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# SIMULATING THE SPREAD OF THE BSE DISEASE: A CELLULAR AUTOMATA APPROACH

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**Abstract:** The rules of evolution applied in the cellular automata approach may correspond to the propagation of the mad cow disease. In a computer simulation of the BSE disease's spread both inherited and infectious mechanisms are accounted for. The initial population of items is randomly distributed on a two-dimensional square lattice, $N_x \times N_y = 1000 \times 1000$, with a fraction of 1 percent the items already infected. Alternatively, faulty prions may spontaneously develop during the simulation with a very small frequency. Our results indicate a critical probability, $p_c$, of BSE transmission, so that for $p$ below the threshold the population recovers. For $p > p_c$ the disease is launched in the population with a dynamic equilibrium between the healthy and infected fractions of the population. The threshold is very sensitive to spatial clustering of the population and the detailed rules for the disease's onset, evolution and propagation.

**Keywords:** computer simulations, disease spreading, BSE, cellular automata method

## 1. Introduction

Bovine spongiform encephalopathy (BSE) is a disease associated with the misfolding of the prion protein [1] which leads to a fatal neurodegenerative disorder [2]. This lethal disease is characterized by a very long incubation period, followed by a relatively brief clinical phase. In the first stage of its development the disease is hardly transmissible; later it may be transmitted while it is still not recognized. The onset of BSE seems to arise spontaneously at a very low rate [3]. The prion infection's dynamics and propagation involves both inherited and infectious cases.

In this paper, BSE is discusses in terms of the case known as the mad cow disease. We are interested in simulating various mechanisms of the disease's

propagation and the possible channels of BSE appearing in a population. The disease may by introduced with the initial population. We refer to that possibility as the i-case. Alternatively, we may consider the faulty protein appearing spontaneously; this rare occurance is controlled by the small frequency of BSE appearances. If this happens to a newborn baby, we shall refer to it as an n-case, while affected grown-ups are g-cases. As already mentioned, the disease's hidden phase lasts long enough before it may be recognized. (Had it been recognized, the item would have been eliminated in order to stop the spread of the disease among the population.) Meantime, the disease may be transmitted to others. If the number of infected items exceeds the number of those affected by the disease and eliminated, the disease creeps into the population and we define the population as BSE-ill. It may be characterized by a fraction $R>0$ of infected items, say in the reproduction age. We may consider vertical transmission from parent to baby, or horizontal transmission to another item. (This may also include indirect infection through same foodstuff, *etc.*) We shall concentrate on the study of how the control parameter, the disease's probability transmission, $p$, gives $R>0$.

The cellular automata technique [4] has been used as a convenient tool to describe the effects of short distance interactions in dense populations, which may be assumed in the case of infection from neighbors (see [5, 6]). Each individual item may be infected or free of the disease and the dynamics is governed by a set of rules for transition from time $t$ to the next time step, $t+1$. It includes the Verhulst factor [7] of item elimination due to the limited environmental capacity, birth and elimination caused by BSE or other factors. A single one-step cycle is completed with suitable biological ageing and other updates. If the system tends to a dynamic equilibrium, we can extract from the computer experiment,after a sufficient number of iterations, all relevant characteristics such as the space and/or age distribution of items at various phases of the infection's development. We intend to study the possible scenarios of the onset of the disease, mechanisms of its transmission and the role of spatial distribution of items.

## 2. The model

An initial population of cows is randomly distributed on a two-dimensional square lattice, $N_x \times N_y = 1000 \times 1000$. Only for the i-case, a one percent fraction of this population is infected. Alternatively, BSE is introduced as a spontaneous process which happens with the frequency of $10^{-6}$ either when a baby is born (the n-case) or among grown-ups (the g-case). The latter may also include a situation when infected food is served to cows. For each simulation time step from time $t$ to time $t+1$, we scan the net and apply the evolution rules given below to non-empty sites. Each site may be empty or occupied by one item only, and the initial population at $t=0$ is 50 percent of the net's capacity. Each individual item is characterized by a set of parameters, including its age, $a$, and possible BSE infection, $v$, which is zero for disease-free individuals or a positive value indicating the degree the disease's development. For each time step the item's age is increased, $a \to a+1$. The maximum biological age has been assumed to be 120, which may correspond to a time step of about 2 months. After several hundreds of iteration steps we approach a dynamic equilibrium when

all crucial parameters do not vary on average, except for statistical fluctuations. We have applied 1 200 iteration steps and the output data have been averaged over the last 200 iterations.

At each time step we scan the lattice and the algorithm applied to each individual is as follows:

- an item is eliminated with probability proportional to the current population, the Verhulst factor;
- or it may be removed with a fixed probability of 0.01 if its age is at least 6, possibly for consumption;
- if it survives and its age, $a$, is within the reproduction age (from 12 to 60), some babies may be born at a presumed birth rate. Only when the randomly chosen cell where we intend to place the newborn is empty, the actual number of offspring is the presumed birth rate; otherwise the number of newborns, $b$, is smaller than the intended number. We aim to get $b = 0.1$, the ratio of born items to the population in the reproduction age;
- we continue elimination by poor health conditions or other factors, including the BSE disease;
- to complete the transition from $t$ to the $t+1$ era, we update grown-up items' age by 1, decrease slightly their health condition parameter, which is responsible for biological ageing, and take other actions such as increasing $v$ by 1 if an item has been infected or contracting BSE from the nearest neighbor (with probability $p$) or spontaneously (with the probability of $10^{-6}$).

Infection may take place only for a moderately developed disease, when $v \geq 15$. For $v = 25$, the item is eliminated, which means that the disease kills the item or it is noticed and reported leading to elimination of the infected cow by the medical services.

## 3. Results and discussion

As has been mentioned in the preceding section, one may consider a fraction of the initial population being infected as the begining the disease's spread in the population, the i-case. Even if the initial population is disease-free, sporadic outbursts of BSE with moderate frequency may be seen as the source of the disease's spread, referred to as either the g-case (the seed among grown-ups) or the n-case (newborns). Figure 1 shows fraction $R$ of infected items in the reproduction age against probability $p$ of either vertical or horizontal transmission of the disease to baby or neighbor. The initial random distribution of items on the lattice is supported by random location of newborns. Some areas of vacancies may still be observed, which results from increased extinction of individuals in the vicinity of a center of the disease's outburst, a direct consequence of the horizontal infection mechanism of neighbors (see Map 1).

Apparently, the onset of the disease in the population takes place for $p$ exceeding a critical value, $p_c$, which depends on the mechanism of the disease's introduction. Below the critical value, $p_c$, the dynamics of the system's evolution leads to a self-recovery of the population which becomes non-infected after a number of iteration steps. For a sufficiently large $p$, the fraction of infected items does not depend on the

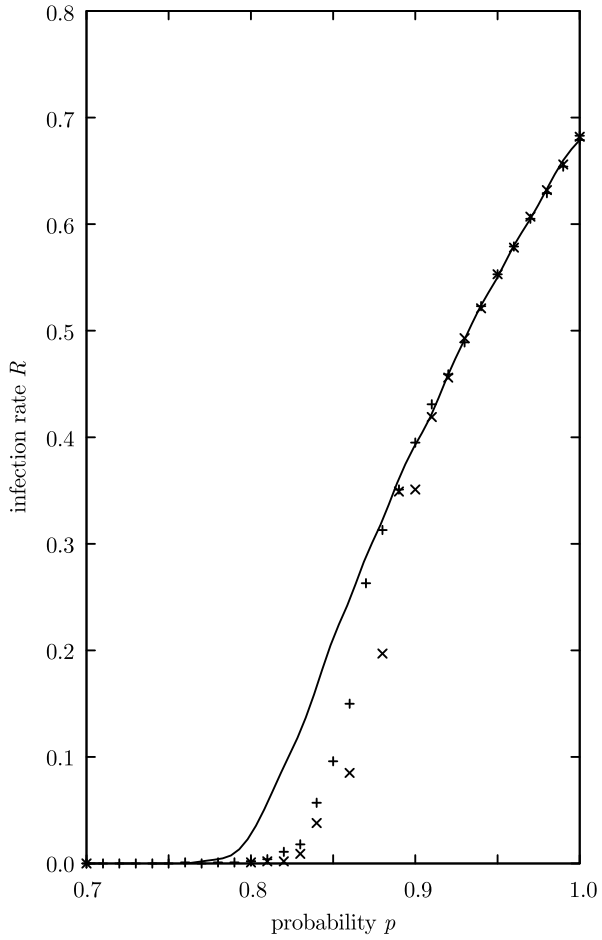



**Figure 1.** Normalized population $R$ of infected items in the reproduction age *vs* probability $p$ of BSE transmission for a random distribution of items on the lattice; the various ways of the disease's introduction are marked by the solid line (i-case), '+' sign (n-case) and '×' sign (g-case)

**Map 1.** Population distribution for offspring randomly located on the lattice; disease-free items are marked '+', infected items are marked 'o', and seriously ill items are marked 'X'

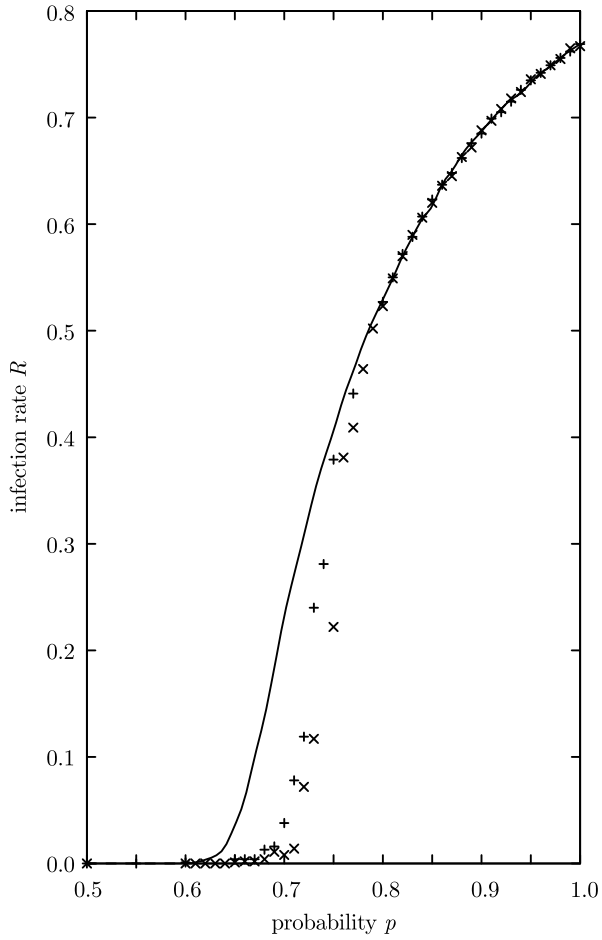
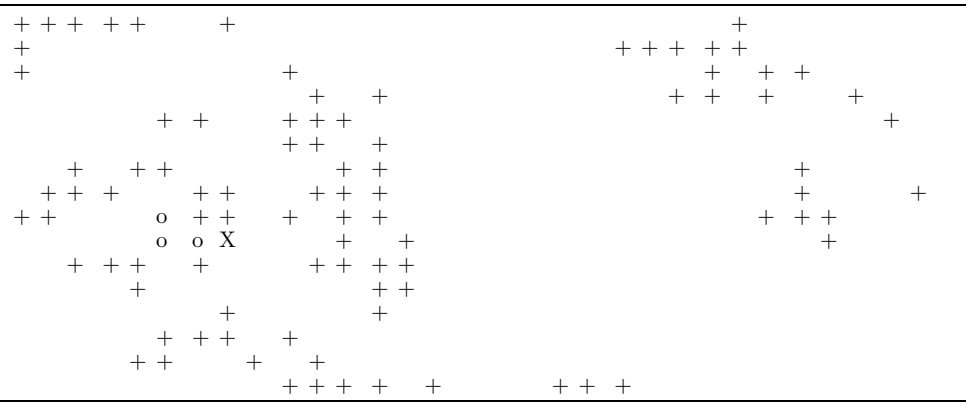



**Figure 2.** Normalized population $R$ of infected items in the reproduction age as a function of the probability $p$ of either vertical or horizontal infection with the BSE disease of a baby or a neighbor; babies are confined to stay close to parents; the various ways of the disease's introduction are marked by the solid line (i-case), '+' sign (n-case) and '×' sign (g-case)



**Map 2.** Population distribution for babies placed close to parents; disease-free items are marked '+', infected items are marked 'o', and seriously ill items are marked 'X'

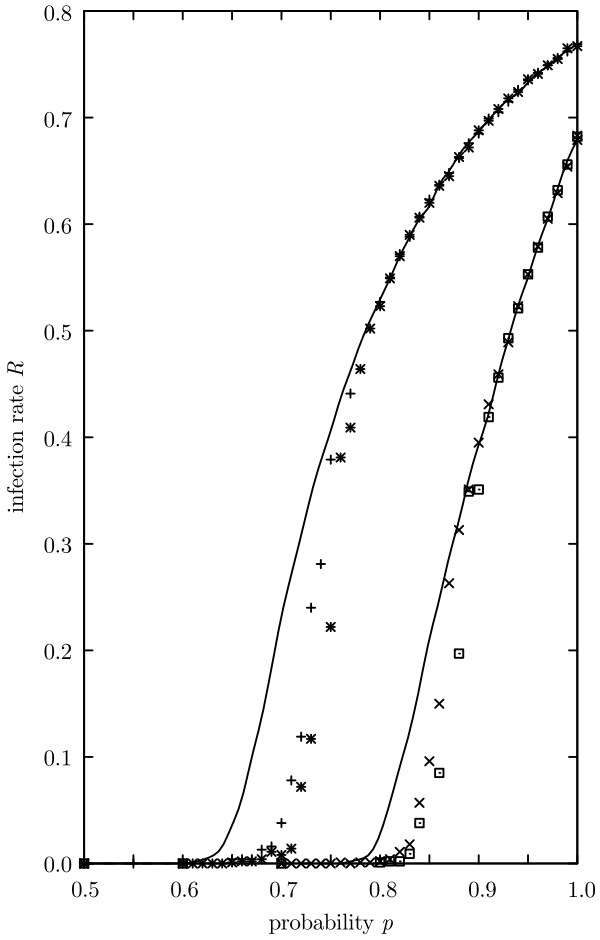



**Figure 3.** Normalized population $R$ of infected items in the reproduction age as a function of the probability $p$ of either vertical or horizontal infection with the BSE disease of a baby or a neighbor; comparison of the cases of babies forced to stay with parents and randomly located offspring

initialization of the disease. Obviously, the fraction $R$ of infected items increases with increasing $p$. However, there is still room for healthy individuals, $R<1$. This may be interpreted as a result of a dynamic equilibrium in a limited environment of the birth rate and the death toll between disease-free and infected items.

Figure 2 is a plot similar to Figure 1 for the case when offspring are placed near their parents instead of random locations. This leads to a non-uniform spatial distribution of individuals, as can be seen in Map 2.

Also in this case, the disease's distribution is non-uniform since both vertical and horizontal transmition operates on a local scale only. Both cases have been compared in Figure 3. The case when children are bound to stay close to their parents helps the disease to propagate. Results are the same for simulations run with different initial condition parameters, *e.g.* when we start with an initial population other than 1 percent, or with a frequency of spontaneous outbursts of BSE other than $10^{-6}$. A clear tendency can be seen that fot the g-case infection rate $R$ stays below that of the n-case. Then, the infection rate $R$ for the n-case stays below that of the i-case.

## 4. Conclusions

There is a critical probability, $p_c$, of BSE transmission such that for $p < p_c$ the disease disappears; the evolutionary rules remove the infected items from the population at a rate sufficiently high to prevent a spread of the disease. For the i-case, this leads to a totally BSE-free population, other cases of spontaneous entry of BSE at an extremely low rate are of no importance. For $p > p_c$, the horizontal component of disease transmission makes agglomerations more vulnerable to the disease's distribution. This, however, is not necessarily equivalent to an overall higher rate $R$ of infected items in the whole population. The evolution dynamics may have the opposite result if only clusters of infected individuals would die and give room to healthy individuals in the limited environment. The birth rate, $b$, plays an important role in the population's structure. For a small $b$, the population vanishes since the number of deaths for various reasons is than above the reproductive limit, $b_0$. Higher birth rates, just above $b_0$, give $R = 0$ even if the maximal disease transmission rate is assumed. The $R = 0$ case is the only solution for any $b$ if only vertical transmission is considered. Also horizontal transmission alone always yields $R = 0$. It is only when both transmission channels are open that we obtain $R > 0$ at some critical $b_c$.

These conclusions are not firm statement, they are rather indicative than decisive in character, for two reasons. Firstly, the set of model parameters cannot be established well due to the lack of well-grounded experimental data, as details of BSE's spread are to some extent questionable. Secondly, the dynamics of the system's evolution is rather sensitive to the choice of model parameters, such as the lower limit of $v = 15$ (that is about 30 months) for the disease's duration before it becomes infectious and may be transmitted. We believe, however, that the overall picture is correct and may represent essential features of BSE's spread.

As has been mentioned, both critical values, the birth rate, $b_c$ (at $p = 1$), and the probability of the disease's transmition, $p_c$ (for $b = 0.1$), are sensitive to possible spatial clustering of the population and depend on the mechanism responsible for the disease's propagation. As our next step, we plan to examine more carefully the effect of migration, which seems to be an important factor in the results obtained so far.

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