**Appendix 1:** Equation Variables.

|  |  |  |
| --- | --- | --- |
| *c* | Constant | Equation 1 |
| *a* | Constant | Equation 1 |
| *P(x,t)* | Osteoblast recruitment stimulus at surface location x as a function of time t (in mol mm-2day-1) | Equation 1, 4, 5 |
| *(dmtot(x,t)/dt)* | Total bone density | Equation 3 |
| *(dmbl(x,t)/dt)* | Osteoblast bone formation | Equation 3 |
| *(dmcl(x,t)/dt)* | Osteoclast bone resorption | Equation 3 |
| *(dm/dt)* | Change in bone density | Equation 4 |
| τ | Proportionality constant | Equation 4 |
| *ktr* | Osteoblast recruitment threshold | Equation 4 |
| *roc* | Amount of mineral resorbed by osteoclasts per day | Equation 4 |
| *n* | Number of osteocytes in the region of the area considered | Equation 5 |
| *fi* | Exponential decay function for signal from osteocyte i to surface location x | Equation 5 |
| μi | Mechanosensitivity of osteocyte | Equation 5 |
| *Rti(t)* | SED rate in the location of osteocyte I (in J m-3s-1) | Equation 5 |
| ρ | Relative (apparent) density in each point x of Ω | Equation 6, 7 |
| *Y* | Design domain within trabeculae (microscale) | Equation 6, 7 |
| Ω | Design domain within whole bone (macroscale) | Equation 6, 7 |
| μ | Volume fraction in each point y of Y | Equation 6, 7 |
| *u* | Displacements along another defined axis at macroscale | Equation 7 |
| *P* | Mechanical Load | Equation 7 |
| *k* | Metabolic Cost | Equation 7 |
| αr | Weight for the rth load | Equation 7 |
| *EHijkl* | Homogenized properties for the trabecular bone at point xϵΩ | Equation 7 |
| ε(*u)r* | Strain tensor for the displacement field **ur** for the rth load | Equation 7 |
| *Soc* | Mechanosensitivity of osteocyte | Equation 8, 9 |
|  | Angle between x1-axis and the projection of n onto the x1x2-plane, measured anticlockwise | Equation 8 |
| *pc(n)* | Volume fraction of osteocytes orientated to n at position x | Equation 8 |
| *rp* | Radius of osteocyte process | Equation 8 |
| *rc* | Radius of canaliculus | Equation 8, 11 |
| τ*p(n)* | Shear stress | Equation 8, 11 |
| ϴ | Angle between x3-axis and vector n | Equation 8 |
| *Ssf* | Intercellular mechanical signal sensitivity | Equation 9 |
| *xsf* | Cell location | Equation 9 |
| Ω | Region | Equation 9 |
| *w(l)= 1-l/lL* | Decreasing function of stimulus distance *(l≤ lL)* | Equation 9 |
| *lL* | Maximum stimulus effective distance | Equation 9 |
| ψ | Mechanobiological signal | Equation 10 |
| *W* | Weight factor | Equation 10 |
| *f* | Function of each component of the signal | Equation 10 |
| γ | Dimensionless parameter γ=*rc /* | Equation 11 |
| *I0, I1, K0, K1* | Modified Bessel functions | Equation 11 |
| *q* | Ratio of the radius of the canaliculus, *rc*, to that of the radius of the process, *rp : (q = rc/rp)* | Equation 11 |
| *n* | Direction | Equation 11 |
|  | Interstitial fluid velocity | Equation 12 |
|  | Fluid viscosity | Equation 12 |
|  | Permeability of bone | Equation 12 |
|  | Bone density | Equation 12 |
|  | Initial Condition for fluid velocity | Equation 12 |
|  | Canaliculus length | Equation 12 |
|  | See reference for calculation | Equation 12 |
|  | See reference for calculation | Equation 12 |
|  | Radial strain at location 1 | Equation 12 |
|  | Radial strain at location 2 | Equation 12 |
|  | Point at edge of cell process | Equation 12 |
| *dCa/dt* | Rate of change in interstitial bone fluid calcium concentration | Equation 13 |
|  | Rate of flow of calcium from bone fluid to bone | Equation 13 |
|  | Rate of flow of calcium from bone to bone fluid | Equation 13 |
|  | Rate of accumulation of calcium in bone fluid due to osteocytic osteolysis | Equation 13 |
|  | Rate of flow of calcium from blood capillary to bone fluid | Equation 13 |
|  | Rate of flow of calcium from bone fluid to blood capillary | Equation 13 |
|  | Calcium degradation rate | Equation 13 |
| *Ca* | Calcium concentration | Equation 13 |
| *Q* | Total bone | Equation 14 |
| *QB* | Mean rate of refilling in mm2/day | Equation 14, 15, 18 |
| *NF* | Number of osteons forming is cross section A | Equation 14, 18 |
| *QC* | Mean rate of resorption | Equation 14, 16, 18 |
| *NR* | Number of BMUs resorbing per mm2 cortex | Equation 14, 18 |
| *Rc* | Mean radius of an osteon’s cement line | Equation 15, 16 |
| *Rh* | M radius of the Haversian Canal | Equation 15 |
| *TF* | Average time it takes to complete the formation phase | Equation 15 |
| *TR* | Average time it takes to complete the resorption phase | Equation 16 |
| *pv* | Bone porosity | Equation 17, 18 |
| *Av* | Void area of the bony matrix | Equation 17 |
| *A* | Cross-sectional area | Equation 17 |
| *(dAm/dt)* | Rate of change of cortical bone area in a cross-section sample | Equation 18 |
| *B* | Concentration of Osteoblasts | Equation 18 |
| *B0* | Initial concentration of osteoblasts | Equation 18 |
| *C* | Concentration of Osteoclasts | Equation 18 |
| *C0* | Initial Concentration of Osteoclasts | Equation 18 |
| *tn* | Stress tensor | Equation 19-22 |
| *ΔA* | Small reference area | Equation 19 |
| *ΔF* | Summation of forces | Equation 19 |
| *n* | Normal vector | Equation 20, 22 |
| σ*n* | Normal stress | Equation 20, 21 |
| s | Shear stress | Equation 21 |
| *λ and μ* | Lame’s Constants | Equation 31 |
| α | Coefficient of Linea Expansion | Equation 32 |
| *T0* | Uniform constant temperature | Equation 32 |
| *T* | Temperature | Equation 32 |
|  | Velocity | Equation 33 |
| *F* | Force acting over the cell | Equation 33 |
| η | Viscosity | Equation 33 |
| μ | Spring Constant | Equation 33 |
| *t =(σ,τ)T* | Normal and tangential cohesive traction for bone formation and resorption | Equation 34 |
| ϱ=( ϱn, ϱT)T | Displacements related to opening and sliding | Equation 34 |
| Ϭ | Energy per unit mass | Equation 35-43 |
| *S* | Entropy per unit mass | Equation 35-43 |
| *T* | Temperature | Equation 35-43 |
| *p* | Pressure | Equation 35-43 |
| *V* | Volume | Equation 35-43 |
| *Ρ* | Density | Equation 35-43 |
| σij | Stress | Equation 35-43 |
| ϵij | Strain | Equation 35-43 |
| σij’ ϵij’ | Stress-strain deviations | Equation 35-43 |
| *f and Q* | Functions describing the bounding and unbounding of energy processes | Equation 43 |