OPTIMAL CONTROL OF TWO COMPETING DISEASES WITH STATE-DEPENDENT INFECTION RATES

E. G. KYRIAKIDIS * ** AND

T. D. DIMITRAKOS,* University of the Aegean

Abstract

A two-dimensional simple stochastic epidemic process is introduced in which the infection rates depend on a power of the number of the infectives. It is assumed that one of the diseases is serious while the other is relatively harmless. Policies for introducing infection by the harmless disease or for isolating infectives with the serious disease are considered. Suitable dynamic programming algorithms are given for the determination of the policy, which minimises the expected future cost at any stage. For the corresponding deterministic model, the optimal policy is found analytically in two cases, and is compared numerically with the optimal policy for the stochastic model.

Keywords: Two-dimensional epidemic process; infection power; optimal intervention; dynamic programming

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1. The model

Consider a population of size N in continuous time $t \ge 0$, in which susceptibles are simultaneously exposed to two diseases. It is assumed that at any time t at most one susceptible can become infected. Once an individual becomes infected by disease t (t = 1, 2), he or she remains an infective for that disease and cannot be infected by the other.

Let X(t), Y(t) $(0 \le X(t) + Y(t) \le N)$ be the random numbers of infectives at time t having the diseases 1 and 2, respectively. It is assumed that the probabilities for a new infective with disease 1 and 2 in a time interval $(t, t + \delta t)$ when X(t) = x and Y(t) = y are equal to $c_1 x^{\alpha} (N - x - y) \delta t + o(\delta t)$ and $c_2 y^{\beta} (N - x - y) \delta t$, respectively, where $c_1, c_2, \alpha, \beta > 0$. All other transitions have probability $o(\delta t)$. The process terminates when the total number of infectives with diseases 1 and 2 becomes N, which will almost surely happen within finite time. The random walk embedded in the process has transitions

$$(x, y) \rightarrow (x + 1, y)$$
, with probability $\frac{c_1 x^{\alpha}}{c_1 x^{\alpha} + c_2 y^{\beta}}$, (1)

$$(x, y) \rightarrow (x, y + 1)$$
, with probability $\frac{c_2 y^{\beta}}{c_1 x^{\alpha} + c_2 y^{\beta}}$. (2)

If $\alpha = \beta = 1$, the model coincides with the two-dimensional simple epidemic process introduced by Billard *et al.* (1979). The parameters α and β are referred to as the infection

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^{*} Postal address: Department of Statistics and Actuarial Science, University of the Aegean, Karlovassi 83200, Samos, Greece.

^{**} Email address: kyriak@aegean.gr

powers of diseases 1 and 2, respectively. The notion of infection power was introduced by Severo (1969), who considered a generalization of the simple stochastic epidemic process and obtained its transient probabilities.

Suppose that disease 1 causes serious symptoms which reduce the productivity of the infected individual. The cost to society of an individual becoming infected by disease 1 is assumed to be fixed, and we define this to be the unit of cost. Disease 2 is assumed to be relatively harmless and no cost is assigned to individuals infected by it. We shall consider policies which at any time allow us to infect deliberately any number of the remaining susceptibles with disease 2, each at a cost K. For example, this controlling action could be carried out by vaccinating some or all of the remaining susceptibles with the milder disease 2. We shall also consider policies that, at any time, isolate any number of the infectives with disease 1. The cost of isolating each infective with disease 1 is equal to L > 0. We state four optimization problems for this model.

Problem 1. Find the policy which minimises the expected future cost for every initial state, if it is possible at any time to infect deliberately with disease 2 any number of the remaining susceptibles.

Problem 2. Find the policy which minimises the expected future cost for every initial state, if it is possible at any time to isolate any number of the infectives with disease 1.

Problem 3. Find the policy which minimises the expected future cost for every initial state, if it is possible at any time to isolate all or none of the infectives with disease 1.

Problem 4. Find the policy which minimises the expected future cost for every initial state, if it is possible at any time to infect deliberately with disease 2 any number of the remaining susceptibles, or to isolate all or none of the infectives with disease 1.

In two previous papers by Kyriakidis (1995), (1999), suitable dynamic programming algorithms were developed for Problems 1 and 3 in the case in which $\alpha = \beta = 1$. Furthermore, the corresponding deterministic problems were studied and the optimal policies were found analytically and compared with the optimal policies for the stochastic problems. The above optimisation problems are related to two optimisation problems introduced by Abakuks (1973), (1974), which are concerned with optimal isolation and immunisation policies, respectively, in the general stochastic epidemic. Abakuks proved that for a given number of susceptibles the optimal policy initiates the controlling action (i.e. isolation of infectives or immunisation of susceptibles) if and only if the number of infectives is smaller than a critical level or exceeds a critical level, respectively. Clancy (1999) recently extended Abakuks's results by considering epidemic models with more general infection and removal rate functions.

The rest of the paper is organized as follows. In the next section, suitable dynamic programming algorithms are developed for Problems 1, 3 and 4. In Section 3 the corresponding deterministic model is considered. For Problem 1 the optimal policy is found analytically when $\alpha \neq 1$ and $\beta = 1$. For Problem 2 the optimal policy is found analytically when $\alpha = 1$ and $\beta \neq 1$. These optimal policies are compared numerically with the optimal policies for the stochastic version of the problems.

2. Dynamic programming algorithms

According to the above assumptions, we know what state (x, y) we are in at any time, and in finding the optimal policy we need only consider the space of paired values (x, y), where $0 \le x, y \le N$ and $0 < x + y \le N$. We will consider Problems 1, 3 and 4 below.

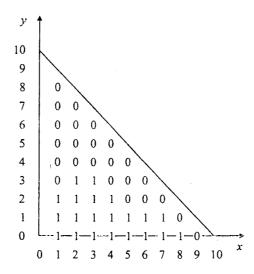


FIGURE 1: The optimal policy for Problem 1 when $(N, K, \alpha, \beta, c_1, c_2) = (10, 1, 2, 1, 1.5, 1)$.

2.1. Problem 1

According to the hypothesis for this problem, in any state (x, y) with x + y < N we may either (i) allow (x, y) to make a transition according to the random walk defined by (1) and (2), the transitions to (x + 1, y) and to (x, y + 1) costing 1 and 0 units, respectively, or else (ii) infect one susceptible deliberately with disease 2 at a cost K; this corresponds to making the instantaneous transition $(x, y) \rightarrow (x, y + 1)$. Note that, if $y \le N - n - x$, a sequence of n choices of controlling action (ii) will result in the infection of n susceptibles; this corresponds to making the instantaneous transition $(x, y) \rightarrow (x, y + n)$. Defining V(x, y) to be the expected future cost of adopting an optimal policy when the epidemic is in state (x, y), and W(x, y) to be the expected future cost of waiting for one transition to occur naturally and adopting an optimal policy from then on, then

$$V(x, N - x) = 0, 0 \le x \le N,$$

$$W(x, y) = \frac{c_1 x^{\alpha}}{c_1 x^{\alpha} + c_2 y^{\beta}} [1 + V(x + 1, y)] + \frac{c_2 y^{\beta}}{c_1 x^{\alpha} + c_2 y^{\beta}} V(x, y + 1),$$

$$0 < x + y < N, (4)$$

$$V(x, y) = \min\{K + V(x, y + 1), W(x, y)\}, 0 < x + y < N. (5)$$

Equation (5) is known as the dynamic programming equation (see, for example, Ross (1983, p. 3)). When the epidemic is in state (x, y) and K + V(x, y + 1) < W(x, y), the optimal policy prescribes the deliberate infection with disease 2 of at least one susceptible. This is effectively action (ii). If $W(x, y) \le K + V(x, y + 1)$, the optimal policy prescribes no intervention in the evolution of the process. Equations (3)–(5) enable us to find V(x, y) numerically for every state (x, y) such that 0 < x + y < N; they also determine the corresponding action prescribed by the optimal policy.

As an example we consider the case in which N=10, K=1, $\alpha=2$, $\beta=1$, $c_1=1.5$, $c_2=1$. The optimal policy for these values of the parameters is presented in Figure 1, where for each state (x, y) $(0 < x + y \le 9)$ the action (i) is denoted by 0 and the controlling action (ii) is denoted by 1. Note that in Figure 1 there is no 1 lying above a 0. Extensive numerical results

for various values of the parameters indicate that the optimal policy always has this property. Thus we are led to the following conjecture concerning the form of the optimal policy.

Conjecture for Problem 1. For each integer x (0 < x < N) two cases are possible:

- 1. The optimal policy prescribes no intervention in the evolution of the process at all states (x, y), $(0 \le y < N x)$.
- 2. There exists an integer \tilde{y} $(0 \le \tilde{y} < N x)$ such that the optimal policy prescribes the controlling action (ii) at all states (x, y) $(0 \le y \le \tilde{y})$ whereas it does not intervene in the evolution of the process at all states (x, y) $(\tilde{y} < y < N x)$.

2.2. Problem 3

According to the hypothesis for this problem, in any state (x, y) with x + y < N we may either (i) allow (x, y) to make a transition according to the random walk defined by (1) and (2), or else (ii) isolate all infectives with disease 1 at a cost Lx; this corresponds to making the instantaneous transition $(x, y) \rightarrow (0, y)$. The dynamic programming equation is now given by

$$V(x, y) = \min\{Lx, W(x, y)\}, \quad 0 < x + y < N.$$

When the epidemic is in state (x, y) and Lx < W(x, y), the optimal policy prescribes the isolation of x infectives with disease 1. This is effectively action (ii). If $W(x, y) \le Lx$, it prescribes no intervention in the evolution of the process. This is effectively action (i).

As an example, we consider the case in which N=10, L=0.6, $\alpha=1$, $\beta=0.5$, $c_1=0.8$, $c_2=1.2$. The optimal policy for these values of the parameters is presented in Figure 2, where for each (x, y) $(0 < x + y \le 9)$ the action (i) is denoted by 0 and the controlling action (ii) is denoted by 2. Note that in Figure 2, there is no 2 lying to the right of a 0. Extensive numerical results for various values of the parameters indicate that the optimal policy always has this property. Thus, we are led to the following conjecture concerning the form of the optimal policy.

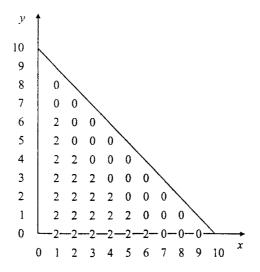


FIGURE 2: The optimal policy for Problem 3 when $(N, L, \alpha, \beta, c_1, c_2) = (10, 0.6, 1, 0.5, 0.8, 1.2)$.

Conjecture for Problem 3. For each integer y such that $0 \le y < N$ two cases are possible:

- 1. The optimal policy prescribes no intervention in the evolution of the process at all states (x, y) $(0 \le x < N y)$.
- 2. There exists an integer \tilde{x} $(1 \le \tilde{x} < N y)$ such that the optimal policy prescribes the controlling action (ii) at all states (x, y) $(1 \le x \le \tilde{x})$, whereas it does not intervene in the evolution of the process at all states (x, y) $(\tilde{x} < x < N y)$.

Note that if we consider Problem 2, which permits a wider class of intervention policies, the implementation of the corresponding dynamic programming algorithm does not seem possible.

2.3. Problem 4

According to the hypothesis for this problem, in any state (x, y) with x + y < N we may (i) allow (x, y) to make a transition according to the random walk defined by (1) and (2), or (ii) infect one susceptible deliberately with disease 2 at a cost K or (iii) isolate all infectives with disease 1 at a cost Lx. The dynamic programming equation is now given by

$$V(x, y) = \min\{K + V(x, y + 1), Lx, W(x, y)\}, \qquad 0 < x + y < N.$$

In any state (x, y), if $W(x, y) \le \min\{K + V(x, y + 1), Lx\}$ we choose action (i), if $\min\{K + V(x, y + 1), Lx\} < W(x, y)$ and $K + V(x, y + 1) \le Lx$ we choose action (ii), and if $\min\{K + V(x, y + 1), Lx\} < W(x, y)$ and Lx < K + V(x, y + 1) we choose action (iii).

As an example we consider the case in which N=10, K=0.6, L=0.7, $\alpha=1.1$, $\beta=1.3$, $c_1=0.8$, $c_2=0.9$. The optimal policy for these values of the parameters is presented in Figure 3, where for each state (x, y) ($0 < x + y \le 9$) the action (i) is denoted by 0, the action (ii) by 1 and the action (iii) by 2. Note that in Figure 3, three separate regions appear that include 0s, 1s and 2s. There is no 2 lying to the right of a 0 and there is no 1 or 2 lying above a 0. Extensive numerical results for various values of the parameters indicate that the optimal policy always has these properties. An analytic proof seems to be difficult.

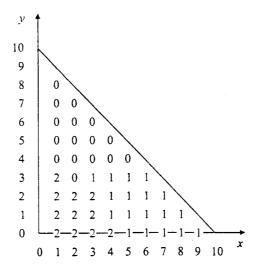


FIGURE 3: The optimal policy for Problem 4 when $(N, K, L, \alpha, \beta, c_1, c_2) = (10, 0.6, 0.7, 1.1, 1.3, 0.8, 0.9)$.

3. The optimal policy for the deterministic model

In the corresponding deterministic model, the numbers x and y ($0 \le x, y \le N$) of infectives with diseases 1 and 2, respectively, are regarded as continuous variables and they satisfy the differential equations

$$\frac{\mathrm{d}x}{\mathrm{d}t} = c_1 x^{\alpha} (N - x - y), \qquad \frac{\mathrm{d}y}{\mathrm{d}t} = c_2 y^{\beta} (N - x - y). \tag{6}$$

The process terminates when x + y = N. As for the stochastic case, suppose that the cost to society of an individual infected by disease 1 is fixed, and we define this to be the unit of cost. We shall consider policies which at any time $t \ge 0$ allow us to infect deliberately with disease 2 any number of the remaining susceptibles, each at a cost K > 0, and policies which at any time $t \ge 0$ allow us to isolate any number of the infectives with disease 1, each at a cost L > 0. We present below analytic solutions for Problem 1 in the case in which $\alpha \ne 1$ and $\beta = 1$, and for Problem 2 in the case in which $\alpha = 1$ and $\beta \ne 1$.

3.1. Problem 1, if $\alpha \neq 1$, $\beta = 1$

Suppose that (x_0, y_0) is the initial state. From (6) it follows that the two-dimensional deterministic epidemic lies on the curve

$$y = y_0 \exp[c(1-\alpha)^{-1}(x^{1-\alpha} - x_0^{1-\alpha})], \qquad x_0 \le x \le \xi(x_0, y_0),$$

where, $c = c_2/c_1$ and $\xi(x_0, y_0)$ is the unique root in (x_0, N) of the equation for x,

$$y_0 \exp[c(1-\alpha)^{-1}(x^{1-\alpha}-x_0^{1-\alpha})] + x - N = 0.$$
 (7)

If the initial state of the epidemic is $(0, y_0)$ with $y_0 \neq 0$, then the curve of the epidemic is x = 0, $y_0 \leq y \leq N$, and consequently no controlling action has to be taken during the epidemic. If the initial state of the epidemic is $(x_0, 0)$ with $x_0 \neq 0$, then the cost of the epidemic if we never intervene in its evolution is equal to the number of individuals infected by disease 1. Hence,

$$C(x_0, y_0) = \xi(x_0, y_0) - x_0.$$
 (8)

Suppose that when the epidemic is in state (x_0, y_0) , we infect Δy_0 susceptibles, and then do not intervene any further in the evolution of the epidemic. The cost of such a policy is $K \Delta y_0 + C(x_0, y_0 + \Delta y_0)$, which is smaller than $C(x_0, y_0)$ if

$$\frac{C(x_0, y_0 + \Delta y_0) - C(x_0, y_0)}{\Delta y_0} < -K.$$

If Δy_0 is small, the above inequality is approximately equivalent to $\partial \xi(x_0, y_0)/\partial y_0 < -K$ and we are led to the conjecture that the optimal policy at the state (x_0, y_0) prescribes the deliberate infection with disease 2 of some of the remaining susceptibles if $\partial \xi(x_0, y_0)/\partial y_0 < -K$, whereas if $\partial \xi(x_0, y_0)/\partial y_0 \ge -K$, the optimal policy does not prescribe any controlling action at (x_0, y_0) . This conjecture can be proved in a way similar to the case in which $\alpha = 1$, $\beta = 1$ (see Kyriakidis (1995)). The relevant result is presented in Proposition 1 and corresponds to the conjecture for Problem 1 for the stochastic model. For notational convenience, let P_θ ($0 < \theta \le N - x_0 - y_0$) denote the policy in which θ susceptibles are infected with disease 2 at the initial state (x_0, y_0) , with no further intervention in the evolution of the process.

TABLE 1: Values of \bar{y} and y^* .

X	1	2	3	4	5	6	7	8	9
							-	0	

Proposition 1. (a) If the initial state of the epidemic is (x_0, y_0) , $x_0 \neq 0$, and $\partial \xi(x_0, y_0)/\partial y_0 \geq -K$, then the optimal policy never intervenes in the evolution of the epidemic.

- (b) Assume that the initial state of the epidemic is (x_0, y_0) , $x_0 \neq 0$, and $\partial \xi(x_0, y_0)/\partial y_0 < -K$. We distinguish two cases:
 - 1. If there exists a state (x_0, y^*) such that $[\partial \xi(x_0, y_0)/\partial y_0]_{(x_0, y^*)} = -K$, then the policy $P_{y^*-y_0}$ is optimal.
 - 2. If there exists no state (x_0, y^*) such that $[\partial \xi(x_0, y_0)/\partial y_0]_{(x_0, y^*)} = -K$, then the policy $P_{N-x_0-y_0}$ is optimal.

Differentiation of (7), in which $x = \xi(x_0, y_0)$, with respect to y_0 yields an expression for $\partial \xi(x_0, y_0)/\partial y_0$ in terms of x_0, y_0, α and $\xi(x_0, y_0)$. For each x_0 (0 < x_0 < N) we can check that the partial derivative $\partial \xi(x_0, y_0)/\partial y_0$, $0 \le y_0 \le N - x_0$, is increasing with respect to y_0 . If $[\partial \xi(x_0, y_0)/\partial y_0]_{(x_0, 0)} \ge -K$, or equivalently,

$$K \ge \exp[c(1-a)^{-1}(N^{1-a} - x_0^{1-a})],$$
 (9)

from the monotonicity of $\partial \xi(x_0, y_0)/\partial y_0$, it follows that $\partial \xi(x_0, y_0)/\partial y_0 \ge -K$ ($0 \le y_0 \le N - x_0$). Hence, according to Proposition 1(a), the condition (9) implies that the optimal policy never intervenes in the evolution of the epidemic, if the initial state is (x_0, y_0) ($0 \le y_0 \le N - x_0$). If $[\partial \xi(x_0, y_0)/\partial y_0]_{(x_0, N - x_0)} < -K$, or equivalently,

$$K < [1 + c(N - x_0)x_0^{-a}]^{-1}, \tag{10}$$

again from the monotonicity of $\partial \xi(x_0, y_0)/\partial y_0$, it follows that $\partial \xi(x_0, y_0)/\partial y_0 < -K$ (0 $\leq y_0 \leq N - x_0$). Hence, according to Proposition 1(b), the condition (10) implies that the policy $P_{N-x_0-y_0}$ is optimal if the initial state is (x_0, y_0) (0 $\leq y_0 \leq N - x_0$).

For each x_0 ($0 < x_0 < N$) when (9) and (10) fail, the critical value y^* mentioned in Proposition 1(b) can be found numerically, since it satisfies the equation $[\partial \xi(x_0, y_0)/\partial y_0]_{(x_0, y^*)} = -K$. Extensive numerical results indicate that, when (9) holds, then the optimal policy in the corresponding stochastic model prescribes no further intervention in the evolution of the epidemic, if the initial state is (x_0, y_0) ($0 \le y_0 < N - x_0$). When (10) holds, there is again strong numerical evidence that the critical integer \tilde{y} in the corresponding stochastic model is equal to $N - x_0 - 1$. In the case in which both (9) and (10) fail, extensive numerical results indicate that $\tilde{y} < y^*$. Thus we are led to the interesting conjecture that the stochastic infection boundary is bounded above by the deterministic infection boundary. The same conjecture arose in the case in which $\alpha = 1$, $\beta = 1$ (see Kyriakidis (1995)). As an illustration, in Table 1, for each x ($0 < x \le 9$), we present the corresponding values of \tilde{y} and y^* when $(N, K, \alpha, \beta, c_1, c_2) = (10, 1, 2, 1, 1.5, 1)$. The dash '-' indicates that case 1 of the conjecture for the stochastic version of Problem 1 holds.

Note that it seems difficult to solve Problem 1 analytically for the deterministic model when $\alpha = 1$ and $\beta \neq 1$ or when $\alpha \neq 1$ and $\beta \neq 1$.

3.2. Problem 2, if $\alpha = 1$, $\beta \neq 1$

Suppose that (x_0, y_0) is the initial state. In this problem, it is preferable to express x as a function of y. Hence, from (6) it follows that the two-dimensional deterministic epidemic lies on the curve

$$x = x_0 \exp[\tilde{c}(1-\beta)^{-1}(y^{1-\beta} - y_0^{1-\beta})], \quad y_0 \le y \le \tilde{\xi}(x_0, y_0),$$

where, $\tilde{c} = c_1/c_2$ and $\tilde{\xi}(x_0, y_0)$ is the unique root in (y_0, N) of the equation for y,

$$x_0 \exp[\tilde{c}(1-\beta)^{-1}(y^{1-\beta}-y_0^{1-\beta})] + y - N = 0.$$
 (11)

Let us first consider two extreme cases. If the initial state of the epidemic is $(0, y_0)$ $(0 < y_0 < N)$, the curve of the epidemic is x = 0 $(y_0 \le y \le N)$. In this case the future cost of the epidemic is zero since no cost is attached to disease 2. If the initial state is $(x_0, 0)$ $(0 < x_0 < N)$, then the curve of the epidemic is y = 0 $(x_0 \le x \le N)$. In this case, given the cost structure of the problem, it can be readily checked that if $L < Nx_0^{-1} - 1$, then the optimal policy isolates all the infectives with disease 1 at the initial state, thus terminating the epidemic. If $L \ge Nx_0^{-1} - 1$, then the optimal policy does not intervene in the evolution of the epidemic.

If the initial state of the epidemic is (x_0, y_0) with $x_0 \neq 0$ and $y_0 \neq 0$, then the future cost $C(x_0, y_0)$ of the epidemic, if we do not intervene in its evolution, is given by

$$C(x_0, y_0) = N - \tilde{\xi}(x_0, y_0) - x_0$$

Proposition 2 below provides the answer to Problem 2 and corresponds to the conjecture for the stochastic model. It can be proved in a way similar to the case in which $\alpha = 1$, $\beta = 1$ (see Kyriakidis (1999)). For notational convenience, let P_{θ} ($0 < \theta \le N - x_0 - y_0$) be the policy in which θ infectives with disease 1 are isolated at the initial state (x_0, y_0) , with no further intervention in the evolution of the process.

Proposition 2. Assume that the initial state of the epidemic is (x_0, y_0) $(0 < y_0 < N)$. If

$$L+1 \ge \exp[\tilde{c}(1-\beta)^{-1}(N^{1-\beta}-y_0^{1-\beta})],\tag{12}$$

then the optimal policy does not intervene in the evolution of the epidemic for all x_0 ($0 < x_0 < N - y_0$). If (12) does not hold, then there exists a critical number x^* ($0 < x^* < N - y_0$) such that the optimal policy is the policy P_{x_0} when $0 < x_0 \le x^*$, while the optimal policy does not intervene in the evolution of the epidemic when $x^* < x_0 < N - y_0$. The number x^* ($0 < x^* < N - y_0$) satisfies the equation $C(x^*, y_0)/x^* = L$.

Note that for each y_0 (0 < y_0 < N) the expression $C(x_0, y_0)/x_0$ is decreasing with respect to x_0 (0 < x_0 < $N - y_0$). When (12) fails for each y_0 (0 < y_0 < N) the critical value x^* (0 < x^* < $N - y_0$) can be found numerically, since it satisfies the equation

$$\frac{C(x^*, y_0)}{x^*} = \frac{N - \tilde{\xi}(x^*, y_0)}{x^*} - 1 = L$$

Extensive numerical results indicate that, when (12) holds, then the optimal policy in the corresponding stochastic model prescribes no further intervention in the evolution of the epidemic, if the initial state is (x_0, y_0) ($0 < x_0 \le N - y_0$). When (12) fails, there is strong numerical evidence that $\tilde{x} < x^*$. This inequality leads us to conjecture that the stochastic

TABLE 2: Values of \tilde{x} and x^* .

у	0]	2	3	4	5	6	7	8
								_	
<i>x</i> *	6.25	5.10	4.30	3.53	2.79	2.06	1.34	0.63	×

isolation boundary is bounded above by the deterministic isolation boundary. The same conjecture arose in the case in which $\alpha=1$ and $\beta=1$ (see Kyriakidis (1999)). As an illustration, when $(N,L,\alpha,\beta,c_1,c_2)=(10,0.6,1,0.5,0.8,1.2)$ Table 2 presents for each $y\in (0\leq y<9)$ the corresponding values of \tilde{x} and x^* . The dash '-' indicates that case 1 of the conjecture for the stochastic version of Problem 3 holds, and the symbol '×' indicates that (12) is valid.

Note that it seems difficult to solve Problem 2 analytically for the deterministic model when $a \neq 1$ and $\beta = 1$ or when $\alpha \neq 1$ and $\beta \neq 1$.

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