Dynamic Properties of Lednev’s Parametric Resonance Mechanism

Stefan Engström

Research Service, J.L. Pettis Memorial Veterans Hospital, Loma Linda, California

This paper presents a further development of the mechanism for the detection of weak magnetic fields proposed by [Lednev (1991): Bioelectromagnetics 12:71–75]. The fraction of excited oscillator states of an unhydrated ion is studied in a dynamic model driven by the predicted (time-varying) transition probability in the presence of thermal noise and an unspecified excitation mechanism. The main results of Lednev are confirmed. In addition, I conclude that ultraharmonic and ultrasubharmonic resonances may also be observed, provided that the response time of the dynamic system is similar to the period of the oscillating magnetic field. I discuss the time scales involved in the mechanism and present theoretical constraints on these parameters. The crucial requirement for the theory’s applicability is that the lifetime of the excited states of the affected ion oscillator exceeds the period of the applied magnetic field. I discuss the time scales involved in the mechanism and present theoretical constraints on these parameters. The main result is that the lifetime of the excited states of the affected ion oscillator exceeds the period of the applied magnetic field. Numerical solutions of the dynamic system are given and are shown to correspond well to theoretical expectations. The main discrepancy between the theories of Lednev and of Blanchard and Blackman [Blanchard and Blackman (1994): Bioelectromagnetics 15:217–238] appears to be due to an inconsistency in the latter paper. The general problem of robust analysis of experimental data is discussed, and I suggest a test of compliance with the Lednev model that is independent of all parameters except for the ratio of oscillating and static field strength \( B_0/B_s \) for many resonance conditions and experimental models.

Key words: ion parametric resonance, AC/DC magnetic fields, excitation and deexcitation mechanisms

INTRODUCTION

The first transductive step in the chain of events that could result in the detection of a weak magnetic field in a biological system remains elusive. One of the main hypotheses currently in vogue is the parametric resonance effect, which was first discussed in this context by Lednev [1991]. Similar to earlier theories, the main obstacles we encounter are thermal and electromagnetic noise. Had it not been for experimental evidence (see section 5) showing effects for very weak fields, one would be tempted to reject out of hand any theory that has to shield its mechanism from the destructive bombardment of intrinsic noise at the level required. In the present paper, I take the stance that as long as no other theory provides a better framework to explain the experiments, one should be willing to accept some seemingly far-fetched assumptions (see section 2A) in order to be able to guide further experiments.

Section 2 discusses Lednev’s original method and previous work. The following section develops our extensions to the model and discusses its general implications. Section 4 explores the model numerically and forms the quantitative predictions we can make. The following section deals with existing experimental results and the problem of analyzing experiments that can support or reject the theory. Conclusions are presented in the final section.

LEDNEV’S ORIGINAL MODEL

It is useful to rederive the model for several reasons. 1) I want to review the assumptions that this model shares with Lednev’s original model. 2) There is a controversy between Lednev [1991, 1993] and Blanchard and Blackman [1994] regarding a numerical factor of 2 in the argument of the Bessel function; I try to resolve that issue. 3) My alternative derivation of the basic transition probability may be useful for others who seek to investigate the effect of, e.g., a finite averaging time for the mean value of this quantity.

The basic physical model is a degenerate three-dimensional oscillator physically realized by a bare (unhydrated) ion located in a protein complex like

Received for review October 6, 1994; revision received May 12, 1995.
Address reprint requests to Stefan Engström, Research Service, J.L. Pettis Memorial Veterans Hospital, 11201 Benton Street, Loma Linda, CA 92357.
Calmodulin. The oscillator’s orbital momentum has an associated magnetic momentum that is in the locus of magnetic field interaction. The mechanism capitalizes on a match between the frequency, $\Omega$, of an applied oscillating magnetic field, $B_0$, and the frequency difference between transitions of excited ion states down to the ground state. A degeneracy of the first excited state is broken through a Zeeman splitting by the combined oscillating magnetic field and parallel static field, $B_0$. The effect appears because the applied field mixes the split states, and it manifests itself by modifying the total transition probability, $p(t)$, of these excited states down to the ground state. In principle, one could consider transitions between arbitrary states as long as one of the energy-levels is nondegenerate [Podgoretskii and Khrustalev, 1964].

Assumptions of the Model

If this mechanism is to operate, then there must exist excited states that are long lived enough so that the spontaneous transitions are an important contribution to the transitions to the ground state. The time between (de) excitations due to thermal and electrical noise also has to be similar to or longer than the period of the oscillating field, or else the spin mixing mechanism that accounts for the alteration of the transition probability will not function. The mechanism that populates the excited states must generate the relative phases, $\delta$, of the two sublevels in a nonuniform distribution, or else there will be no effect. The ion must not be hydrated. If it has water bound to it, the mass will be much larger and more uncertain than if the ion is bare. Furthermore, the presence of an excited ion state must somehow make a difference biochemically: It must represent a biologically meaningful change so that the signal can proceed in the biological pathway.

Adair [1992] levels severe criticism aimed at the noise and coherence problems mentioned above. Apart from these two points, he argues that an imperfect symmetry of the potential in which the ion is located will break the degeneracy before the Zeeman splitting is able to affect the transition probability. He also puts forward an argument that claims that the basic resonant phenomenon is impossible due to the orthogonality of the initial and final states.

I cannot provide satisfying answers or justifications to all issues raised above. However, some points can be addressed at least partially:

One can imagine a situation in which the ion is shielded in a hydrophobic region that might prevent the ion from becoming hydrated [Chiabrera et al., 1985a]. A hydrophobic cleft of this type has been observed in Calmodulin [Babu et al., 1987], the molecule Lednev [1991] cites as a possible interaction site.

Adair’s argument regarding state orthogonality concerns the case when we average the transition probability over all possible angles. We must require that a special direction exists from which the transition is observed by the oscillator’s environment. This might be the most severe problem of the proposed model.

There are several coherence aspects of the mechanism. One that does not constitute a problem is the spatial coherence required by Adair [1992]. It is a misconception that different ions have to have correlated phases. The present model’s requirement is that the excitation mechanism should provide the relative phase, $\delta$, of the states of a single ion in some nonuniform distribution. Although an ensemble of ion oscillators is considered below (“An Extended Model”), I do not postulate any collaborative action between different oscillator sites.

Lednev [1994] claims that x-ray diffraction studies of Calmodulin [Babu et al., 1987] support the contention that the oscillator is sufficiently isotropic. However, it is not clear that the data provide sufficient resolution to settle the dispute, because the isotropy required by Adair is well beyond the available experimental resolution.

Results of the Basic Model

In Appendix A, I derive the main result of Lednev [1991, 1993]:

$$ p(t) = A_1^2 + A_2^2 + 2A_1A_2 \cos \left( \Omega t + \alpha \sin (\Omega t) + \delta \right) $$

(1)

$$ \bar{p} = \lim_{t_0 \rightarrow \infty} \int_0^{t_0} p(t) \, dt = $$

$$ \begin{cases} 
A_1^2 + A_2^2 + 2A_1A_2 \cos \delta (-1)^\nu J_\nu (\alpha) & \nu \text{ integer} \\
A_1^2 + A_2^2 = \gamma & \text{otherwise} \end{cases} $$

(2)

$A_1$ and $A_2$ parameterize the unperturbed transition rate (g) and the initial condition of the oscillator along with $d$, which is the phase difference between the upper and the lower excited states. For the other quantities, we have $\Omega = g \Delta q B / 2m$ (frequency difference of the two split states); $\nu = \Omega / \Omega$ (frequency index, resonance for integer $\nu$); and $\alpha = g \Delta q B / 2m \Gamma = \nu B / B_0$ (Bessel function argument). The quantity $g$ is a generalized Landé factor, $\Delta$ is the difference in orbital momentum along the component parallel to the field, $q$ is the charge of the ion, and $m$ is its mass.

In Appendix A, I calculate the average of $p(t)$ up to a finite time $t_0$. If one is satisfied with knowing the mean only at whole periods of the applied field, then the result is:


$$\bar{p}_K = A_1^2 + A_2^2 + 2 A_1 A_2 J_1 (\alpha) \frac{1}{K} \sum_{k=1}^{K} \cos \bigl( q \pi (2k-1) + \delta \bigr) ,$$

(3)

where $$\delta = 2\pi k / \Omega$$ ($$K$$ integer). $$J_1 (\alpha)$$ is the Anger function [section 3.2.3 of Abramowitz and Stegun, 1964]. For integer $$\nu$$, $$J_{\nu} (\alpha)$$ coincides with the Bessel function $$J_{\nu} (\alpha)$$, and we recover the result of Equation 2.

### Controversy About a Factor of 2

The argument $$\alpha$$ to the Bessel function differs between the results of Lednev [1991, 1993] and Blanchard and Blackman [1994], although the authors appear to utilize the same basic physical model. The latter paper uses the argument $$2\alpha$$, which is inconsistent with their expression for $$\Omega$$, if we assume that the static and oscillating fields operate through the same mechanism. The amplitudes $$B_s$$ and $$B_r$$ are equivalent in their effect on level splitting [see section 113 in Landau and Lifshitz, 1977] and must appear with the same prefactor in Equation 13. For the reader who wishes to compare the different versions of the derivation, Table 1 summarizes the notations of Lednev [1993], of Blanchard and Blackman [1994], and of this paper. In order to understand the results of Blanchard and Blackman [1994], we must assume that there are two different interaction mechanisms; one for the DC field (Zeeman splitting) and one for the AC field (unspecified). Furthermore, the effect that is sensitive to the AC field must somehow cancel the effect predicted by Lednev and must, instead, deliver $$2\alpha$$ for the argument of the Bessel function.

We can see a reason for the controversy between the papers of Lednev [1991, 1993] and Blanchard and Blackman [1994] in Equation 18 (see Appendix A). One can say that the latter paper implicitly uses different values of $$g\Delta$$ for calculating $$\Omega$$, and $$\alpha$$. $$g\Delta$$ may be negotiable, but the same value must be used for the static and oscillating fields (see also section 2B). The source of the inconsistency is probably the ad-hoc definition of a “frequency modulation index” in Equation 3 of the Appendix of Blanchard and Blackman [1994].

I conclude that Lednev’s expression (Eq. 2) is consistent with a choice of $$g\Delta = 2$$. This particular choice is implicitly assumed by considering a model with three levels. The number of levels is determined by the total orbital momentum, $$L$$, and the total spin, $$S$$, of the ion state. With $$L = 1$$ and $$S = 0$$, we obtain the above-mentioned levels and also predict $$g\Delta = 2$$. The resonance condition is also affected by this quantity, and, so far, experimental findings [McLeod et al., 1987; Ross, 1990; Blackman et al., 1994] tend to support $$g\Delta = 2$$ for the observed primary resonance, although several negative results from studies that expressly searched for resonance at the “cyclootron resonance” have also been published [Saalman et al., 1992; Coulton and Barker, 1993]. See Liboff [1992] for a review of experiments that tested resonant effects due to combinations of static and oscillating fields. Even if this is not the true resonance condition, the form $$\alpha = vB_s / B_r$$ for the Bessel function argument is unambiguous, because it hides the $$g\Delta$$ factor in the definition of $$\nu$$.

### AN EXTENDED MODEL

I extend the basic model by taking a plausible first step down the pathway of biological response. Assuming that only the first excited state is going to communicate with the ground state, one can construct a model for the state of one ion (cf. Fig. 1).

Now, consider an ensemble of such ions that are all subjected to the same magnetic field. We can write down a differential equation for the fraction of excited ions, $$f(t)$$. Because the rate of change of $$f$$ is $$(\rho + \sigma)(1 - f) - [p(t) + \rho]f$$ (cf. Fig. 1), we get:

$$\frac{df}{dt} + (2\rho + \sigma + p(t)) f = \rho + \sigma .$$

(4)

### TABLE 1. A Guide to the Notation of the Different Papers That Address the Ion Oscillator Parametric Resonance Model*

<table>
<thead>
<tr>
<th>Quantity</th>
<th>Lednev [1993]</th>
<th>Blanchard and Blackman [1994]</th>
<th>This paper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Static magnetic field</td>
<td>$$B_0$$</td>
<td>$$B_m$$</td>
<td>$$B_0$$</td>
</tr>
<tr>
<td>Osc. field amp. (peak)</td>
<td>$$B_1$$</td>
<td>$$B_{1m}$$</td>
<td>$$B_1$$</td>
</tr>
<tr>
<td>Resonant angular freq.</td>
<td>$$\Omega = qB_s / m$$</td>
<td>$$\omega_1 - \omega_2 = qB_s / m$$</td>
<td>$$\Omega = qB_s / m$$</td>
</tr>
<tr>
<td>Resonant index</td>
<td>$$n = \Omega / \Omega$$</td>
<td>$$n = (\omega_1 - \omega_2) / \Omega$$</td>
<td>$$v = \Omega / \Omega$$</td>
</tr>
<tr>
<td>Bessel function arg.</td>
<td>$$\alpha_1 - \alpha_2 = qB_s / B_0$$</td>
<td>$$\alpha_1 - \alpha_2 = 2nB_s / B_0$$</td>
<td>$$\alpha = vB_s / B_0$$</td>
</tr>
</tbody>
</table>

*Omega ($$\Omega$$) denotes the angular frequency of the applied oscillating magnetic field in all cases; $$q/m$$ is the charge-to-mass ratio of the considered ion.
In this equation, \( p(t) \) is the spontaneous transition probability derived in the preceding section, \( p \) is the (de-)excitation probability due to noise, and \( \sigma \) is an as yet unspecified source of excitations. The quantity \( f(t) \) lends itself better to physical intuition than does \( p(t) \), particularly in its time-averaged form.

The dynamic time scale, \( t_r \), for this system is set by the transient solution to Equation 4 for a constant \( p(t) = \gamma = A_1^2 + A_2^2 : t_d = 1/(2\rho + \sigma + \gamma) \). Next, I consider the limits of fast and slow dynamic response times relative to the forcing time scale, \( t_f \), over which \( p(t) \) varies.

**Slow Dynamic Response—(\( t_s \gg t_f \))**

A sluggish dynamic system will only be able to observe the average value of \( p(t) \). The differential Equation 4 can therefore be approximated by:

\[
\frac{df}{dt} + (2\rho + \sigma + \bar{p}) f = \rho + \sigma
\]

which has the stationary solution

\[
f = \frac{\rho + \sigma}{2\rho + \sigma + \bar{p}}.
\]

In this case, we expect resonant behavior for \( f \) at the same frequencies as in Lednev's model, i.e., for \( v = 1, 2, 3 \ldots \), because only then does \( \bar{p} \) differ from \( \gamma = A_1^2 + A_2^2 \).

**Fast Dynamic Response—(\( t_s \ll t_f \))**

If the dynamic response is much faster than the forcing, then the dynamic system will be able to follow the forcing dictated by \( p(t) \) at all times, and, again, we can look at a stationary solution:

\[
f(t) = \frac{\rho + \sigma}{2\rho + \sigma + p(t)}.
\]

Averaging this solution over time will produce resonant behavior for integer \( v \), and, due to the nonlinear dependence of \( f(t) \) on \( p(t) \), possibly also for rational \( v \). This happens because the distribution of \( p(t) \) is radically different for rational and irrational \( v \) (Appendix B). This possibility is demonstrated by numerical simulation in section 4A.

Adair [1992] estimates the unperturbed spontaneous transition rate, \( \gamma \), to 0.1 s\(^{-1} \) by assuming that the energy of the first excited state of a calcium ion, \( h\omega_0 \), equals the average thermal energy of the environment [Adair, 1992: Eq. 6]. A higher value for \( \omega_0 \), a different transition mechanism, or a lighter ion could conceivably increase the value of \( \gamma \). However, there is a more serious limit imposed by the period of the oscillating field. If \( \gamma \) or \( \rho \) greatly exceeds the forcing frequency, \( \Omega \), then the quantum state mixing does not have time to act before the excited state is disrupted and Equation 1 is replaced with Equation 19, which does not exhibit resonant behavior. It follows that we will not be able to observe the case \( t_s \ll t_f \); thus, Equation 7 can only guide our expectations of the case \( t_s = t_f \).

**Resonance Width**

In the model, we see a pure mathematical resonance that has zero width in the limit of long averaging times relative to the period of the forcing frequency. Extending the model to a distribution of parameters \( \rho, \sigma, A_1, A_2, \delta \) may not affect the width of this resonance.

Consider a distribution \( h \) of the parameters and the initial condition. Denote these parameters \( (\rho, \sigma, A_1, A_2, \delta, f) \) by \( s \) and normalize \( h(s) \) such that \( \int h(s)ds = 1 \). Then, for each set of parameters, we have

\[
\frac{df}{dt}(s;t) + (2\rho + \sigma + p(s;t)) f(s;t) = \rho + \sigma
\]

and the total mean of \( f \) is:

\[
\bar{f} = \int dt \int ds h(s) f(s;t).
\]

If all solutions \( f(s;t) \) exhibit zero width resonant behavior at integer \( v \) (and possibly at rational \( v \)), then \( \bar{f} \) will experience the same resonances. This assertion is difficult to demonstrate in the general case of intermediate response times for the dynamic system. However, the statement is provable in the limit of a fast dynamic response where \( f(t) \) is directly dependent on \( p(t) \) (Eq. 7). The proof...
relies on showing that the long-term distribution of $p(t)$ is different between rational and irrational $v$ (cf. Appendix B) and that this resonant behavior does not depend on any of the parameters $s$.

Thus, neither the mean lifetime of the states $\left(\gamma = A_1 + A_2^2\right)$ nor the magnitude of the noise level ($p$) or any other of the parameters that constitute $s$ can generate a finite width resonance in this limit. A parameter that would change the resonance width (assuming that $\Omega$ is constant) is $\Omega$, the energy difference between the excited levels. One can imagine a situation in which the potential well of the ion varies between ion sites. This variation could give rise to a broadening of the resonance.

Another factor is the lifetime of the protein complex itself. If the complex is structurally altered after a time $t_c$, then this corresponds directly to a finite averaging time $t_0$ in our model. The resonance width is inversely proportional to $t_0$ for large $t_0$. Therefore, it is possible to obtain information about the life time of the protein complex by measuring the width of any resonance if this is the main cause of broadening.

### Numerical Investigation

I solve Equation 4 numerically by calculating $f(t)$ in an interval $[0,t_c]$ using a Bulirsch-Stoer integrator [see section 16.4 in Press et al., 1992] with a relative error of $10^{-5}$. The output from the integration is the average of $f(t)$ over the investigated interval. The initial condition for the solution is somewhat arbitrarily set to

$$f(0) = f = \frac{p + \sigma}{2p + \sigma + \gamma},$$

which is the value we approach when there is no field effect and the transition probability is constant $P(t) = \gamma$. Also, $f_0$ is our reference for normalization throughout this paper; all excited ion fractions are given in units of $f_0$.

### Resonant Behavior

By scanning $v = \Omega/\Omega$, the parameter that controls whether we are on or off resonance, the expectations for the slowly responding system (Fig. 2a) are confirmed. In compliance with Equations 2 and 6, the system exhibits the expected harmonic resonance for $v = 1$, and the first few subharmonics can be seen as well ($v = 2, 3$).

Turning instead to a system with a dynamic response time comparable to the period of the applied oscillating field (Fig. 2b), the third strongest resonance is the first ultraharmonic, $v = 1/2$. Overall, the $v = 1/2$ response is weaker than most of the main integer resonances, but not by a large factor. This statement appears (as seen from numerical investigation) to be true for all ultra(sub)harmonic responses. For very weak fields, $v = 1/2$ has an advantage over all subharmonics in that it has a nonvanishing first derivative. This means that, if this mechanism is active at low AC fields, then the two strongest responses should be expected for $v = 1$ and $v = 1/2$. A few more ultraharmonics can be seen in a more detailed view of the region $v < 1$, and some ultrasubharmonic resonances (in particular, $v = 3/2$ and $v = 2/3$) are present as well.

### Dependence on $\alpha$

Next, I study the influence of $\alpha = gBqB/m\Omega$, the quantity that appears as the Bessel function argument in Lednev’s model. Turning first to the case of a slowly responding system (Fig. 3), we see the effect predicted by Equation 6: The normalized fraction of excited ions is very close to 1 for noninteger $v$ and is qualitatively similar to the predictions of Lednev’s original model.

Figure 4 displays the functional dependence on $\alpha$ for the fraction of excited ions. For a general description, one can say that the harmonic and subharmonic resonances follow the prediction of Equations 2 and 6 rather closely. The ultraharmonic and ultrasubharmonic resonances are also described by oscillating functions in general, and their “period” is a consistent continuation of the integer-v results. The difference between the curves in Figures 3 and 4 is due to a response lag introduced by the dynamic response of the extended model.

### Noise-Limited Response

If we increase the noise, then, at some point, we will remove the possibility of a Lednev effect. In Table 2, I demonstrate this for a range of noise levels ($p$) and, for comparison, one-directional excitation rates ($\sigma$). The maximum effect of the mechanism is estimated by the two quantities

$$f_1 = \text{extremum}\left[\tilde{f}(v = 1, \alpha = \alpha_1)\right] \quad \text{and}$$

$$f_2 = f_1 \tilde{f}(v = 1, \alpha = 0),$$

as seen from numerical investigation.
where $\alpha_0$ denotes the point at which $f$ has its first extremum.

Table 2 shows that the maximum response declines approximately like $\gamma/\rho$ when $\gamma < \rho$, and a similar relation holds for the $\sigma$ variation. The rapid decline in response with $\gamma/\rho$ leads us to require that $\gamma$ is somewhat similar to the dominant term of $\rho$ and $\sigma$ if there is to be a measurable effect. To some extent, we may be able to invoke amplification at later stages but probably not by a large factor, because our mechanism does not vanish at the no-effect level ($\rho = \gamma$ in the absence of any fields), and I am considering an ensemble response in this model.

**EXPERIMENTAL RESULTS AND THEIR INTERPRETATION**

Due to the nontrivial dependence on several field parameters, the Lednev mechanism makes many predic-
tions that are subject to experimental verification or rejection. In designing experiments to test the method, one should be aware that the transductive step occurs at the molecular level and should try to reduce the use of parametric interpretations of experimental data that are biologically very remote from the point of magnetic field interaction. Some workers have explored the mecha-
nism with carefully controlled field parameters ($B_o$, $B_1$, and $\Omega$) in rather high-level experimental models that make the interpretation more difficult, e.g., counts of neurite outgrowths in PC-12 cells [Blackman et al., 1994; Trillo et al., 1994] and attenuation of analgesia in land slails [Prato et al., 1994]. Shuvalova et al. [1991] have tested the model in a biological system that lies closer to the mechanism by examining Calmodulin-dependent phosphorylation of myosin. Yost and Liburdy [1992] report consistency with the Lednev model in a experi-
ment that examined a magnetic field’s ability to alter the role of calcium signalling in the lymphocyte.
Using a minimal assumption of a locally (around the no-effect value) monotonic response function and targeting a single ion so that \( q / m \) is fixed, we can make the following predictions, which can be experimentally examined. 1) We should expect a response for the conditions as outlined in sections 3 and 4. If the resonance width is moderate, then this should be detected as on/off conditions. 2) The magnitude of the response should be largest for \( v = 1 \) and, in general, should decrease for less significant resonances in a manner depicted in Figure 2. 3) If \( v \) is selected on resonance, then varying \( \alpha \) should produce a response that oscillates and takes both positive and negative values. The magnitude of the oscillations should be damped for large \( \alpha \). The zeros and extrema are well defined regardless of the response function (consult Figs. 3, 4 for the location of the zeros and extrema). For integer \( v \), the appropriate Bessel functions provide a good approximation.

One particular feature of the mechanism that has not been substantiated experimentally is the increase and decrease of excited ion states. The references cited above saw only a decrease of the response regardless of field parameter combinations. It appears that the response function involves a rectification or a saturation around the no-effect value. This might be an expression of a biological response, which has adapted a form that is maximal in a no-field situation, and, when the field is turned on, the response goes down regardless of the sign of the change in the fraction of excited ions. Alternatively, one side of the response function may experience a saturation that would cancel positive or negative responses. Obviously, the list of model predictions above has to be adapted to the chosen type of response scenario.

**Location of the First Extremum in \( \alpha \)**

An interesting property of the functional form of the original model as well as our extended version lies in the dependence on \( \alpha \), i.e., \( B / B_0 \). Although we may be able to determine that a resonance is observed, it might be impossible to say which ion is active (there are many possible candidates). Therefore, we cannot know with certainty the resonance index \( v \). Fortunately, the fraction of excited ion states, \( f(\nu,\alpha) \), has its first extremum approximately at the same position of \( B / B_0 = \alpha / \nu \) for most \( \nu \) (Table 3), and the information concerning which resonance is active is less crucial.

This observation provides a test that is capable of determining whether a set of experiments agrees with the basic Lednev model or not: determining the position of the first extremum of a set of experiments. The response has to be minimal or maximal for a value of \( B / B_0 \in (1.16, 1.99) \) in order to be consistent with the model. The provision is that one of the resonances listed in Table 3 is causing the effect. Under these conditions, this result is independent of the specific resonance model \( (g\Delta) \) as well as what ion is affected \( (q/m) \). From a theoretical point of view, the ion parametric resonance (IPR) model of Blanchard and Blackman [1994] appears to be inconsistent, but I recognize the excellent data of the companion paper [Blackman et al., 1994], which is in the form discussed here and which cannot be explained by the Lednev model, because their first minimum occurs at approximately \( B / B_0 \approx 0.9 \). The main difference between the IPR model and Lednev [1991, 1993] is a numerical factor of 2, which lands \( 2B_0 / B_0 \) in the required range and which is why especially the \( v = 1 \) resonance for Mg\(^{2+} \) fits their experimental data well in the IPR model.

**CONCLUSIONS**

The main theoretical concern about the parametric resonance model as a means of sensing weak magnetic fields lies in thermal and electrical noise. However, if we retain the possibility that the rate of deexcitations due to thermal and electrical noise can be very small, then the model makes many predictions regarding the response of any biological mechanism that is sensitive to the biochemical difference of an excited state vs. an ion in-the-ground state.

The time scales that control the behavior of the mechanism are: \( \rho \), time between (de-)excitations due to thermal and electrical noise (see section 3B); \( \gamma^{-1} \), time before a spontaneous transition occurs in the no-field situation \([\gamma^{-1} \text{ is expected to be of the order } 8 \text{ s for a calcium ion with an excitation energy of the first state of } kT]\).
TABLE 3. The First Extremum for the Extended Model*

<table>
<thead>
<tr>
<th>ν</th>
<th>α₁</th>
<th>α₁/ν</th>
<th>r₁</th>
<th>α₂</th>
<th>α₂/ν</th>
<th>Jₙ(α₁)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.699</td>
<td>1.699</td>
<td>0.221</td>
<td>1.841</td>
<td>1.841</td>
<td>0.582</td>
</tr>
<tr>
<td>2</td>
<td>3.225</td>
<td>1.612</td>
<td>0.148</td>
<td>3.054</td>
<td>1.527</td>
<td>0.486</td>
</tr>
<tr>
<td>3</td>
<td>4.044</td>
<td>1.348</td>
<td>0.173</td>
<td>4.201</td>
<td>1.400</td>
<td>0.434</td>
</tr>
<tr>
<td>4</td>
<td>5.501</td>
<td>1.375</td>
<td>0.097</td>
<td>5.318</td>
<td>1.329</td>
<td>0.400</td>
</tr>
<tr>
<td>12</td>
<td>14.09</td>
<td>1.173</td>
<td>0.075</td>
<td>13.88</td>
<td>1.157</td>
<td>0.286</td>
</tr>
<tr>
<td>∞</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.000</td>
</tr>
<tr>
<td>1/2</td>
<td>0.994</td>
<td>1.988</td>
<td>0.035</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>1/3</td>
<td>0.575</td>
<td>1.725</td>
<td>0.005</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2/3</td>
<td>1.300</td>
<td>1.951</td>
<td>0.008</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>3/2</td>
<td>2.242</td>
<td>1.495</td>
<td>0.027</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

* α₁ : f (ν, α₁) = min/max and it’s relative strength r₁ = |f (ν, α₁)| / f (ν, 0) - 1.

For comparison, I list the first maxima of the relevant Bessel functions α₁ : Jₙ(α₁) = max and the value at the maximum. The Lednev model predicts that B₁/B₁ = α/ν assumes it’s first minimum or maximum at approximately the same value (1.55 ± 0.4) for all of the strongest resonances.

for a hydrogen ion with an excitation energy of 3 kT, γ⁻¹ drops to about 20 msec, and γ⁻¹ has to be within two orders of magnitude of ρ⁻¹ in order for the immediate dynamic response to be observable at the percentage level (see section 4C); 2πΩ₁⁻¹, period of the oscillating magnetic field |Ω| cannot be much larger than (ρ + γ)⁻¹, or the quantum-state mixing mechanism will not operate to produce Eq. 1 (cf. section 3.2); r₁, lifetime of the protein complex |r₁| has to be larger than the period of the oscillating field and will affect the width of the resonance (see section 3C).

The mechanism under study requires two kinds of coherence: 1) The lifetime of a single ion excitation must be long enough, so that Equation 1 for the transition probability holds for all times. 2) At the dynamic level, the parameter δ must be consistently generated, so that the time-average of P(t), or a dynamic variable driven by it, can utilize the possible resonances between Ω₁ and Ω₂.

The first condition is difficult to defend from a physical point of view, and, at the same time, it is crucial for the mechanism to work. The alternative to very long-lived excited states is a memory mechanism that could preserve the information summed by Equation 16 over long time scales. Unfortunately, no such mechanism comes readily to mind. Investigations of a fast dynamic response time prepared for this paper reveal that the conditions imposed by the second condition are not very strict. So long as δ is drawn from a nonuniform distribution, we will see an effect, provided that Equation 1 holds for all t, even if Ω/(γ + ρ) << 1.

In a recent contribution, Lednev [1994] reinterprets the ion-oscillator model as a continually excited vibrational level. He disregards the interpretation of p(t) as a transition probability and, instead, views this quantity as the probability to find the ion oscillating along a particular fixed direction in space. This property is identified as the starting point of the transductive step into the biological pathway. The continuity of p(t) is explained by an assumption of coherence that requires δ and A₁A₂ to be independent of time, i.e., the excitation mechanism provides exactly the same relative strength and phase for the two split states. It is not clear that this interpretation overcomes the objections that suggest that p(t) should have the form of Equation 19 when ρ >> Ω. If it does, then the implication is that the option proposed in this paper in which the (de)-excitation time is faster than the period of the oscillating field is also viable (still provided that γ is similar to ρ).

The rich functional structure of the model should be tested experimentally. Considering the microscopic level at which the mechanism operates, care should be taken to test the model in a robust fashion. Properties like zero crossings, extrema, and relative intensities can be expected to be reflected directly in the response and can be used to test predictions of the model. A particularly informative set of experiments is one that tries
values of the resonance index \(v\) (by varying static field amplitude or oscillating field frequency). If successful, it would provide us with information about the value of \(g \Delta q / m\), and the relative strength of resonances could be compared to predictions like those of Figure 4. A less detailed experiment is provided by scanning the \(\alpha\) parameter (oscillating field amplitude). The location of the first extremum is a direct test of compliance with the model regardless of targeted ion, quantum model, and which resonance is active. In order to be consistent, the first extremum of the response must occur in the interval \(B_1 / B_0 \in [1,2]\). If we restrict the resonances that may have an effect to integer values in the range from 1 to 12, the range explored by Blackman et al. [1994], then we obtain the stricter range of \(B_1 / B_0 \in [1.16, 1.84]\), using the position of the relevant Bessel functions as indicators of the extremum location. High values of \(v\) are probably not very relevant, because the required coherence time (\(\rho \Omega\)), which is probably the limiting parameter for this model, increases linearly with \(v\).

Future studies should address the problem of preserving the phase information of the oscillator over long time periods, so that we can approach realistic time scales for the perturbations from thermal and electrical noise. Another interesting direction of research is the investigation of the effects of fields at angles other than parallel and perpendicular orientations. There is reason to believe that nonparallel fields will produce an effect other than a mere projection of one field onto the other (see section 6 in Macomber, 1976), particularly if the primary transductive step is occurring at time scales much faster than those of the applied oscillating field.

ACKNOWLEDGMENTS

I am grateful for discussions with my colleagues at the J.L. Pettis Memorial VA Medical Center. Dr. Asher Sheppard in particular supplied many valuable comments throughout this project. This work was supported by the U.S. Department of Energy under grant DE-A101-90LE35035.

REFERENCES


APPENDIX A

Derivation of the Basic Mechanism

In the Lednev model, a magnetic field influences the rate of spontaneous transitions of quantum states of a bare ion located in a protein complex. I will assume that a spinless particle (the ion) populates the degenerate state of a three-dimensional linear oscillator. In the presence of an external magnetic field, this degenerate first state \( \Psi_1 \) is split into three levels \( \left( \Psi_1^{-1}, \Psi_1^0, \Psi_1^+ \right) \). The separation of these states will depend on the total magnetic moment of the ion, \( \mu \). In our case, \( \mu \) stems from the orbital momentum \( L = 1 \) of this state. Of these three states, the transition \( \Psi_1^0 \rightarrow \psi_1^0 \) is forbidden, and we are left with two states that can communicate with the ground state.

Using a static field \( B_0 \) with a superimposed parallel oscillating field \( B_\perp \cos \Omega t \), the energy levels \( E_i \) and the corresponding characteristic frequencies \( \omega_i(t) \) will experience a separation that is proportional to \( \mu \) [see section 113 in Landau and Lifshitz, 1977]:

\[
E_1 - E_2 = \hbar \left( \omega_1(t) - \omega_2(t) \right) = \mu B_{\text{tot}} \Rightarrow (12)
\]

\[
\omega_1(t) - \omega_2(t) = \Delta \left[ B_0 \cos \Omega t - \left( B_1 + B_0 \cos \left( \Omega t + \phi_0 \right) \right) \right], \quad (13)
\]

where \( \Delta \) is the difference in orbital magnetic moment of the component parallel to the field between the two states. In our case, \( \Delta = 2 \); \( \phi_0 \) determines the phase of the oscillating field at the time that the state we are considering is excited \( t = 0 \).

The total emission amplitude from the excited state [Podgoretskii and Khristalev, 1964] can be calculated from the state mixing introduced by the time-dependent Hamiltonian associated with Equation 13:

\[
A(t) = A_1 \exp \left[ i \left( \int_0^t \omega_1(\tau) d\tau + \delta_1 \right) \right] + A_2 \exp \left[ i \left( \int_0^t \omega_2(\tau) d\tau + \delta_2 \right) \right]. \quad (14)
\]

In this equation, \( \omega_i(t) \) represents the frequencies associated with the \( \left( \Psi_1^{-1} \rightarrow \Psi_0^0 \right) \) and \( \left( \Psi_1^0 \rightarrow \Psi_0^0 \right) \) transitions, respectively, and \( \delta_1, \delta_2 \) represents the phases that allow us to select the amplitude of the initial states, \( A_i \), as real numbers without loss of generality.

With the magnetic splitting in the form of Equation 13, a sufficient parametrization of \( \omega_i(t) \) is

\[
\omega_1(t) = \omega_1 + \alpha_1 \cos(\Omega t + \phi_0) \quad (15)
\]

\[
\omega_2(t) = \omega_2 + \alpha_2 \cos(\Omega t + \phi_0) \quad (15)
\]

which leads to

\[
A(t) = A_1 \exp \left[ i \left( \omega_1 + \alpha_1 \sin(\Omega t + \phi_0) + \delta_1 \right) \right] + A_2 \exp \left[ i \left( \omega_2 + \alpha_2 \sin(\Omega t + \phi_0) + \delta_2 \right) \right]. \quad (16)
\]

We can now calculate the transition probability perpendicular to the field

\[
p(t) = \left| A(t) \right|^2 = A(t) A^{\ast}(t) = A_1^2 + A_2^2 + 2 A_1 A_2 \cos(\Omega t + \phi_0 + \delta_1). \quad (17)
\]

with

\[
\Omega_c = \omega_1 - \omega_2 = g \Delta q B_0 / 2 m
\]

\[
\alpha = \alpha_1 - \alpha_2 = g \Delta q B_1 / 2 m \Omega
\]

\[
\delta = \delta_1 - \delta_2.
\]

Note that the expression of Equation 17 is only valid as long as the state excited at \( t = 0 \) is active. The lifetime of the state is \( t_s = (\rho + \gamma)^{-1} \), where \( \rho \) is the decay rate due to collisions, and \( \gamma = A_1^2 + A_2^2 \) is the spontaneous transition probability in the absence of a magnetic field. If \( t_s \) is short compared to the period of the oscillating field, then

\[
p(t) = A_1^2 + A_2^2 + 2 A_1 A_2 \cos(\alpha \sin \phi_0 + \delta) + O(\Omega t)
\]

for \( \Omega t \ll 1 \).

The transition probability will still be weakly modulated by the field as states are continually excited and deexcited, but the possibility for resonant behavior disappears in this limit.
Assuming that the excited state is long-lived, we can calculate the mean of \( p(t) \) over time:

\[
\bar{p}(t_0) = \frac{1}{t_0} \int_0^{t_0} \left( A_1^2 + A_2^2 + 2 A_1 A_2 \cos(\Omega_0 t + \alpha \sin(\Omega t + \phi_0) + \delta) \right) dt
\]

\[
\left\{ x = \Omega t + \phi_0 ; dx = \Omega dt ; \nu = \Omega / \Omega_0 \right\}
\]

\[
= A_1^2 + A_2^2 + \frac{2 A_1 A_2}{\Omega_0} \int_{\Omega_0 t_0 + \phi_0}^{\Omega_0 t_0 + \phi_0 + \delta} \cos(\nu x + \alpha \sin x + \delta) dx = \left[ N = 2 \left( \Omega_0 t_0 + \phi_0 / 2 \pi \right) \left[ \right. \right]
\]

\[
\left[ x_0 = \Omega_0 t_0 + \phi_0 - N\pi \right]
\]

\[
= \frac{N-1}{2} \int_0^{\pi} \cos(\nu x + \nu k \pi + \alpha \sin(x + k\pi) + \delta) dx + \left[ \sum_{k=1}^{N/2} \cos(\nu \pi(2k - 1) + \delta) + \frac{1}{\Omega_0} \int_0^{\pi} \cos(\nu x + \nu N\pi + \alpha \sin(x + N\pi) + \delta) dx \right].
\]

We can stop here and consider Equation 21 for the case of integer \( \nu \), in which case the integrand is periodic, and the integral evaluated over one period recovers Equation 1.

However, I press on and evaluate the integrals in the sum without any assumptions on \( t_0 \) and \( \nu \):

\[
I_k = \int_0^{\pi} \cos(\nu x + \nu k \pi + \alpha \sin(x + k\pi) + \delta) dx = \int_0^{\pi} \left[ \cos(\nu x - (-1)^{k+1} \alpha \sin x) \cos(\nu k \pi + \delta) - \sin(\nu x - (-1)^{k+1} \alpha \sin x) \sin(\nu k \pi + \delta) \right] dx = \frac{\pi \cos(\nu k \pi + \delta) J\nu \left( (-1)^{k+1} \alpha \right) - \pi \sin(\nu k \pi + \delta) E\nu \left( (-1)^{k+1} \alpha \right)}{\Omega_0}.
\]

\[
J\nu(\alpha) \text{ and } E\nu(\alpha) \text{ are Anger and Weber functions, respectively [see section 12.3 in Abramowitz and Stegun, 1964]:}
\]

\[
J\nu(\alpha) = \frac{1}{\pi} \int_0^{\pi} \cos(\nu x - \alpha \sin x) dx \quad \text{and} \quad E\nu(\alpha) = \frac{1}{\pi} \int_0^{\pi} \sin(\nu x - \alpha \sin x) dx
\]

By grouping the integrals of the sum in Equation 22 in pairs and using the following symmetry properties [see section 8.581 in Gradshteyn and Ryzhik, 1980]:

\[
J\nu(\alpha + \beta) = \cos(\nu \beta) J\nu(\alpha) + \sin(\nu \beta) Y\nu(\alpha)
\]

\[
E\nu(\alpha + \beta) = \cos(\nu \beta) E\nu(\alpha) - \sin(\nu \beta) X\nu(\alpha)
\]

where \( X\nu(\alpha) \) is an even function, and \( Y\nu(\alpha) \) is odd, I find that

\[
\bar{p}(t_0) = A_1^2 + A_2^2 + 2 A_1 A_2 \left( \sum_{k=1}^{N/2} \cos(\nu \pi(2k - 1) + \delta) + \frac{1}{\Omega_0} \int_0^{\pi} \cos(\nu x + \nu N\pi + \alpha \sin x + \delta) dx \right).
\]

When is integer-valued \( J\nu(\alpha) \) coincides with the Bessel functions \( J\nu(\alpha) \) and in the limit of \( t_0 \rightarrow \infty \), we retrieve the original result. Note that the sum of cosines of Equation 28 vanish for all rational \( \nu \) (except integers) when \( k \) runs through a full cycle.

\textbf{APPENDIX B}

\textbf{Resonant Behavior for Rational \( \nu \)}

I need to establish that the distribution of

\[
q(t) = \cos(\nu \Omega t + \alpha \sin(\Omega t + \phi_0) + \delta)
\]

\textbf{(29)}
is radically different for rational and irrational \( v \). To this end, I expand \( q(t) \) in Legendre polynomials using the method described in Appendix C:

\[
q(t) = \sum_{n} C_n P_n \left( \frac{\theta}{\theta_0} \right)
\]

Using [see section 22.3.13 in Abramowitz and Stegun, 1964], we can write \( C_n \) as

\[
C_n = \frac{2n+1}{2t_0} \frac{\partial^n}{\partial t_0^n} \int_{0}^{1} \cos \left( (n-2m) \left( \pi t + \phi_0 \right) + \delta \right) dt.
\]

\[\text{APPENDIX C}\]

Orthogonal Basis Expansion of the Distribution of a Continuous Function

Consider a smooth function \( q(t) \) defined on \( t \in [0, t_0] \), which has no finite-length segments where \( q(t) \) is constant. In an interval \( t \in [t_k, t_k + \tau] \) where \( q(t) \) increases monotonically, the cumulative distribution function for \( q \) in this interval equals

\[
D(q) = \begin{cases} 
\frac{s(q)}{\tau} & q(t_k) < q \leq q(t_k + \tau) \\
0 & q \leq q(t_k) \\
1 & q > q(t_k + \tau).
\end{cases}
\]

where \( s(q) \) is the inverse of \( q(t) \). A similar expression is valid in an interval where \( q(t) \) decreases monotonically. The distribution of \( q \) for both monotonically increasing and decreasing segments can be expressed as

\[
d(q) = \frac{D(q)}{dq} = \frac{1}{\tau} \left| \frac{ds(q)}{dq} \right|.
\]

The integral has already been calculated in Appendix A. Restricting ourselves to a whole number of periods, \( t_0 = 2\pi K/\Omega \), we obtain

\[
C_n = \frac{2n+1}{2t_0} \sum_{m=0}^{n} \frac{a_m}{m} \int_{0}^{1} \cos \left( (n-2m) \left( \pi \delta + \alpha \sin \left( \pi t + \phi_0 \right) \right) \right) dt.
\]

\[\text{The integral has already been calculated in Appendix A. Restricting ourselves to a whole number of periods, } t_0 = 2\pi K/\Omega, \text{ we obtain}
\]

\[
C_n = \frac{2n+1}{2t_0} \sum_{m=0}^{n} \frac{a_m}{m} \int_{0}^{1} \cos \left( (n-2m) \left( \pi \delta + \alpha \sin \left( \pi t + \phi_0 \right) \right) \right) dt.
\]

\[\text{APPENDIX C}\]

Orthogonal Basis Expansion of the Distribution of a Continuous Function

Consider a smooth function \( q(t) \) defined on \( t \in [0, t_0] \), which has no finite-length segments where \( q(t) \) is constant. In an interval \( t \in [t_k, t_k + \tau] \) where \( q(t) \) increases monotonically, the cumulative distribution function for \( q \) in this interval equals

\[
D(q) = \begin{cases} 
\frac{s(q)}{\tau} & q(t_k) < q \leq q(t_k + \tau) \\
0 & q \leq q(t_k) \\
1 & q > q(t_k + \tau).
\end{cases}
\]

where \( s(q) \) is the inverse of \( q(t) \). A similar expression is valid in an interval where \( q(t) \) decreases monotonically. The distribution of \( q \) for both monotonically increasing and decreasing segments can be expressed as

\[
d(q) = \frac{D(q)}{dq} = \frac{1}{\tau} \left| \frac{ds(q)}{dq} \right|.
\]

The integral has already been calculated in Appendix A. Restricting ourselves to a whole number of periods, \( t_0 = 2\pi K/\Omega \), we obtain

\[
C_n = \frac{2n+1}{2t_0} \sum_{m=0}^{n} \frac{a_m}{m} \int_{0}^{1} \cos \left( (n-2m) \left( \pi \delta + \alpha \sin \left( \pi t + \phi_0 \right) \right) \right) dt.
\]

\[\text{The integral has already been calculated in Appendix A. Restricting ourselves to a whole number of periods, } t_0 = 2\pi K/\Omega, \text{ we obtain}
\]

\[
C_n = \frac{2n+1}{2t_0} \sum_{m=0}^{n} \frac{a_m}{m} \int_{0}^{1} \cos \left( (n-2m) \left( \pi \delta + \alpha \sin \left( \pi t + \phi_0 \right) \right) \right) dt.
\]

\[\text{APPENDIX C}\]

Orthogonal Basis Expansion of the Distribution of a Continuous Function

Consider a smooth function \( q(t) \) defined on \( t \in [0, t_0] \), which has no finite-length segments where \( q(t) \) is constant. In an interval \( t \in [t_k, t_k + \tau] \) where \( q(t) \) increases monotonically, the cumulative distribution function for \( q \) in this interval equals

\[
D(q) = \begin{cases} 
\frac{s(q)}{\tau} & q(t_k) < q \leq q(t_k + \tau) \\
0 & q \leq q(t_k) \\
1 & q > q(t_k + \tau).
\end{cases}
\]

where \( s(q) \) is the inverse of \( q(t) \). A similar expression is valid in an interval where \( q(t) \) decreases monotonically. The distribution of \( q \) for both monotonically increasing and decreasing segments can be expressed as

\[
d(q) = \frac{D(q)}{dq} = \frac{1}{\tau} \left| \frac{ds(q)}{dq} \right|.
\]

The integral has already been calculated in Appendix A. Restricting ourselves to a whole number of periods, \( t_0 = 2\pi K/\Omega \), we obtain

\[
C_n = \frac{2n+1}{2t_0} \sum_{m=0}^{n} \frac{a_m}{m} \int_{0}^{1} \cos \left( (n-2m) \left( \pi \delta + \alpha \sin \left( \pi t + \phi_0 \right) \right) \right) dt.
\]

\[\text{The integral has already been calculated in Appendix A. Restricting ourselves to a whole number of periods, } t_0 = 2\pi K/\Omega, \text{ we obtain}
\]

\[
C_n = \frac{2n+1}{2t_0} \sum_{m=0}^{n} \frac{a_m}{m} \int_{0}^{1} \cos \left( (n-2m) \left( \pi \delta + \alpha \sin \left( \pi t + \phi_0 \right) \right) \right) dt.
\]
For each $c_{kn}$ we have

$$c_{kn} = \pm \frac{1}{h_n} \int_{q(t_k)}^{q(t_k + \tau_k)} d_k(q) w(q) g_n(q) dq,$$  

(41)

where the minus sign should be used when $q(t_k) > q(t_k + \tau_k)$. Using a properly labeled version of Equation 36, and changing variables to integrate over time in each segment, we obtain

$$c_{kn} = \frac{1}{h_n \tau_k} \int_{t_k}^{t_k + \tau_k} \left| \frac{ds}{dq} \right| w(q) g_n(q) \left| \frac{dq}{dt} \right| dt,$$  

(42)

where

$$C_n = \frac{1}{h_n t_0} \int_{0}^{t_0} w(q(t)) g_n(q(t)) dt.$$  

(46)

The last absolute value on the first line takes care of the sign ambiguity associated with Equation 41. Finally, we can assemble the total distribution function:

$$= \frac{1}{h_n \tau_k} \int_{t_k}^{t_k + \tau_k} w(q(t)) g_n(q(t)) dt.$$  

(43)