1953125D−01	COUNT3	=	1.00
COUNT1	=	518.00	COUNT2	=	256.00			

The combined methods of Runge-Kutta and Simpson cannot be used at discontinuities of the state variable in time. For instance, when a crop is harvested, the contents of the state variable in the model must be removed instantaneously. In principle, states can only be changed by integration of rates over time. If a state variable's content, A_t, must be removed instantaneously, i.e. in one time interval Δt, the rate of change must be defined as $R_t = A_t/\Delta t$, and the rectangular integration method should be used. Rewriting Equation 7 for the moment of harvesting yields:

$$A_{t+\Delta t} = A_t - \Delta t \cdot (A_t/\Delta t)$$

Exercise 12

Let A_t be 100, Δt be 2, and define the rate of change R_t as $R_t = A_t/\Delta t$:

a. Compute the amount $A_{t+\Delta t}$ according to the rectangular and trapezoidal integration routines.

b. What do you conclude about the method of integration to be applied when division by Δt occurs in a rate variable?

There are many more numerical integration routines available, but the methods discussed here are usually sufficient to tackle the problems encountered in biological models.

Figure 10 summarizes the line of reasoning to be followed in order to select the appropriate integration method.

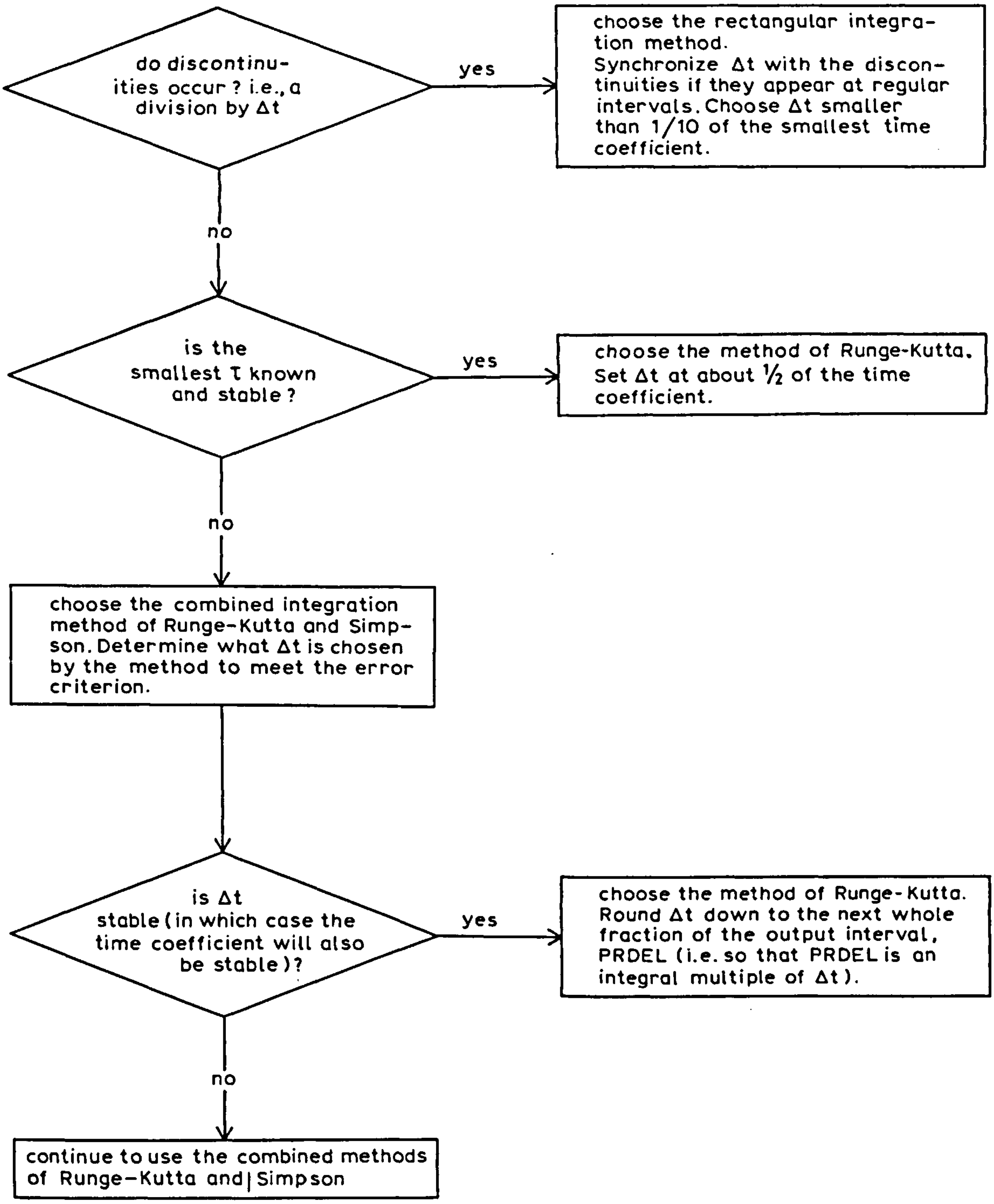

Figure 10. Flow diagram for choosing the appropriate integration method.

2.1.7 Error analysis; a case study of integration with and without feedback

The accuracy of numerical integration is influenced by the choice of Δt (Subsection 2.1.5). An error criterion was introduced in Subsection 2.1.6 (see Figure 9) to determine which Δt should be chosen to obtain integration results with errors smaller than, or equal to, this preset limit. Error analysis is used to quantify these errors in terms of Δt and τ. As many rates in nature are proportional to the amounts present, the error analysis will be demonstrated for the model of exponential growth (Equations 2, 2a, 5 and Figure 6).

In the analysis of propagation of errors in integration, two situations should be distinguished. In the first situation, rate as a function of time is known in advance, e.g. a driving force. Then, results of integration are independent of the state variable that is changed by integrating the rate (situation without feedback), and the same relative error is made each time interval. In the second situation, the rate depends at each moment on the state of the system. This situation usually occurs in simulation, and the error in the calculations will accumulate: in exponential growth, an underestimation of the state will cause an underestimation of the rate, and hence state (situation with feedback).

Integration of a driving force (no feedback) When a driving force is integrated, its value is known in advance as a function of time; for instance, a series of data of rates of change which may be represented by an exponential curve. Figure 11 shows such a curve (solid line), drawn according to Equation 2a, with $A_0c = v_0$, the initial velocity. Integration by the rectangular and trapezoidal methods yields the hatched areas. In this case, the exact error in the result obtained by the rectangular integration method could be derived, but a good approximation is given by the area of the triangles that are included using the trapezoidal integration method.

The relative error in an integration method of order n is defined as

$$E_{rel,n} = \frac{A(n^{th}\text{ order method}) - A((n+1)^{th}\text{ order method})}{A((n+1)^{th}\text{ order method})} \qquad \text{Equation 10}$$

where A stands for surface area. (This definition has already been used in the program in Figure 9.) Examples of first, second, third and fourth order integration methods are the rectangular, trapezoidal, Simpson and Runge-Kutta methods, respectively.

Applying Equation 10 to calculate the relative error in the first order rectangular integration method gives:

$$E_{rel,1} = \frac{v_0 \cdot \Delta t}{(v_0 + v_0 \cdot e^{c \cdot \Delta t}) \cdot \Delta t/2} - 1$$

From the numerator and denominator, $v_0 \cdot \Delta t$ cancels, and $e^{c \cdot \Delta t}$ can be written according to a Taylor expansion: $1 + c \cdot \Delta t + \frac{1}{2}(c \cdot \Delta t)^2 + \ldots$ (see Appendix 1 for details). Since $c \cdot \Delta t$ is much smaller than 1, higher order terms can be omitted, and, after some algebra, one obtains:

$$E_{rel,1} \cong -\tfrac{1}{2} \cdot c \cdot \Delta t = -\tfrac{1}{2} \cdot \frac{\Delta t}{\tau} \qquad \text{Equation 11}$$

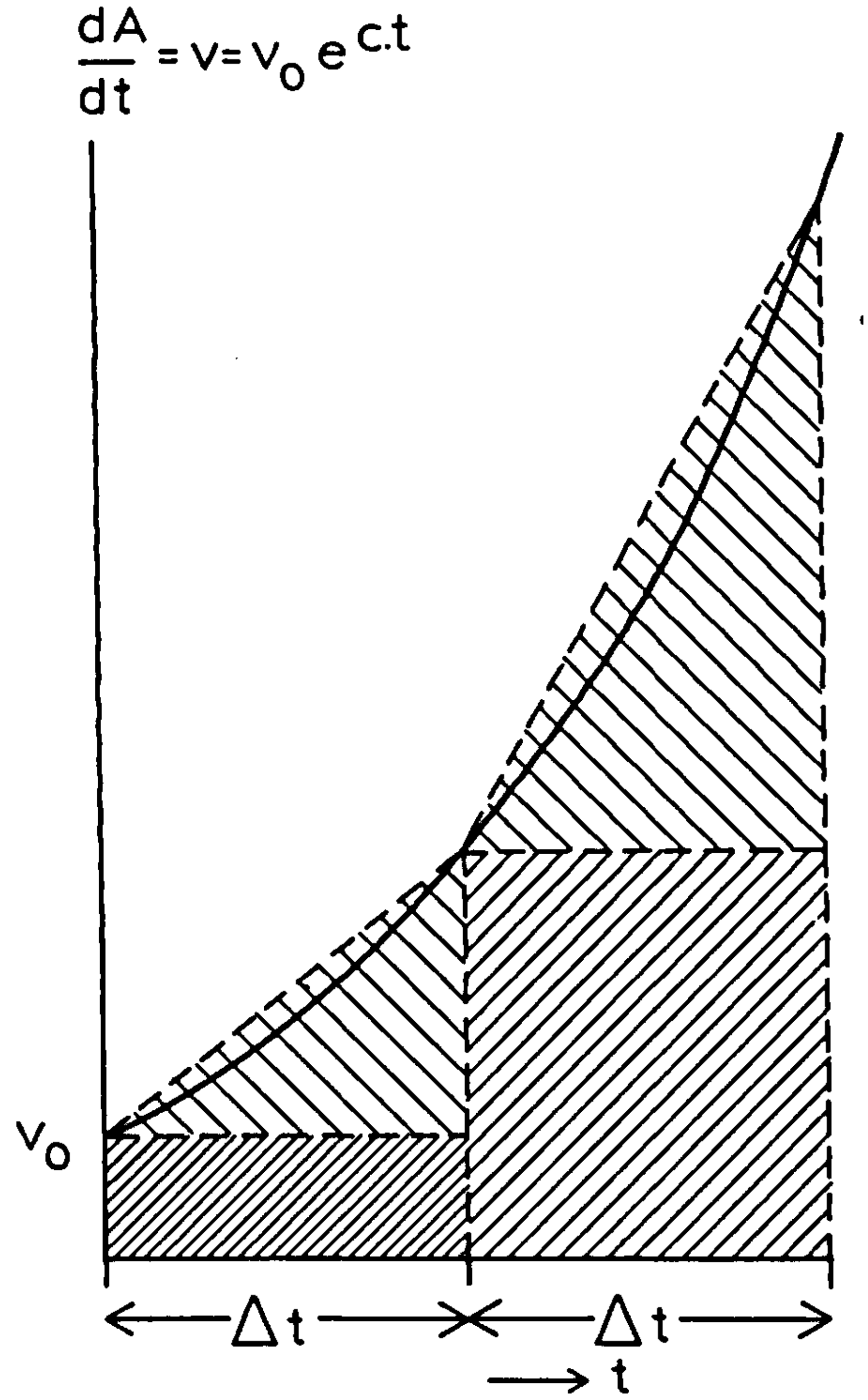

Figure 11. Graphical representation of the surface areas that are calculated by the rectangular integration method ( ) and by the trapezoidal integration method (+), when the exponential rate curve is given as a function of time (solid curved line).

This derivation is given in detail in Appendix 1. Equation 11 shows that the relative error is proportional to the ratio of the time interval of integration and the time coefficient of the model. The minus sign reveals the underestimation of the surface area beneath the curved solid line in Figure 11. As the rate of change grows exponentially, the same relative error is added each time interval. Thus, the final absolute error is $E_{abs,1} = -\frac{1}{2} \cdot (\Delta t/\tau) \cdot A$. In the trapezoidal integration method, the triangles are taken into account, so the error is much smaller. The remaining error is estimated from the area between the straight line that is formed by connecting the corners of the vertical bars and the parabola constructed through the values of the exponential rate function at times t, $t + \frac{1}{2} \cdot \Delta t$ and $t + \Delta t$. The relative errors for the trapezoidal and Runge-Kutta integration methods have been calculated by Goudriaan (1982) and are given in Table 3. Note that for integration without feedback, the relative error is independent of the simulation time.

Exercise 13

a. Use the estimates of the relative errors without feedback from Table 3 to calculate which Δt (expressed as a fraction of τ) must be chosen to yield a relative error of 1% in the integration of an exponential curve, for all three methods.

b. Calculate analytically the area beneath an exponential curve between $t = 0$ and $t = 1$, with $v_0 = 1$ and $c = 1$. Also, calculate this area using the three numerical methods with $\Delta t = 1$. Since in integration without feedback all rates are known in advance, it is neither necessary to know the initial condition nor to calculate the intermediate areas.

c. From the answer to b, calculate the exact absolute and relative errors in the integration results using the three numerical methods, with respect to the analytical solution. Compare these exact relative errors with the estimates from Table 3.

Table 3. Estimates of the relative errors of three integration methods.

Method	Without feedback	With feedback
rectangular	$-(\Delta t/\tau)/2$	$-(t \cdot \Delta t/\tau^2)/2$
trapezoidal	$(\Delta t/\tau)^2/12$	$-(t \cdot \Delta t^2/\tau^3)/6$
Runge-Kutta	$(\Delta t/\tau)^4/2880$	$-(t \cdot \Delta t^4/\tau^5)/120$

Integration of a differential equation with feedback In dynamic simulation, the rate variable is usually not known as a function of time; instead, new values are calculated from the current state, as for example in Equations 2 and 3. For instance, in the case of exponential growth of an animal population, an underestimate of the growth rate will result in an underestimate of the population at time $t + \Delta t$, and thus also of the growth rate at that moment. This occurs in numerical integration of differential equations with feedback, and a new error will be added each time interval. Thus, in contrast to the integration of a driving force, relative errors increase during the time of simulation. The error analysis is slightly different from that for a driving force, because the relative error will refer to the total integral value, which consists of the integrated amount together with the initial value.

For the rectangular method this implies the following. The rate at time t equals (Equation 2): $(dA/dt)_t = c \cdot A_t$. So the value of the integral after one time interval is $A_{t+\Delta t} = A_t + \Delta t \cdot c \cdot A_t$. To calculate the value of the integral according to the trapezoidal method, the rate at $t + \Delta t$ is calculated:

$$(dA/dt)_{t+\Delta t} = c \cdot A_t \cdot (1 + \Delta t \cdot c).$$

It then follows that

$$A_{t+\Delta t} = A_t + \Delta t \cdot (c \cdot A_t + c \cdot A_t \cdot (1 + \Delta t \cdot c))/2.$$

All the terms required to calculate $E_{rel,1}$ according to Equation 10 are now available. After some algebra, and neglecting higher order terms, the relative error in the rectangular integration method is determined as

$$E_{rel,1} \cong -\tfrac{1}{2} \cdot (\Delta t \cdot c)^2 = -\tfrac{1}{2}\left(\frac{\Delta t}{\tau}\right)^2 \qquad \text{Equation 12}$$

This derivation is given in detail in Appendix 2. The relative error occurs in each integration step and, in contrast to the situation without feedback, these errors accumulate. At time t, when $t/\Delta t$ integration steps have been performed, the relative error is

$$E_{rel,1} \cong -(t \cdot \Delta t/\tau^2)/2$$

Interestingly, the relative error is proportional to Δt, as for integration without feedback, but is now also linearly dependent on the simulation time. The relative errors for integration with feedback for the trapezoidal and Runge-Kutta integration methods, as derived by Goudriaan (1982), are also given in Table 3.

Exercise 14

a. Perform the calculations in Exercise 13a for the situation with feedback and a simulation time equal to τ.
b. For the situation with feedback, the differential equation is $dA/dt = v = c \cdot A$ (Equation 2). Calculate A at $t = 1$ when the initial condition, A_0, equals 1, $c = 1$, and $\Delta t = 1$, using the three numerical methods. Also calculate A at $t = 1$ for this situation, analytically.
c. Perform the calculations in Exercise 13c for the situation with feedback.

At a discontinuity, no derivative exists. When an integration interval overlaps a discontinuity, the error in any integration method will be large, as seen in Exercise 12 where an attempt was made to nullify a state variable in one time step, using the trapezoidal integration method. Error analysis as described above can, however, be applied before and after such discontinuities. The numerical error due to the discontinuity itself is avoided by using the rectangular integration method and synchronizing the time interval with the discontinuity.

2.1.8 An example

The different steps which are distinguished in systems analysis of living systems are demonstrated below.

Objectives and definition of the system A microbiologist plans to develop a technical system in which yeast can be grown continuously. To do this he wishes to use a vessel of constant volume, through which a sugar solution will flow. To gain insight into the proper technical system parameters, such as the volume of the vessel (v, m^3), the concentration of sugar in water (c_s, kg kg^{-1}) and the flow rate of water (q, m^3 d^{-1}), he decides to design a model of the system.

The physiological parameters pertaining to the yeast cannot be adjusted like the technical parameters. Therefore, some experiments are performed which reveal that the absolute growth rate of the yeast (dy/dt, kg d^{-1}) is proportional to the amount of yeast (y, kg) present, and to the sugar concentration. At a sugar concentration of 10%, c_{s10}, the relative growth rate and amount of sugar in the vessel are termed μ_{10} and s_{10}, respectively. The rate of sugar consumption per unit yeast (s_y, kg kg^{-1} d^{-1}) is known. The maximum possible quantity of sugar (s_m, kg) in the vessel is determined by the incoming sugar concentration and the volume of the vessel.

Exercise 15

The following table gives fictitious data on the changing amount of yeast at different constant sugar concentrations.

sugar concentration in water (kg kg^{-1})	time (h) 0	2	4	10
0	2000	2000	2000	2000
0.02	1950	2119	2304	2958
0.05	1900	2340	2882	5384
0.10	2050	3110	4717	16464

a. Derive the relative growth rate of yeast, μ, at these four different sugar concentrations.
b. Plot the relative growth rate, in units of day^{-1}, against the sugar concentration, c_s. Express μ in terms of c_s, c_{s10} and μ_{10}.
c. Rewrite the expression for μ in terms of the current amount of sugar, s, and s_{10}.

The relational diagram Figure 12 shows the relational diagram of the model. Note that this figure is constructed from the elementary system units used throughout this text. For instance, the lower left input rate together with the integral of the sugar (s, kg) is equivalent to the relational diagram of the car from Figure 6; and the upper integral of the yeast, together with the right output rate, forms an exponential decrease. The representation of the model by one integral

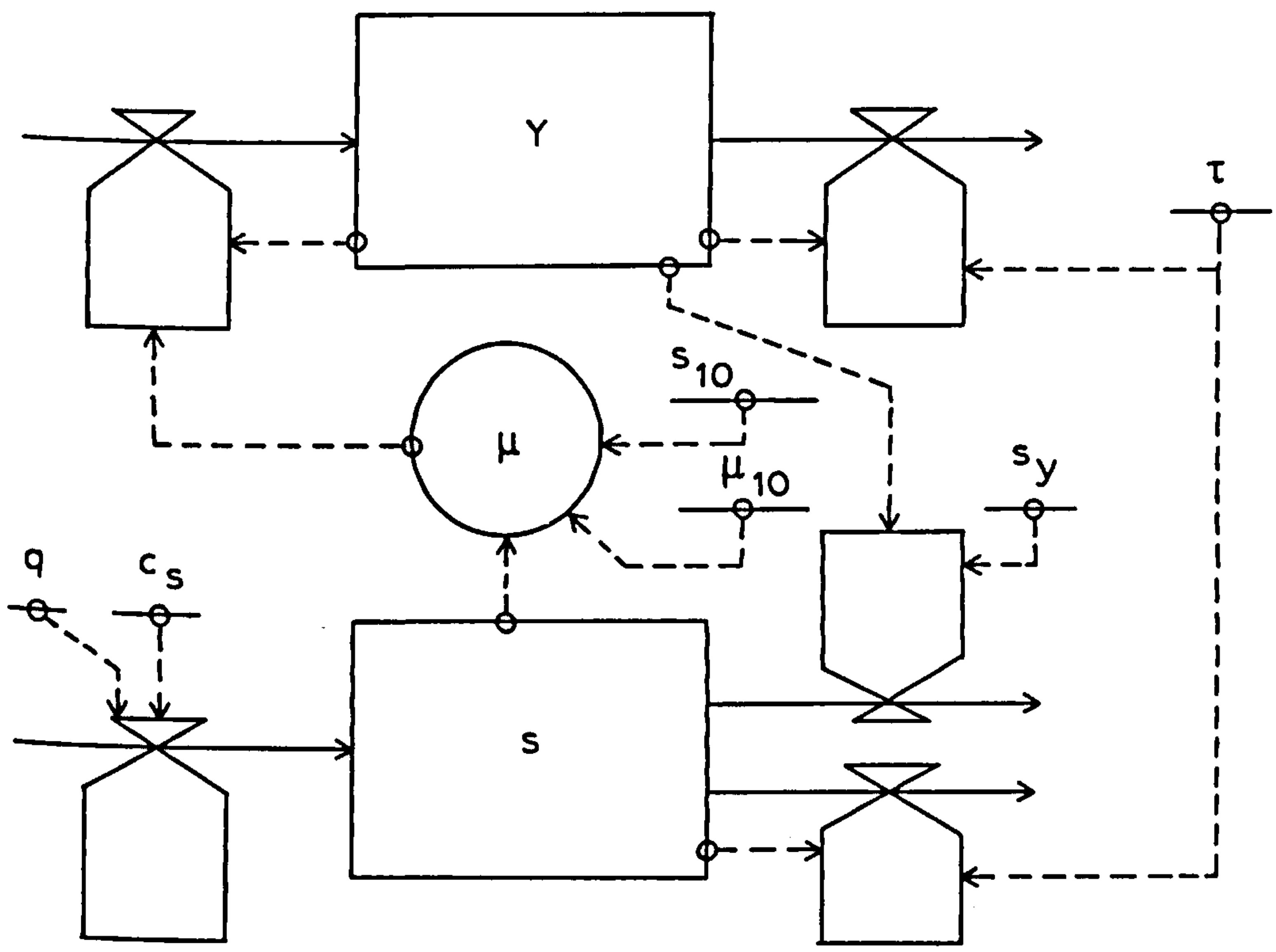

Figure 12. Relational diagram of a continuous yeast culture fed by a sugar solution.

for y and one for s, implies that the yeast and the sugar solution are well mixed throughout the vessel; the integral contents as a whole influence both input and output rates. The relational diagram does not contain yeast mortality: the time coefficient of the vessel (τ, d) influences only the outflow rate of yeast. The τ of the vessel has a similar influence on the outflow rate of the sugar, but here a second outflow is present as sugar is consumed by the yeast. The time coefficient of the vessel represents the average residence time of yeast and sugar in the vessel. In the real system, this characteristic time can be adjusted, as it is defined as $\tau = v/q$ (d).

Differential or rate equations The relational diagram in Figure 12 can help to derive the differential equations. It is immediately clear which variables will appear in a particular rate or flow. For example, for the input flow of yeast: $dy/dt = f(y, \mu)$, with $\mu = f(\mu_{10}, s_{10}, s)$; and for the output flow: $dy/dt = f(y, \tau)$.

This information, together with information on the proportionalities and dimensions of variables, yields the net flow rate for yeast:

$$\frac{dy}{dt} = \mu \cdot y - \frac{y}{\tau} \qquad \text{Equation 13}$$

where

$$\mu = \frac{s}{s_{10}} \cdot \mu_{10} \qquad \text{Equation 14}$$

$$s_{10} = c_{s10} \cdot v \cdot 1000 \qquad \text{Equation 15}$$

$$\tau = \frac{v}{q} \qquad \text{Equation 16}$$

By analogy, the net flow rate for sugar is

$$\frac{ds}{dt} = c_s \cdot q \cdot 1000 - y \cdot s_y - \frac{s}{\tau} \qquad \text{Equation 17}$$

Exercise 16

a. Examine the dimensions of all variables and constants in Equations 13 to 17.

b. What does the number 1000 denote in Equations 15 and 17?

Further analysis of Equations 13 to 17 To study the dynamic behaviour of the yeast-sugar model, Equations 13 and 17 should be solved by numerical integration. However, several model properties can be analysed without a computer; for example by studying simplified equations or equilibrium properties.

An example of needing to simplify equations, is the calculation of the time needed to equilibrate a water-filled vessel, which is initially free of sugar, with the sugar solution but in the absence of yeast. The relational diagram for this problem is represented by the lower half of Figure 12 when the outflow of sugar, due to consumption by the yeast, is omitted. The differential equation for the sugar, when $y = 0$, is $ds/dt = c_s \cdot q \cdot 1000 - s/\tau$, which can be solved analytically. For the condition that at $t = 0$, $s = 0$, this gives

$$s = s_m \cdot (1 - e^{-t/\tau}) \qquad \text{Equation 18}$$

where $s_m = c_s \cdot v \cdot 1000$, which is the maximum amount of sugar that can be achieved with given c_s and v.

Equations 18 and 6, when $W_0 = 0$, are similar in form, although their differential equations describe quite different systems and express a dynamic and a static flow model, respectively.

Exercise 17

Derive from Equation 18, in general terms, the time needed to reach 95% of the final equilibrium level of sugar in the vessel.

Such equilibrating processes may take a long time when large time coefficients are involved. It is preferable, therefore, to start an experiment by filling an empty vessel with the desired sugar solution.

Exercise 18
How much time, expressed in terms of the time coefficient, is needed to reach 100 % of the equilibrium level of sugar when an empty vessel is filled at a constant rate with the sugar solution? There is no outflow until the vessel is full.

Equations 13 and 17 can be analysed to determine whether equilibrium levels of yeast and sugar can be reached, and if so, what levels. In a dynamic equilibrium the state variables are constant, and the sum of the inflow rates is equal to the sum of the outflow rates. Thus, the net rate of change of the state variable is zero. In the case of the continuous culture, this means that dy/dt and ds/dt in Equations 13 and 17, respectively, are zero. The equilibrium levels of sugar and yeast can be calculated from

$$s = \frac{s_{10}}{\mu_{10} \cdot \tau} \qquad \text{Equation 19}$$

and

$$y = \frac{1}{\tau \cdot s_y} \cdot (s_m - s) \qquad \text{Equation 20}$$

A special case of dynamic equilibrium is obtained when y is zero. Such a dynamic equilibrium is established when the yeast culture is washed out, because the time coefficient for the vessel is smaller than that for the yeast. This is the case when $q > c_s \cdot v \cdot \mu_{10}/c_{s10}$.

Exercise 19
Derive Equations 19 and 20 from Equations 13 to 17.

Equation 20 shows that the equilibrium level of yeast depends on the (manipulable) time coefficient for the vessel.

The microbiologist is interested in the combination of manipulable parameters yielding maximum yeast production with the minimum amount of sugar. The only manipulable variables in Equation 20 are s_m and τ. From Equation 19 it follows that s is a hyperbolic function of τ, indicating that at very low τ values s will be very large, and at high τ values s will be small; i.e. there is no practical minimum value of the amount of sugar. To investigate whether a maximum exists in the curve of yeast production against the time coefficient, Equation 19 is inserted into Equation 20, which is then differentiated with respect to τ, to obtain

$$\frac{dy}{d\tau} = \frac{1}{\tau^2 \cdot s_y} \cdot \left(\frac{2 \cdot s_{10}}{\tau \cdot \mu_{10}} - s_m \right) \qquad \text{Equation 21}$$

Exercise 20

a. Derive Equation 21.

b. At what value of τ is there a maximum or minimum value of y?

If the second derivative of y with respect to τ is negative at the τ value found in Exercise 20b, y is at a maximum. The second derivative is

$$\frac{d}{d\tau}\left(\frac{dy}{d\tau}\right) = \frac{d^2y}{d\tau^2} = \frac{2}{\tau^3 \cdot s_y} \cdot \left(s_m - \frac{3 \cdot s_{10}}{\tau \cdot \mu_{10}} \right) \qquad \text{Equation 22}$$

Substituting the answer from Exercise 20b into Equation 22 yields a negative value for the second derivative. The maximum yeast level, at that value of τ, can be calculated from Equation 20 as

$$y = \tfrac{1}{4} \cdot \frac{\mu_{10}}{s_{10} \cdot s_y} \cdot s_m^2 \qquad \text{Equation 23}$$

The quantity of sugar is then

$$s = \tfrac{1}{2} \cdot s_m. \qquad \text{Equation 24}$$

Equations 23 and 24 show that at the optimum value of τ ($= v/q$), the amounts of yeast and sugar can still be changed by adjusting the inflow concentration of sugar which determines s_m.

Exercise 21

a. Check the dimensions of Equations 19 to 24.

b. Express the water flux q in terms of the other parameters to calculate the inflow rate resulting in the maximum amount of yeast at a given sugar concentration and vessel volume.

It has been shown which tools are needed to develop and solve simple models. Although the treatise is far from complete, it will be seen that most of the models described in the following chapters are composed of the elementary feedback loops discussed in this chapter, and that the above simple mathematical techniques are adequate to solve them. Analysing and solving more complex problems, requires more knowledge, expecially about the relationships that may characterize system structure, rather than sophisticated mathematics. Today, the lack of such knowledge is the major restriction, but is also the major challenge, of future research.