15

Physical Bases for Bioelectric Effects in Mineralized Tissues*

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INTRODUCTION

The electrical and electromechanical properties of mineralized tissue have been investigated only recently and on a rather limited scale. This is somewhat surprising in view of the wide interest shown in bioelectric effects over the past few decades, but perhaps it is understandable that hard tissues were thought to be less likely to exhibit such effects than other tissues more intimately connected with the nervous system. At any rate, it is now clear that electrical effects can be observed in bone. However, there is some lack of agreement as to their underlying physical bases.

The initial work in this field was done by Fukada and Yasuda in Japan. These investigators, the former a physicist and the latter an orthopaedist, published a series of classic papers, beginning in 1954, on the piezoelectric effect in bone and related tissues.[7,8] They used small plates of bone and collagen in their experiments, stressing the samples in various ways. This work, which will be described below, seems to have established the basic mechanism of the stress-induced potentials observed in such tissues.

In 1962, Bassett and Becker published their initial findings[1] on the potentials produced in freshly prepared bone subjected to bending stresses, and shortly afterward the present authors published some preliminary results[10] on bone subjected to both bending and compressive stresses. Bassett and Becker, comparing their results with the output from a quartz crystal, concluded that because the potentials in bone decay more slowly and were sustained during the time that the stress was applied, they could not be caused solely by a classic piezoelectric effect. On the other hand, our own results indicated no reason to look beyond this effect for a satisfactory explanation.

Subsequently, Becker, Bassett and Bachman[3] proposed a semiconductor rectifier theory, primarily to account for a unidirectional current flow rather than an alternating potential, upon repeated application and release of stress, and also to account for the sustained potentials observed during the time that the bone is under stress. We believe that it will be made clear that these can be accounted for without having to invoke so elaborate a mechanism.

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NOTE: Some of the material in this paper was presented at the Gordon Research Conference on the Biochemistry, Physiology and Structure of Bones and Teeth, July, 1963.

TABLE 1. Electrical Properties of Some Calcified Tissues and Dielectrics

Sample	Density (Gm./cm.^{3})	Resistivity (@ 300 °K.; ohm-cm.)	Dielectric Constant
1. Cortical bone (femur)	2.02	1.7×10^{11}	8.0
3. Cortical bone (femur)	2.13	1.2×10^{12}	9.2
7. Anorganic bone (cow cortical, ED treated)	1.55	10^{10}-10^{13}*	4.9
4. Clam shell (prismatic layer)	2.79	2.2×10^{12}	7.5
5. Clam shell (pearly layer)	2.83	7.0×10^{12}	8.0
8. Bone collagen (5% formic acid)	.80	8.0×10^{9}†	4.0
Bakelite (micarta)	1.8-2.0	2.5×10^{10}	5-7
Wood (maple)	.6	1.1×10^{10}	4.4
Italian marble	2.7	5.0×10^{10}	9.0

* Extremely dependent upon humidity.
† Values in excess of 10^{15} ohm-cm. have been reported by Eley and Spivey for vacuum dried, powdered collagen.

MATERIALS AND METHODS

To permit comparison of calcified tissues with other materials, various samples were examined for their ordinary electrical properties. Measurements were made of density, resistivity at room temperature ($\sim 300°$ K.) and dielectric constant at 100 kc. for a number of representative materials. In addition, the temperature coefficient of resistance was determined for several samples. Resistance measurements were made with a Keithley 610 used as an ohmeter, while dielectric constants were measured with a Tektronix-130 L-C meter. The samples used were in the form of small plates about 1 cm. on a side by 1 or 2 mm. thick. These were cleaned, dried and coated with silver conducting paint (Dupont No. 4817) to which contacts were generally made with light pressure springs, the same material being used on both sides of the sample to avoid contact electromotive forces. Resistance measurements at these high values are complicated by surface leakage due to moisture; hence, even at moderate humidity, it is not unusual to find variations in resistance of as much as an order of magnitude unless great care is taken to keep the samples very dry. In fact, in the case of anorganic bone it was suspected that the wide range of values may be due to the very large surface area and consequent leakage in so porous a material.

Another type of measurement was performed that was thought might have some bearing on the nature of these materials. Dr. Martin Pope, of New York University, was kind enough to measure the surface ionization energies of several materials by his ingenious new technic which uses finely powdered specimens in a "Millikan oil drop" type of apparatus.[9] Powder grains are balanced in an electric field against the gravitational attraction and then illuminated with light of varying wave length until electrons are ejected, as evidenced by a sudden motion of the grains. The ionization potentials so measured are analogous to the work function of a metal and are thus a measure of the height of the surface barrier, or, what is the same thing, the strength of the electron bonds in the surface molecules.

It was decided that animals with exoskeletons might be suitable subjects for the study of stress-induced potentials in vivo, since observations could be made without the disturbing influence of body fluids or of soft tissues. Accordingly, some preliminary experiments were performed on live clams to determine the magnitude of stress-induced potentials in the shell. The horny outer layer was removed from several spots by grinding, and then electrodes were attached at these points. The clam was induced to stress its own shell by stimulating the adductor muscle with a needle probed through the excurrent opening. Pulse voltages were observed with a vibrating reed electrometer (Applied Physics Corp. model 31) superimposed on a large background potential in the order of several volts. In fact, normally the shell of a clam is so highly stressed that when it is removed from the animal, several hours are required for the polarization to relax to the zero point. Subsequent stressing of the shell mechanically gives rise to the typical piezoelectric effect observed in well-ordered structures.

RESULTS

Table 1 shows the results of the conventional electrical measurements. It will be noted that the 2 samples of cortical bone (cut from the same femur) exhibit a difference in resistivity and in dielectric constant. It is perhaps significant that the dielectric constant of apatite is 9.5 when measured perpendicular to its optic axis and 7.4 when measured parallel with it. While no effort was made to obtain precisely oriented samples here, it is quite possible that the difference was due to structural alignment of the samples. This is seen more clearly in the case of the clam shell samples. Here, the 2 layers are known to have different crystal orientations with respect to the surface of the shell (Fig. 1). The middle or prismatic layer consists largely of calcium carbonate crystals arranged perpendicularly to the surface, while the pearly or nacreous layer consists mostly of thin sheets of calcium carbonate laid down parallel with the surface. Since the samples were cut parallel with the surface, one might expect to find the dielectric constant, which is a measure of the polarizability of the substance, to show this anisotropy. For example, the dielectric constants of calcite are 8.5 perpendicular to the optic axis and 8.0 in the parallel direction.

In the case of demineralized bone, one also has the problem of large surface area for a given volume and hence considerable leakage under any but the driest conditions. While our sample was desiccated for several days prior to the measurements, it may be significant that Eley and Spivey[4] found a value in excess of 10^{15} ohm-cm. for powdered collagen in vacuum, a value that seems to be extremely high, for it places collagen among the better insulators.

Included for comparison in the tabulation are 3 common substances that generally are regarded as insulating materials. Note that their resistivities, as taken from the literature, generally are lower than those of the calcified materials. There is no rigid rule that distinguishes an insulator from a semiconductor on the basis of resistivity. Generally, semiconductors are thought of as having resistivities (at room temperature) in the range of $\sim 10^{-2}$ to 10^{9} ohm-cm., which is intermediate between good conductors ($\sim 10^{-5}$ ohm-cm.) and good insulators ($\sim 10^{14}$ to $\sim 10^{22}$ ohm-cm.). Hence, the region in question is more nearly in the class of insulators than of conductors. A more meaningful distinction may be found in terms of the band theory of solids by considering the energy gap ($\triangle E$) between the valence and the conduction bands of a given material. In ordi-

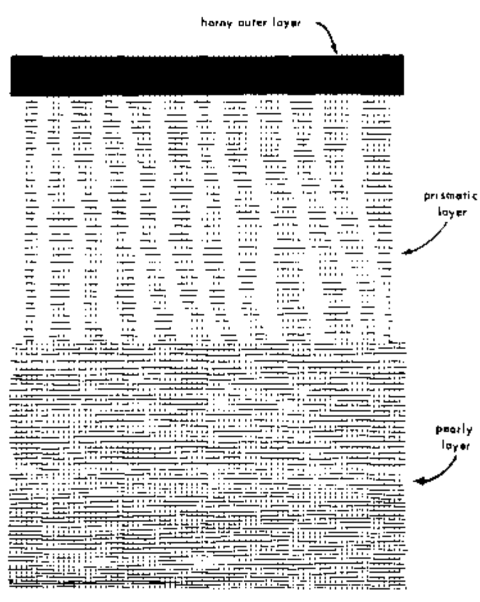


FIG. 1. Clam shell layers.

nary semiconductors, this gap is very small, of the order of kT (thermal energy) at room temperature; hence, electrons are easily excited into the conduction band. In insulators, on the other hand, the gap is quite large, of the order of several volts, so that very few electrons are raised to the conduction band at ordinary temperatures. There is an additional feature of semiconductors that is responsible for most of their conductivity at room temperatures. They generally contain appreciable numbers of impurity atoms which give rise to electronic energy levels lying between the empty and the filled bands. Thus, to raise electrons from these impurity levels to the upper conduction band requires a much smaller $\triangle E$ than the width of the gap and may be small enough to give rise to appreciable conduction at room temperature. It is generally possible to distinguish between intrinsic and impurity conduction by examining the temperature dependence of resistivity. In an intrinsic semiconductor (or insulator), this increases exponentially with temperature, while impurity conduction depends to a much smaller degree on temperature.

Figure 2 shows the temperature dependence of resistivity for a number of the samples studied. There is no evidence that any of these could exhibit typical semiconductor effects except perhaps at very high temperatures, where insulators show appreciable conductivity. But this would be at many hundreds or thousands of degrees. If anything, they *might* be considered as intrinsic semiconductors (or possibly, "semi-insulators") with rather large energy gaps. For example, the energy gap calculated from these measurements for the cortical bone turns out to be ~ 2.4 electron volts, much too large for appreciable effects to occur at body tempera-

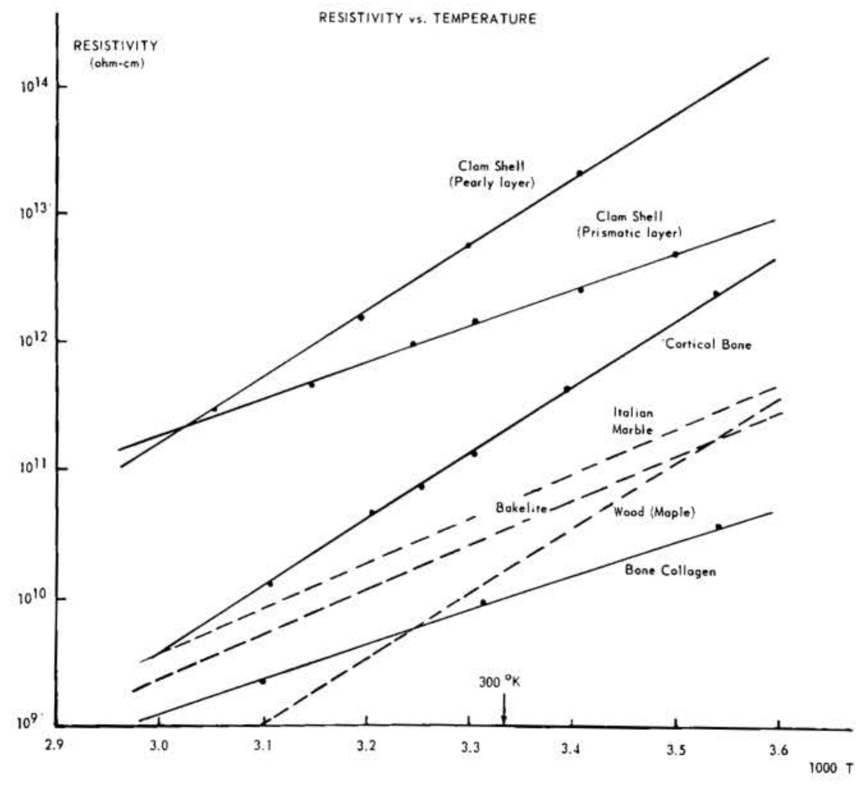


FIG. 2. Resistivity versus temperature.

ture (~ 0.03 electron volt). In fact, the energy gaps for most proteins appear to be of this magnitude or higher, which in itself ought to cast some doubt on semiconductor theories involving these materials. Of course, it may be that the in-vivo situation is quite different in this respect, because of the presence of body fluids, but this could hardly be inferred from measurements on dried specimens. Nor is photoconductivity evidence of any special semiconductor behavior, for good insulators also exhibit this property.

No dependence on voltage was found in the samples measured, nor was there any evidence of non-ohmic behavior or rectifying property in these materials.

The results of the surface ionization measurements are shown in Table 2. It will be noted that all values are in excess of 6.7 electron volts, which was the limit of the apparatus used, except for the hide collagen and the unpurified kangaroo tail tendon. There may be some significance in the fact that hide collagen has a lower ionization potential that bone collagen, and the difference may be related to cross-linking of the collagen fibrils. If this is so, then extending these measurements to the higher energy region may prove to be one of the most useful tools in the study of tissue structure.

These results lead to the conclusion that at least for dried specimens, we are dealing with dielectric materials having a highly ordered structure and that there is no compelling evidence of any special semiconducting or rectifying properties in these materials. In further support of this view, let us look at their piezoelectric properties, particularly as shown by the work of Fukada and Yasuda.

TABLE 2. Surface Ionization Energies of Calcified Tissues*

Sample	ϕ (e.v.)
Bone ash	>6.7
Calcium apatite	>6.7
Synthetic apatite	>6.7
Molar dentin	>6.7
Cortical bone (femur)	>6.7
Hide collagen	5.0-5.5
Kangaroo tail tendon (unpurified)	5.5
Rat tail tendon	>6.7
Bone collagen (femur)	>6.7
Bone collagen (ilium)	>6.7

* (From Dr. Martin Pope).

PIEZOELECTRIC EFFECT

First, we shall review briefly the basic features of the classic piezoelectric effect. This is the reciprocal relationship between the stress (or strain) produced in certain dielectric crystals and the electric polarization of the crystal. Applying a mechanical stress to a piezoelectric crystal results in a polarization, i.e., an electric dipole moment per unit volume, which is proportional to this stress. In an isolated crystal, this polarization produces a voltage across the crystal and a flow of charge in an external circuit connected to the crystal for a time that depends, as we shall see, on the circuit constants and the elastic and the electrical characteristics of the crystal itself. Conversely, application of a voltage between certain faces of the crystal results in a mechanical distortion of the material. It is this reciprocal relationship that characterizes the classic piezoelectric effect. The generation of voltage under mechanical stress is known as the *direct* piezoelectric effect, while the mechanical strain produced in the crystal under electric stress, which is a thermodynamic consequence of the direct effect, is called the *converse* piezoelectric effect.

Piezoelectricity often is regarded as a special property of certain crystals, but actually it is only in very special crystal structures that it does not exist. Of the 32 crystal classes, 20 exhibit piezoelectric properties, and 12 do not. All crystalline materials are anisotropic, which means that most physical properties are different when measured in different directions.* However, this anisotropy obviously is not the sole criterion for piezoelectricity. Instead, what determines whether or not a given crystal is piezoelectric

* Note, for example, that the refractive index and the dielectric constant of a cubic crystal are isotropic properties, requiring only one coefficient to specify their values, but the elastic constants of such a crystal are different in different directions.

is the symmetry of its internal structure. A crystal that is centrosymmetric cannot be piezoelectric because no combinations of stresses will separate the centers of gravity of its positive and negative charges to produce an induced dipole moment. Thus, it is the asymmetry of charge distribution upon application of stress that determines the piezoelectricity of a crystal. That is to say, the crystal must have a structural bias or "one-wayness" that determines the type of charge that will appear on a given surface as the result of a stress.

In the most general case, a component X_i of strain is related to a component E_j of electric field by a power expansion such as the following:

$$X_i = C_{1ij} E_j + C_{2ij} E_j^2 + C_{3ij} E_j^3 + \ldots$$

where the subscripts refer to constants and components along a given crystal axis. In a number of crystals, symmetry requires that in certain directions a reversal of the electric field produces exactly the same strain, and in centrosymmetric crystals this is the case for all directions. In such cases, the strain is an even function of E, and the odd coefficients must be zero, including C_1 (commonly known as the d-coefficient) which is the main contributor to the classic piezoelectric effect. Such a strain is said to be "electrostrictive" and occurs in *all* substances, whether crystalline, amorphous or fluid. The 2 types of strain can be seen in graphic form in Figure 3; thus, the converse effect serves to test whether a given crystal is piezoelectric or not. In fact, it is the best confirmation, since the direct effect is easily confused with contact potentials and "frictional" electricity.

ELECTRICAL OUTPUT FROM PIEZOELECTRIC CRYSTAL

The electrical response of a stressed crystal depends on a number of factors, such as whether the stress is applied suddenly or gradually (i.e., adiabatically or isothermally), whether or not the crystal is clamped along any of its strain axes, whether there is any creep and the circuit constants associated with it.

Consider a crystal, without electrodes, stressed as shown in Figure 4. Applying the load produces a dipole moment which results in an electric field inside the crystal and bound charges on the surface. It should be

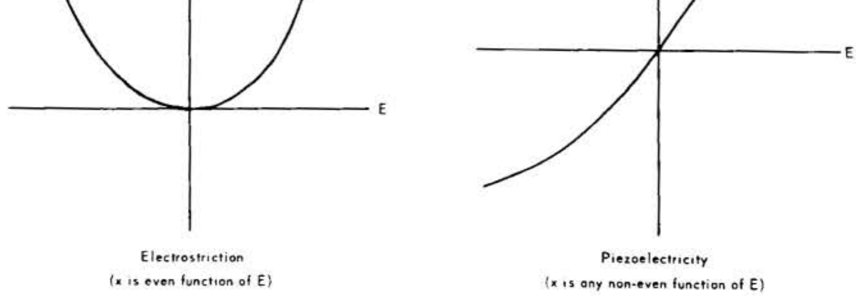
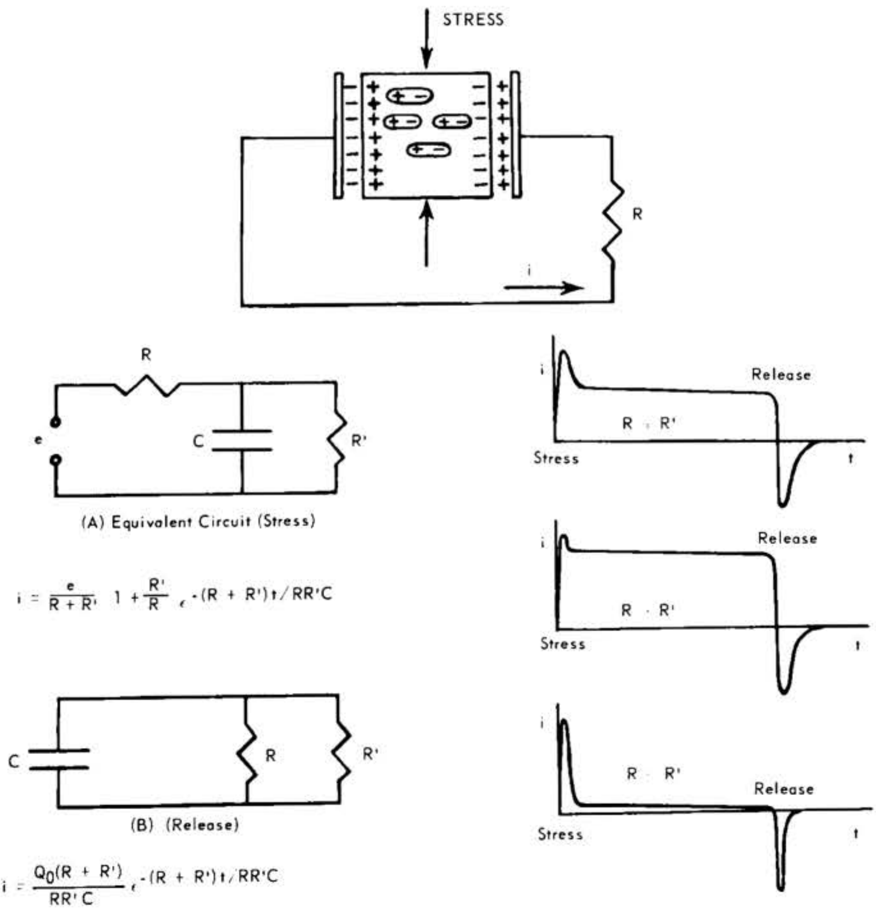


FIG. 3. Electrostriction versus piezoelectricity. (Forsbergh, P. W., Jr.: Handbugh Der Physik, vol. 17, p. 265, Berlin, Springer)

emphasized that as long as the crystal is stressed, the polarization field will persist, since it is caused by the actual displacement of charge. In order to observe the field, one must place electrodes on the crystal and connect them to an external circuit containing an electrometer or a similar device for measuring voltage. If the impedance of this circuit is very high, the voltage so measured will decay with time according to the conductivity of the sample itself. The "open circuit" voltage of a piezoelectric crystal is the voltage across it in the absence of voltmeters, or, what is the same thing, the voltage measured by a capacitanceless voltmeter, a situation clearly impossible to achieve in practice. It is perhaps better to think of the open circuit voltage in terms of the field across the crystal in the absence of electrodes, either attached or nearby.

The dielectric is shown in the polarized state in Figure 4, as indicated by the alignment of some representative dipoles. Connecting electrodes and an external circuit to the crystal results in a flow of charge through the external circuit until the surface charges on the crystal are neutralized, at which point there is no further flow of charge until the stress is removed. The electrodes are shown separated from the crystal simply for greater



$$i = \frac{e}{R + R'}\left(1 + \frac{R'}{R}\,\epsilon^{-(R + R')t/RR'C}\right)$$

$$i = \frac{Q_0(R + R')}{RR'C}\,\epsilon^{-(R + R')t/RR'C}$$

FIG. 4. Crystal under stress.

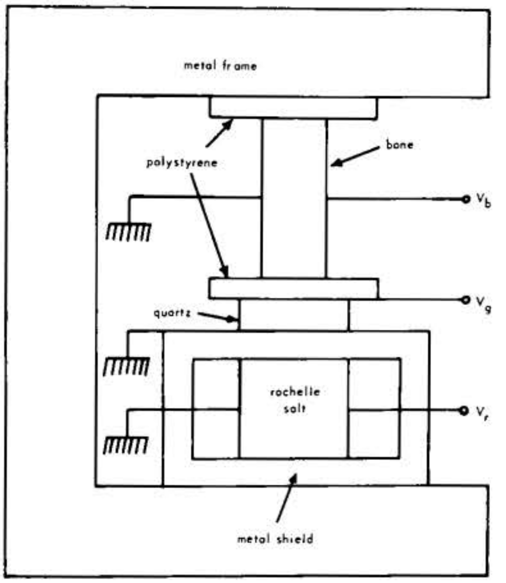


FIG. 5. Fukada apparatus. Schematic diagram of measuring device. (J. Phys. Soc. Japan 12:1158)

clarity, although in the usual case they would generally be in close contact with the dielectric. Note that if the external circuit were broken and the electrodes removed, the polarization charge would remain on the dielectric because the dipoles are oriented as long as the stress is applied.

A simplified equivalent circuit analysis was made to determine the shape of the electrical output pulse to be expected from a piezoelectric crystal under abrupt stress conditions. The results are also shown in Figure 4. Here, C is the capacitance of the system (crystal plus circuitry), R is the resistance of the external measuring circuit, and R′ the resistance of the crystal itself. If e is the piezoelectric voltage produced by the stress, the current i flowing in the external circuit is found by solving Circuit (A):

$$i = \frac{e}{R+R'}\left[1 + \frac{R'}{R}\epsilon^{-\frac{R+R'}{RR'C}t}\right]$$

On releasing the stress, the circuit conditions are changed since now the capacitance of the system simply discharges through the parallel combination of R and R′, as shown in Circuit (B).

It is instructive to look at the output for several different values of the circuit constants. Three such curves are shown, the first for $R \approx R'$, the second for the external resistance R greater than R′ and the last for the reverse condition. The initial current pulse in each case has the same amplitude, since this depends only on e and R. Note particularly the second case, which is a situation that is not too difficult to obtain in the case of bone, because of its relatively low internal resistance, while the last curve is what would be expected from a quartz crystal with its very high leakage resistance. The similarities between these curves and those obtained by Bassett and Becker in their initial experiments[1] should be noted. Of course, the release pulses do not show a "steady" potential.

PIEZOELECTRICITY IN POLYCRYSTALLINE MATERIALS

One would not expect to observe a true piezoelectric effect in amorphous or polycrystalline materials unless the material has a highly ordered structure, in which case the individual dipole moments (which can be caused by distortion of covalent or molecular bonds as well as by displacement of ions) add rather than balance out as in the case of random orientations. Such an ordered structure is found in many materials, certainly in most mineralized tissues. Hence, even though a single hydroxyapatite crystal may not belong to a class that is piezoelectric, nevertheless the ordered assemblage of small crystallites might be expected to show this property.

Fukada and Yasuda have carried out a series of measurements on a number of materials ranging from high polymers to samples of bone and collagen.[7,8] All are piezoelectric, as evidenced by measurements of both the direct and the converse effects. Because of the fundamental importance of this work, it may be useful to describe their method and their results in some detail, limiting ourselves at present to bone and collagen. They used square plates of dried bone cut at various angles from the femurs of a man and an ox. The direct effect was measured first by a static method, in which the potentials were observed with a vacuum tube electrometer. Subsequently, both the direct and the converse effects were measured in an ingenious fashion with the apparatus shown in Figure 5. Here, the rochelle salt crystal served as the actuator for the direct measurement and as the transducer for the converse effect: that is, by using the converse effect in rochelle salt, the bone sample was stressed and its direct coefficients determined, whereas by applying a potential to the bone its strain is transmitted to the rochelle salt, and thereby the converse coefficients were measured.

The results show rather conclusively the classic piezoelectric effect in bone. In the direct effect, the polarization was shown to be linear with pressure, while in the converse effect the strain was directly proportional to electric field. The dependence of this effect on direction of stress was determined from the samples cut at various angles with the bone axis. This is shown in Figures 6 and 7 for man and for ox, where the angles are measured clockwise from the bone axis. Note that the piezoelectric effect disappears when the bone is stressed at an angle of about 10° with the bone axis and also when the stress is almost perpendicular to the axis. Fukada and Yasuda conclude from this that the effect is exhibited only when a shearing force acts on the highly ordered collagen fibers so that they tend to slip past one another. If this is the correct interpretation, it presumably means that the effect is due to a distortion of the cross-linking bonds in collagen.

The authors point out that x-ray diffraction studies also show that the symmetry axis is inclined to the bone axis and suggest that this may result from the fact that the bone axis of the femur is not vertical when man or ox is in the standing position, while the collagen axis does lie in the vertical plane.

More recently, Fukada and Yasuda carried out similar measurements on tendon taken from the leg of a horse. The tendons were immersed in dehydrated alcohol for 1 or 2 weeks and then dried under vacuum. Test specimens were cut in the form of square plates (approximately $1 \times 1 \times 0.4$ cm.) at various angles to the tendon axis, and both

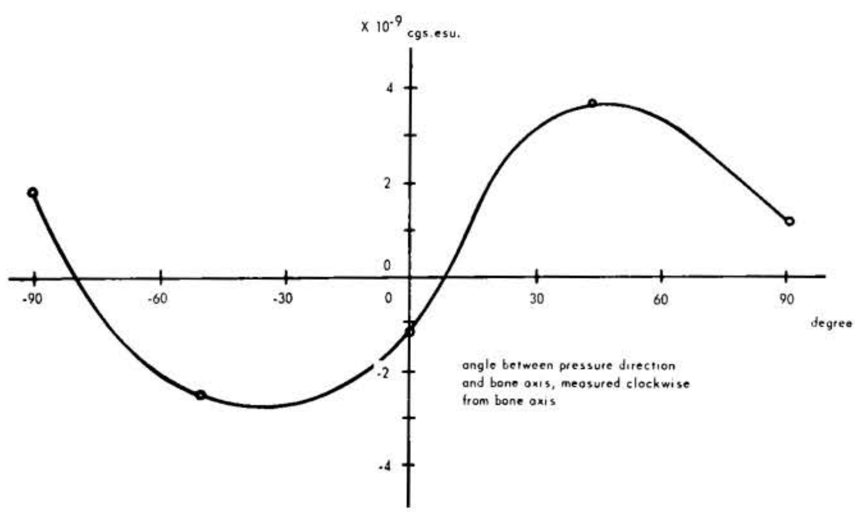


FIG. 6. Dependence of the piezoelectric constant of femur of man on the angle between the pressure direction and the bone axis. (Fukada and Yasuda, J. Phys. Soc. Japan 12:1158)

the direct and the converse effects were measured. Here, again, the results were similar to the case of bone, including the directional effect. The collagen fibers appear to be highly oriented along the tendon axis and isotropic in a plane at right angles to the axis. The magnitude of the effect in dry collagen was particularly high, of the same order of magnitude as in quartz, but decreased rapidly with water content. This is possibly due to a large decrease in resistivity of the sample, causing the polarization charge to leak off too rapidly for reliable measurement. It is interesting to note that the effect also disappears in dried samples above about 100° to 120°C., where dry collagen begins to shrink, probably due to the melting of crystallites of collagen, according to these authors. Bassett and Becker, incidentally, were unable to detect stress-induced potentials in wood, polyethylene and tendon,[1] while Fukada[5,6] not only detected such potentials but measured the piezoelectric coefficients and even constructed phonograph pickups out of tendon and pieces of bone.

CONCLUSIONS

Becker *et al.*[3] have used as the main argument favoring their rectifier model the fact that an alternating signal is produced on application and release of stress in a bone. Actually, however, the reverse pulse is an electrical artifact caused by the release of charge from the capacitance of the system when the polarization is released in the stressed bone. It is not as though the stress were reversed (e.g., a compression replaced by a tension), in which case the electric field in the sample would reverse, as well as the sign of charge on its surface. Instead, as was pointed out in connection with the equivalent circuit and as Becker *et al.*[3] point out as well, the potential change on release of stress is quite different from that upon the application

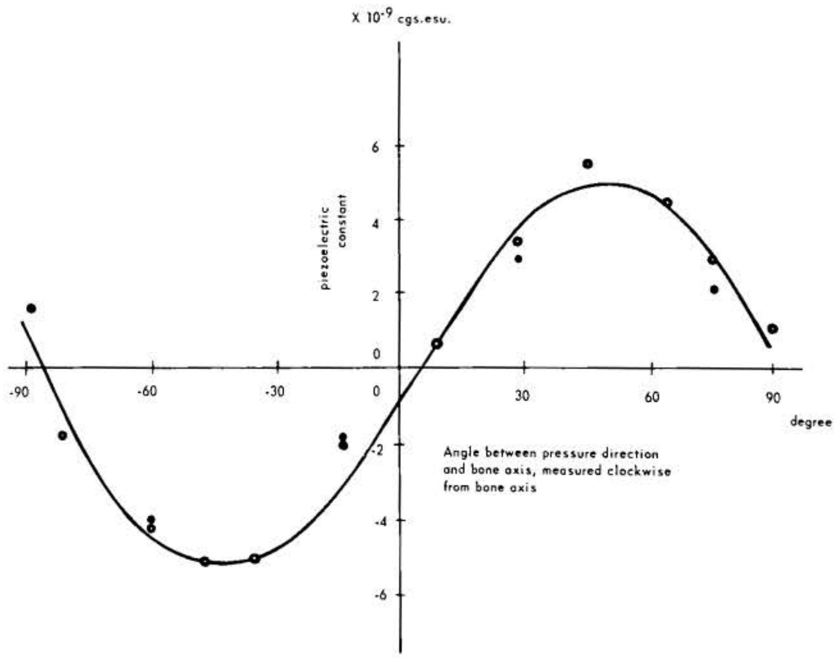


FIG. 7. Dependence of the piezoelectric constant on femur of ox on the angle between the pressure direction and the bone axis. (Fukada and Yasuda: J. Phys. Soc. Japan 12:1158)

of stress. Nor, in the usual in-vivo situation is a bone subjected to alternate compression and tension. Rather, a bone such as the femur is subjected to relatively large compressive forces but comparatively small tension forces. And the same is generally true of the entire skeletal system. Hence, it is quite unnecessary to invoke a rectifier mechanism in order to provide unidirectional currents; the stresses normally placed on mineralized tissues in the animal kingdom are essentially unidirectional. Nor does the temperature dependence of the stress-induced potentials provide evidence of a rectifying property, for such effects are also to be expected in piezoelectricity. In fact, many piezoelectric materials are pyroelectric as well.

There is another cogent argument against a rectifier mechanism as the basis for the observed effects. Stress-induced potentials have been observed in pure collagen,[8] while according to the theory of Becker *et al.*[3] the collagen in bone forms part of a collagen-apatite PN rectifying junction.

Recently, Becker reported on some electron paramagnetic resonance measurements in nonirradiated cortical bone.[2] His purpose was to seek supporting evidence for his semiconduction mechanism by looking for free charge carriers in the bone samples. One would expect to find resonances on such a theory if adequate concentrations of donors were present in bone. Some resonance signals were observed but could not be definitely established as being due to a population of free-charge carriers.

Therefore, we must conclude that the semiconductor-rectifier theory is unnecessarily elaborate to account for the experimental evidence and is probably not the correct mechanism. Instead, all of the observed effects seem to be accounted for in terms of a classic piezoelectric effect.

One can imagine how bone remodeling *might* take place on the basis of piezoelectricity alone, using the polarity distribution given by Bassett and Becker.[1] Since the compressed regions of bone develop a negative charge with respect to the regions under tension one might imagine that free Ca^{++} ions could migrate to the former regions and deposit thereon, perhaps later to nucleate hydroxyapatite. Whether or not this is the mechanism, one can see that the in-vivo situation is quite different from the in-vitro case. In the former, as long as the bone is stressed, polarization charges are present, and ions or polarizable molecules can deposit thereon. Since these would most probably deposit along the polarization vector, one can see how the process might continue far beyond the point where the polarization charges may be imagined to become neutralized by the accretion of charged ions.

It is clearly important to understand the basic mechanism underlying the stress-induced potentials in mineralized tissues if one hopes to learn more about the process of mineralization itself. Electron microscopy and x-ray diffraction studies show the orientation and certain structural features of these materials but do not provide sufficient information on a molecular level, such as can be inferred from dielectric constant measurements (as a function of frequence) or from surface ionization potentials. We believe that much can be learned about the structure of collagen and the relation of collagen to bone apatite from studies of the electrical characteristics of these materials. In particular, we wish to emphasize the potential value of dielectric constant measurements as a means of learning more about the "cooperative structure" of these materials on a molecular level. Perhaps, it is too early to say whether this information will help one to a much better understanding of bone processes, but it seems rather likely that it may.

SUMMARY

Stress-induced potentials in hard tissues have been demonstrated by several investigators. The origin of these potentials is shown to be attributable to a classic piezoelectric effect. Other workers have postulated a semi-

conductor-rectifier mechanism based on an assumed difference in majority charge carrier between the organic and the inorganic portions of tissue. Measurements of the ordinary electrical properties of hard tissues show them to lie in the region between good insulators and poor semiconductors, with energy gaps at room temperature in the order of 2.5 electron volts. Dielectric constant measurements indicate a highly ordered structure for these materials, in agreement with morphologic studies. Arguments are presented against the semiconductor-rectifier theory as being unnecesarily elaborate to account for the observed effects. A hypothesis is proposed to account for bone remodeling in terms of the charges produced on the surface of such tissue when it is subject to mechanical stress. These studies appear to be particularly useful in learning about the cooperative structure of mineralized tissues on a molecular level.

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