CHAPTER 9

Mechanisms of Biological Effects Of Electromagnetic Energy

Introduction

When we inquire about the mechanism of a biological effect, we have implicit reference to a picture of how nature is organized and how it should be approached. In one view, the biological system is seen as more than a sum of its parts and it is held that one cannot understand an organism's essential characteristic-life-by studying subsystems below a certain structural level because life does not exist below that level. This idea was precisely stated by Paul Weiss (1):

> If *a* is indispensable for both *b* and *c*; *b* for both *a* and *c*; and *c* for both *a* and *b*; no pair of them could exist without the third member of the group, hence any attempt to build up such a system by consecutive additions would break down right at the first step. In other words, a system of this kind can exist only as an entity or not at all.

Thus, for example, even complete knowledge of the properties of a protein solution would not tell us how the protein functioned *in vivo*; we would not even know whether its in vitro properties had any relevance at all. Under this approach, the proper starting point to study nature is the whole organism in its normal environment. It is recognized that, considering the organism's physiological control processes, not all biological phenomena can be localized to specific tissues in the organism. In contrast to this cybernetic approach is the idea that, ultimately, living things will be describable solely in terms of the physical laws governing inanimate things. Methodologically, this analytical approach consists of the study of increasingly more complex models of the organism's parts, with the goal of explaining the organism's characteristics and behavior in terms of the characteristics and behavior of the models. The amount of whole-animal data presently available is much greater than that involving model systems and, for this reason, the cybernetic approach gives a more general and more useful picture of bioelectrical phenomena. This approach is described below; work that can be considered to have arisen from an analytical approach is described in the following section.

Cybernetic Approach

The cybernetic approach to EMF-induced biological effects begins with a view of the living system as a black box. The animal is considered to have an unknown internal organization, and the only factors regarded as accessible to investigation are the applied EMF (input) and the biological effect (output). Empirical data that describe relationships between various inputs and outputs is generalized into empirical laws that furnish insights into the relevant component processes. The empirical laws cannot conflict with known physical law, but they need not conform to a process or behavior observed only in a model system. The reports described in the preceding chapters provide a basis for this approach, and they may be summarized this way:

1. EMFs can alter the metabolism of all body systems, including the nervous, endocrine, cardiovascular, hematological, immune-response, and reproductive systems.
2. The effects on each tissue or system are largely independent of the type of EMF. The studies suggest that there are common physiological pathways for spectrally different EMFs, and that the major consequence associated with specificity of the EMF is that it determines the magnitude or direction—as opposed to the existence—of the biological effect. On the other hand, certain spectral characteristics—pulse modulation frequency seems to be one of the most important—can fundamentally modify the biological response.
3. An organism's response to an EMF is determined in part by its physiological history and genetic predisposition; individual animals, even in an apparently homogeneous population, may exhibit changes in opposite directions in a dependent biological parameter.
4. Although high-field-strength and long-duration studies are exceptions, EMF-induced biological effects seem best characterized as adaptive or compensatory; they present the organism with an environmental factor to which it must accommodate.

If attention were restricted to EMF-related changes in individual body systems such as intermediary metabolism, the immune-response system, or the adrenal gland, it might be hypothesized that the action of the field involved certain enzymes, specific antibody regions of certain cells or particular organs. But the studies clearly showed that EMFs produce a

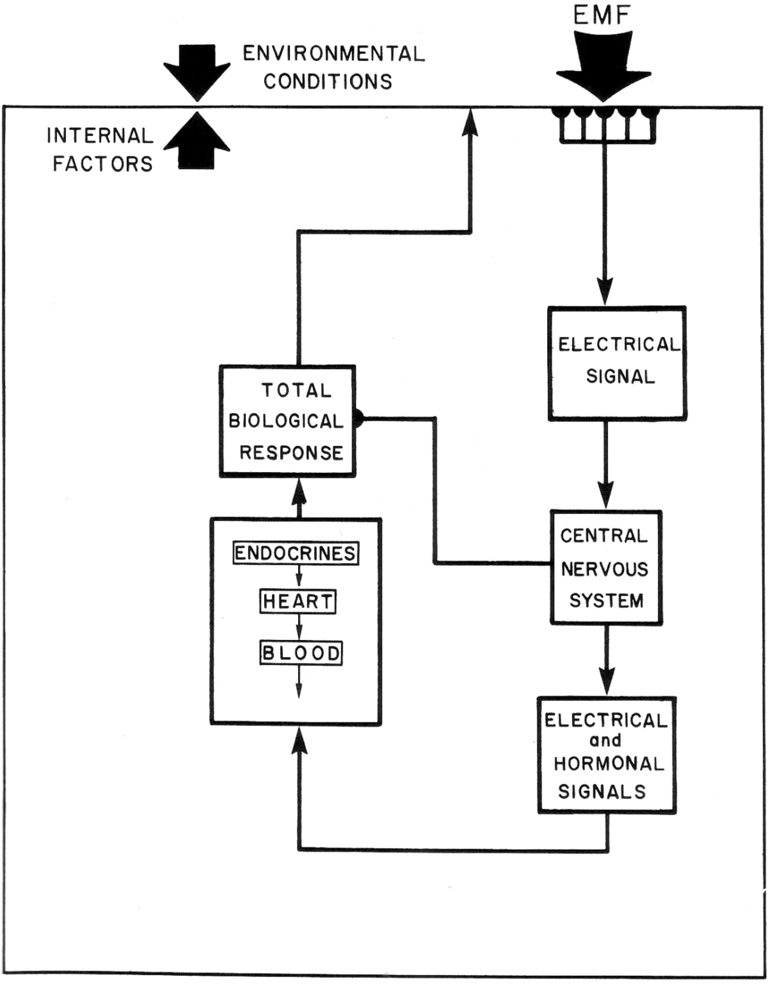

Fig. 9.1. The basic control system that mediates EMF-induced biological effects. The field is detected and transduced into a biological signal which is received in the CNS. The resulting hormonal and electrical signals to the various body systems initiate the appropriate adaptive physiological responses.

complex interrelated series of physiological changes (see Figure 8.4). It follows that the consequences of EMF exposure must be understood in terms of an integrative response of the entire organism. In our view, after the EMF is detected, information concerning it is communicated to the central nervous system which then activates the broad array of physiological mechanisms that are available to furnish a compensatory response (Fig. 9.1). As is generally true of an adaptive response, the particular biological system that is invoked, and the nature of its response, will depend on numerous factors including the animal's internal conditioning and its external environment. With one notable exception, the biological proces ses that follow detection of an EMF are the same as those associated with the response to any biological stressor. Thus, for example, the cellular or molecular mechanisms that operate in the adrenal following a cold stress to produce altered serum corticoid levels will also operate following an electromagnetic stress, because adrenal activity is initiated by neuronal and hormonal signals, not by the actual presence of the stressor agent in the tissue. Thus, advances in the understanding of EMF-induced systemic effects are tied to general progress in physiology. Even so, electromagnetic stress has a characteristic which sets it apart from other stressors: electromagnetic stress is not consciously perceived. This suggests that sub-cortical brain centers are the first mediators of the electromagnetic stress response. The physical processes that occur in this as-yet-unidentified center must, therefore, be different than those associated with the mediation of other stressors—heat, cold, trauma, for example—all of which are detected peripherally and are then consciously perceived.

Bearing in mind the studies described in part two of this book, it can be concluded that the adaptive response occurs primarily when the EMF is outside the frequency range to which the organism is intrinsically sensitive. Inside the range, the EMF can supply information to the organism concerning its environment.

Analytical Approach

The analytical approach is a mixture of empirical data and physical models which, hopefully, leads to laws that predict undiscovered phenomena. The physicist, unlike the biologist, approaches nature using constructs that do not exist—simple geometric models with perfect conductivity, for example—in an attempt to reduce the number of variables and establish functional relationships. This methodology has not yet been systematically applied to bioelectric phenomena, and hence there are no physicist-type explanations for EMF-induced biological effects. Despite this, evidence of the existence of many interesting molecular processes that may explain the effects has been discovered. In what follows, we present an overview of the physical mechanisms applicable to bioelectrical phenomena.

When an EMF is applied to a material, many types of molecular processes can occur (Fig. 9.2): (1) electronic excitation; (2) polarization; (3) field-generated force effects; (4) heat; and (5) other electronic and ionic effects. If the material is also alive, additional processes that are associated with cells and higher levels of structural organization can also occur. We shall regard such consequences as biological effects, in distinction to effects that occur regardless of whether the material is alive or dead (physical effects).

Electronic excitation involves the transition of electrons to a higher energy level following the absorption of electromagnetic energy. If the electrons are bound to enzyme molecules, for example, then the excited molecules might behave differently in a metabolic reaction, thereby resulting, ultimately, in a biological effect. Since, however, the thermal energy at 37°C is about 0.02 electron volts (ev), it has traditionally been argued that photons having a lower energy would not produce electron excitation—hence, no biological effects—because molecules with energy states less than 0.02 ev would already be excited as a result of thermal motion. This view, although popular, is not correct because the thermal energy is only the average energy of a collection of molecules: at any given time, some molecules are in a state of less than 0.02 ev. The salient—and presently unexplored- questions associated with Type-I processes relate to the density of states that are h*v* ev (h is Planck's constant, v is the frequency of the EMF) below a specific average energy, and to the minimum change in the density of such states that would be required to produce a biological effect.

Type-2 processes involve electronic, atomic, and orientational polarizations produced when a material is exposed to an EMF: the total dipole moment of a group of molecules depends on these polarization properties and on the strength of the local electrical field. EMF-induced alterations in dipole moments could theoretically account for biological effects. For example, Figure 9.2 depicts a material containing a linear array of permanent dipoles. In the absence of an EMF, the dipoles remain randomly oriented because of thermal motion, but when the field is present a preferential alignment becomes established. If the dipoles were attached to a cell membrane, for example, then the preferential alignment might correspond to a state of altered membrane permeability. Every EMF produces some preferential alignment, but one cannot determine, before

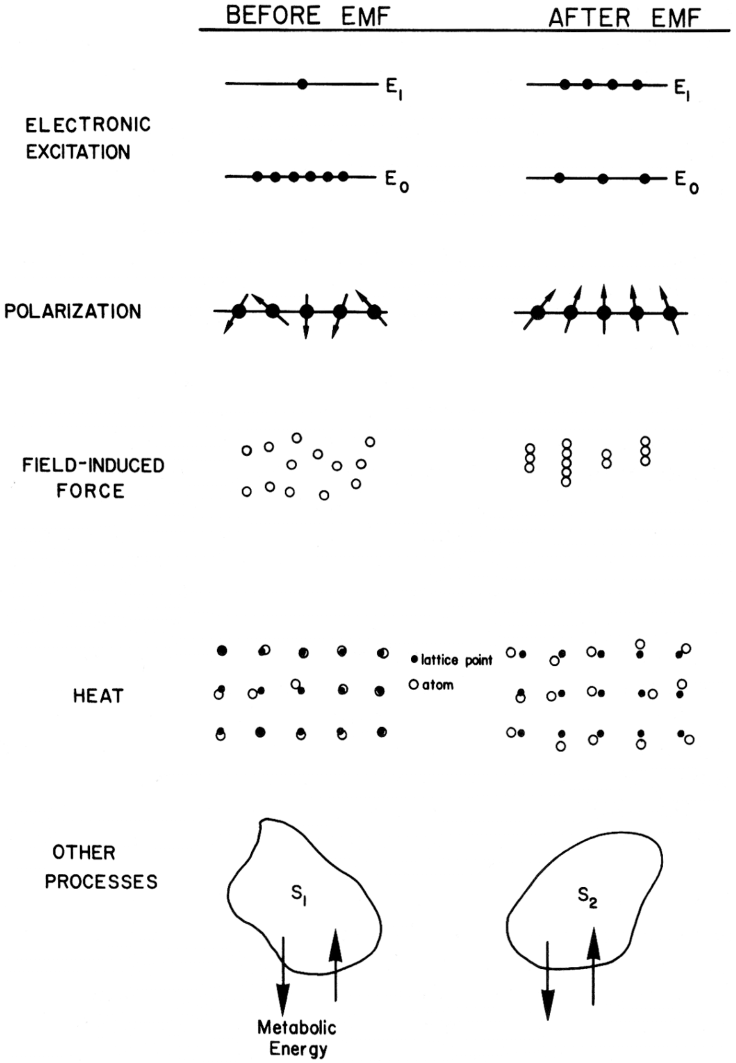

Fig. 9.2. Classes of physical processes in biological tissue exposed to EMFs: Types 1-4 can occur in living and nonliving tissue They are thermodynamically closed in the sense that they are directly proportional to the applied EMF. The biological consequences, if any, are thermodynamically open because they can occur only if metabolic energy is also present—that is, if the system is alive. For Type 5, in contrast, both the physical process *and* the biological consequence can be thermodynamically open. As an example, we have depicted a metabolically maintained superconducting region in a cell organelle. State S_1 is associated with one biological function and S_2 -induced by the presence of the EMF—with a different function.

the fact, how much alignment would be biologically significant. Historically, the notion has been that something approaching saturation would be required, but this view is based on inappropriate models of living organisms (low-pressure gasses and dilute solutions of polar solutes).

In addition to permanent dipoles, which may or may not be present in a material, applied EMFs can induce a dipole moment as a result of electronic and atomic polarization. Field-generated forces (Type 3) occur when the field interacts with the induced dipole moment, and they can produce interesting orientational and translational effects in *in vitro* systems. One of the best known such effects, pearl-chain formation (Fig. 9.2), has been observed with many kinds of particles including blood cells (alive and dead) and plastic microspheres. Present theory suggests that field strengths needed to produce pearl-chains are of the order of 10^4-10^6 v/m, depending on particle size. If this is true of all Type-3 processes—the latest evidence suggests that it is not—they would be of little biological interest.

Heat is an ubiquitous consequence of EMFs and it has long been associated with gross, irreversible changes in tissue - the microwave oven is perhaps the latest and most familiar example. In theory, any heat input to a biological system (hence any EMF) could alter one or more of its functions. This idea, however, directly conflicts with the prominent view (at least in the West) that only heat inputs that are an appreciable fraction of the organism's basal metabolic rate can lead to biological effects. We shall have more to say concerning the implications of this view in chapter 10.

Since heat is always produced when an organism is exposed to an EMF, one cannot experimentally determine whether a resulting biological effect could occur in the absence of heat production. (Conversely, although it is a heavy burden for such a humble process, it is always possible to assert that any EMF-induced biological effect is due to heat.) Thus it seems pointless to relate heat—a thermodynamic concept that is independent of the pre cise details of molecular activity—to observed biological effects which can, ultimately, be explained in more fundamental terms.

The most fertile ground for understanding the physical basis of EMF-induced biological effects involves those processes that we have lumped together in Type 5. They are quantum mechanical and classical processes and include, for example, superconductivity, Hall effect, converse piezoelectric effect, cooperative dipole interactions, Bose-Einstein condensation, and plasma oscillations. Type-s processes have sensitivities as low as 10-9 $\mu W/cm^2$ and 10-9 gauss, and, therefore, are theoretically capable of serving as the underlying physical mechanism for any known EMF-induced biological effect. Some direct evidence for Type-5 processes has already been described in previous chapters; other developments in this area that also deserve mention are the initiative of Pilla, Frolich, Zon, and Cope.

Pilla's model originated with his and Bassett's work regarding the effects of localized pulsed magnetic fields on bone growth in dogs (2) and humans (3). Pilla reasoned that there must exist generalized mechanisms by which diverse electrical stimuli could alter cell function. He proposed a theory of electrochemical information transfer in which field-induced changes in the ionic microenvironment were responsible for alterations in cell permeability (4,6). The theory allows for three non-faradaic electrochemical processses: the binding of specific ions; the passage of ions through the membrane; and changes in the membrane double-layer. Because the kinematics of each process differed -measured in impedance studies of the cell's cytoplasmic membrane- it would be possible, in theory, to couple to either of the three processes by choosing an appropriate magnetic pulse. The theory has been successfully applied to the study of the rate of limb regeneration in the salamander (7): it was found that the degree of dedifferentiation could be accelerated or decelerated (depending on the spectral characteristics of the magnetic field) as predicted.

The ideas of resonant absorption and resonant interactions have also been proposed as an explanation for the marked sensitivity of living systems to EMFs. Zon speculated that the electrons in cell mitochondria constituted a plasma state (8). He calculated that the frequency of resonant absorption would be in the gigahertz range for typical values of the dielectric constant and the density of charge carriers. This would make the mitochondria extremely sensitive to microwave EMFs. Zon's idea could also apply to other biostructures and other frequency ranges.

Frolich has proposed another form of resonance. Biological structures frequently consist of electric dipoles that are capable of vibratory motion—hydrogen bonds in DNA and proteins, for example. Long-range coulomb interactions between the oscillatory units produce a narrow band of frequencies corresponding to the normal modes of electromagnetic oscillations. Frolich showed that when energy is supplied to such a system—either from metabolism or from external sources—above a critical rate, it is automatically channeled into the lowest frequency mode, thereby resulting in coherent excitation of the vibratory components (a phenomenon known as Bose-Einstein condensation) (9). Theoretically, such electromagnetic oscillations could affect cell dynamics, and the sharp frequency resonances in biological effects predicted by Frolich have been observed in studies of the rate of yeast growth (10) and the rate of cell division (11). The latency of the biological effect is an important parame ter, because the biological effect is associated with the condensed phase which occurs a finite time after irradiation has begun. It is not yet clear to what extent the observed time thresholds are consistent with theory. Future work may lead to an extension of Frolich's concept to higher systems.

A Josephson junction consists of a thin (approximately 10Å) insulating barrier between two superconducting regions. The current through a Josephson junction is highly sensitive to applied EMFs, and this has been exploited in the design of EMF detectors (SQUIDS). Theoretical and experimental evidence for the existence of superconductivity in biological tissue has already been discussed (chapter 4); it suggests the existence of fractional superconductivity in which the superconducting regions are dispersed in tissue that has normal macroscopic electrical characteristics (a concentration in the order of parts per million). As Cope has pointed out (12), the existence of Josephson junctions in biological tissue would provide a physical mechanism of sufficient sensitivity to explain the observed biological effects of applied EMFs. Antonowicz has observed what seems to be a room temperature Josephson effect in carbon films (13), but there are no similar reports involving biological tissue. This may only mean, of course, that the right measurements have not yet been performed.

Summary

As was seen in chapter 3, living organisms have evolved a means for receiving information about the environment in the form of nonvisual electromagnetic signals. To process it, organisms must also have developed an ability to discriminate among the infinite number of possible signals and to ignore those that were not useful. Although EMFs can be physiologically informational or can have characteristics that simulate intrinsic electrical signals found in growth-control and neural processes (see chap ter 2), the bulk of the studies done to date used EMFs whose characteristics had no special physiological significance. The studies in part three show that the organism's prototypical response to such EMFs is the detection of the fields by the CNS and the subsequent adaptive activation of the organism's various physiological systems. Only when the organism's compensatory mechanisms are exhausted—when the EMFs are present too long, or at too high a strength, or when other factors are simultaneously present—do the effects become irreversible.

The cellular and molecular mechanism underlying the CNS's detection of applied EMFs are (for the most part) unstudied, and hence unknown. As we have shown in chapter 1 the study of bioelectrical phenomena has had a complex history involving many scientific, political, and economic factors. This combined with, ironically, the great intellectual triumphs of early twentieth century physics, produced a scientific Procrustean Bed[1] regarding the biological effects of EMFs. The Bed consisted of an almost exclusive emphasis on the role of dipole orientation and heat-production as the molecular mechanisms for bioelectrical phenomena. Commonly, reports of biological effects were stretched to fit the Bed: the notion of "strong" and "weak" EMFs evolved in relation to how much heat was deposited in saline-filled beakers which were considered to represent the average electrical properties of living organisms. EMFs of 10,000-100,000 $\mu W/cm^2$ were considered to be strong because they would noticeably heat the saline animal. Fields of 1000-10,000 μW/cm2, however, were held to be weak, because the saline animal's temperature change was so small that it was said, that if it were a real animal, the heat generated would probably be handled by the animal's homeostatic mechanisms. It was argued that fields below 1000 $\mu W/cm^2$ were no more than electrical noise to the organism, and thus were entirely without physiological significance.

The thermal fiction took such firm root that it became impossible to establish that other mechanisms besides heat could be involved in the production of biological effects above 10,000 $\mu W/cm^2$. This occurred despite the fact that no EMF-induced biological effects above 10,000 $\mu W/cm^2$ have been replicated with heat applied via some other means. When reports of effects in the 1000-10,000 $\mu W/cm^2$ range began to surface in the 1950's, the thermal hypothesis was extended to also apply in this range. The notion of differential heating was advanced, and its proponents argued that there were "hot spots" in the real animal, and *that* accounted for the observed biological effects. When reports of EMF-induced biological effects that extended beyond the Bed—below 1000 $\mu W/cm^2$, 50 kv/m, 10^2 gauss-began to surface in the 1960's they were simply cut off: there developed unprecedented attacks against investigators who reported such effects.

The EMF Procrustean Bed has been destroyed by the weight of the number of excellent EMF studies: they exist, and it now becomes the business of science to investigate them and to learn their laws. Despite the interesting and provocative thoughts of some theoreticians and the tentative results of some experimentalists involving *in vitro* systems, there is still

[1] Procrustes lived in ancient Greece, and it was his practice to make travelers conform in length to his bed. If they were too short he stretched them and if they were too long he chopped off their legs. Later, Procrustes wrote a learned paper entitled "On the Uniformity of Stature of Travelers."

much to learn. Molecular processes that could explain EMF-induced biological effects are found in inanimate nature and, if they also occur in living systems, they would constitute one class of possible explanatory mechanisms. in addition, since the structural complexity of even the simplest living organism greatly exceeds that found in inanimate nature, it would be a mistake to expect that only molecular processes identified in purified materials could be candidates for the mechanism by which the organism detects an EMF. As we have frequently pointed out, solid-state biology may ultimately provide the answer—it may reveal mechanisms that simply do not exist in purified crystals.

Our best guess (and at the moment it is no more than that) is that the organism detects EMFs via cooperative dipole, or higher order, interactions in neural tissue-possibly peripheral nerves. An engagingly simple mechanical model of this notion has been described by Bowman (14). He assembled an array of dime-store magnetic compasses (Fig. 9.3), and described as follows the remarkably diverse range of states of the system that resulted when he passed a bar magnet nearby:

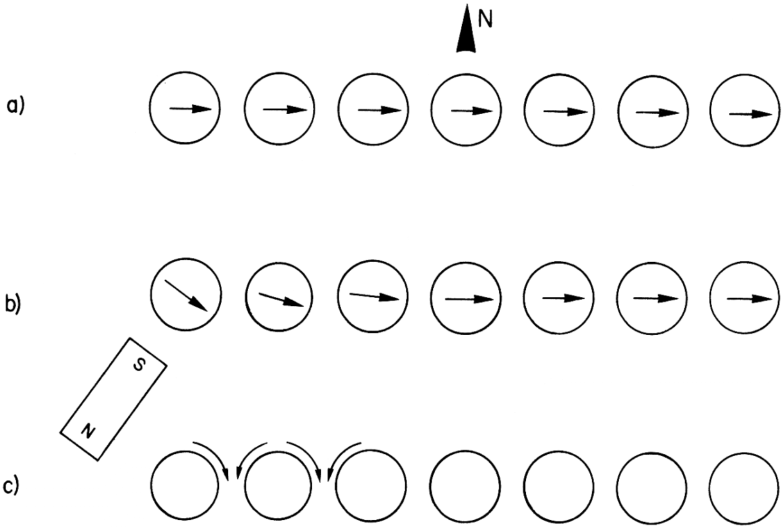

Fig. 9.3. Linear array of magnetic compasses (14).

> The idea was first to set [the compasses] nearly touching in a row. The individual needles have a time constant, in pointing somewhere near to the magnetic north pole, of the order of a second. When they are close to one another, however, they interact to an extent that overshadows the field of the earth, and the time constant is of the order of, say, a tenth of a second. Thus they will point north to south, north to south, on down the line [Fig. 9.3a]. The experiment was set up so that north was normal to the axis of the array, and that gives a very stable sort of array. Bringing up a south pole gives a repulsion that will tend to displace the end needle. You can see, I am sure, that a quasi-static system will result, where we get something as shown in [Fig. 9.3b]. The angles of displacement will decrease, so that after the initial impulse a dynamic situation is established and the signal moves along, not too fast.
>
> You can bring up the bar magnet slowly and dose, and maintain a static situation where equilibrium is propagated, so that the needles assume angles equally. The behavior is an exact analog of a gear train; that is, one turns this way, one that way, and so on [Fig. 9.3c]. It is very much like the bar where you turn one end and observe that the other end turns too. That is not too interesting.
>
> However, if you look upon this as a dynamic rather than a quasi-static system, you can get some extraordinary phenomena that I cannot draw. With a little practice, bringing a south pole up just right, you can make the first compass spin all around and nothing is propagated down the line. The skill in my hand automatically introduces some random numbers, so the experiments were not reproducible. I can tell, nevertheless, of several things that can happen. If you bring the south pole up in a certain fashion, a nice signal goes along, with a complete flip-flop of every needle in the row, and a truly binary, bistable system exists.
>
> On the other hand, if you do not do it in quite the same way, the signal will go down only so far, sometimes apparently even amplified through resonance, and somewhere along the line one of the needles will turn all the way around, and the signal will be reflected and go back again, never getting past a certain point. In other instances—you can run several hundred experiments an hour—you will have a section of several needles that just start spinning in a synchronous fashion until it finally dies out. Eventually it will settle down in one of the two stable states.
>
> If you set up an (NxN) array of this sort, and then poke the thing with a bar magnet, I challenge any IBM machine to compute what will happen. The interactions are now exceedingly complicated.

We expect that something akin to this goes on at the molecular level when an organism detects an EMF. As Szent-Gyorgyi said (15): "Single molecules are not necessarily sharply isolated and closed units. There is more promiscuity among them [than] is generally believed."

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