Metabolic Control of Body Temperature via Thyroid Hormones

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By: Andrew Harris, Jacinda Martinez, Michael Megally, Riya Varma, Iris Zaretzki

Background (Thyroid Physiology)

- Thyroid is activated by the Anterior Pituitary and response for the release of Thyroid Hormone
  - Tetraiodothyronine (T4)
  - Triiodothyronine (T3)
- Releases Thyroid Hormones into the bloodstream attached to transport proteins
- T4 is converted into T3 in target tissues
- One function of the Thyroid is the regulation of metabolism, and by extension body temperature

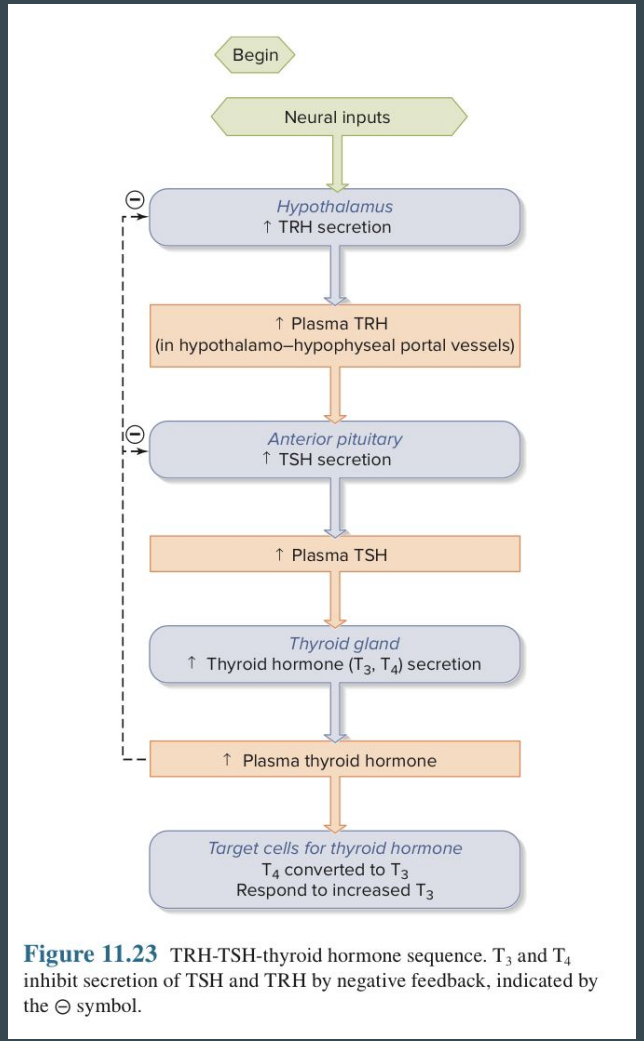


Figure 11.23 TRH-TSH-thyroid hormone sequence. T_3 and T_4 inhibit secretion of TSH and TRH by negative feedback, indicated by the ⊖ symbol.

Scope of Project / Thermoregulation / Metabolism

- Thermoregulation of the body by the thyroid gland
- Thyroid hormone binds to the receptors of the target cells → activates genes for increasing metabolism/thermogenesis (heat production) → increased consumption of oxygen and energy
- Thyroid hormone increases the basal metabolic rate
- Increased thyroid function → body temperature rises.

Equations

(1) $\frac{dT_3}{dt} = k_f\left[\frac{1}{3}T_4\right] + \alpha_3 e^{\beta_3/T_3} - \gamma_3 T_3$

(2) $\frac{dT_4}{dt} = \alpha_4 e^{\beta_4/T_4} - \gamma_4 T_4$

(3) $H_c \frac{dT_{body}}{dt} = f(t) - k(T_{body} - T_{environment}) + b\left(\frac{dT_3}{dt} + a\right)$

(4) $f(t) = k_d \frac{d}{dt}(e(t)) + k_p e(t) + k_i \int e(t)dt$

(5) $e(t) = T_{body} - T_{target}$

Assumptions for the Model

- Not modeling the role of TRH/TSH in T3/T4 production
- Single direction view on thyroid hormone-temperature relationship
- Linearization assumes we are only operating w/i a small range for thyroid concentrations
- Constants
  - Not much data on Thyroid-temperature relationship
  - b [sensitivity to T3] was based on the correlation between this temperature-thyroid
  - Hc estimated for a person of 70kg, and skin specific heat of 3.6 kJ/(kg*K)

Linearized Equations

$$(6)\ \frac{d\widetilde{T_3}}{dt} = \left(-\gamma_3 + \frac{\alpha_3\beta_3}{\overline{T_3}^2} e^{\beta_3/\overline{T_3}}\right)\widetilde{T_3} + k_f\left[\frac{1}{3}\widetilde{T_4}\right]$$

$$(7)\ \frac{d\widetilde{T_4}}{dt} = \left(-\gamma_4 + \frac{\alpha_4\beta_4}{\overline{T_4}^2} e^{\beta_4/\overline{T_4}}\right)\widetilde{T_4}$$

Transfer function

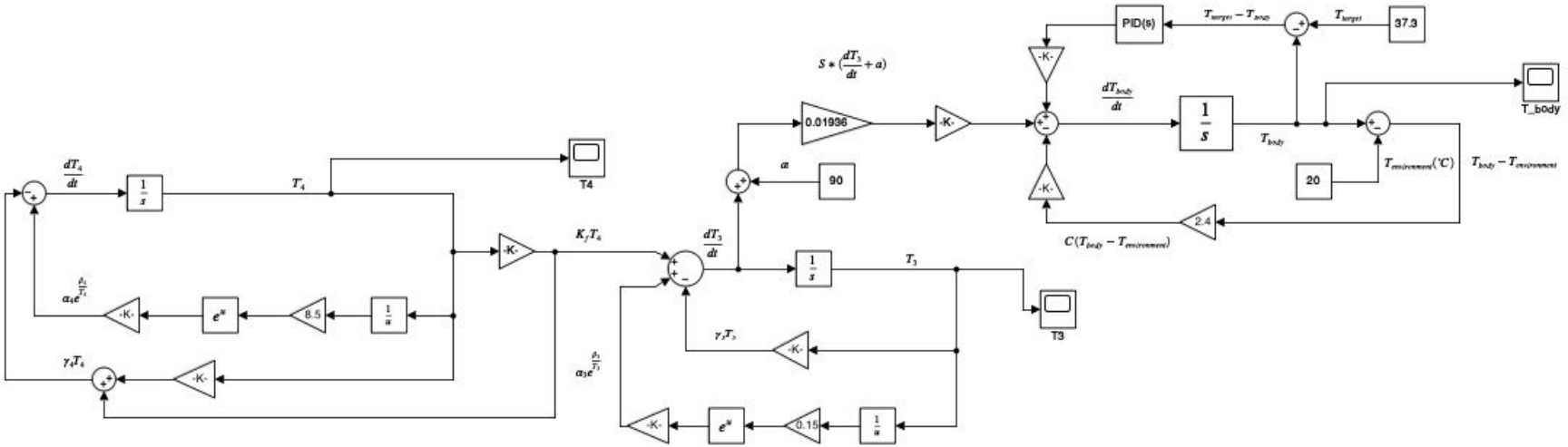
$$H(s) = \frac{T_{body}(s)}{T_3(s)} = \frac{N(s)}{D(s) * T_3(s)}$$

$$N(s) = \left[T_{target}\left(K_d s^2 + k_p s + K_i\right) + ab + kT_{environment}\right] * (A - B)(s - B)(s - A) + bs^2[C * C_1 * (s - B) + k_1(A - B)(s - A)]$$

$$D(s) * T_3(s) = [k_1(A - B) * (s - A) + C_1 * C * (s - B)][s^2(K_d + H_c) + s\left(K_p - k\right) + K_i]$$

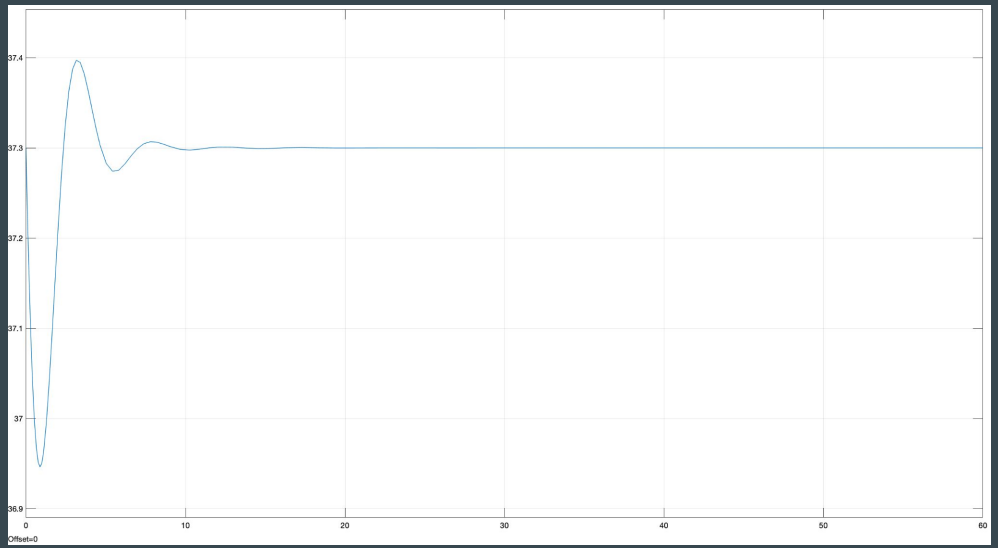
$$\mathrm{A} = \left(-\gamma_4 + \frac{\alpha_4 \beta_4}{\overline{\mathrm{T}_4}^2} \mathrm{e}^{\beta_4 / \overline{\mathrm{T}_4}}\right) \qquad B = \left(-\gamma_3 + \frac{\alpha_3 \beta_3}{\overline{\mathrm{T}_3}^2} \mathrm{e}^{\beta_3 / \overline{\mathrm{T}_3}}\right) \qquad \mathrm{C} = \frac{1}{3} \mathrm{k_f}$$

Block Diagram

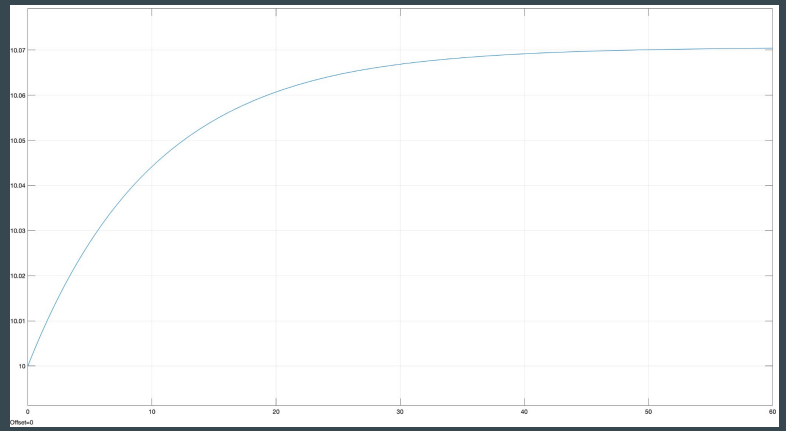


Simulink Response: Low T_3

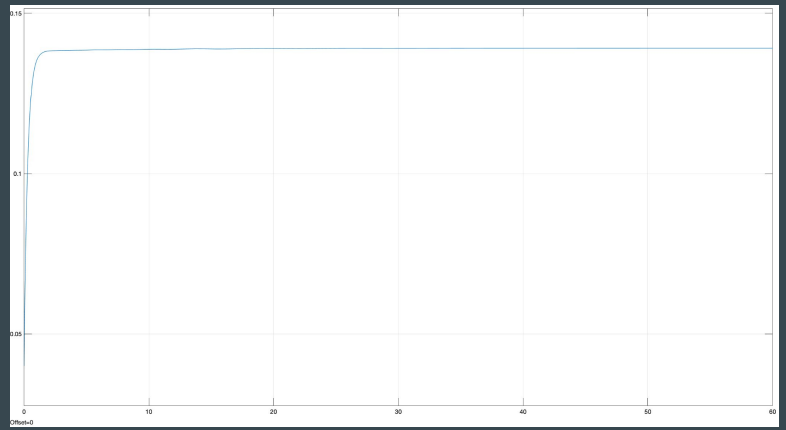
dT_body/dt



dT4/dt

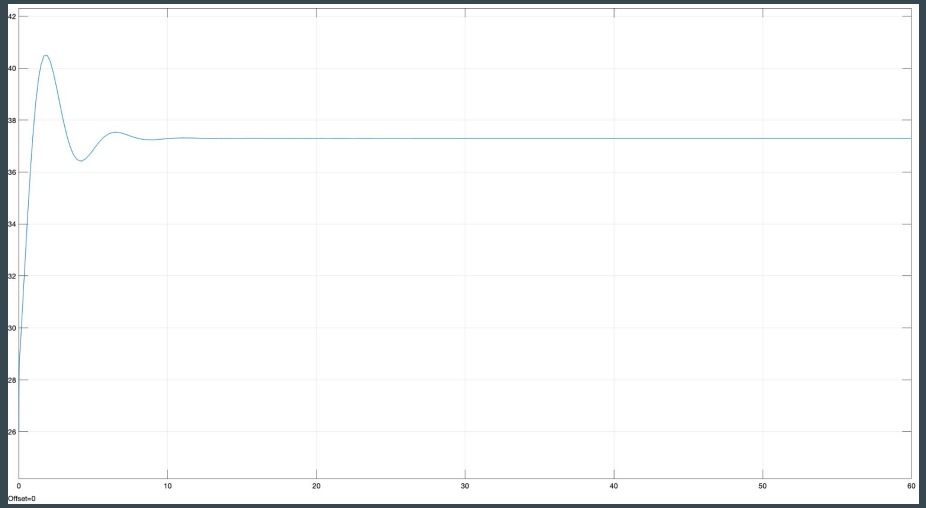


dT3/dt

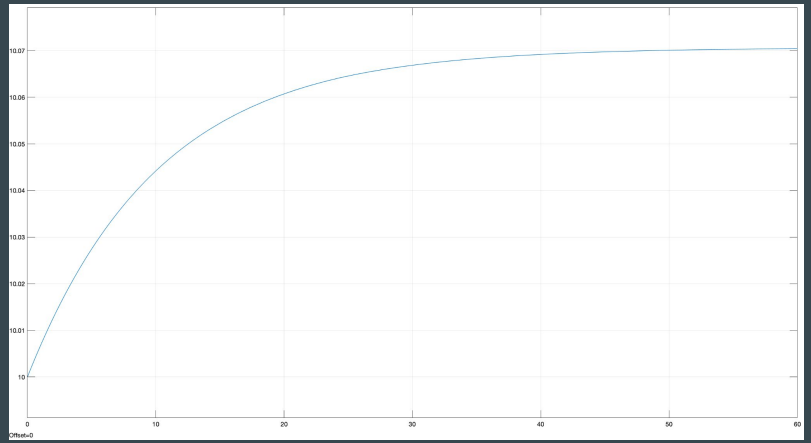


Simulink Responses: Low Body Temperature

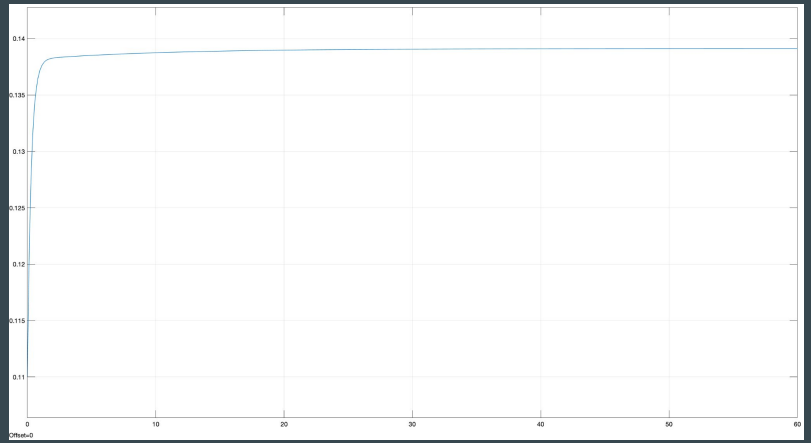
dT_body/dt



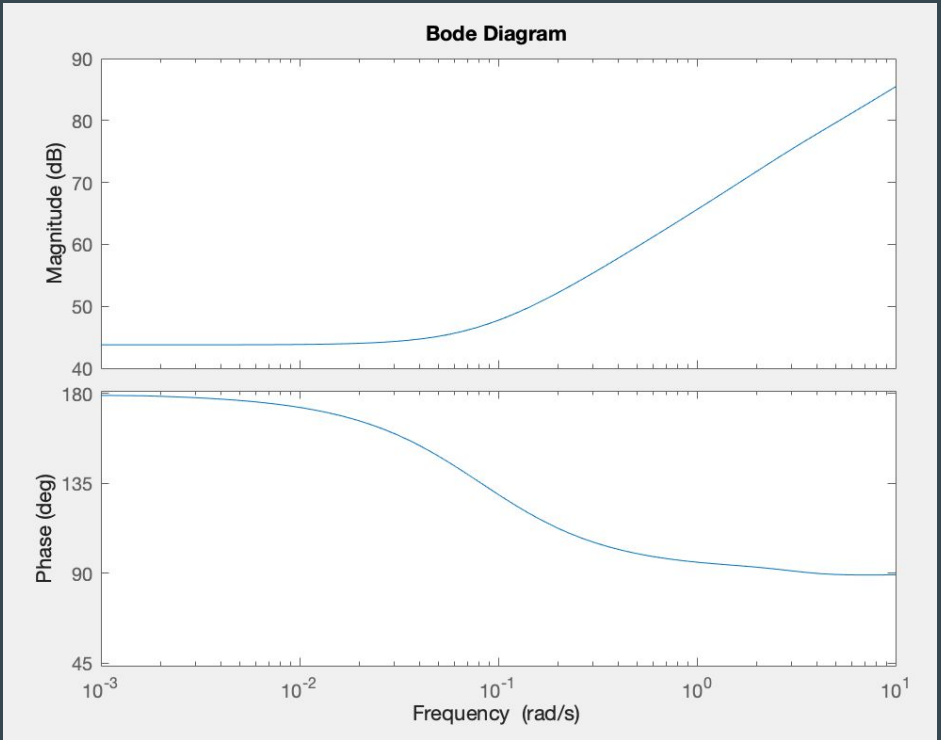
dT4/dt

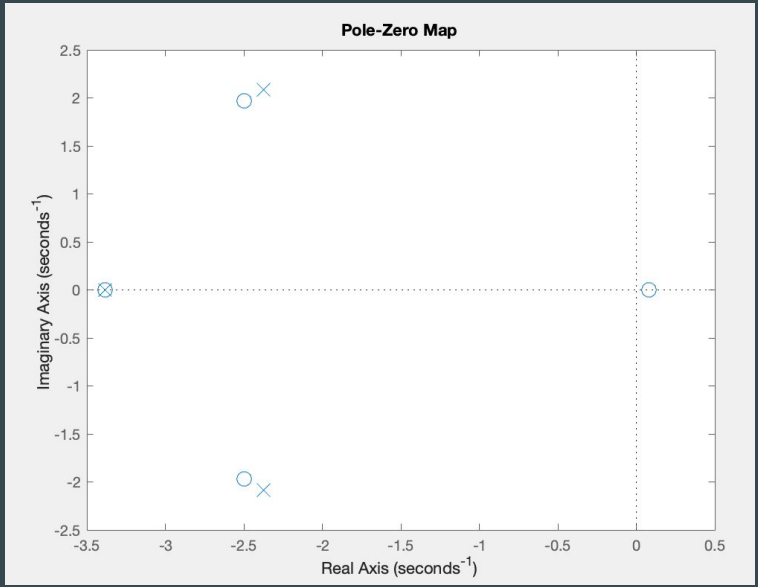


dT3/dt



Bode Plots





LHP: 2 complex zeros & 2 complex poles

RHP: 1 real zero

- Effect is similar to that of a single zero response
- Losing information during linearization and transfer function derivations

Improvements and Future Directions

Improvements

- Account for more drastic changes in environmental temperature
- More supporting literature for constant values
- Add bi-directional relationship between Thyroid-Body temperature

Future Work:

- Disease and treatment models
- Look at different time scales (Thyroid impact over days, change PID to have less contributions for this scale)

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Thank You!

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