

Breakdown of a chemostat exposed to stochastic noise

JOHAN GRASMAN, MAARTEN DE GEE and ONNO A. VAN HERWAARDEN

Biometris, Wageningen University and Research Centre, Postal Box 100, 6700 AC Wageningen, The Netherlands

(E-mail: johan.grasman@wur.nl)

Received 29 November 2004; accepted in revised form 7 June 2005

Abstract. The stochastic dynamics of a chemostat with three trophic levels, substrate-bacterium-worm, is analyzed. It is assumed that the worm population is perturbed by environmental stochastic noise causing extinction in finite time. A diffusion model of the process is formulated. With singular perturbation methods applied to the corresponding Fokker-Planck equation an estimate of the expected extinction time is derived. This chemostat can be seen as an experimental sewage-treatment system in which the worm population facilitates the reduction of remaining sludge.

Key words: chemostat, Fokker-Planck equation, white noise, WKB-method

1. Introduction

Investigations of the dynamics of biological populations that are based on the deterministic theory of ordinary differential equations are numerous and cover a wide variety of phenomena that can arise in nonlinear systems. In this study we focus on a class of models having other qualitative properties: systems that are subjected to random perturbations. These perturbations may be from external sources (environmental stochastic noise) or inherent in the biological process itself (random birth and death or random mating). Deterministic models with an asymptotically stable limit solution (equilibrium, limit cycle or strange attractor) will have a solution with all the populations remaining present for infinitely long time. Introduction of noise may result in a system in which one or more populations will get extinct with probability one in finite time. This property of limited persistence cannot be described with a deterministic model. Studies on the stochastic dynamics of a population consisting of genetically different subpopulations already have a long history [1]. Later on, this type of analysis was extended to ecological systems [2], including the study of metapopulations [3].

The problem of extinction of a (sub)population in a system of interacting populations cannot be analyzed quantitatively to its full extent because of the complexity of such problems. Application of the theory of singular perturbations yields an asymptotic approximation method that offers the possibility of computing estimates of certain quantities under the assumption that the random perturbations are small. Various applications in population biology are given by [4]. In epidemiology, for example, the expected duration of the endemic period is an important parameter that is worth to be estimated. For the general theory of random perturbation of dynamical systems and the exit problem we refer to [5–7].

In the present study we deal with a problem from the environmental sciences: the modeling of a sewage treatment plant in which bacteria feed on organic matter as well as phosphates and other minerals in the waste. In this way the sewage is purified and cleaner wastewater, that meets the health standards, can be brought into the environment. Still at the plant one

is left with the sludge consisting of indigestible sewage and the remains of the bacteria [8]. It is found that the amount of sludge can be reduced if an organism is added that lives on the bacteria. If the efficiency of transforming the bacterium biomass into the organism's own biomass is low, then a reduction of the sludge can be achieved. The worm *Nais elinguis* is an organism with such a property. In an experimental setting of a laboratory chemostat it was observed that this worm population fluctuates strongly and may even, for a long period of time, remain below the minimum level at which it can be detected. We will compute an estimate for the time scale of disappearance of these worms. To this end we formulate a model of three trophic levels, substrate – bacterium – worm. The worm population will be subjected to noise of which the amplitude is proportional to the size of the population.

As an introduction we deal in the next section with the stochastic logistic differential equation and find the expected extinction time for this population model. This one-dimensional problem has an exact solution. However, we will only give the asymptotic approximation, because for our main problem, the 3-dimensional model of the sewage treatment plant analyzed in Section 3, an exact solution is not available and an asymptotic expression is the best we can produce. In Section 4 we discuss the possibilities and limitations of our approach based on singular perturbations.

2. Logistic dynamics with environmental noise

Let $N(t)$ be the size of the biological population at time t . In addition to the deterministic dynamics of a logistic type, we consider fluctuations in birth and death due to environmental noise acting upon the population. Such an external perturbation is assumed to result in a change that is proportional to the size of the population: during a time interval $(t, t + \Delta t)$ an individual is added or deleted with a probability that is proportional to the length Δt of the time interval and the size of the population $N(t)$. The transition probabilities over the time interval $(t, t + \Delta t)$ are given in Table 1. Note that due to this mixed approach the population is no longer an integer number. The probability of two or more stochastic events taking place in that time is of the order $o(\Delta t)$ and is not taken into consideration.

Using the scaling

$$N = Kx, \tag{2.1}$$

we find for the change Δx over the time interval $(t, t + \Delta t)$:

$$E\{\Delta x\} = \alpha(1-x)x \Delta t, \quad \text{var}\{\Delta x\} = (2\beta x/K) \Delta t. \tag{2.2}$$

Table 1. Change over the time interval $(t, t + \Delta t)$.

Type	Transition	Probability
Deterministic	$N \rightarrow N + \alpha N(1 - N/K)\Delta t$	1
Stochastic	$N \rightarrow N + 1$	$\beta N \Delta t$
	$N \rightarrow N - 1$	$\beta N \Delta t$
	$N \rightarrow N$	$1 - 2\beta N \Delta t$

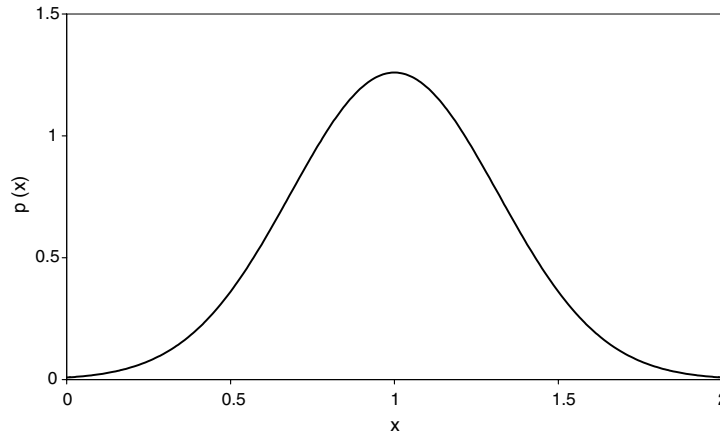


Figure 1. The quasi-stationary probability density approximated by (2.5) with values $\alpha=0.1$, $\beta=2.5$, $K=250$ and $C=1.26$.

2.1. DIFFUSION PROCESS

For the corresponding diffusion process we derive the Fokker-Planck equation, also called the forward Kolmogorov equation. It is a linear diffusion equation that holds for the time-dependent probability-density function $p(t, x)$; see [4, Chapter 7]:

$$\frac{\partial p}{\partial t} = -\frac{\partial}{\partial x}\{\alpha(1-x)x p\} + \frac{1}{2} \frac{\partial^2}{\partial x^2} \left\{ \frac{2\beta x}{K} p \right\}. \tag{2.3}$$

For an initial distribution $p_0(x)$, we can solve this diffusion problem. It is noted that the boundary $x=0$ is absorbing. Consequently, for increasing t the sum of the density will decrease for $x > 0$. This process takes place on a large time scale because arrival at the boundary requires a random motion that is directed opposite to the deterministic flow. Therefore, the distribution for $x > 0$ is actually *quasi-stationary*, as it is slowly decreasing. The quasi-stationary probability-density function $p^{(s)}(x)$ satisfies the stationary Fokker-Planck equation

$$-\frac{d}{dx}\alpha(1-x)x p + \frac{1}{2K} \frac{d^2}{dx^2}\{2\beta x p\} = 0. \tag{2.4}$$

This equation can be solved exactly and for $K \gg 1$ an asymptotic approximation, valid away from the origin, can be made:

$$p^{(s)}(x) \approx C \exp\{-2K\Phi(x)\} \text{ with } \Phi(x) = \frac{\alpha}{2\beta} \left[\frac{1}{2} - x + \frac{1}{2}x^2 \right] \tag{2.5}$$

with C a constant having a value in agreement with the total density; see Figure 1.

2.2. EXTINCTION TIME

If we start at $t=0$ in a point $x > 0$, then extinction (absorption at $x=0$) will occur in finite time τ with probability 1. Let $T(x)$ be the expected value of the stochastic variable τ ; it satisfies

$$\alpha(1-x)x \frac{dT}{dx} + \frac{1}{2K} 2\beta x \frac{d^2T}{dx^2} = -1 \text{ with } T(0)=0 \text{ and } T'(\infty)=0 \tag{2.6}$$

A derivation of this result can be found in [6, Section 5.2.7]. Note the difference between the differential operator in this equation and the one in the stationary forward Kolmogorov equation; here we are dealing with a so-called backward Kolmogorov equation. Again the exact solution can be approximated asymptotically. For values of x away from the origin it gives

$$T(x) \approx D(K) \exp\{2K\Phi(0)\} \quad \text{or} \quad \log\{T(x)\} \approx 2\Phi(0)K + O(\log(K)) \quad \text{for } K \gg 1. \quad (2.7)$$

We remark that the expected extinction time is approximately constant as a function of x and so independent of the starting point, provided it is not taken close to the origin. This may be understood as follows: since the random force is weak, drift prevails and the system will tend to its internal equilibrium $\underline{x}=1$. In the period that follows the initial state plays no role anymore in the value of the actual state. Near equilibrium the system keeps wandering until some successive random contributions will accidentally push the system towards the boundary equilibrium $\underline{x}_0=0$, where it will slow down. Then absorption in the origin is likely to occur.

2.3. SIMULATION RESULTS

Due to the noise, different solutions $x(t)$ satisfying a given initial condition $x(0)=x_0$ can be realized. Taking a sufficient large family of solutions, we find that their value of x at some time t will approach a distribution $p(t, x)$ satisfying the Fokker-Planck equation with the delta-function $\delta(x-x_0)$ as initial value. For the purpose of a Monte Carlo simulation we take the Langevin equation as our starting point:

$$\frac{dx}{dt} = \alpha(1-x)x + \sqrt{\frac{2\beta x}{K}} \xi(t) \quad (2.8)$$

with $\xi(t)$ representing standard white noise. As numerical approximation we use a forward Euler scheme:

$$x(t + \Delta t) = x(t) + \alpha(1-x)x \Delta t + \sqrt{\frac{2\beta x}{K}} \xi(t) \Delta t. \quad (2.9)$$

In this scheme standard white noise is produced as follows. The random number $\xi(t)$ is produced by a random generator. It should have the following properties

$$E\{\xi(t)\} = 0, \quad \text{var}\{\xi(t)\} = 1/\Delta t, \quad \text{cov}\{\xi(t), \xi(t+k\Delta t)\} = 0, \quad k = \pm 1, \pm 2, \dots \quad (2.10)$$

We take a normal distribution with appropriate standard deviation $\xi(t) \cong N(0, 1/\sqrt{\Delta t})$. In Figure 2 a realization with starting value $\underline{x}_0=1$ is presented. It is seen indeed that the solution stays in a neighborhood of $x=1$ most of the time. Extinction occurs at time τ when x gets below the value $1/(2K)$; then, if we round off to integer N -values, the population will be exactly zero in size. In Figure 3 we carry out a Monte Carlo simulation with 100 runs for each of the different values of K and compare the result with the almost linear dependence of $\log(T)$ upon K derived in (2.7). The next term of order $O(\log(K))$ can also be computed.

3. The chemostat

A chemostat is a device consisting of a chamber in which chemical and/or biological processes take place continually, usually in a liquid medium. There is an inflow at some volume rate of substances that feed the processes and an outflow at a same rate of a mixture of substances in the same composition as that of the well-stirred fluid in the chamber. In this way a culture of some organism such as bacteria can be harvested continually, as their nutrients are part of the inflowing substances. Here we consider a chemostat with three trophic levels: sewage-bacterium-worm. It can be regarded as an experimental sewage-treatment plant. In the thesis of [8] it is investigated whether or not the presence of worms would lead to a reduction of the sludge that consists of the part of the sewage not digested by the organisms in the chemostat and the

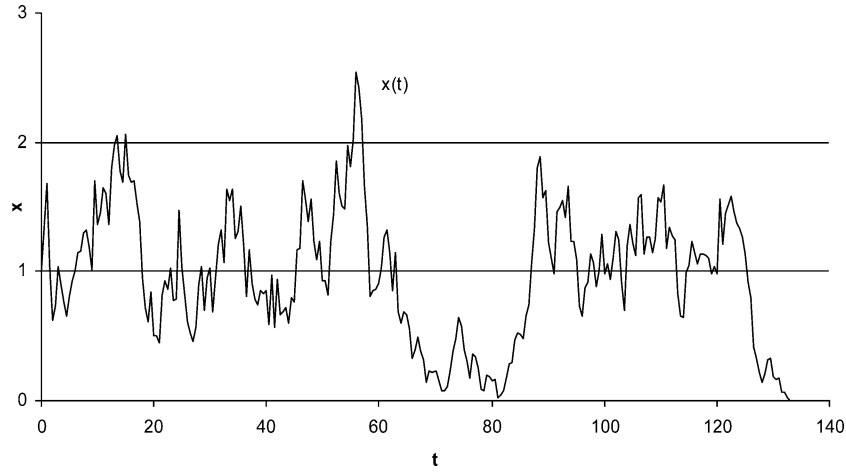


Figure 2. Simulation of the system (2.8) using the difference scheme (2.9) with $\alpha = 0.1$, $\beta = 2.5$ and $K = 50$. It is noted that the population density fluctuates most of the time around the equilibrium value $x = 1$. The second large excursion to lower density values results in extinction: $x < 1/(2K)$.

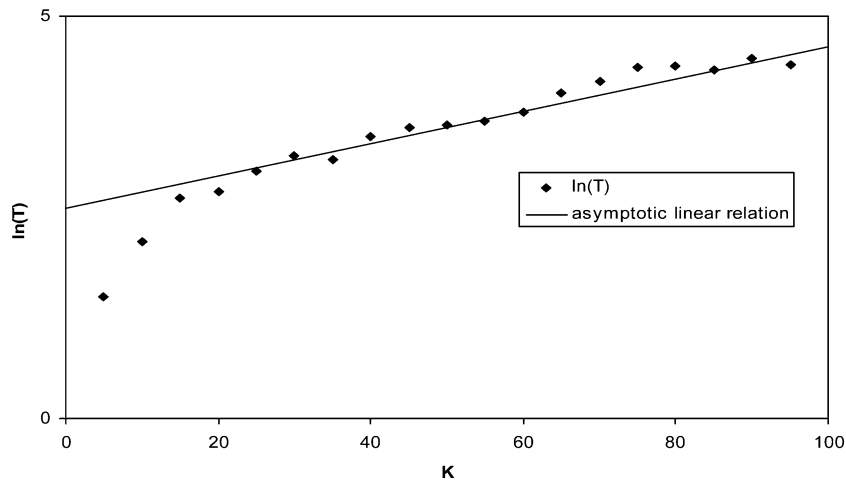


Figure 3. Expected extinction times given by (2.5) and (2.7) with $\alpha = 0.1$ and $\beta = 2.5$ and simulation results. For each value of K the average of 100 simulation runs was taken.

remains of the bacteria that have fed on the sewage. Such a reduction can be expected as the worms have a restricted efficiency in transforming the biomass of the bacteria into their own biomass. A good functioning sewage-treatment plant produces sufficiently cleaned wastewater and as little sludge as possible. Let x , y , z be the dry organic densities (dry weight per volume) of, respectively, the sewage, the bacteria and the worms. Moreover, it is assumed that worms are subjected to environmental noise of the type we described in the previous section. Then the process is modeled by the following set of three coupled Langevin equations:

$$\begin{aligned}
 \frac{dx}{dt} &= d(x_r - x) - \frac{i_0 x}{k_0} y, \\
 \frac{dy}{dt} &= \frac{\mu_0 x}{k_0} y - \frac{i_1 y}{k_1 + y} z - dy, \\
 \frac{dz}{dt} &= \frac{\mu_1 y}{k_1 + y} z - dz + \varepsilon \sqrt{z} \xi(t).
 \end{aligned}
 \tag{3.1}$$

Table 2. The parameters of Equation (3.1) for the case of a stable internal equilibrium.

Parameter	d	i_0	μ_0	k_0	i_1	μ_1	k_1	x_r
Value	0.001	0.5	1.25	1000	0.167	0.01	50.0	25

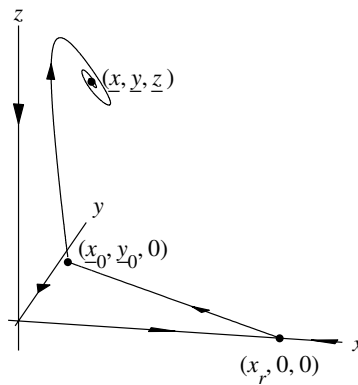


Figure 4. Deterministic dynamics of the system (3.1) with $\varepsilon=0$. The system has three equilibria. Its trajectories are given as solid lines with an arrow indicating the path for increasing t . Note that the axes coincide with trajectories.

At first we ignore the noise component ($\varepsilon = 0$). Then the system is deterministic and has three equilibria: the internal equilibrium: $(\underline{x}, \underline{y}, \underline{z})$ and the boundary equilibria $(x_r, 0, 0)$ and $(x_0, y_0, 0)$. A picture of the deterministic dynamics in the state space is given in Figure 4. Parameter values have been chosen in the range given by [9]; see Table 2. The parameter k_1 is a bifurcation parameter with a Hopf bifurcation at $k_1^h = 25$. For $k_1 > k_1^h$ a stable equilibrium solution is found and for $k_1 < k_1^h$ a stable periodic solution arises; see Figure 5.

3.1. DIFFUSION PROCESS AND EXTINCTION TIME

For $\varepsilon > 0$ the noise term will lead to a considerable change in the dynamics. Over a short time interval with a worm population not at the point of extinction, the difference is not

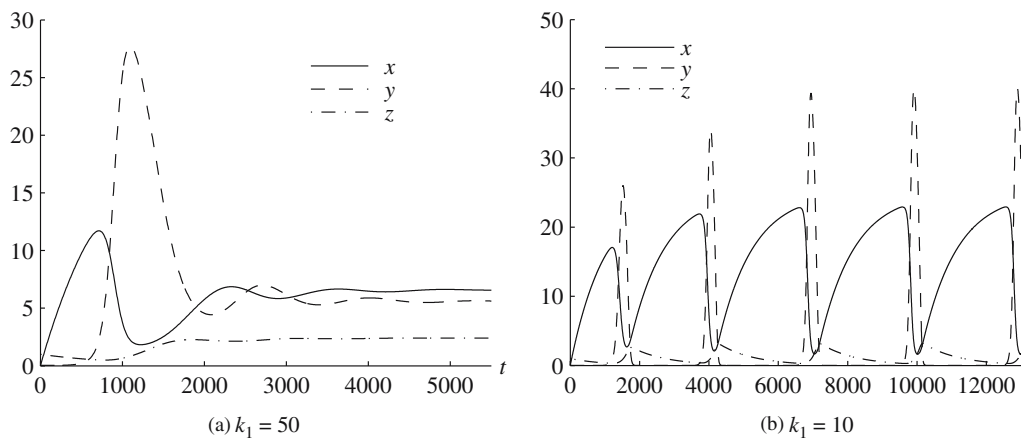


Figure 5. Two solutions of the system (3.1) with $\varepsilon=0$.

so dramatic and is in line with our expectation: the possible states at some time $t > 0$ form a small cloud around the state of the deterministic system at that time. However, eventually larger deviations may occur and even extinction of the worm population is possible. Let the number of worms in the equilibrium state with biomass density \underline{z} be K . Then, for $z < \underline{z}/(2K)$, the worm population has come to the point of extinction. From then onwards the deterministic dynamics applies in the plane $z = 0$.

Rewriting the system (3.1) as follows,

$$x' = f(x, y), \quad y' = g(x, y, z), \quad z' = h(y, z) + \varepsilon \sqrt{a(z)} \xi(t), \tag{3.2}$$

we obtain the stationary Fokker-Planck equation

$$-\left\{ \frac{\partial}{\partial x}(fp) + \frac{\partial}{\partial y}(gp) + \frac{\partial}{\partial z}(hp) \right\} + \frac{\varepsilon^2}{2} \frac{\partial^2}{\partial z^2}(ap) = 0. \tag{3.3}$$

For this equation we cannot find an exact solution. From the analysis of the one-dimensional system of Section 2 we infer that the following *ansatz* should be made for the quasi-stationary solution

$$p^{(s)}(x, y, z) \approx C \exp\{-\Phi(x, y, z)/\varepsilon^2\} \tag{3.4}$$

with $\Phi(x, y, z)$ satisfying

$$f \frac{\partial \Phi}{\partial x} + g \frac{\partial \Phi}{\partial y} + \left(h + \frac{1}{2} a \frac{\partial \Phi}{\partial z} \right) \frac{\partial \Phi}{\partial z} = 0 \quad \text{and} \quad \Phi(\underline{x}, \underline{y}, \underline{z}) = 0. \tag{3.5}$$

Near $(\underline{x}, \underline{y}, \underline{z})$ the solution is approximated by the quadratic form

$$\Phi(v) = \frac{1}{2} v^T P v \quad \text{with} \quad v = \begin{pmatrix} x - \underline{x} \\ y - \underline{y} \\ z - \underline{z} \end{pmatrix}, \tag{3.6}$$

where P is a symmetric positive definite matrix. The value of the solution away from internal equilibrium is found by integration along a characteristic that starts from a small sphere with the internal equilibrium as center and with initial value given by (3.6). For the present low-dimensional problem, the correct starting point at the sphere can be found by application of a shooting method. For higher-dimensional systems this is not possible, so that other methods have to be employed [10, Chapter 4]. In [4, Section 7.1] it is deduced that the most likely exit point must be near a boundary equilibrium (and for $\varepsilon \rightarrow 0$ the equilibrium itself). From the boundary equilibria the one with the smallest value of the function $\Phi(x, y, z)$ has to be chosen; in the present case this is $(\underline{x}_0, \underline{y}_0, 0)$. We need the value $\Phi(\underline{x}_0, \underline{y}_0, 0)$ for an approximation of the expected extinction time. Consequently, we have to find the starting point on the sphere for which the characteristic approaches $(\underline{x}_0, \underline{y}_0, 0)$ and compute $\Phi(\underline{x}_0, \underline{y}_0, 0)$. Integration of the partial differential Equation (3.5) along a characteristic means solving a system of seven ordinary differential equations for $x, y, z, u = \partial\Phi/\partial x, v = \partial\Phi/\partial y, w = \partial\Phi/\partial z$ and Φ itself:

$$\begin{aligned} \frac{dx}{ds} &= f, & \frac{dy}{ds} &= g, & \frac{dz}{ds} &= h + a w, \\ \frac{du}{ds} &= -\frac{\partial f}{\partial x} u - \frac{\partial g}{\partial x} v, & \frac{dv}{ds} &= -\frac{\partial f}{\partial y} u - \frac{\partial g}{\partial y} v - \frac{\partial h}{\partial y} w, & \frac{dw}{ds} &= -\frac{\partial g}{\partial z} v - \frac{\partial h}{\partial z} w - \frac{1}{2} \frac{da}{dz} w^2, \\ \frac{d\Phi}{ds} &= \frac{1}{2} z w^2, \end{aligned}$$

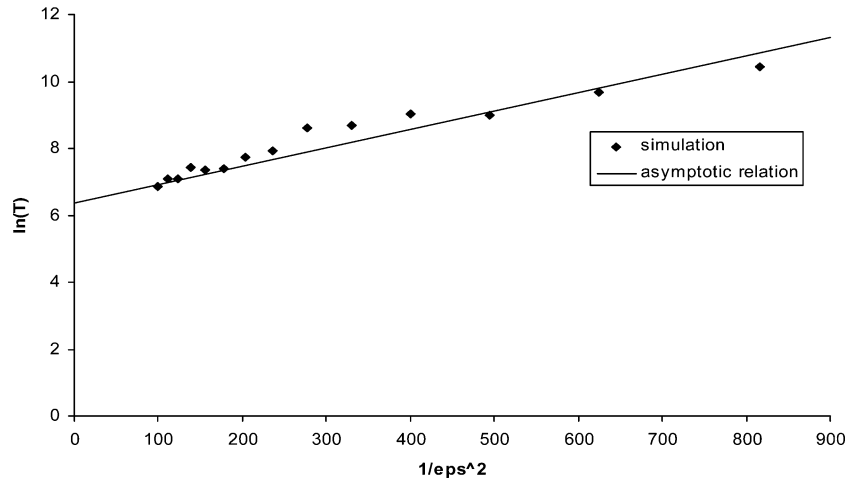


Figure 6. Estimated expected extinction times given by (3.7) compared with simulation results. For each value of ε the average of 50 simulation runs was taken (for the two smallest ε values 25 runs have been made).

where s denotes the path variable. Near the path of the correct characteristic, the trajectories of the system of the first six ordinary differential equations of the above system are extremely sensitive to the initial values. The fact that we try to find the heteroclinic orbit connecting the internal equilibrium $(\underline{x}, \underline{y}, \underline{z}, 0, 0, 0)$ with the boundary equilibrium $(\underline{x}_0, \underline{y}_0, 0, 0, 0, 0)$ explains this sensitivity: both equilibria have three positive (and negative) eigenvalues. On the other hand, in practice $\Phi(x, y, z)$ changes slowly near the boundary equilibrium, so a high shooting accuracy is not required. It may occur that characteristics intersect; then a choice has to be made. The Lagrangian related with the above Hamilton system of six differential equations determines the correct way to proceed; see [10, Chapter 6] for an analysis of such a situation.

The expected extinction time $T(x, y, z)$, if starting in a point (x, y, z) not at the boundary, satisfies the backward Kolmogorov equation

$$f \frac{\partial T}{\partial x} + g \frac{\partial T}{\partial y} + h \frac{\partial T}{\partial z} + \frac{1}{2} \varepsilon^2 a \frac{\partial^2 T}{\partial z^2} = -1.$$

For starting points sufficiently bounded away from the boundary the result for the present problem is

$$\log T \approx \Phi(\underline{x}_0, \underline{y}_0, 0) / \varepsilon^2 + O(-\log \varepsilon) \quad \text{with } \Phi(\underline{x}_0, \underline{y}_0, 0) = 0.0055. \tag{3.7}$$

3.2. SIMULATION RESULTS

As we did for the logistic system of Section 2, we now compare the asymptotic result (3.7) with the results of a Monte Carlo simulation; see Figure 6. For each value of ε 50 runs were made, all starting in the internal equilibrium. It is noted that, for the higher-dimensional system we are dealing with now, the approximation still has an accuracy comparable with the one-dimensional logistic system. In Figure 7 we give the position of the exit points in the plane $z = 0$ for two different values of ε . It is seen that trajectories are followed that approach the saddle point equilibrium $(\underline{x}_0, \underline{y}_0, 0)$ in the 3-dimensional state space. For the intermediate value $\varepsilon = 0.08$ the plane $z = 0$ is hit earlier because of the larger stochastic perturbations. For the small value $\varepsilon = 0.04$ the exit points are closer to the boundary equilibrium but still the

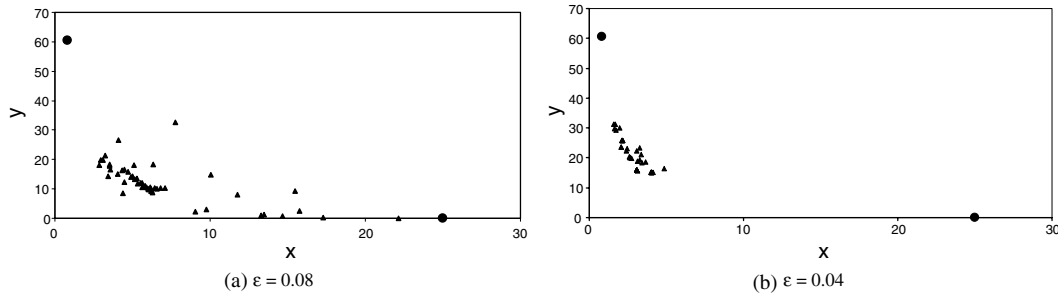


Figure 7. Distribution of exit points in the plane $z = 0$. The two boundary equilibria are indicated by (\bullet) .

distance remains quite large. The simulation result is in agreement with the observation that the function $\Phi(x, y, z)$ does not vary strongly near this boundary equilibrium.

4. Concluding remarks

The estimate we constructed for the expected breakdown time of the chemostat of Section 3 focuses on the limit situation that the amplitude ε of the random perturbations tends to zero. In Figure 6, the asymptotic value of the exit time follows from the slope of the line approached by the almost linear graph for $\varepsilon \rightarrow 0$. The intercept of this line is not calculated. In order to compute it, a higher-order asymptotic analysis has to be carried out. This is a rather complex task and the numerical calculations it requires turn out to be quite tedious.

A second problem that may arise is more or less inherent in perturbation theory: to apply it means that a small parameter value has to be chosen. In certain situations, such as in the epidemiology of human diseases, the value of ε should be very small (order of 10^{-3}) to obtain an acceptable numerical accuracy of the approximation. This will limit the practical use of the method for many problems in the applied sciences. In the type of problem we are dealing with in this study such a complication may arise if the boundary equilibrium $(\underline{x}_0, \underline{y}_0, 0)$ is far away from the projection $(\underline{x}, \underline{y}, 0)$ of the internal equilibrium on the plane $z=0$ and if, in addition, \underline{z} is small. Even if the asymptotic results are not so accurate, we may learn much from the analysis of the limit situation of random perturbations tending to zero. If we are mainly interested in the long-term behavior we have found that the system remains near the stable internal equilibrium most of the time on a time scale that is exponentially large with respect to $1/\varepsilon^2$. Furthermore, time spent near the boundary equilibrium $(\underline{x}_0, \underline{y}_0, 0)$ is of the order $O(-\log \varepsilon)$. The transitions between these two domains are short. Based on this observation the dynamic behavior of the worm population can be modeled by a logistic stochastic differential equation with parameter values that can be expressed in the parameters of the full system [11,12].

The two problems we analyzed with our asymptotic method both have a stable internal equilibrium. It is also possible to study the problem when it has an oscillatory solution; see Figure 5b. In [13] such a situation arises. Although in that study there is also a stable internal equilibrium, the analysis concerns the exit probability in the initial stage when the solution is strongly oscillating.

Finally, returning to the chemostat experiment, we have to consider the use of this mathematical analysis for the proposed way of reducing sludge in a sewage treatment plant. Here we studied the risk of disappearance of the worm population. When in the chemostat experiment the population is below the detection level, it is not clear if the population is completely

extinct. It may quite well continue to be present at a low level. This would not change our analysis much, because the formulation of the problem of arriving at the detection level is similar to the problem of arriving at the zero-level (extinction). In fact, the worm population always recovers by itself after some randomly fluctuating time. It can be that the population has disappeared and that new worms have arrived from outside. It may also be that below the detection level the worm population has stayed present and recovers after some time in a type of predator-prey cycle structure. This suggests a model with a stable limit cycle. Still, stochastic elements are needed to account for the fluctuating time intervals during which the population remains below the detection level. Various mechanisms with a dynamics comparable with a randomly perturbed self-sustained oscillation should be considered, such as a strange-attractor structure or a Markov-chain model with three states (near internal equilibrium, near boundary equilibrium and extinction). In [4, Chapter 10] it is demonstrated how the last type of model can be derived from a differential-equation model in other applications, such as in meteorology (preferent states of the atmospheric circulation) and in ecology (changing densities in metapopulations).

Acknowledgements

The authors are grateful to Bob Kooi (Free University, Amsterdam) for bringing this topic to their attention and to Bas Buys (Wageningen University) for sharing his experiences with chemostat experiments on wastewater treatment.

References

1. J.F. Crow and M. Kimura, *An Introduction to Population Genetics Theory*. New York: Harper and Row (1970) 591 pp.
2. J. Roughgarden, *Theory of Population Genetics and Evolutionary Ecology: An Introduction*. New York: Macmillan (1979) 634 pp.
3. I. Hanski, *Metapopulation Ecology*. Oxford: Oxford University Press (1999) 313 pp.
4. J. Grasman and O.A. van Herwaarden, *Asymptotic Methods for the Fokker-Planck equation and the Exit Problem in Applications*. Heidelberg: Springer-Verlag (1999) 220 pp.
5. M.I. Freidlin and A.D. Wentzell, *Random Perturbations of Dynamical Systems*. New York: Springer (1984) 326 pp.
6. C.W. Gardiner, *Handbook of Stochastic Methods for Physics, Chemistry and the Natural Sciences*. Heidelberg: Springer-Verlag (1983) 442 pp.
7. Z. Schuss, *Theory and Applications of Stochastic differential Equations*. New York: Wiley (1980) 321 pp.
8. C.H. Ratsak, *Grazer Induced Sludge Reduction in Wastewater Treatment*. PhD thesis. Amsterdam: Free University (1994) 193 pp.
9. B.W. Kooi, J.C. Poggiale and P. Auger, Aggregation methods in food chains. *Math. Computer Model.* 27 (1998) 109–120.
10. H. Roozen, *Analysis of the Exit Problem for Randomly Perturbed Dynamical Systems in Applications*. PhD thesis. Wageningen: Wageningen University (1990) 156 pp.
11. J. Grasman, The expected extinction time of a population within a system of interacting biological populations. *Bull. Math. Biol.* 58 (1996) 555–568.
12. J. Grasman, Stochastic epidemics: the expected duration of the endemic period in higher dimensional models. *Math. Biosci.* 152 (1998) 13–27.
13. O.A. van Herwaarden, Stochastic epidemics: the probability of extinction of an infectious disease at the end of a major outbreak. *J. Math. Biol.* 35 (1997) 793–813.