Modeling Hypocalcemia due to Parathyroid regulation of Plasma Calcium Concentration

Viha Ukani | Samuel Carlson | Nicholas Schwartz |Longyu Zhang| Chelina Wong

Background - Calcium

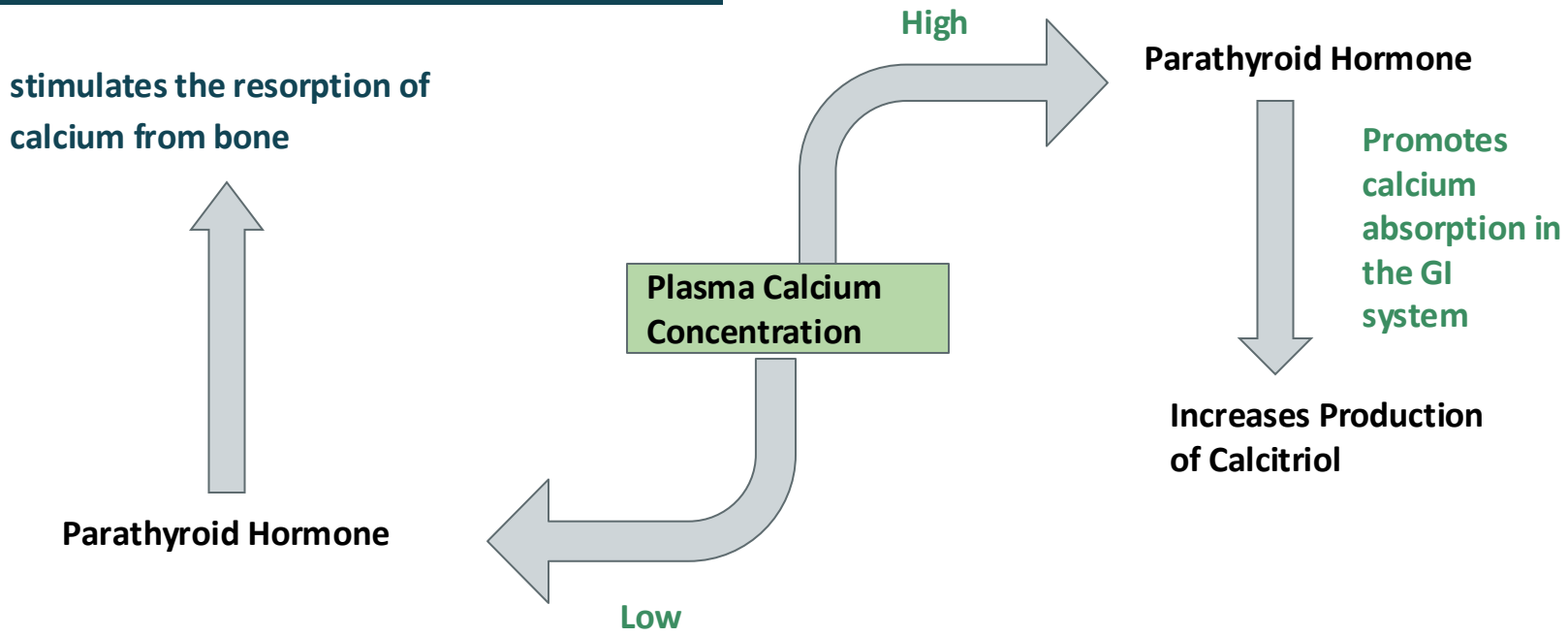
Role in the Human Body

- maintains the structural integrity of bones
- allows for the muscular contraction of heart and skeletal muscle
- acts as an enzymatic signal in biochemical pathways

Regulation

The body tightly regulates blood calcium levels through the calcium-sensing receptors (CaSRs), the parathyroid hormone (PTH), calcitonin, and calcitriol (vitamin D)

How is Calcium regulated by PTH?



Hypocalcemia

- Accounted for 27.72% of hospital inpatients from 2011 - 2014.
- Low Blood Calcium Concentration (> 8.8 mg/dL)
- Caused by Advanced Cancers, Hypoparathyroidism and/or damage to parathyroid glands.
- Symptoms vary from cramping and fatigue to cognitive impairment and heart failure.

Goals

- Model and Create a control system including: Parathyroid Hormone (PTH), Calcitriol (Vitamin-D derivative), and abnormally low Calcium concentrations.

- Utilize a Simulink model representing the system at various abnormal concentrations of Calcium

Assumptions

- All governing equations, transfer functions, and data from literature applies to physiological conditions.
- Parathyroid Hormone production is directly proportional to Plasma Calcium concentration
- The scope of our model is limited to the Parathyroid hormone regulating Plasma Calcium concentration.

Terminology in the Model

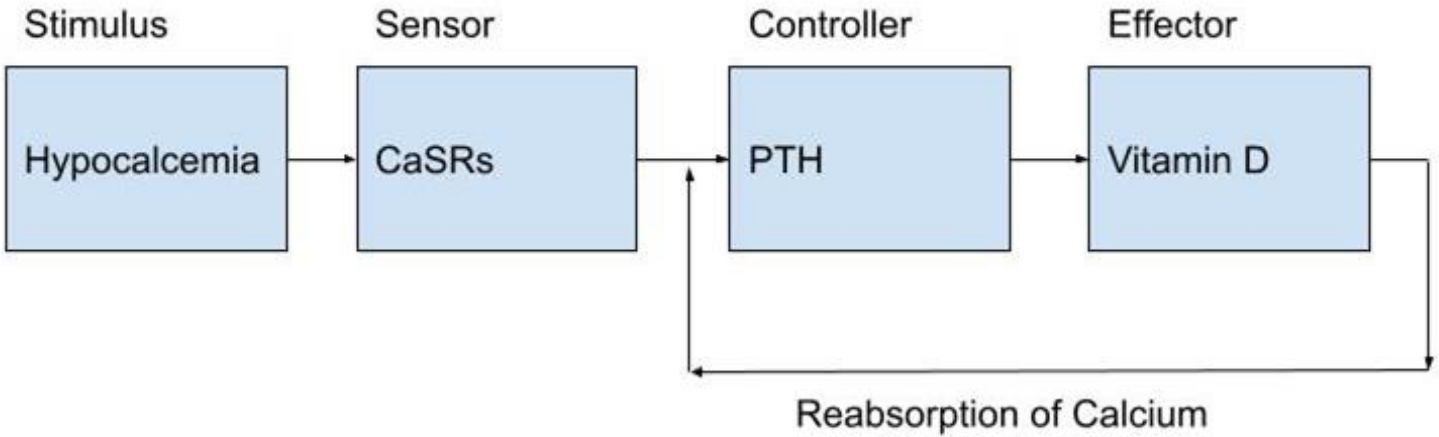
- PTH(t) = Secretion of Parathyroid hormone by Parathyroid gland (mg/dL)
- K = Rate at which Parathyroid gland secretes PTH and Vitamin D level (dL/min)
- T = Target Calcium levels (mg/dL)
- C(t) = Current plasma calcium concentration
- M(t) = Vitamin D secretion (mg/dL)
- N(t) = Vitamin D concentration (mg/dL)
- a & b = rate constants (1/min)

Governing Equations and values

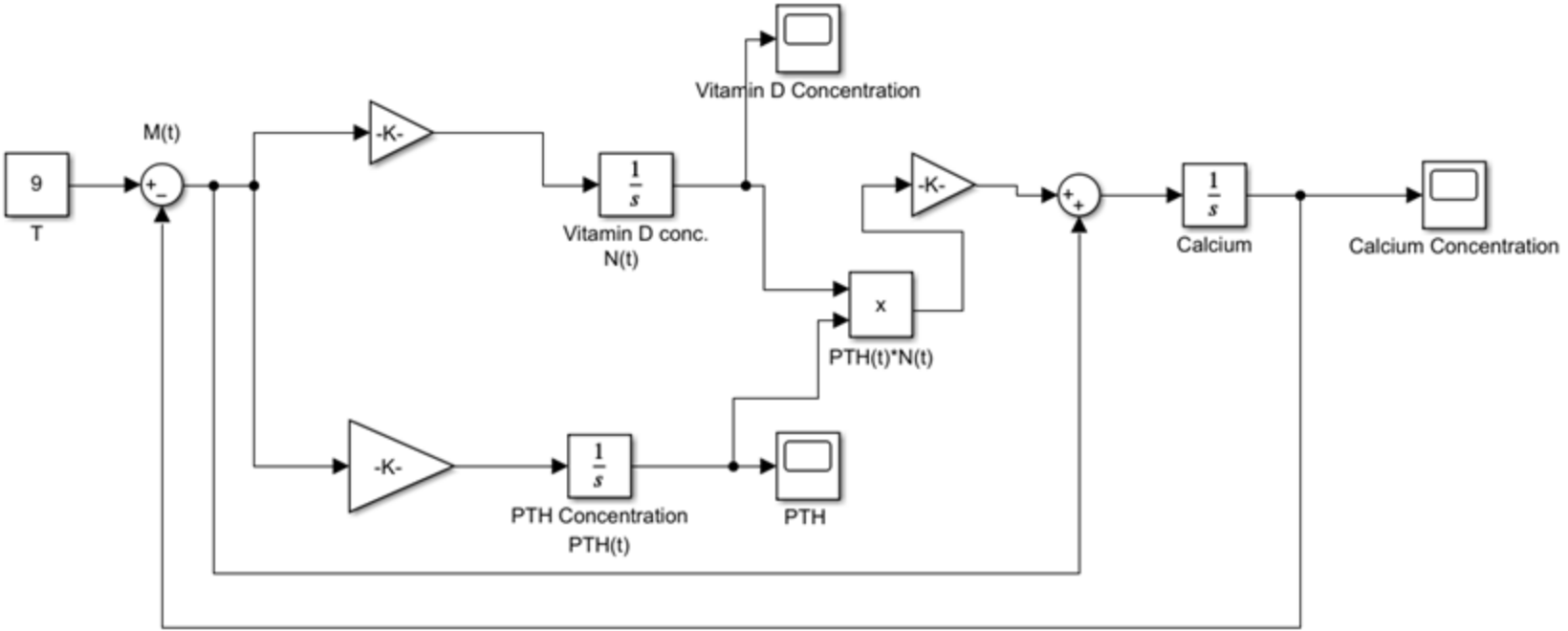
- $M(t) = K(T - C(t))$
- $\frac{dN(t)}{dt} = aM(t)$
- $\frac{dPTH(t)}{dt} = -bM(t)$
- $\frac{dC(t)}{dt} = K \cdot PTH(t) \cdot N(t) + M(t)$

Parameter	Value	Units
T	9	mg/dL
K	0.0001	dL/min
a	0.000001	1/min
b	-0.000001	1/min

General Model of Hypocalcemia



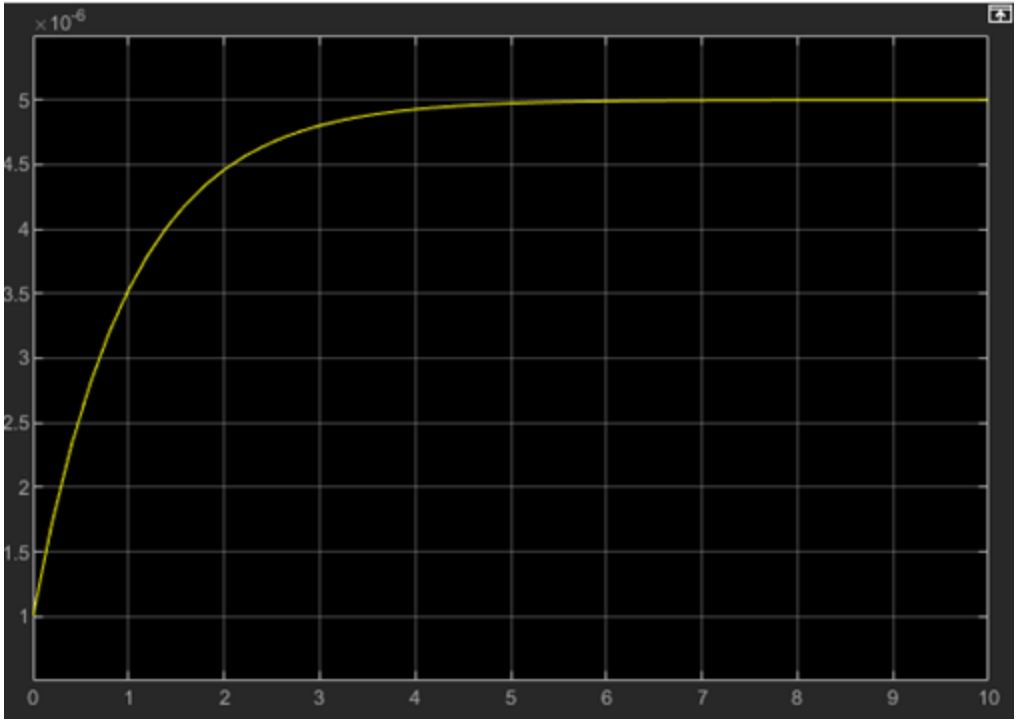
Simulink Model of Hypocalcemia



Vitamin D concentration

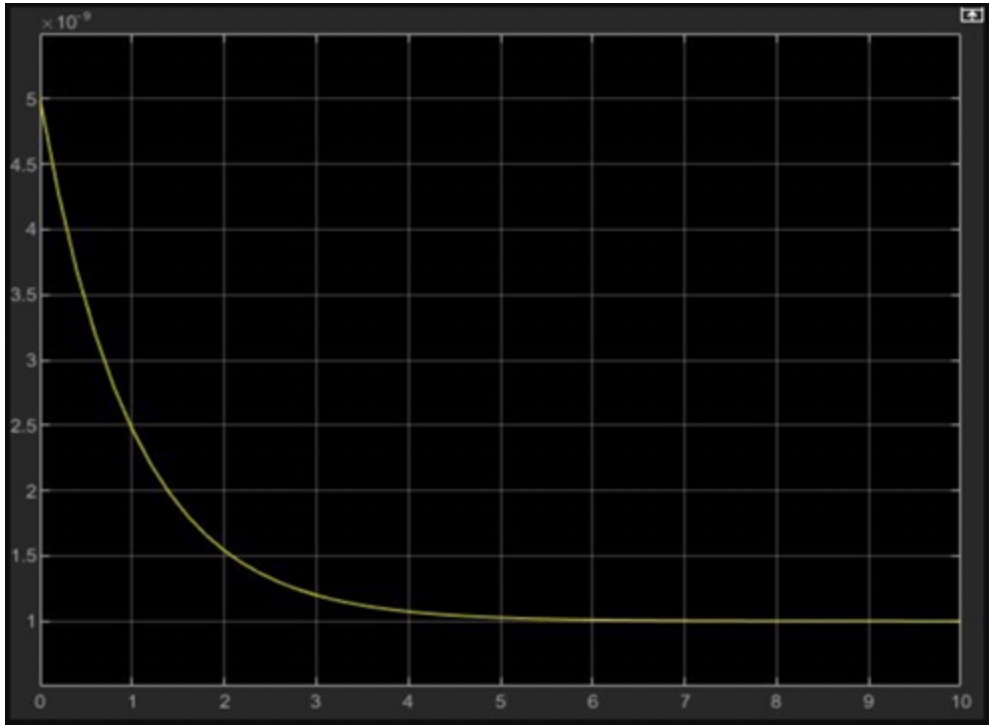
$$M(t) = K(T - C(t))$$

$$\frac{dN(t)}{dt} = aM(t)$$



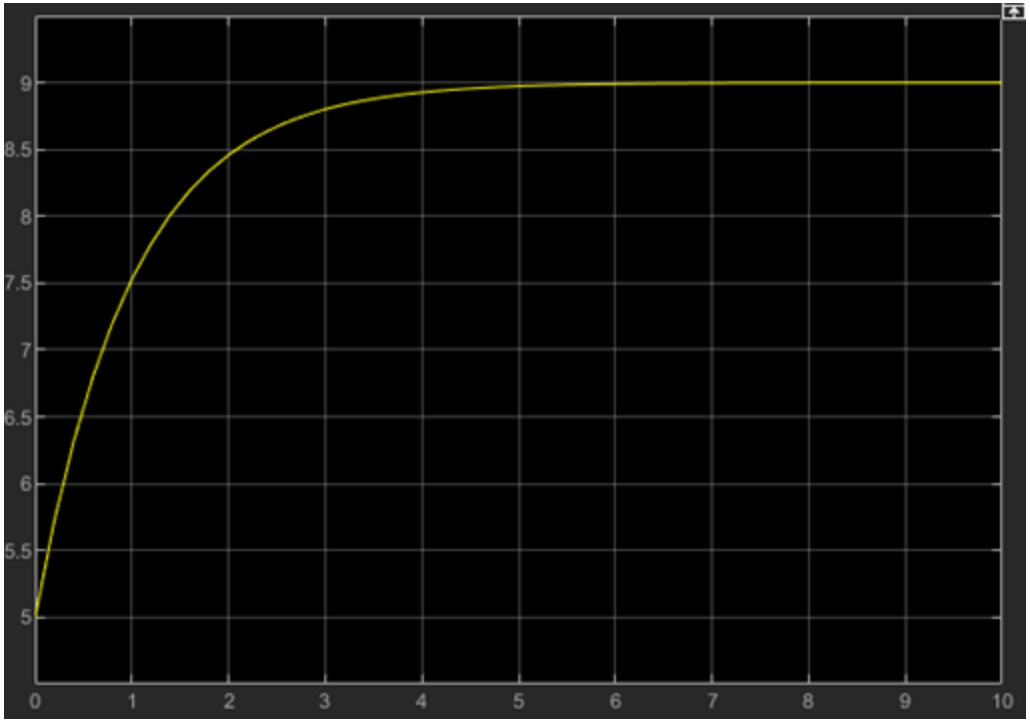
PTH Concentration

$$\frac{dPTH(t)}{dt} = -bM(t)$$



Calcium Concentration

$$\frac{dC(t)}{dt} = K \cdot PTH(t) \cdot N(t) + M(t)$$



Biosystem Transfer Function

$$M(s) = \frac{kT}{s} - kC(s)$$

$$sN(s) - N(0) = aM(s)$$

$$\frac{sN(s) - N(0)}{a} = M(s)$$

$$sPTH(s) - PTH(0) = -bM(s)$$

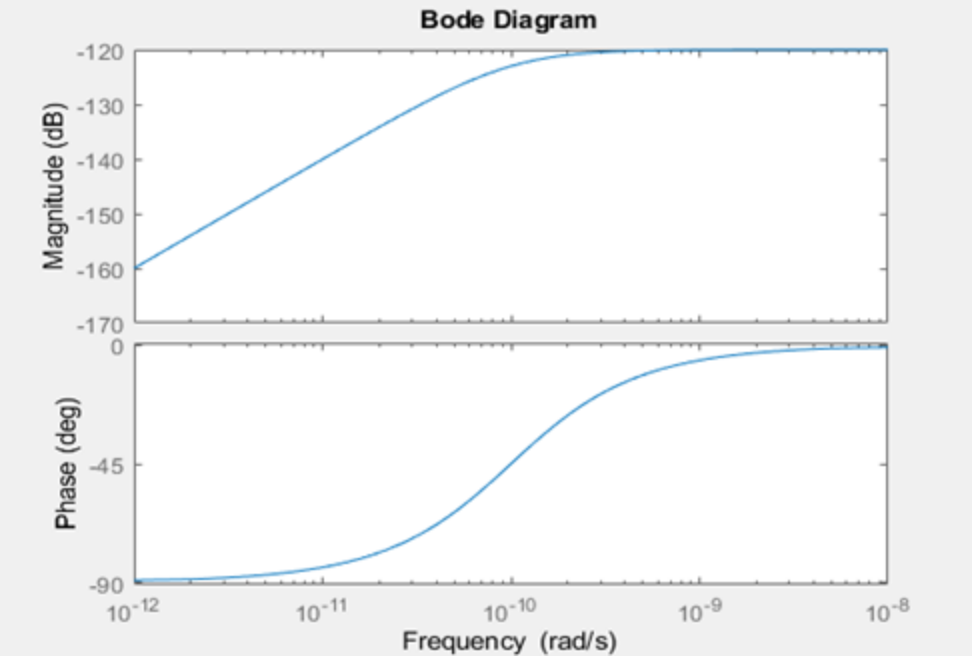
$$sC(s) - C(0) = kPTH(s)N(s) + M(s)$$

Assuming,
N(0) <<< 0
C(0) <<< 0
PTH(0) = 0.000005 <<< 0

$$C(s) = \frac{-kbN(s)}{sa} + \frac{N(s)}{a}$$

$$H(s) = a\left(\frac{s}{s - kb}\right)$$

Bode Plot


Bode Diagram
Magnitude (dB)
-120
-130
-140
-150
-160
-170
Phase (deg)
0
-45
-90
10^{-12}
10^{-11}
10^{-10}
10^{-9}
10^{-8}
Frequency (rad/s)

Advantages and Limitations of our Model

Advantages

- Allows for a variety of inputs, at various simulated concentrations of hypocalcemic systems.
- System parameters may be manipulated to account for differences between patients.

Limitations

- Each hormone interacts with systems outside this pool so simulations are constrained to relevant hormone interactions.
- Parameters could vary from different patients.
- Time delays are not optimal, so simulations based on the assumptions are constrained.
- Biological systems are often nonlinear, it's hard to predict their behavior using linear models alone.

Thank you!