Mathematical Modeling in the Kidney: Characterizing a Long-Looped Nephron

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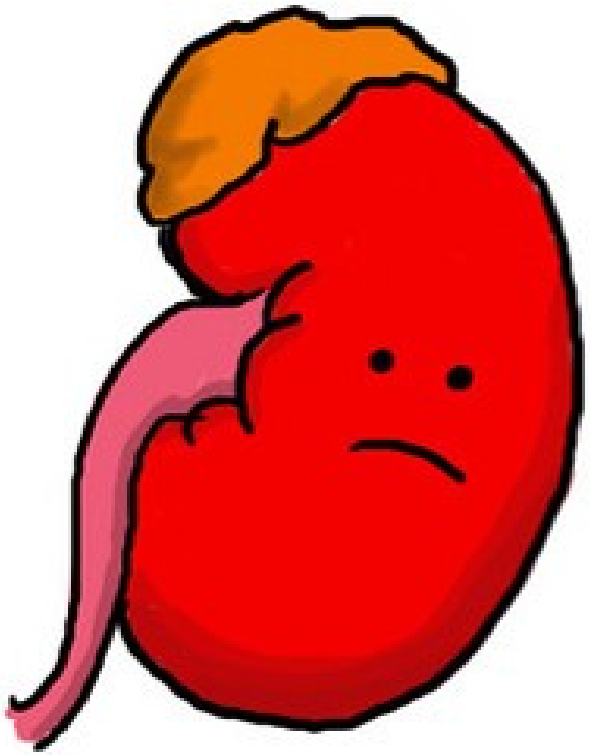
What is this "Kidney" you speak of?

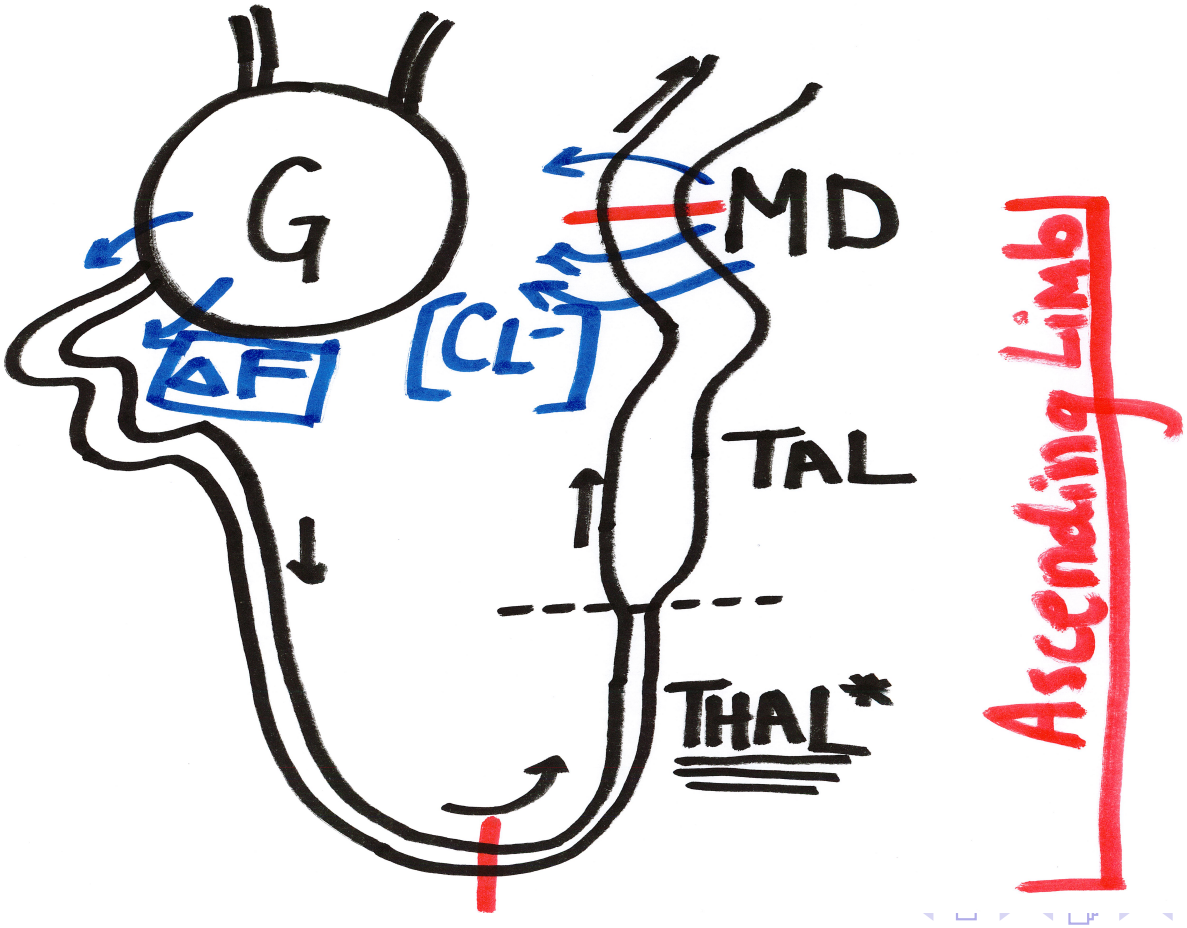
- Production of urine
- Functional unit: Nephron
- Nephron $\rightarrow$ Kidney as the Neuron $\rightarrow$ Brain



I make pee...

Structure of the Long-Looped Nephron

G : Glomerulus, **THAL** : Thin Ascending Limb, **TAL** : Thick Ascending Limb, **MD** : Macula Densa



Tubuloglomerular Feedback (TGF) System

Purpose

- Regulate chloride concentration

Key Features of Long-Looped Model

- Long-looped nephrons $\rightarrow$ slightly higher concentrated urine
- Thin ascending limb (THAL)

That's riveting, but where's the math?

Mathematical Analysis

- Partial Differential Model of Long-Looped Nephron
- Simplify PDE $\rightarrow$ ODE
- Bifurcation Analysis of the TGF System

Key Parameters of Analysis

- **Delay** : TGF time delay (τ)
- **Gain** : TGF sensitivity to signal (γ)

Chloride and Flow Rate Model Equations

C : Chloride Concentration, F : Fluid Flow Rate
R : Tubular Radius, P : Permiability

$$\pi R^2(x)\frac{\partial}{\partial t}C(x,t) = -F(t)\frac{\partial}{\partial x}C(x,t)$$
$$-\pi R(x)\left(\frac{V_{\text{max}}(x)C(x,t))}{K_M + C(x,t)} + P(x)(C(x,t) - C_e(x))\right) \textbf{(Conservation)}$$

$$F(t) = 1 + K_1 \tanh(K_2(C_{\text{ss}} - C(1, t-\tau))) \textbf{(TGF Response)}$$

Derivation of the Characteristic Equation

Model equations for $C(x,t)$ and $F(t)$

$\Downarrow$

Nondimensionalization

$\Downarrow$

Linearization; $C(x,t) = S(x) + \epsilon D(x,t)$

$\Downarrow$

Seperation of Variables; $D(x,t) = f(x)\mathrm{e}^{\lambda \mathrm{t}}$

$\Downarrow$

Characteristic Equation

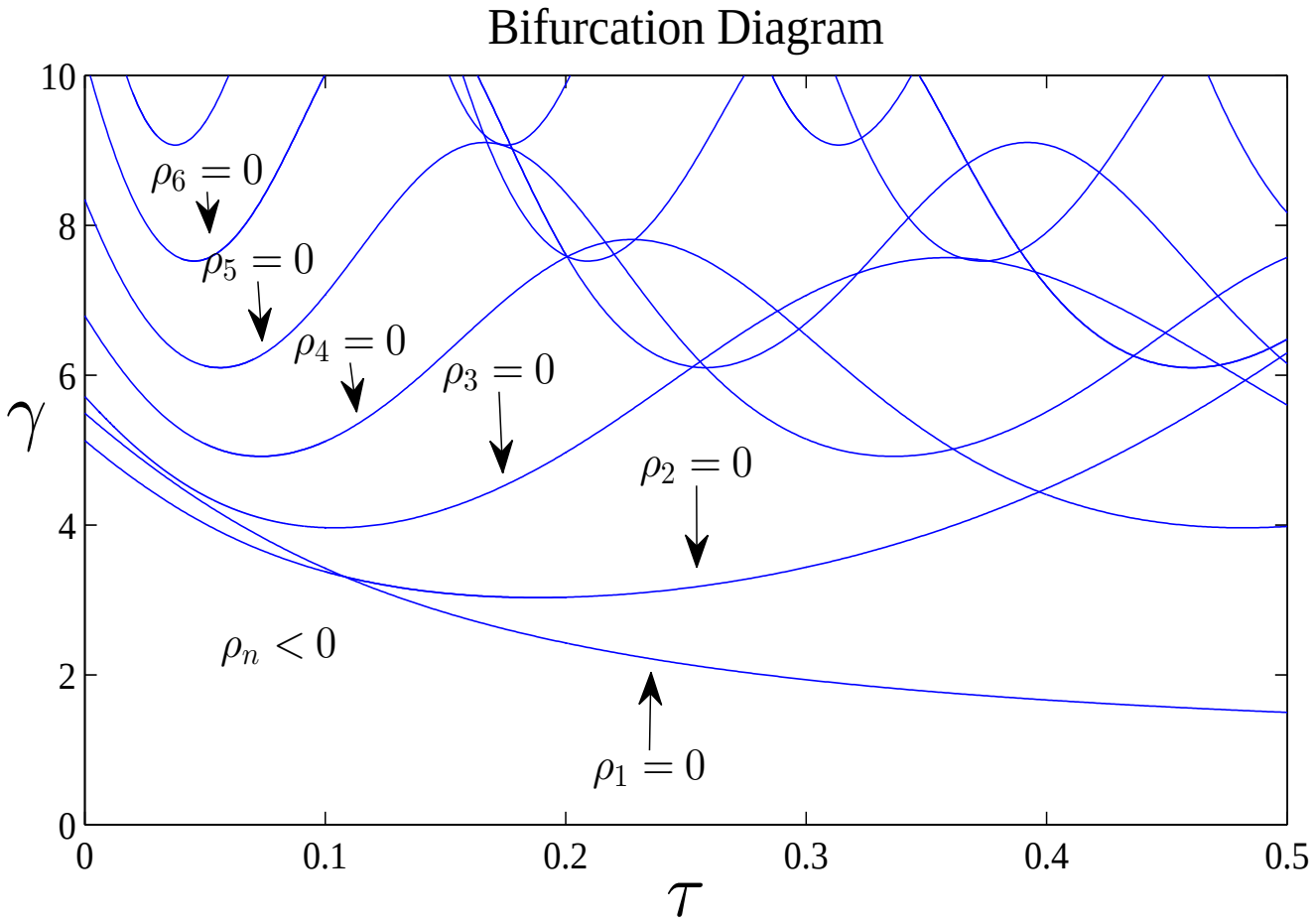
C : Chloride Concentration, R : Tubular Radius
S : Steady State Chloride Concentration, P : Permiability

$$1 = \frac{-\gamma e^{-\lambda\tau}}{R(1)} \int_0^1 R(x) \cdot exp\left(-\int_x^1 f(R, V'_{\text{max}}, S, P, C_e)\,\mathrm{d}y\right)\,\mathrm{d}x.$$

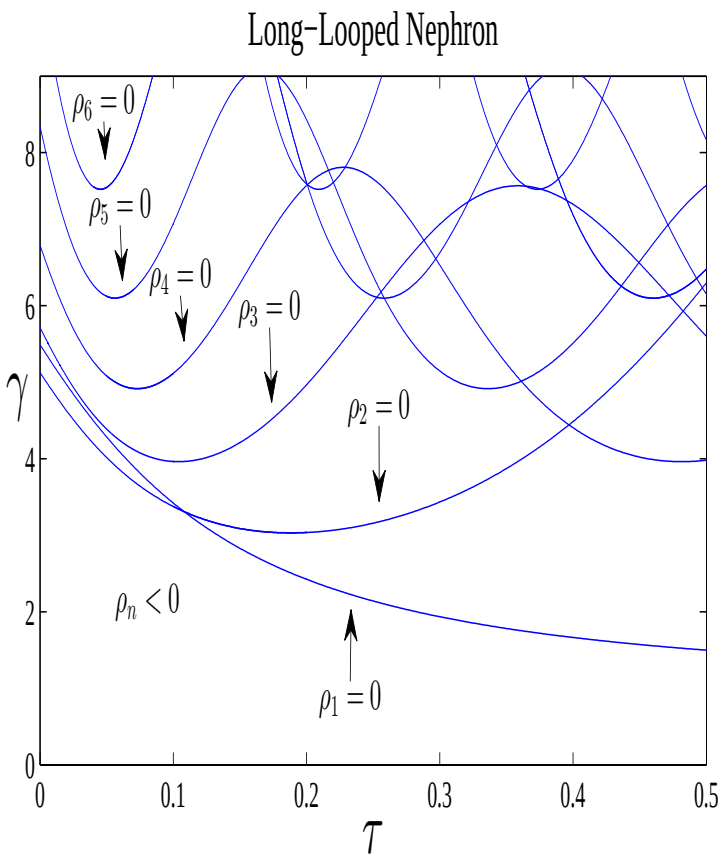
Key Parameters

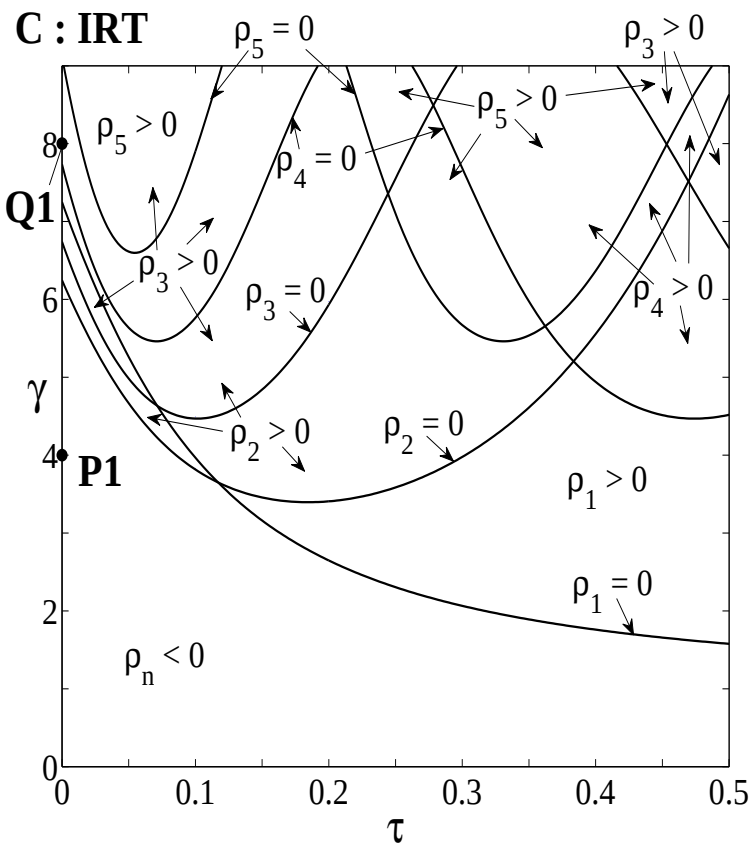
- **Delay** : Time (τ)
- **Gain** : Sensitivity (γ)
- **Solution Behavior** : $\lambda = \rho + i\omega$ ($\lambda \in \mathbb{C}$)
- **Real Part** : Growth/Decay (ρ)
- **Imaginary Part** : Frequency (ω)

Bifurcation Diagram or Rorschach Test?



Long-Loop vs. Short-Loop Bifurcation

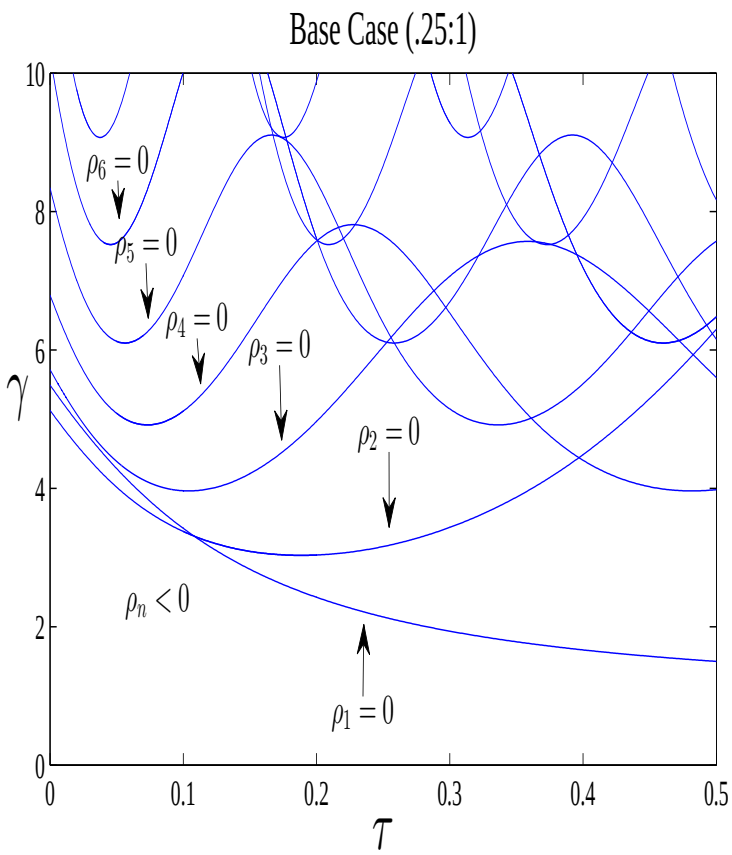


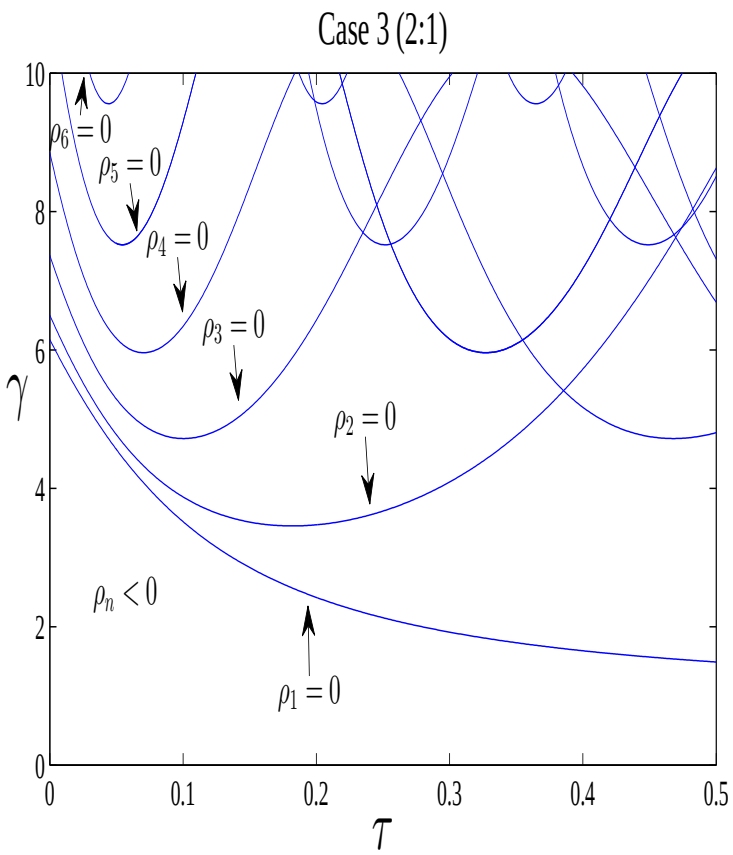


Varying Lengths of Model THAL

Case	THAL Length (cm)	TAL Length (cm)	Ratio
Base Case	0.125	0.5	.25:1
Case 1	0.25	0.5	.5:1
Case 2	0.5	0.5	1:1
Case 3	1.0	0.5	2:1

Bifurcation Variance in Model Cases





But what does it all mean?!

Bifurcation Analysis

- Higher tendency towards oscillatory solutions in Long Loop vs. Short Loop
- Within Long Loop, longer THAL $\implies$ more stable TGF system

What's Next?

- Numerical analysis of full model equations
- Verify bifurcation analysis results

Thank you!
Any Questions?

Slides and references are available upon request:

- *H. Ryu and A.T. Layton/ Math. Med. Biol. (2013)*