

Dear reader/scientist,

We have noted several aspects of the model described in Bone 2010 Jan;46(1):49-63 that either warrant clarification or require correction to enable reproduction and extension of this work. The following erratum is divided into two portions. The first (PART 1: CLARIFICATIONS) provides the reader clarification on how to interpret the text and approach solving the mathematics for variables that are not listed and are solved for under an assumption of steady-state conditions. The second (PART 2: EDITS AND UPDATES) provides corrections to typographical errors in the tables and equations that may impede reproduction and extension of this work. References to the paper have been provided to allow the reader to link these comments to the paper as seamlessly as possible. If additional errors or points of clarity are identified, please forward them to the authors for correction and updating of this website.

Lastly, please note in correspondence the date of upload or last edit to this erratum when sending any findings or suggestions.

PART 1: CLARIFICATIONS

Clarification regarding equation nomenclature: The dashes indicate movement between 'compartments', e.g., H_{1-4} is a hyperbolic describing Ca moving from the gut (1) to the vasculature (4) and so the concentration of Ca in the gut drives the hyperbolic. As another example, H_{4-u} is Ca going from vasculature to the urine (u). Same notation is used with ν_{12-4} which is flux of Ca from bone (12) back to vasculature.

Another set of nomenclature that appears uses separation of compartment numbers by a comma. In these cases, the first number is the concentration of that compartment affecting the second; e.g., $H_{4,10-7}$ describes the effect of Ca in the vasculature (4) on the release of PTH from the PT gland (10) into the vasculature (7). In this case, the vasculature compartments, (4) and (7), are different as the quantities describe two different concentration pools (Ca and PTH).

Clarification on adding disease or exogenous (e.g., drug) effects: This was done one of two ways. For hyper and hypo-parathyroidism, the equations were modified to either increase or decrease the endogenous PTH production rates. For drug administration (e.g., intermittent PTH and denosumab), additional differential equations were written that described the pharmacokinetics of these substances based on the referenced publications. The administered PTH, for example, was added into the existing PTH vascular compartment (A(7)).

Clarification regarding steady-state solutions: Many of these were never actually assigned a value in the code, but rather were just expressed algebraically within the code, e.g., hyperbolic equations were often solved at a set point of unity (1). Here's an example, where we solved for the EC50 (aka 'H 6,11 - delta' in the Bone paper) for effect of calcitriol (C8 in the equation below, which is equal to A(6)/V_{vasc} in the

paper and so C8 had an initial condition = 90) on the PT gland:

CtrialPTeff =

$$\begin{aligned} & \text{CtrialMax} - (\text{CtrialMax} - \text{CtrialMin}) * \text{C8}^{\text{CtrialPTgam}} / (\text{C8}^{\text{CtrialPTgam}} + \text{Ctrial50}^{\text{CtrialPTgam}}) \\ & = 1 (\text{where } 1 \text{ is the null setpoint}) @ \text{C8} = 90 \end{aligned}$$

$$\text{INparenCtrial} = ((\text{CtrialMax} - \text{CtrialMin}) * (90)^{\text{CtrialPTgam}}) / (\text{CtrialMax} - 1) - 90^{\text{CtrialPTgam}}$$

$$\text{Ctrial50} = \text{EXP}(\text{LOGN}(\text{INparenCtrial}) / \text{CtrialPTgam})$$

Nonetheless, not all of the set points for the algebra were straightforward or explicit and so here are solutions for the following parameters:

| | |
|----------------|---------------------------|
| | $\delta_{7,22} = 1.183$ |
| | $k_{12-13} = 6.086E - 03$ |
| $H_{2,1}$ | $\alpha = 0.9094$ |
| H_{4-u} | $\alpha = 6.811$ |
| $H_{7,4-u}$ | $\delta = 0.2366$ |
| $H_{4,10-7}^-$ | $\delta = 1.818$ |
| $H_{7,9}$ | $\alpha = 1.904$ |
| $H_{5,9}^-$ | $\rho = 1.02$ |
| $H_{6,11}$ | $\delta = 68.38$ |
| $H_{20,16}$ | $\delta = 3.622$ |
| $H_{20,17}$ | $\delta = 1.977E - 09$ |
| $H_{20,17D}^-$ | $\delta = 0.1077$ |
| $H_{28,17D}$ | $\delta = 29.67$ |
| $H_{24,18S}$ | $\delta = 2.634E - 04$ |
| $H_{20,18D}$ | $\delta = 14.90$ |
| $H_{22,18D}^-$ | $\delta = 1.3E - 05$ |
| $H_{7,26D}^+$ | $\delta = 30.04$ |
| $H_{7,27S}^+$ | $\delta = 22.31$ |
| $H_{18,12-4}$ | $\delta = 5.423E - 03$ |

PART 2: EDITS AND UPDATES

Table 1: Initial conditions

| | |
|-----|--|
| Gut | Ca initial value = 1.585 mmol Units for Calcitriol and PTH = pmol |
|-----|--|

Table 2: Estimates for non-hyperbolic parameters.

k_{15-14} should be k_{13-12}

$\alpha_{20,21}$ should be $\gamma_{20,21}$

$\alpha_{17,22}$ should be $\gamma_{17,22}$

$D(1) = 1.5625$ mmol/h

$D(3) = 0.4375$ mmol/h

add $k_{27D} = 2.795E - 03$

add $\gamma_{4,10} = 0.9$

delete $\gamma_{18,12-4}$

Note: Vic, Vbone were used to scale amounts in the intracellular (e.g., phosphate) and bone compartments to concentrations for various user outputs (not required variables)

Table 3: Estimates for hyperbolic function parameters.

| | | | |
|--------------------------------------|----------|--------|--|
| $H_{2,1}^+$ should be just $H_{2,1}$ | | | |
| delete $H_{2,1}$ | ρ | 0.25 | |
| add $H_{2,1}$ | α | 0.9094 | |

$H_{1-4} \quad \delta = 11.88$
 $H_{4,10-7}^-$ values for ρ and α should be switched
 $H_{28,17D}$ first α should = 3.903E-03
 $H_{28,17D}$ second α (3.816) should be γ
 add $H_{18,12-4} \quad \alpha \quad 0.5435$
 add $H_{18,12-4} \quad \gamma \quad 1.6971$

Differential equations:

$H_{2,1}^+$ should be just $H_{2,1}$

for d/dt A(10), missing parentheses have been corrected in the following expression:

$$\begin{aligned}
 T_{6'4}^{\pm} = & \\
 & 1 \pm (EXP(b_{T64} * (A(6)/Vvasc - \delta_{T64} * (A(4)_0/A(4))^{\gamma_{4,10}})) - \\
 & EXP(-b_{T64} * (A(6)/Vvasc - \delta_{T64} * (A(4)_0/A(4))^{\gamma_{4,10}})) / \\
 & (EXP(b_{T64} * (A(6)/Vvasc - \delta_{T64} * (A(4)_0/A(4))^{\gamma_{4,10}})) + \\
 & EXP(-b_{T64} * (A(6)/Vvasc - \delta_{T64} * (A(4)_0/A(4))^{\gamma_{4,10}}))
 \end{aligned}$$

For clarification:

$$\begin{aligned}
 H_{1-4} &= A(1) * \alpha / (A(1) + \delta) \\
 H_{4-u} &= (A(4)/Vvasc) * \alpha / ((A(4)/Vvasc) + \delta)
 \end{aligned}$$