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Noise effects on the health status in a dynamic failure model for living organisms

H Kang[1], J Jo[1], M Y Choi[1,2], J Choi[3] and B-G Yoon[4]

[1] Department of Physics and Centre for Theoretical Physics, Seoul National University, Seoul 151-747, Korea
[2] Korea Institute for Advanced Study, Seoul 130-722, Korea
[3] Department of Physics, Keimyung University, Daegu 704-701, Korea
[4] Department of Physics, University of Ulsan, Ulsan 680-749, Korea

E-mail: bgyoon@ulsan.ac.kr

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Abstract

We study internal and external noise effects on the healthy–unhealthy transition and related phenomena in a dynamic failure model for living organisms. It is found that internal noise makes the system weaker, leading to breakdown under smaller stress. The discontinuous healthy–unhealthy transition in a system with global load sharing below a critical point is naturally explained in terms of the bistability for the health status. External noise present in constant stress gives similar results; further, it induces resonance in response to periodic stress, regardless of load transfer. In the case of local load sharing, such periodic stress is revealed more hazardous than the constant stress.

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1. Introduction

Living organisms constantly suffer stresses from the external world, which may lead them into failures. Cells in an organism may become dead due to such an external load and the stress carried by the dead cells should be transferred to other living cells. The resulting increase of stress then induces additional deaths of the remaining cells and possibly failure of the whole system. This kind of failure is common in many other systems, which is well described by the fibre bundle models [1–3]. What makes living organisms distinctive, however, is that cells may be regenerated (or healed); those effects have been considered in a recently proposed dynamic failure model for living organisms [4].

The dynamic model displays characteristic time evolution that the system tends to resist stress for rather a long time, followed by sudden failure with some fraction of cells surviving when the external stress exceeds a certain value f_t. This is called the 'unhealthy' state.

Otherwise, there is no such breakdown and the system is regarded to be in the 'healthy' state. It has also been shown that the transition stress f_t beyond which the system breaks down increases rapidly as the regeneration or healing ability is increased. A discontinuous transition between the two states may also take place as the system parameters are varied. With these features, the model turns out to reproduce the characteristic time course of degenerative disease progression such as diabetes [5], Alzheimer's disease [6] and possibly AIDS [7]. When the system is subject to periodic stress, the average fraction of living cells or the 'health status' exhibits oscillatory behaviour, appearing similar to the periodic synchronization [8]. In particular the oscillation amplitude exhibits a peak as the healing parameter is varied, dubbed healing resonance [9].

An important factor to affect the health of a living organism is the randomness present in real situations, e.g., due to imperfections and random variations. This is usually taken into consideration by resorting to a probabilistic description, which is controlled by the effective 'temperature'; such *internal* noise tends to weaken the system (namely, in its presence f_t in general reduces). The system also exhibits a healthy–unhealthy transition as the temperature is varied. In this paper, we elucidate this transition further by means of fixed point calculations as well as direct Monte Carlo (MC) simulations. Further, we note that environmental influences are likely to induce noise in the external stress, and accordingly a living organism may experience the resulting *external* noise as well. It is shown that the external noise added in constant external stress plays a similar role to the internal noise in the model, giving rise to the healthy–unhealthy transition as the (external) noise level is varied. In particular, such noise added in periodic stress has some interesting consequences: for peak values of the periodic stress sufficiently smaller than f_t, the health status oscillates in the healthy state at small noise levels. As the noise level is raised, the overall health status becomes worse, while the oscillation amplitude exhibits a peak, typical of resonance-like behaviour. Induced by the (external) noise, this is appropriately called stochastic resonance [10] and observed in systems with global load sharing (GLS) as well as with local load sharing (LLS). In the LLS case, the peak is in general broader, and periodic stress, albeit weaker on the average, is more hazardous than constant stress.

This paper consists of four sections: section 2 presents the dynamic failure model for living organisms as well as the MC algorithms used in this work. Section 3 describes the healthy–unhealthy transition as the (effective) temperature is varied. Discussed in section 4 are external noise effects including resonance-like behaviour of the system under noisy periodic stress. Finally a summary is given in section 5.

2. Dynamic failure model for living organisms

The basic ingredients of the dynamic failure model for a living organism consisting of N cells are as follows [4, 9].

(i) $N \equiv L^2$ cells are placed at sites of a square lattice of linear size L under periodic boundary conditions. Each cell i is characterized by a spin variable $s_i = -1(+1)$ according to whether it is alive (dead), and subject to external stress f_{ext}.

(ii) Each cell i has its own tolerance h_i, taken from a probability distribution $g(h)$, beyond which the cell may become dead. We take a Gaussian distribution for $g(h)$ with mean $\bar{h}$ and standard deviation σ.

(iii) For time interval $[t, t + \delta t]$, cell i, chosen at random, becomes dead according to the probability

$$p_i(\text{death}) = \frac{\delta t}{2t_r}\left[1 + \tanh\frac{E_i}{T}\right], \tag{1}$$

where $E_i \equiv (\eta_i - h_i)(1 - \bar{s})/2$ is the local field felt by cell i at time $t - t_d$ with the local stress $\eta_i \equiv f_{\text{ext}} + f_{\text{exc}}$ given by the sum of the external stress f_{ext} and the excess stress f_{exc} transferred from dead cells and $\bar{s} \equiv N^{-1}\sum_i s_i$ is the average spin of the system. Note that we introduce the time delay t_d for the stress to be transferred from dead cells to living ones and the refractory period t_r setting the relaxation time of the cell. The (effective) temperature T measures the width of the threshold region of the cells or the internal noise level in the system.

(iv) The excess stress f_{exc} is determined as follows: the stress carried by the dead cell ($s_i = +1$) is transferred to intact (living) cells on the 3×3 square centred at the dead cell. Each neighbour receives an equal amount of the excess load. If there is no living cell on the first (3×3) square, the load is transferred to the living cells on the second (5×5) square, and so on. If there is no living cell up to the tenth square of linear size 21, the load is shared by all living cells in the system, each getting an equal amount.

(v) In step 3, if cell i is dead, it is regenerated (or healed) with the probability

$$p_i(\text{heal}) = \frac{\delta t}{t_0}, \tag{2}$$

where t_0 denotes the time needed for a cell to be regenerated (or healed).

(vi) A regenerated cell gets its load from nearby living cells similarly to step 4: Each living neighbour chosen gives an equal amount of the load to the regenerated cell, in such a way that the load on the regenerated cell is equal to the average load of the chosen cells before the load transfer.

(vii) Measure the average fraction of living cells or the health status $\bar{x}$, which completes one time step.

There are three different time scales in the model: the time delay t_d, the refractory period t_r and the regeneration time t_0. Hereafter we rescale time in units of t_d and introduce the relaxation time $\tau \equiv t_r/t_d$ and the healing parameter $a \equiv t_r/t_0$, which measures the regeneration probability during the relaxation time.

We point out that step 4 or 6 is just one of many possible ways to realize LLS. We have thus considered several other realizations of LLS, only to find that qualitative behaviours of the system do not change. For a system with GLS, the load of the failed cell is transferred equally to all remaining living cells. In the latter case the equation of motion for the average living fraction $x_k \equiv (1 - \langle s_k \rangle)/2$ for the kth cell takes the simple form [4]

$$\tau \frac{\mathrm{d}}{\mathrm{d}t} x_k(t) = a - \left(\frac{1}{2} + a\right) x_k(t) - \frac{1}{2} x_k(t) \tanh[(f_{\text{ext}} - h_k \bar{x}(t-1))/T]. \tag{3}$$

The stationary solutions of equation (3), upon averaging over the tolerance distribution $g(h)$, leads to the self-consistency equation for the average (stationary) fraction of living cells or the health status $\bar{x}$:

$$\bar{x} = \int \mathrm{d}h\, g(h) \frac{2a}{(1 + 2a) + \tanh[(f_{\text{ext}} - h\bar{x})/T]}. \tag{4}$$

The results in this work, obtained from MC simulations and from equation (3), are average values over 20 initial configurations with $\tau = 5$ and time step $\Delta t = 0.5$, mostly in a system of size $L = 64$. For the Gaussian distribution of tolerance $g(h)$, we set $\bar{h} = 1$, and $\sigma = 0.2$. These parameter values have also been varied, only to give no qualitative difference.

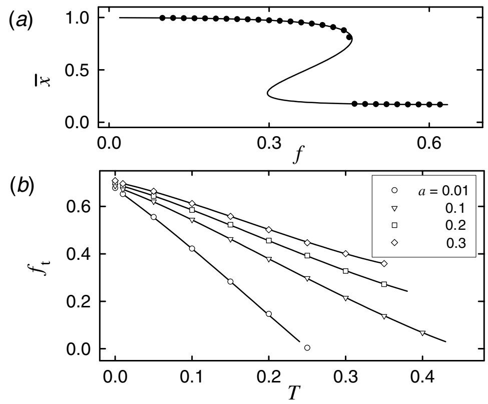

Figure 1. (a) Health status $\bar{x}$ versus (constant) stress f in a system with GLS, for the healing parameter $a = 0.2$ and temperature $T = 0.2$. Symbols represent the data obtained from MC simulations with the number of cells $N = 4096$; the line represents the fixed-point solutions of equation (4). (b) Transition stress f_t versus temperature T for several values of a shown in the legend. Data points are obtained by integrating equation (3) with the number of cells $N = 4096$ and lines represent the fixed-point curves obtained from equation (4).

3. Internal noise and healthy–unhealthy transition

The dynamic failure model described in the previous section is known to undergo a (discontinuous) healthy–unhealthy transition depending on the external stress $f_{\rm ext}$, healing parameter a and temperature T [4, 11]. We re-examine this transition in more detail by means of fixed points given by equation (4) and present the results for systems with GLS; the behaviour of the LLS systems is qualitatively similar [11].

We first consider the system under constant stress $f_{\rm ext} = f$ and examine the behaviour as a function of f. Figure 1(a) shows the health status $\bar{x}$, i.e., the average fraction of living cells in the stationary state, versus stress f in the GLS system with healing parameter $a = 0.2$ and temperature $T = 0.2$. The line represents the fixed-point solutions of equation (4) while symbols denote the data obtained from MC simulations for the system size $L = 64$. Note that there exists a bistable region in some range of f, in which there are two stable and one unstable fixed points. In direct MC simulations, however, only uppermost solutions are realized, as seen from the data points in figure 1(a), since all cells are taken to be alive initially. From this fixed-point line, we can determine the transition stress $f_{\rm t}$ beyond which the system breaks down and show in figure 1(b) that $f_{\rm t}$ reduces with the temperature T. As the healing parameter a or the temperature T is raised the bistable region shrinks to disappear: The discontinuous transition disappears and $\bar{x}$ decreases gradually with f. For comparison, we have also integrated equation (3) numerically and plot the obtained data points represented by symbols in figure 1(b); observed is perfect agreement with the lines obtained from the fixed-point analysis.

Next we describe the transition as the temperature T is varied. Figure 2(a) shows the health status $\bar{x}$ versus temperature T, obtained from equation (3) for a GLS system with the healing parameter $a = 0$ under several values of the external stress f. When there is no healing, the internal noise, however small, may lead the system to breakdown, even for the stress smaller than the transition stress at $T = 0$. Recall that $a = 0$ in equation (4) leads to $\bar{x} = 0$. At a finite value of a, the transition with T may also be understood in terms of the

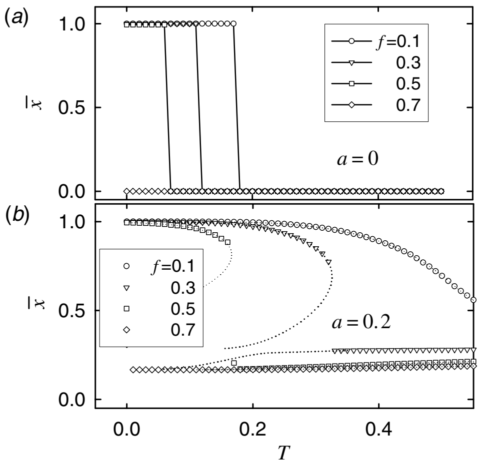

Figure 2. Health status $\bar{x}$ versus temperature T in the GLS system with the healing parameter $a =$ (a) 0 and (b) 0.2 for several values of the external stress f shown in the legends. Symbols represent the data obtained from integration of equation (3) with the number of cells $N = 4096$; solid lines in (a) are guides to the eye whereas dotted lines in (b) depict fixed-point solutions of equation (4).

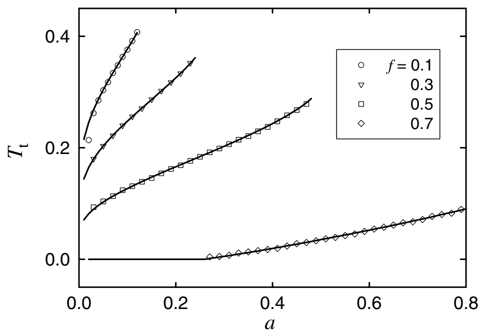

Figure 3. Transition temperature T_t versus healing parameter a for several values of external stress f shown in the legend. Other parameters of the system are the same as those in figure 1. Symbols denote the data obtained from integrating equation (3); lines are from equation (4).

fixed-point solutions of equation (4). The dotted lines in figure 2(b) show $\bar{x}$ versus temperature T for $a = 0.2$. Here the bistable region is again observed for larger values of stress, and the transition can be understood as before. For stress smaller than a critical value, the health status changes continuously with T (see the data for $f = 0.1$ in figure 2(b)), implying that the transition disappears.

Before moving on to the next issue, we probe the behaviour as the healing parameter a is varied and present in figure 3 the transition temperature T_t versus a for several values of stress f, in the same system as before. The lines represent fixed-point solutions whereas the symbols are obtained from equation (3). The transition temperature is shown to increase with the healing parameter or the regeneration probability, as expected. Here the healthy–unhealthy transition disappears again for a above the critical value.

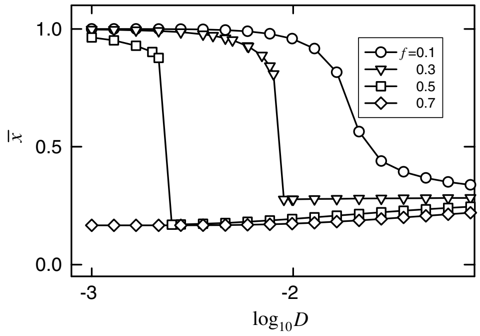

Figure 4. Health status $\bar{x}$ versus (external) noise level D in the same system as figure 1. The system suffers the stress given by equation (5) with $\Omega = 0$ at $T = 0$. Symbols represent the data obtained from MC simulations and lines are guides to the eye.

4. External noise and resonance

We now discuss the effects of random noise directly added to the external stress. Specifically we consider the stress of the form:

$$f_{\text{ext}}(t) = \frac{f_0}{2}(\sin\Omega t + 1) + \gamma(t), \tag{5}$$

where Ω is the stress frequency and $\gamma(t)$ represents Gaussian white noise characterized by the average $\langle\gamma(t)\rangle = 0$ and correlations $\langle\gamma(t)\gamma(t+\tau)\rangle = 2D\delta(\tau)$. Via MC simulations, we compute the health status $\bar{x}$ for various values of the noise level D.

We first consider the case $\Omega = 0$, i.e., constant stress $f = f_0/2$ in the presence of noise of strength D, and show in figure 4 the average stationary fraction $\bar{x}$ versus D for $a = 0.2$ and several values of f. Note that the behaviour of $\bar{x}_s$ is remarkably similar to that in figure 2(*b*), except for that the logarithm of D plays the role of the temperature T. We therefore conclude that the effects of external noise is qualitatively the same as those of internal noise and henceforth consider only the case of $T = 0$ to study the effects of external noise.

When the external stress is periodic ($\Omega \neq 0$) in the absence of any noise ($T = D = 0$), the system is known to exhibit interesting time evolution [9]: without healing, the health status $\bar{x}$ either decays stepwise to zero or approach a constant value far from zero, depending on the peak value f_0. When the healing parameter a is raised from zero, $\bar{x}$ exhibits oscillatory behaviour, similar to periodic synchronization. Further, as a is increased, the power spectrum at the stress frequency grows at first and then reduces, manifesting resonance-like behaviour hence termed healing resonance.

Similar phenomena also emerge when noise is added and the temperature T or the noise level D is varied. Here we only present effects of the latter while keeping $T = 0$, since effects of T and D are qualitatively the same. Figure 5 shows the time evolution of the health status $\bar{x}$ for several values of the noise level D. The system is under the sinusoidal stress with noise, given by equation (5) with period $\mathcal{T} \equiv 2\pi/\Omega = 128$ and the peak stress (*a*) $f_0 = 0.6$ and (*b*) $f_0 = 0.7$. We recall that under constant external stress the transition stress is given by $f_t(T = 0) \approx 0.69$ for $a = 0.2$. When the (external) noise is sufficiently small, the health status in the stationary state oscillates within the healthy/unhealthy region if the peak stress f_0 is smaller/larger than f_t. As the noise level D is increased, oscillations of the health status moves to the unhealthy region from the healthy one. This happens even when the peak stress f_0 is somewhat smaller than f_t. Further, in this case, the oscillation amplitude first grows

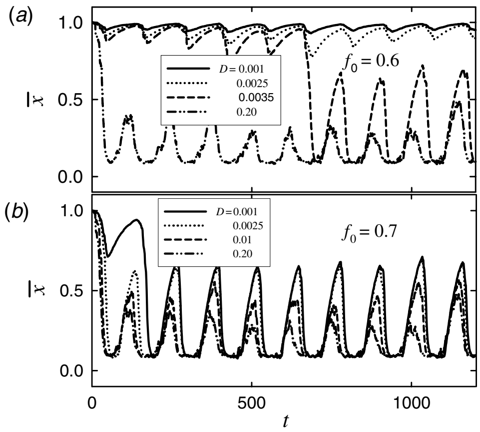

Figure 5. Time evolution of the health status $\bar{x}$ (with time t in units of the delay time) for several values of the noise level D. The organism suffers the sinusoidal stress in the presence of noise, given by equation (5), with period $\mathcal{T} = 128$ and peak stress $f_0 =$ (*a*) 0.6 and (*b*) 0.7. There is no internal noise ($T = 0$) while other parameters of the system are the same as those for figure 1.

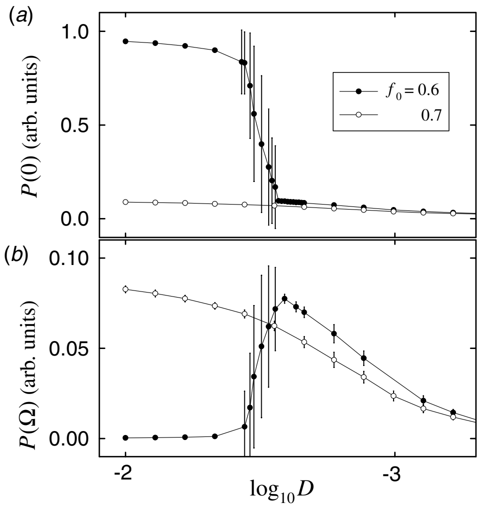

Figure 6. Power spectrum (*a*) $P(0)$ at zero frequency and (*b*) $P(\Omega)$ at the driving frequency versus noise level D in the same systems as figure 5. Error bars denote standard deviations.

with D, then decreases. This may be demonstrated more clearly by the power spectrum of $\bar{x}(t)$ versus noise level D. Shown in figure 6 are thus the power spectrum (*a*) $P(0)$ at zero frequency and (*b*) $P(\Omega)$ at the driving frequency. If the peak stress f_0 is larger than f_t, the health status of the system oscillates always in the unhealthy region: $P(0)$ remains more or less constant near zero whereas $P(\Omega)$ gradually reduces with the noise level D. When f_0 is smaller than f_t, on the other hand, $P(0)$ decreases rather sharply with D, similar to the healthy–unhealthy transition discussed in the previous section. In addition, as D is varied, $P(\Omega)$ exhibits a noticeable peak. This behaviour, typical of resonance, is induced by noise and thus appropriate to call stochastic resonance [10].

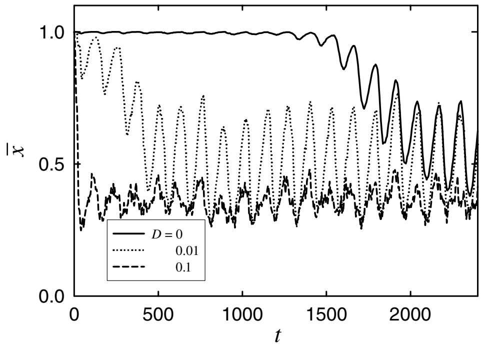

Figure 7. Time evolution of the health status $\bar{x}$ in an LLS system for several values of the noise level D shown in the legend. The stress is given by equation (5), with the peak stress $f_0 = 0.5$ and period $\mathcal{T} = 128$. Other parameters of the system are the same as those in figure 5.

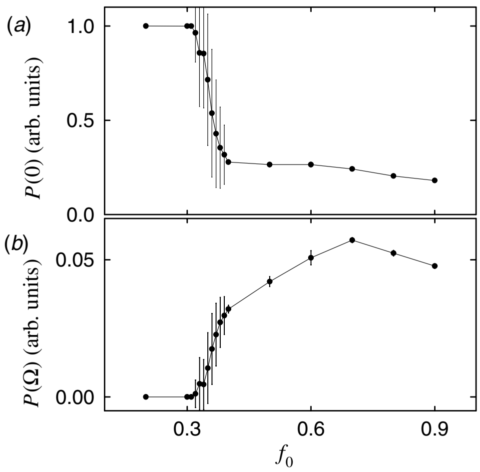

Figure 8. Power spectrum (*a*) $P(0)$ at zero frequency and (*b*) $P(\Omega)$ at the driving frequency versus the peak value f_0 of the stress, in the same system as figure 7.

Finally, we investigate the LLS system under periodic stress, which exhibits another characteristic behaviour. Under constant external stress, the LLS system is in general weaker than the GLS one for the same parameters. Under periodic stress, the LLS system tends to become less healthier, compared with the case of constant stress given by the peak stress f_0. This happens even when f_0 is smaller than the transition stress f_t. Figure 7 shows the time evolution of $\bar{x}$ in the LLS system under periodic stress for several values of the noise level D for $f_0 = 0.5, \mathcal{T} = 128$ and $T = 0$, with other parameters the same as those in figure 1. We point out that $f_0 = 0.5$ is smaller than $f_t \approx 0.58$; nonetheless breakdown still occurs after a long time, even in the absence of external noise ($D = 0$). This is in contrast with the GLS system which never breaks down at this value of stress without noise (the stationary value of $\bar{x}$ is larger than 0.9). To determine the role of f_0 in the LLS system, we display in figure 8 the power spectrum (*a*) $P(0)$ at zero frequency and (*b*) $P(\Omega)$ at the stress frequency versus the peak stress f_0, for the system in figure 7. It is shown that $P(0)$ decreases rather abruptly near $f_0 \approx 0.32$, which is much smaller than f_t in the case of constant stress. At the same

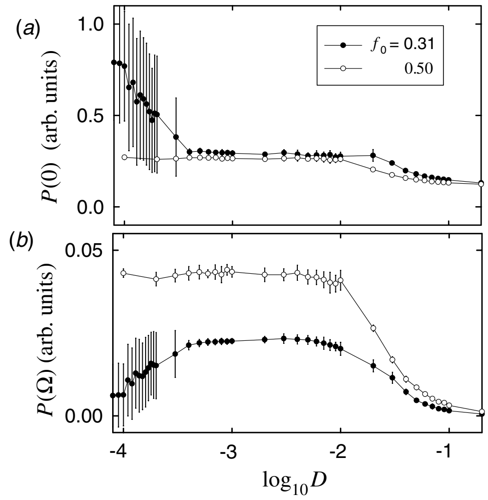

Figure 9. Power spectrum (*a*) $P(0)$ at zero frequency and (*b*) $P(\Omega)$ at the driving frequency versus noise level D, in the same system as figure 7 and in the system under periodic stress with a smaller peak $f_0 = 0.31$.

time $P(\Omega)$ shows a sharp increase and reaches a peak at $f_0 \approx 0.71$. The peak in $P(\Omega)$ is also observed in the GLS system (data not shown).

It is both intriguing and interesting that in the LLS system the periodic stress with the peak stress f_0 could be more hazardous than the constant stress of the same f_0. This seems to reflect that the stress per intact cell after breakdown is not smaller than the transition stress and that state maybe metastable which is accessible only by the LLS system under periodic stress, with regeneration probabilities. The origin is, however, not known at this stage; presumably, it results from an interplay of the delay time, the healing parameter, the stress period, and disorder or noise in the LLS system.

The external noise has similar effects on the health of the LLS system. To see this, we have varied the noise level D in the LLS system under periodic stress, with two values of $f_0 = 0.31$ and 0.50. Figure 9 displays the power spectrum (*a*) $P(0)$ at zero frequency and (*b*) $P(\Omega)$ at the driving frequency versus D, for both values of f_0. When $f_0 = 0.50$, the system breaks down quickly and oscillates in the unhealthy state. The oscillation amplitude or $P(\Omega)$ is rather insensitive to D up to a certain value, then tends to reduce. For $f_0 = 0.31$, on the other hand, as D is increased, $P(0)$ drops to the stationary value quickly while $P(\Omega)$ exhibits a resonance-like peak similar to the GLS system, although the peak is broader and less pronounced.

5. Summary

We have studied noise effects on the behaviour of the failure model for a living organism. The internal noise, resulting from, e.g., imperfections, has been taken into account by introducing appropriate probabilities. It has been shown that the health status of the system, defined to be the average fraction of intact cells, is determined by the external stress, the healing parameter, and the effective temperature measuring the internal noise level, and describes the healthy–unhealthy transition. In a system with global load sharing, the nature of the phase transition has been probed by means of the fixed-point solutions of the self-consistency equation for the health status. At given temperature, there are bistable regions in the health status of the organism in some range of external stress, manifestly explaining the existence of the discontinuous transition as the stress is varied. The transition temperature has been found to increase with the healing parameter. Also shown is the existence of the critical temperature and healing parameter, beyond which the discontinuous transition disappears and the health status varies in a continuous manner.

We have also studied effects of external noise directly present in the external stress. It has been shown that the role of such noise in stress is qualitatively the same as that of the internal one: Namely, the system undergoes a healthy–unhealthy transition, either as the (effective) temperature is varied or as the (external) noise level is varied at zero temperature. The transition disappears and the health status experiences continuous change when the stress is smaller and/or the healing parameter is larger than the critical value. When the noise is added to periodic stress, the average fraction of intact cells oscillates in time. In particular, the oscillation amplitude grows at low noise levels, then reduces as the noise level is raised further, thus displaying a peak; this may be interpreted as the stochastic resonance, regardless of the load transfer mechanism. It is also observed that the local load sharing system is more vulnerable to the periodic stress than the constant stress.

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