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Viscoelasticity of Bone Cells Exposed to Fluid Flow

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Numerous experiments have shown fluid flow to be a potent stimulator of bone cells *in vitro*, suggesting that fluid flow is an important physical signal in bone mechanotransduction. In fluid flow experiments, bone cells are exposed to both time-dependent (*e.g.* oscillating or pulsing) and time-independent (*e.g.* steady) flow profiles. Interestingly, the signaling response of bone cells shows dependence on loading frequency and/or rate that has been postulated to be due to viscoelastic mechanical behavior. However, the time-dependent mechanics of bone cells have not been well characterized.

Using sulfate and collagen coated fluorescent beads of varying sizes as displacement markers, we quantified the frequency dependence of peak deformation, strain, and phase lag in bone cells exposed to 1.0 Pa oscillating flow at frequencies of 0.5-2.0Hz. During oscillatory flow, peak deformation (~0.1 μm) and strain (~1%) were frequency-independent, indicating the cells deformed like elastic bodies. The frequency-independent deformations found in our experiments suggest that frequency-dependent, flow-induced signaling in bone cells may not be attributable to viscoelastic behavior, and instead may be due to other rate-dependent phenomena. During steady flow, the creep response of the cells was well modeled by a Maxwell body. However, when the model was calibrated under steady flow and applied to oscillatory flow, we found that it was able to accurately predict peak deformation, but not phase lag. The ability of the model to accurately predict peak deformation but not phase lag under oscillatory flow suggests that a simple Maxwell body may be adequate for predicting deformations under different flow profiles, but a more complex model is necessary in order to accurately describe the mechanical phenomena which govern phase lag. Note that the model also predicts a transition frequency of ~0.01Hz below which viscous deformations become significant. Finally, the model was used to make an estimate of viscoelastic continuum properties. By assuming the cell is composed of an isotropic continuum, we estimate a cellular Young's modulus of E ~70 Pa, and shear viscosity of η ~200 Pa·s.

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