Chapter 12

Detection of Gravity through Nonequilibrium Mechanisms

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ABSTRACT

Using the principles of physics, could we set a fundamental lower limit for the size of a cell that can respond to gravity? Pollard (1965) tried to obtain such a limit assuming a gravity sensing mechanism that could be described as a system in thermodynamic equilibrium. In this chapter, a dynamic gravity sensing mechanism that is not in thermodynamic equilibrium is considered. It is shown that under some conditions nonequilibrium systems can be more sensitive than equilibrium systems. The dynamic mechanism described here is able to respond to gravity by virtue of its ability to perform a process similar to "signal averaging" used in electronic detection of weak signals. Through this process, a system is able to respond to a small systematic force embedded in a larger but randomly fluctuating force.

INTRODUCTION

One basic difference between systems in thermodynamic equilibrium and systems far from thermodynamic equilibrium is in the way they respond to external factors. When a physical system is far from thermodynamic equilibrium certain transitions, broadly classified as "symmetry-breaking transitions," may occur. Recently it was realized (Kondepudi, 1989) that when a symmetry-breaking transition occurs the system becomes very sensitive to external influences. Influences that have a small effect when the system is in thermodynamic equilibrium can have a much larger effect when it is not in equilibrium.

In this chapter I shall often speak of a "state" of the system. The "state" of the system could be something as simple as the position on an intracellular particle or a more complex organization of a cell with certain well defined geometrical features such as symmetries or asymmetries. In a symmetry-breaking transition, the system makes a transition from an initial (symmetric) state to one of the many possible (asymmetric) final states. (This may correspond to, for example, an intracellular particle initially being localized to one position but, as changes in the cell occur, moving to one of the two or more possible final locations.) A symmetry-breaking transition is such that in the absence of an external biasing influence, such as gravity, each of many possible final states is reached with equal probability. In the presence of a small biasing influence, such as gravity, one of the states is reached with a high probability. The somewhat unexpected sensitivity of such systems is that even when the magnitude of the biasing influence is smaller than the root-mean-square value of the random fluctuations that the system experiences, the transition to one of the many possible states occurs with a high probability. Systematic biases buried in random fluctuations can have strong effects.

Using a simple model, this chapter will describe how sensitivity to gravity may come about in a simple transition that could conceivably occur in a living cell. The main purpose of this chapter is to emphasize the difference between the responses to gravity of a static system in thermodynamic equilibrium and a dynamic system that is not in thermodynamic equilibrium. An awareness of this difference may be helpful in understanding gravisensitivity of living cells.

EQUILIBRIUM SYSTEMS

In equilibrium systems, in accordance with the Boltzmann principle, the response to an external factor is characterized completely by the interaction energy. The Boltzmann principle states that if a system is in thermodynamic equilibrium, the probability that the system will be in a particular state depends only on the energy, $E$, of that state and temperature, $T$, in $\text{K}$. The probability $P(E)$ is proportional to $e^{-E/kT}$ (in which $k$ is the Boltzmann constant). To investigate the response of such a system to an external factor, such as gravity, we must determine the change in the state of the system due to gravity. If the gravitational interaction energy, $\Delta E$, is small then the change in the state will be small. This general idea has been discussed by Pollard (1965) in the context of a cell. (Figure 1 is a schematic representation of Pollard's analysis.)

Pollard's analysis is as follows. Consider an intracellular particle of density $\rho$ and volume $\nu$. The simplest response of such a system to gravity is the change in position, $x$, of this intracellular particle. Let the size of the cell be 1. It is assumed that the particle behaves as if it were suspended in water. In the absence of gravity the state of the intracellular particle is such that it is equally likely to be in any part of the cell as it moves randomly due to Brownian motion. In the presence of gravity, however, the particle is more likely to be
at the bottom of the cell than at the top. If P(1) and P(0) are the probabilities of the particle being at the top, \( x = 1 \), and bottom, \( x = 0 \), of the cell respectively, then (assuming that the whole system is in thermodynamic equilibrium) according to the Boltzmann principle:

\[
P(0)/P(1) = e^V(p - p_0)g/M_kT
\]

Here \( g \) is the acceleration due to gravity and \( p_0 \) is the density of water. \( V \) and \( p \) are the particle's volume and density, respectively. The factor \( V(p - p_0)g \) is an energy difference in the system when the particle is at the top and when it is at the bottom of the cell. The ratio given by Equation (1) may be taken to be a measure of the system's response to gravity. If this ratio is close to one then the system is not sensitive to gravity; if it is much larger than one then it is sensitive to gravity.

One can now look at the "sensitivity" of such an equilibrium system to gravity in various situations. If we consider a spherical particle of radius 0.1 \( \mu \text{m} \) with a density of \( = 1.5 \text{ g cm}^{-3} \) in a cell of size 1 \( \mu \text{m} \times 10^{-4} \text{ cm} \), we find (assuming \( T = 300^\circ \text{K} \) and \( p_0 = 1.0 \text{ g cm}^{-3} \)) that the ratio \( P(1)/P(0) = 0.995 \). If we consider a larger cell of size 5 \( \mu \text{m} \) and a particle of radius 0.5 \( \mu \text{m} \) we find \( P(0)/P(1) = 22 \). These estimates can give an idea of how sensitive a system in thermodynamic equilibrium can be if its response can be modeled as a particle suspended in water.

On the other hand, a living cell is not a system in thermodynamic equilibrium. Its internal structure is extremely complex and dynamic; it is a system capable of "processing" data about its environment and responding to small changes. In view of this, is it possible that a cell can be more sensitive to gravity than the estimates made using the Boltzmann principle lead us to believe? The following section describes a simple dynamic mechanism that enables a system to become very sensitive to gravity. The most fundamental difference between the analysis of Pollard and this mechanism is that the latter is a dynamic nonequilibrium system for which the Boltzmann principle does not apply.

**NONEQUILIBRIUM SYSTEMS**

Nonequilibrium systems are known to exhibit a wide variety of interesting phenomena. One type of phenomenon that is quite generally observed is the transition to a symmetry-breaking state. In a symmetry-breaking transition a system can become extremely sensitive to external influences such as gravity. For an intracellular particle of the type discussed by Pollard, a simple model can be developed to illustrate how this sensitivity comes about.

The model, shown in Figure 2, can be realized in a cell whose internal structure is undergoing certain changes. Here the intracellular particle is not completely free, as in the case discussed above, but confined to a region. In the terminology of physics, it is in a potential well. Initially the particle is assumed to be in a potential well with one minimum as shown in Figure 2a. We assume that with time changes in the cell transform the single-well potential to a double-well potential as shown in Figure 2b. In the latter situation, the particle has two possible positions that it can occupy. Assume also that further changes in the state of the cell depend on which of the two positions the particle occupies. The influence of gravity here is that it makes it more probable for the particle to be in the lower position. Our objective is to obtain this probability (of the particle going to the lower position) in this dynamic process, taking into account the random Brownian motion.

From a fundamental thermodynamic point of view, generally a structural transformation such as the one assumed in this model (from a single-well potential to a double-well potential) occurs in a cell because the cell is a system not in thermodynamic equilibrium. Further, in such dynamic processes, even if the energy of the particle in the final two positions is known, we cannot in general use the Boltzmann principle to predict the probabilities for the two positions.

The equation of motion of a particle of mass, \( m \), subject to a force, \( F(x) \) (which is a function of position), and the force of gravity, \( mg \), in a viscous medium can be written as:

\[
m \frac{dv}{dt} = -\psi v + F(x) - mg
\]

where \( v \) is the velocity, \( \psi v \) is the viscous force which is linearly proportional to the velocity, and \( g \) is the acceleration due to gravity. For a spherical particle of radius \( r \), \( \psi = 6 \pi \eta r \) in which \( \eta \) is the viscosity of the fluid. Since the particle being considered is extremely small, its motion will be heavily damped so that we may take the acceleration \( \frac{dv}{dt} = 0 \).
Then Equation (2) becomes:

\[ v = \frac{dx}{dt} = \frac{F(x)}{\psi} - \frac{mg}{\psi} \]  

(3)

In analyzing the motion of an intracellular particle of radius less than a micron, random forces that generate the Brownian motion cannot be ignored. As a first approximation, one may assume that the random forces that are to be included in Equation (3) represent a "Gaussian white noise," \( \sqrt{\varepsilon} \xi(t) \). This assumption means that the particle's motion can be approximated by small random jumps whose magnitude varies from jump to jump; the probability that the change in \( x \) due to a jump will take a particular value is a Gaussian function with mean equal to zero and standard deviation equal to \( \sqrt{\varepsilon} \). The term "white noise" refers to the assumption that a jump is not correlated with any of the previous jumps. If the motion of the particle is considered to be only due to the jumps, the equation is:

\[ \frac{dx}{dt} = \sqrt{\varepsilon} \xi(t) \]  

(4)

With the two assumptions made above regarding the random force term \( \sqrt{\varepsilon} \xi(t) \), one can show that on a time scale long compared to the time scale of fluctuations (Chandrasekhar, 1943), the motion of the particle obeys the Fick's law of diffusion:

\[ \frac{\partial P(x,t)}{\partial t} = (\varepsilon/2) \frac{\partial^2}{\partial x^2} P(x,t) \]  

(5)

Here \( P(x,t) \) is the probability distribution of the particle's position \( x \) at time \( t \). We can identify \( (\varepsilon/2) \) as the diffusion coefficient. Equation (5) is called the Fokker-Planck equation associated with the random differential Equation (4).

This formalism can be applied to Equation (3).

With the random fluctuations added to (3) the equation becomes:

\[ \frac{dx}{dt} = \frac{F(x)}{\psi} - \frac{mg}{\psi} + \sqrt{\varepsilon} \xi(t) \]  

(6)

The corresponding Fokker-Planck equation is (Haken, 1975):

\[ \frac{\partial P(x,t)}{\partial t} = -\frac{\partial}{\partial x} \left[ \left( \frac{F(x)}{\psi} - \frac{mg}{\psi} \right) P(x,t) - \frac{\varepsilon}{2} \frac{\partial P(x,t)}{\partial x} \right] \]  

(7)

When the system reaches thermodynamic equilibrium,

\[ \frac{\partial P(x,t)}{\partial t} = 0 \]  

Using this in Equation (7), we can solve for the equilibrium distribution, \( P_{\text{eq}}(x) \). It can be shown that:

\[ P_{\text{eq}}(x) = \text{C exp } \left\{ - \frac{1}{2} (V(x) + mgx)/\psi \right\} \]  

(8)

in which \( C \) is the normalization constant and \( V(x) \) is the potential energy given by:

\[ V(x) = -\int F(x')dx' \]  

(9)

From the Boltzmann principle the equilibrium distribution should be:

\[ P_{\text{eq}}(x) = \text{C exp } \left\{ - \frac{1}{2} (V(x) + mgx)/kT \right\} \]  

(10)

Comparing Equations (8) and (10) we obtain the relation:

\[ \frac{\psi \varepsilon}{2} = kT \]  

(11)
which is the Stokes-Einstein equation. For a spherical particle of radius \( r \), \( \psi = 6 \pi \eta r \) and so we have:

\[
\varepsilon = \frac{2kT}{\psi} = \frac{2kT}{6\pi \eta r} \tag{12}
\]

Thus, once the force \( F(x) \) is specified, all the quantities in Equation (7) can be computed for a particle of mass \( m \) and radius \( r \) (we assume the fluid is water, \( \eta = 0.01 \text{ g cm}^{-1} \text{ s}^{-1} \)).

For our model, consider a force \( F(x,t) \) which changes with time such that the potential \( V(x,t) \) has an initial shape as shown in Figure 3a and changes to the shape shown in Figure 3c.

As a model we may consider the function:

\[
F(x,t) = -Ax^3 + (\lambda_0 + \gamma t - \lambda_c) x \tag{13}
\]

in which \( A, \lambda_0, \lambda_c \) and \( \gamma \) are constants. Assume that \( \lambda_0 < \lambda_c \), so that the coefficient of \( x \) is negative for \( t = 0 \) but becomes positive when \( t \) is sufficiently large. If the coefficient of \( x \) is negative, then the corresponding potential has only one minimum as in Figure 3a; if the coefficient is positive, the corresponding potential has two minima as in Figure 3c. If the coefficient is nearly zero, then the potential is somewhat flat as shown in Figure 3b. For this model Equation (6) becomes:

\[
\frac{dx}{dt} = -Ax^3 + (\lambda_0 + \gamma t - \lambda_c) x - \frac{mg}{\psi} \sqrt{\frac{2kT}{\psi}} x \tag{14}
\]

Now we have the formalism to answer our main question — in a physical process described by Equation (14), what is the probability, \( P_{\text{lower}} \), that the particle will be in the "lower" position when the system reaches its final configuration as shown in Figure 3c? The probability for the system to make a transition to the upper position is, of course, \( P_{\text{upper}} = (1 - P_{\text{lower}}) \) since there are only two possible positions. The sensitivity of the system to gravity depends on this \( P_{\text{lower}} \). If \( P_{\text{lower}} = 0.5 \), for example, the system is unable to feel the effects of gravity. If \( P_{\text{lower}} = 1.0 \), then the effects of gravity on the system are very strong. A detailed theory of the computation of \( P_{\text{lower}} \) has recently been developed (Kondepudi, 1989, and references therein). This theory, when applied to the above model, gives the result:

\[
P_{\text{lower}} = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} \exp(-x^2/2)dx \tag{15}
\]

where:

\[
N = \frac{(mg/\psi)}{(kT/\psi)^{1/4}} \tag{16}
\]

As can be seen, \( P \) is expressed in terms of a Gaussian integral with the upper limit \( N \) being the number of standard deviations.

To contrast the difference between equilibrium and nonequilibrium processes it is convenient to define the following ratios as measures of the sensitivities of the respective systems to gravity:

\[
S_{\text{Equilib}} = \frac{P_0}{P(1)} = e^{V(p - \rho_0)g/\kappa T} \tag{17}
\]

\[
S_{\text{Nonequil}} = \frac{P_{\text{upper}}}{P_{\text{lower}}} \tag{18}
\]

For a numerical comparison consider a cell of size 5 \( \mu m \) so that \( l = 5 \mu m \) in Equation (17). Assume that the particle has a density \( \rho = 1.5 \text{ g cm}^{-3} \), \( \rho_0 = 1.0 \text{ g cm}^{-3} \), \( \eta = 0.01 \text{ g cm}^{-1} \text{ s}^{-1} \) and calculate \( S_{\text{Equilib}} \) for various particle radii. These are tabulated in the first two columns of Table I.

For computing \( S_{\text{Nonequil}} \) we must choose appropriate values for the parameters \( \gamma \) and \( \lambda_0 \), in addition to the radius of the particle and its density. The value of \( \lambda_0 \) has the following physical meaning. At time \( t = 0 \), the particle is in its equilibrium position at \( x = 0 \); if this particle is displaced from this position by a small amount then the rate at which it will relax back to the equilibrium position depends on the value of \( (\lambda_0 - \lambda_c) \). Without loss of generality, we may choose \( \lambda_c = 0 \) (because this only fixes the zero of the scale).

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Figure 3. Evolution of the shape of the potential \( V(x,t) \) in time. Initially (a) there is only one minimum so the particle relaxes to essentially a stable position. In the final state (c), the potential has two minima so the particle can be in one of the two possible positions. This transition is mathematically described by Equation (13).
Then if $\lambda_0 < 0$, the relaxation rate is $\psi / \lambda_0$. If we choose $\lambda_0 / \psi = 1 \text{ s}^{-1}$, for example, the displaced particle returns to its equilibrium position in about one second. We shall use this value for $\lambda_0$.

Table I. A Comparison of Equilibrium and Nonequilibrium Responses to Gravity. The values shown are computed using Equations (15)-(18) for a spherical particle. The following numerical values were used: $1 = 5.0 \mu m$, $\rho_0 = 1.0 \text{ g cm}^{-3}$, $\rho = 1.5 \text{ g cm}^{-3}$, $\eta = 0.01 \text{ g cm}^{-1} \text{ s}^{-1}$, $(\lambda_0 / \psi) = 1 \text{ s}^{-1}$, $(\psi / \psi) = 5.0 \times 10^{-4} \text{ s}^{-2}$, $T = 300^\circ K$, $g = 980 \text{ cm} \text{ s}^{-2}$.

<table>
<thead>
<tr>
<th>Particle</th>
<th>$S_{\text{Equilib}}$</th>
<th>$N$</th>
<th>$S_{\text{Nonequilb}}$</th>
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</thead>
<tbody>
<tr>
<td>Equation:</td>
<td>(17)</td>
<td>(16)</td>
<td>(18)</td>
</tr>
<tr>
<td>0.1</td>
<td>1.02</td>
<td>0.065</td>
<td>1.11</td>
</tr>
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<td>0.2</td>
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<td>0.370</td>
<td>1.81</td>
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<tr>
<td>0.3</td>
<td>1.95</td>
<td>1.020</td>
<td>5.50</td>
</tr>
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<td>4.88</td>
<td>2.093</td>
<td>5.40x10^4</td>
</tr>
<tr>
<td>0.5</td>
<td>2.21x10^3</td>
<td>3.657</td>
<td>7.83x10^4</td>
</tr>
<tr>
<td>0.6</td>
<td>2.22x10^4</td>
<td>5.768</td>
<td>&gt;1.0x10^6</td>
</tr>
</tbody>
</table>

Next a value for $\gamma$ must be chosen. This determines the time it takes for the system to evolve from a single-well potential to a double-well potential. When the coefficient of $x$ in Equation (14) is negative then the potential has only one minimum; if it is positive then it has two minima. If we set $(\psi / \psi) = (1/2000)$ s, for example, then in 4000 s, the coefficient of $x$ will change from -1 to +1, which corresponds to a transition time of little over one hour. We choose this value for $\gamma$. The value of the coefficient $A$ establishes the final depth of the well; it is chosen such that when the particle is in one of the two positions (potential wells), the barrier between the two is sufficiently high that it remains there and does not make a transition to the adjacent position. This assumption is necessary to derive the formula (15) - (16), but it is not needed for the computation of $S_{\text{Nonequilb}}$.

The values of $N$ and $S_{\text{Nonequilb}}$ are tabulated in the last two columns in Table I. The results show that for particles of size up to 0.3 $\mu m$ there is no significant difference. Beyond this size the difference markedly increases — for a 0.6 $\mu m$ particle, nonequilibrium sensitivity is about four orders of magnitude larger than equilibrium sensitivity. This example clearly shows a situation in which dynamic nonequilibrium mechanisms in a cell can make it very sensitive to gravity.

The sensitivity of the above nonequilibrium model increases if the entire process occurs on a longer time scale. This happens if the values of $\lambda_0 / \psi$ and $(\psi / \psi)$ are decreased. The total time for the transition is the time it takes for the coefficient of $x$ on the right hand side of Equation (14) to change from $-\lambda_0 / \psi$ to $+\lambda_0 / \psi$ which is equal to $(2\lambda_0 / \psi)$.

Table II shows the enhancement of sensitivity with the decrease of $\lambda_0 / \psi$ for a particle of radius 0.2 $\mu m$ in a cell of size 5 $\mu m$. For a transition that takes several hours, the nonequilibrium system can be a hundred times more sensitive than the equilibrium system. While the difference in sensitivity is not so great for particles smaller than 0.2 $\mu m$, it is even more dramatic for larger particles.

The physical reason for the enhancement of nonequilibrium sensitivity for slower processes is that on a long time scale the system is able to perform what amounts to "signal averaging" to detect the weak gravitational force embedded in the much larger random fluctuations. Signal averaging is a technique used by communication engineers to extract a weak signal embedded in large noise. (For a deeper understanding of these aspects of nonequilibrium sensitivity the reader is referred to Kondepudi, 1989.) In understanding the graviscendivity of cells such processes may be of some relevance.

Table II. Table Showing the Increase of Sensitivity with the Decrease of $(\lambda_0 / \psi)$ and $(\psi / \psi)$.
The values tabulated are for a particle of radius 0.2 $\mu m$ for a cell size of 5 $\mu m$. All the other values are the same as in Table I.

<table>
<thead>
<tr>
<th>$(\lambda_0 / \psi)$, s$^{-1}$</th>
<th>$(2\lambda_0 / \psi)$, s</th>
<th>$S_{\text{Equilib}}$</th>
<th>N</th>
<th>$S_{\text{Nonequilb}}$</th>
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</thead>
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<td>1</td>
<td>$10^4$</td>
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<td>$10^4$</td>
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<td>$10^4$</td>
<td>1.22</td>
<td>2.617</td>
<td>2.24x10$^2$</td>
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<td>10$^{-3}$</td>
<td>8.64x10$^4$ (1 day)</td>
<td>1.22</td>
<td>4.486</td>
<td>2.75x10$^5$</td>
</tr>
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</table>

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REFERENCES


