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## The effect of charge density on the velocity and attenuation of ultrasound waves in human cancellous bone

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#### ABSTRACT

Cancellous bone is a highly porous material, and two types of waves, fast and slow, are observed when ultrasound is used for detecting bone diseases. There are several possible stimuli for bone remodelling processes, including bone fluid flow, streaming potential, and piezoelectricity. Poroelasticity has been widely used for elucidating the bone fluid flow phenomenon, but the combination of poroelasticity with charge density has not been introduced. Theoretically, general poroelasticity with a varying charge density is employed for determining the relationship between wave velocity and attenuation with charge density. Fast wave velocity and attenuation are affected by porosity as well as charge density; however, for a slow wave, both slow wave velocity and attenuation are not as sensitive to the effect of charge density as they are for a fast wave. Thus, employing human femoral data, we conclude that charged ions gather on trabecular struts, and the fast wave, which moves along the trabecular struts, is significantly affected by charge density.

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#### 1. Introduction

Cancellous bone is a highly porous material, so general poroelasticity is appropriate to detect bone diseases when ultrasound is used. Two types of waves are observed in cancellous bone ([Cardoso et al., 2008; Fellah et al., 2004; Haire and Langton,](#page--1-0) [1999; Hughes et al., 2003; Lee et al., 2003; Sebaa et al., 2006;](#page--1-0) [Williams et al., 1996; Williams, 1992; Yoon et al., 2012](#page--1-0)), and general poroelasticity was first formulated by Biot ([Biot, 1956\)](#page--1-0). Hosokawa [\(Hosokawa and Otani, 1998](#page--1-0)) employed the Biot theory for cancellous bone because the two waves are observed in cancellous bone, and they found a close fit with experimental data. Williams [\(Williams, 1992](#page--1-0)) also introduced the Biot theory, or the so-called poroelasticity theory, to cancellous bone. All equations used in these studies have an isotropic assumption for bone materials and are solved numerically. Thus, simple solutions for isotropic generalized equations are given in the literature. Yoon and his colleagues [\(Yoon et al., 2012](#page--1-0)) showed that the shape of trabeculae significantly affects the velocity of wave propagation using the Biot theory.

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Bone cells are exposed to mechanical forces and electrokinetic forces ([Hung et al., 1996; Schneider et al., 2004\)](#page--1-0). Hung et al. ([Hung et al., 1996](#page--1-0)) applied fluid flow to bone cells, exposing mechanical forces as well as electrokinetic forces. Electrokinetic forces are created by an applied convective current that produces mobile ion transport. As a result, the authors found that fluidinduced shear stress is a primary stimulus rather than electrokinetic forces. However, Schneider et al. ([Schneider et al., 2004\)](#page--1-0) found that positively charged hydrogel scaffolds result in greater cell attachment compared to negative and neutral charge densities. The cell attachment is altered by manipulating a fixed charge density ([Alsberg et al., 2001; English et al., 1998\)](#page--1-0). Mesenchymal stem cells are differentiated to osteoblasts during osteogenesis. Mineralization is influenced by extracellular matrix proteins and by substrates ([Schneider et al., 2001\)](#page--1-0). It is believed that the flow of charged ions generates the convective current, and the mechanical deformation of bone generates both piezoelectricity and the electrokinetic effect (or charge density). However, piezoelectricity may be determined by the electrokinetic double layer that remains in dry bone because charged ions remain on the surface of bone after it is dried [\(Pollack et al., 1984b\)](#page--1-0).

Osteoblastic cells respond to charged hydroxyapatite particles ([Liang et al., 2011](#page--1-0)) The positively charged hydroxyapatite nanoparticles have better interaction with osteoblastic cell membranes because the cell membrane is negatively charged and the size of

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hydroxyapatite mineral crystals increases. Also at the early stage of mineralization, charged hydroxyapatites affect the mineralization as well as cell adhesion [\(Bodhak et al., 2009\)](#page--1-0). The wave propagation of ultrasound is similar to the mechanical deformation because the governing equation of wave propagation is solved for the displacement of solid and fluid, respectively. Thus we believe that the wave propagation of ultrasound has the similar effect to mechanical deformation and the charge density affects both mineralization and cell adhesion.

Poroelasticity is widely used for elucidating the bone fluid flow stimulating bone cells, and these bone cells communicate with each other [\(Cowin, 1999\)](#page--1-0). The electrokinetic effect is another parameter in the bone remodeling process. These two parameters – bone fluid flow and the electrokinetic effect - are coupled to each other. The strain-generated potentials induce charged ions, called the charge density, in bone fluid flow through the canalicular network, and excessive positive ions move along the bone fluid flow ([Pollack et al., 1984a; Salzstein and Pollack, 1987; Salzstein et al.,](#page--1-0) [1987\)](#page--1-0). Thus, the general bone poroelasticity equation is combined with charge density in the electrokinetic effect of bone.

#### 2. Poroelasticity theory

The governing equations for the poroelasticity theory are given by [\(Biot, 1956; Neev and Yeatts, 1989\)](#page--1-0), but Neev and Yeatts ([Neev](#page--1-0) [and Yeatts, 1989](#page--1-0)) include the charge densities  $q_s$  and  $q_f$ , which are those of solid and fluid, respectively, into the governing equations of poroelasticity. These two quantities,  $q_s$  and  $q_f$ , can be assumed to be identical, the details of which can be found in Neev and Yeatts ([Neev and Yeatts, 1989](#page--1-0)). The governing equations of poroelasticity, including electrokinetic effects and charge densities  $q_s$  and  $q_f$ , are as follows:

$$
\rho_{11}\ddot{u} + \rho_{12}\ddot{U} - Nu_{ijj} - (A + N)u_{jji} - QU_{jji} + b(\dot{u}_i - \dot{U}_i) + q_s\Phi_{i} = 0
$$
\n(1)

$$
\rho_{22}\ddot{U}_i + \rho_{12}\ddot{u}_i - (RU_{j,j} + Qu_{j,j})_{,i} - b(\dot{u}_i - \dot{U}_i) + q_s\Phi_{,i} = 0
$$
 (2)

$$
\left\{ q_f \left( RU_{j,j} + Qu_{j,j} \right) - \varepsilon b \left[ \dot{\Phi} + (\phi G/\varepsilon) \right] \Phi \right\}_{,ii} = 0 \tag{3}
$$

Here, N, R, Q, and A are poroelastic parameters,  $u$  and U are displacements of the fluid and solid constituents, respectively, and the variable bis defined by  $\phi^2\mu/K$ , where  $\mu$  is the fluid viscosity, K is the permeability of bone fluid,  $\varepsilon$  is the permittivity, and  $\phi$  is the porosity. G is a constant showing the linear relationship between the electric current and electrical potential due to the applied electrical potential, i.e.,  $J_i = -\phi G \Phi_{i,j}$ , where  $J_i$  is the current density. After we define  $P \equiv A + 2N$ , the poroelastic parameters, or the socalled Biot parameters P, Q, and R, are given by [\(Williams, 1992;](#page--1-0) [Yoon et al., 2012\)](#page--1-0)

$$
P = \frac{\phi(K_s/K_f - 1)K_b + \phi^2 K_s + (1 - 2\phi)(K_s - K_b)}{(1 - \phi - K_b/K_s + \phi K_s/K_f)} + \frac{4G}{3},\tag{4}
$$

$$
Q = \frac{(1 - \phi - K_b/K_s)\phi K_s}{1 - \phi - K_b/K_s + \phi K_s/K_f},
$$
\n(5)

and

$$
R = \frac{K_s \phi^2}{(1 - \phi - K_b/K_s + \phi K_s/K_f)},
$$
\n(6)

 $K_i$  is the bulk modulus of *i*, where *i* is substituted by solid (s), fluid  $(f)$ , and bone  $(b)$ . By assuming that the displacements of the fluid and solid,  $u$  and  $U$ , and the potential  $\Phi$  are harmonic, i.e.,

$$
u_i = u_i^0 \exp[i(k_i x_i - \omega t)], \qquad U_i = U_i^0 \exp[i(k_i x_i - \omega t)], \qquad \text{and}
$$
  
\n
$$
\Phi = \Phi^0 \exp[i(k_i x_i - \omega t)], \qquad \text{Eqs. (1), (2), and (3) are expressed by}
$$

 $\mathbf{I} \mathbf{I}^0$  arra $\mathbf{I} \mathbf{I}^1$   $\mathbf{I} \mathbf{I} \math$ 

$$
[Pk^{2} - (\omega^{2}\rho_{11} + i\omega b)]u_{1}^{0} + [Qk^{2} - (\omega^{2}\rho_{12} - i\omega b)]U_{1}^{0} - (iq_{f}k)\Phi^{0} = 0,
$$
\n(7)

$$
\[Qk^2 - (\omega^2 \rho_{12} - i\omega b)\]u_1^0 + \[Rk^2 - (\omega^2 \rho_{22} + i\omega b)\]U_1^0 + (iq_f k)\Phi^0 = 0,
$$
\n(8)

$$
(-iq_f Q k_j)u_1^0 + (-iq_f R k_j)U_1^0 + [(1 - i\omega \varepsilon b)]\Phi^0 = 0.
$$
 (9)

In order to produce non-trivial solutions, the determinant of Eqs.  $(7)$ ,  $(8)$ , and  $(9)$  should be zero, i.e., we can find the wave velocity,  $Re[v] = \frac{\omega}{k}$ . The last term of Eq. (9) is reformulated from Eq. (3) for the case when the electric potential induces charged ion movement though the fluid only. Note that, in this paper, we assume that the charged ions are moving along the fluid only so that the permittivity for this calculation is used for the constant value of a fluid (or water). From the definition of the wave number,  $k$  is a complex number,  $k = Re[k] + i\alpha$ , where  $\alpha$  is the attenuation constant. Because the wave number  $k$  is expressed as [\(Cardoso and](#page--1-0) [Cowin, 2012](#page--1-0))

$$
k = \frac{\omega}{v} = \frac{\omega}{Re[v] + ilm[v]} = \frac{\omega(Re[v] - ilm[v])}{|v|^2} = Re[k] + i\alpha,
$$
 (10)

the attenuation  $\alpha$  is obtained by

$$
\alpha = -\frac{\omega \text{Im}[v]}{|v|^2}.\tag{11}
$$

In this calculation, we set the wave number k to be 1 so that the frequency is identical to the wave velocity because we cannot change the wave velocity but can manually change the frequency.

#### 3. Numerical application to human cancellous bone

To obtain the bulk moduli described in the poroelastic parameters P, Q, and R as illustrated in Eqs.  $(4)$ ,  $(5)$ , and  $(6)$ , the following relation is employed:

$$
K_i = \frac{E_i}{3(1 - 2v_i)},
$$
\n(12)

where the subscript  $i$  can be replaced by  $b$ ,  $s$ , and  $f$  for bone, solid bone material, and fluid (or water), respectively. The elastic modulus and Poisson's ratio of 141 human cancellous bones are theoretically estimated for the porosity  $\phi$  [\(Yang et al., 1999;](#page--1-0) [Yoon et al.,](#page--1-0) [2012](#page--1-0)),

$$
E_b = 822.367 E_t \phi^{1.95}, G_b = 345.540 E_t \phi^{1.99} \text{ and } v_b = 0.198 \phi^{-0.16}.
$$
\n(13)

The unit of the elastic and shear moduli in Eq. (13) is GPa. To obtain the unknown variable,  $E_t$ , we set  $E_b = E_s$ , as the porosity  $\phi$ is zero. The variable  $E_t$  is obtained as 0.023, as the elastic modulus of solid bone material is 18.9 GPa. Then, we can estimate the shear modulus of solid bone material as 7.94 GPa, and the poroelastic parameters P, Q, and R are numerically calculated with the bulk modulus of fluid (or water) to be 2.3 GPa. The parameter b introduced in Eqs. (1), (2), and (3) is  $\phi^2 \mu / K$ , where  $K = \frac{\frac{1}{6}\phi^3}{\mu S \nu^2 (\frac{3}{2} + \frac{1}{6}\phi)}$  and  $Sv = 26.23\phi - 81.73\phi^2 + 121.80\phi^3 - 92.71\phi^4 + 26.55\phi^5$ . The unit for b is  $kg/(m^3 \cdot s)$  [\(Daish et al., 2017\)](#page--1-0). The permittivity  $\varepsilon$  for the fluid, which we assume to be same as that of water, is calculated by the formula  $\varepsilon(\omega, T_{water}) = \varepsilon_{\infty}(T_{water}) + \frac{\varepsilon_0(T_{water}) - \varepsilon_{\infty}(T_{water})}{1 - i\omega r(T_{water})}$ 

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