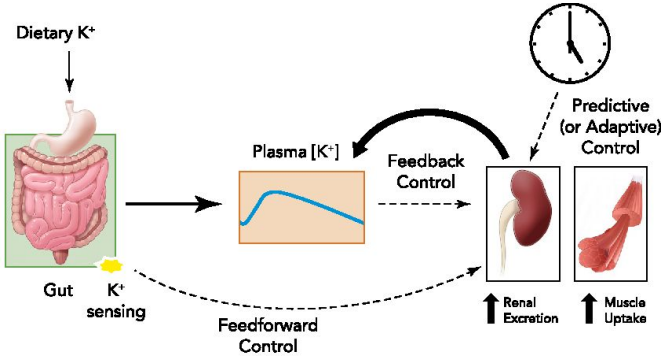
Potassium Homeostasis

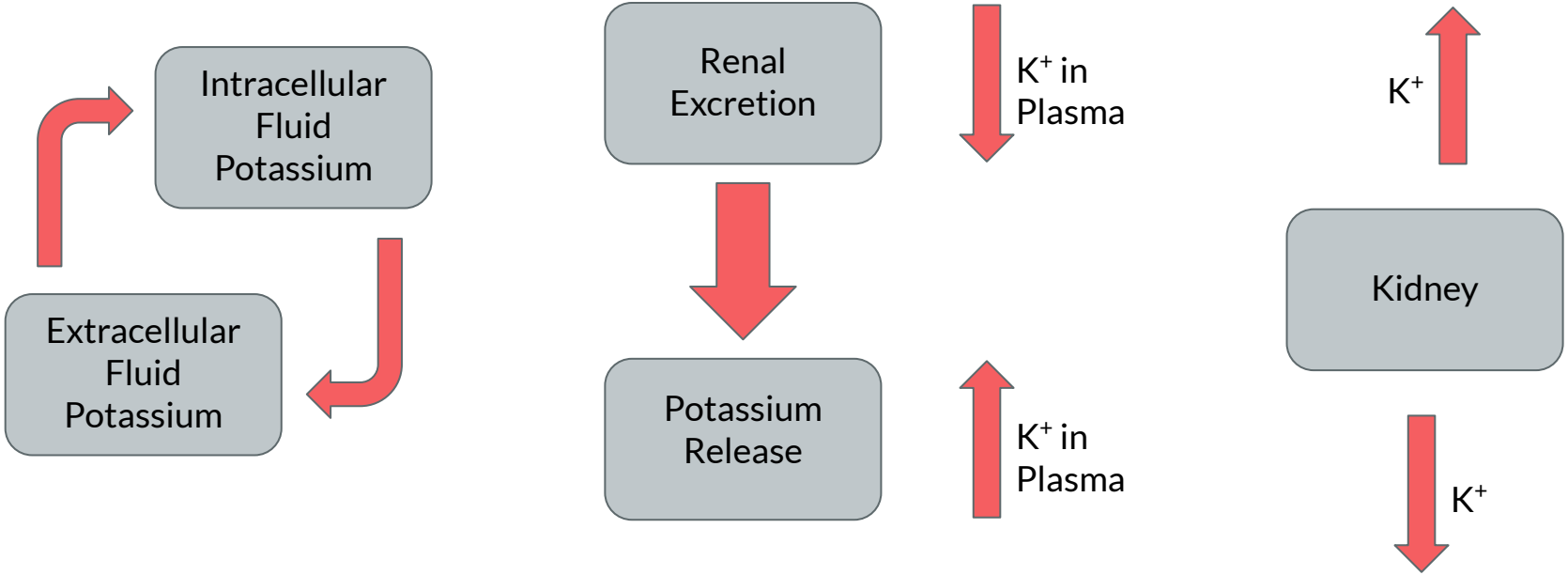
Trisha Ahuja, Benjamin Balster, Andrew Nguyen, Kaitlyn Strandberg, and Tyler Tran

Background



- **Potassium** is one of the most abundant ions in the body
  - Critical for cellular function (and other processes)
  - Main source of potassium intake is through food. (gastrointestinal tract)
  - < 2% of whole body potassium is found in the extracellular fluid (ECF)
- Maintaining ECF to ICF potassium ratio is essential for body homeostasis
  - This is seen through the sodium-potassium ATPase pump, which keeps [K+] in the ICF & ECF balanced
  - Improper regulation of ECF K+ can lead to severe medical conditions
- Potassium is mainly excreted through urine, and in smaller amounts through sweat and stool

Regulation of Potassium Concentration



Clinical Relevance

Hyperkalemia (increased potassium concentration in the blood) - ECF [K+] > 5.0 mEq/L

- Decreases membrane potential
- Disruption of heart electrical conduction (cardiac arrhythmias)
- Can result from:
  - Potassium intake overwhelming kidney's ability to excrete potassium
  - Decrease in renal function
  - Massive tissue breakdown (rhabdomyolysis)
  - Endocrine system disorders (hyperaldosteronism)
- Diabetes is an independent predictor of hyperkalemia (Goia-Nishide K et. al.)
  - Impaired potassium excretion
  - Impaired renal tubular function
  - Reduced uptake of potassium into cells
- Direct negative effect on acid-base homeostasis

Hyperkalemia ECG and Action Potential Response

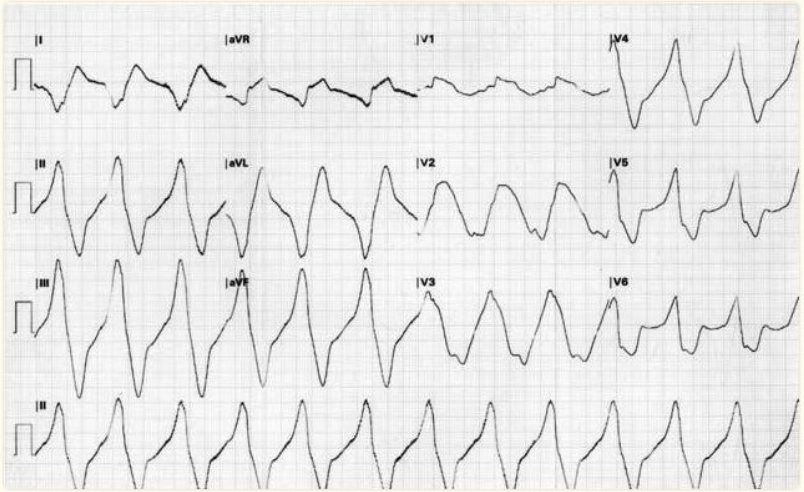
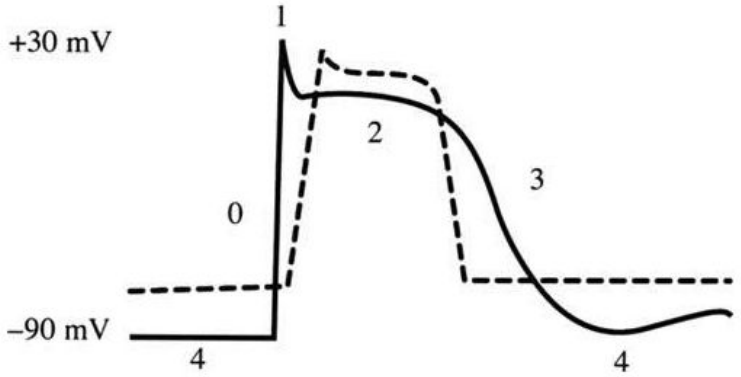


Fig. 1 Admission electrocardiogram.

Source: Parham WA et. al.



Action Potentials:

- **Normal:** Solid Line
- **Hyperkalemia:** Dashed Line

Clinical Relevance Continued

Hypokalemia (decreased potassium concentration in the blood) - ECF [K+] < 2.5mEq/L

- Hyperpolarization and non-responsiveness of cellular membrane
- Disruption of heart electrical conduction (cardiac arrhythmias)
- Can result from:
  - Decreased potassium intake
  - Excessive loss of potassium in urine
    - Diuretic drug use
  - Endocrine system disorders (hyperaldosteronism)
  - Negatively affected renal function
  - Large gastrointestinal loss of potassium
  - Intracellular shift of potassium
- Muscle weakness or ascending paralysis
- Direct negative effect on acid-base homeostasis

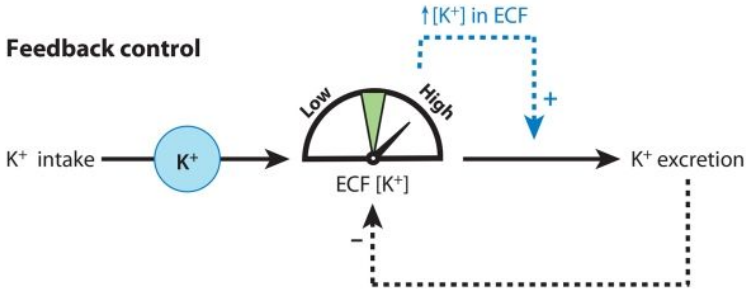
Problem Statement and Model Objectives

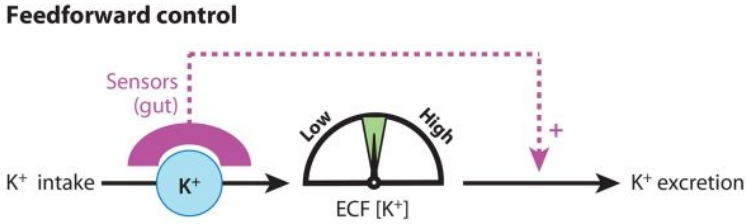
Problem Statement: Complex whole body homeostasis relies significantly on the 2% of bodily potassium that is found in the extracellular fluid to be controlled in order to prevent the adverse effects of hyperkalemia and hypokalemia.

Model Objectives:

1. Model homeostasis of potassium concentration in the extracellular fluid in Simulink and simulate biological responses.
2. Model is capable of showing biologically accurate responses to hyperkalemic and hypokalemic extracellular fluid potassium concentrations.
3. Model possesses both feedback and feedforward control mechanisms.

Feedback vs Feedforward Control





- **Feedback control:**
  - A rise in extracellular fluid (ECF) potassium initiates the stimulation of potassium excretion by the kidney
  - Rise in excretion of potassium brings ECF potassium down to normal levels again

- **Feedforward control:**
  - Localized increase in potassium in the gut initiates an independent potassium excretion by the kidney
  - The potassium excretion in the kidney starts to occur before the potassium in the ECF rises

Assumptions

1. Potassium intake/input is through absorption of the gut
2. Potassium flows out of the body through waste in the gut and kidneys
    a. Stool loss (potassium lost in the gut) is proportional to the potassium intake
3. A majority of the intracellular potassium concentration is found in the muscle cells (ignoring nonmuscle cells)
4. Distribution of potassium between the ICF and ECF are symmetric

Governing Equations & Parameters

Governing Equations:

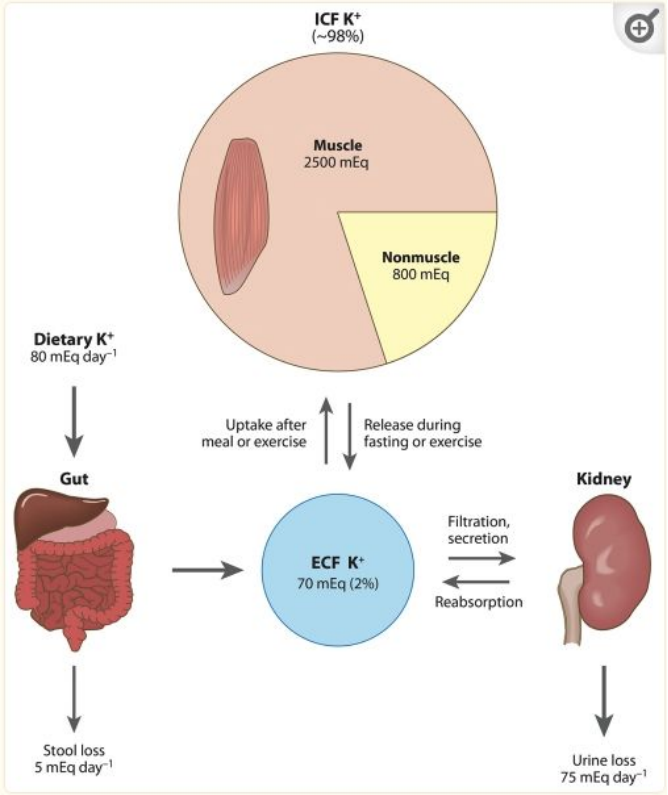
- **Gut:** $dG/dt = f(t) - [5\% \text{ of Potassium Intake in Stool Loss}]$
- **Bloodstream (ECF):** $dE/dt = \Gamma G(t) - Ki(t) + \alpha(I(t)-E(t))$
- **Muscle Cells (ICF):** $dI/dt = \alpha(E(t)-I(t))$
- **Kidneys:** $dKi/dt = K_p e(t) + K_i \int e(t) + K_d e'(t) + K_{ff} d$

Error: $e(t) = E(t)-T$

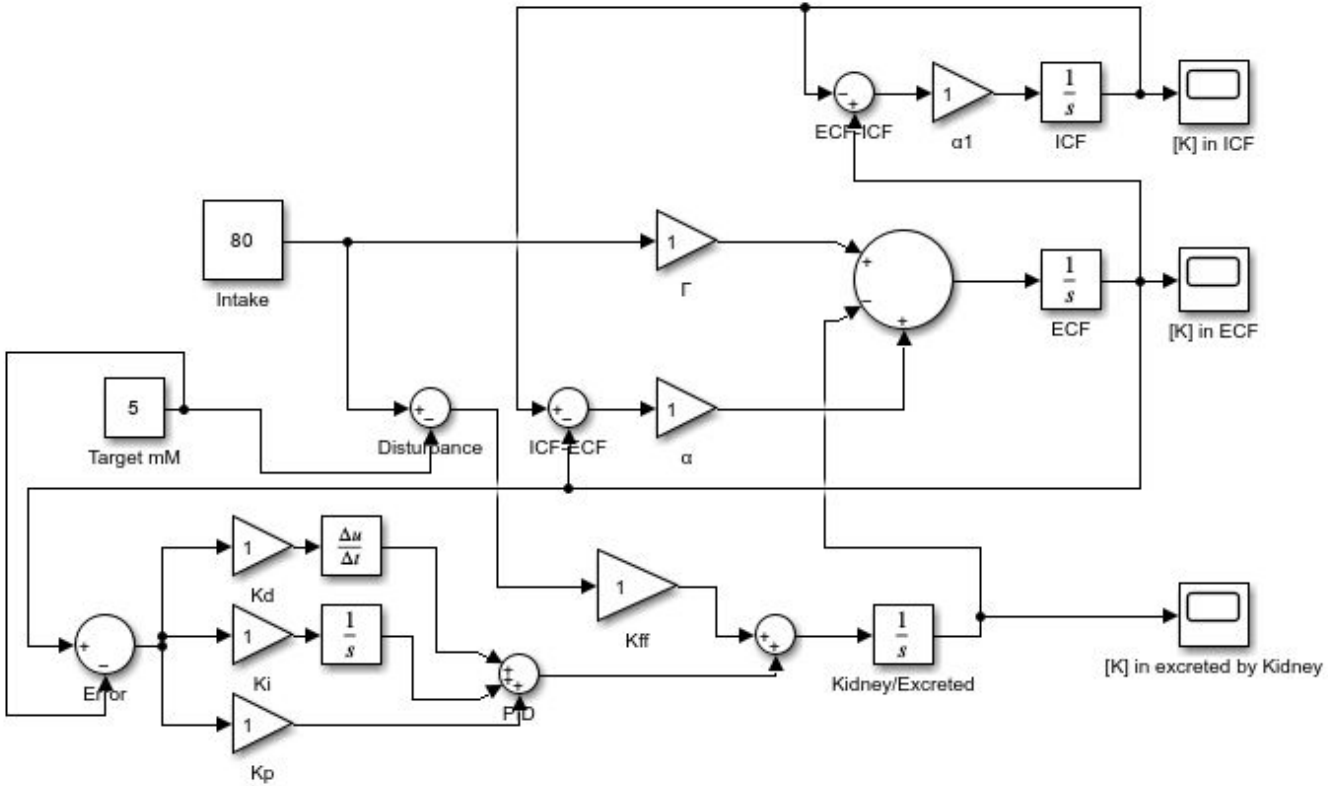
Disturbance: $d(t) = f(t)-T$

Parameters:

α: redistribution of [K+] between ICF and ECF
T: normal [K+] in the bloodstream, ~3.8–5mM
Γ: absorption of [K+] from the gut into the bloodstream/ECF
K_{ff}: feedforward parameter when gut senses intake of [K+]



Simulink Model



Future Directions

- By testing the model and determining control parameters that yield biologically similar responses, we can make inferences regarding the possible mechanisms and pathways in the body exist to control Potassium levels
- Comparing the control parameters can provide insight into what is most important in regulation Potassium concentration
- Analyze the response to a more realistic change in extracellular potassium concentration, such as after eating a meal

Citations

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