Wave Patterns and Their Application to Migraines

By: Erica Pursell, Chenxing Xie, Max Swartz, and Fan Zhang
Mentor: Ildar Gabitov

Overview

- Background Information
- The Model
- Results
- Future Work

Background

- Migraine
  - Throbbing pain in the head-usually on one side
  - Headache attacks associated with:
    - Nausea
    - Vomiting
    - Sensitivity to light, sound, and even movement
  - Two Types of Migraine:
    - Migraines with aura (MA)
    - Migraines without aura (MO)

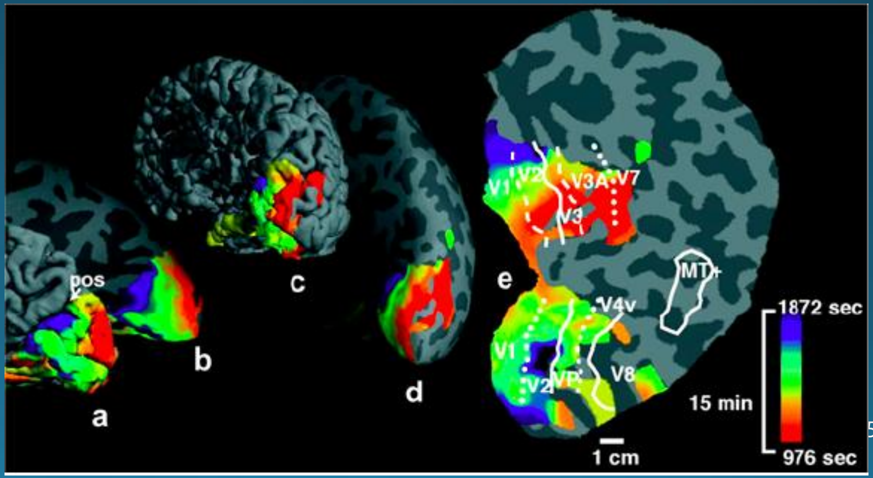
Migraines with Aura (MA)

- In addition to headache: Neurologic symptoms including visual hallucinations
- If SD occurs in MO, physiological phenomena last less than 5 minutes
- Because of short duration of time: Noninvasive imaging is difficult if SD stays silent (clinical symptoms not present).

Spreading Depression (SD)

- A massive but temporary perturbation of ion homeostasis due to seizure-like discharges of neurons.

- Cause the neurological migraine aura symptoms, like visual hallucinations
- Induces hyperemia (increased blood flow) to unaffected area-lowers risk of being effected by SD



The Model

- u is the activator value
- v is the inhibitor value
- t is time
- u_{sat} is the activator saturation value
- D is the diffusion constant
- ε is the time separation constant
- α is the inhibitor scaling coefficient
- β is an initial inhibitor state

NOTE: The activator and inhibitor values model energy states; they do not actually model any physiological phenomena.

The Old Model

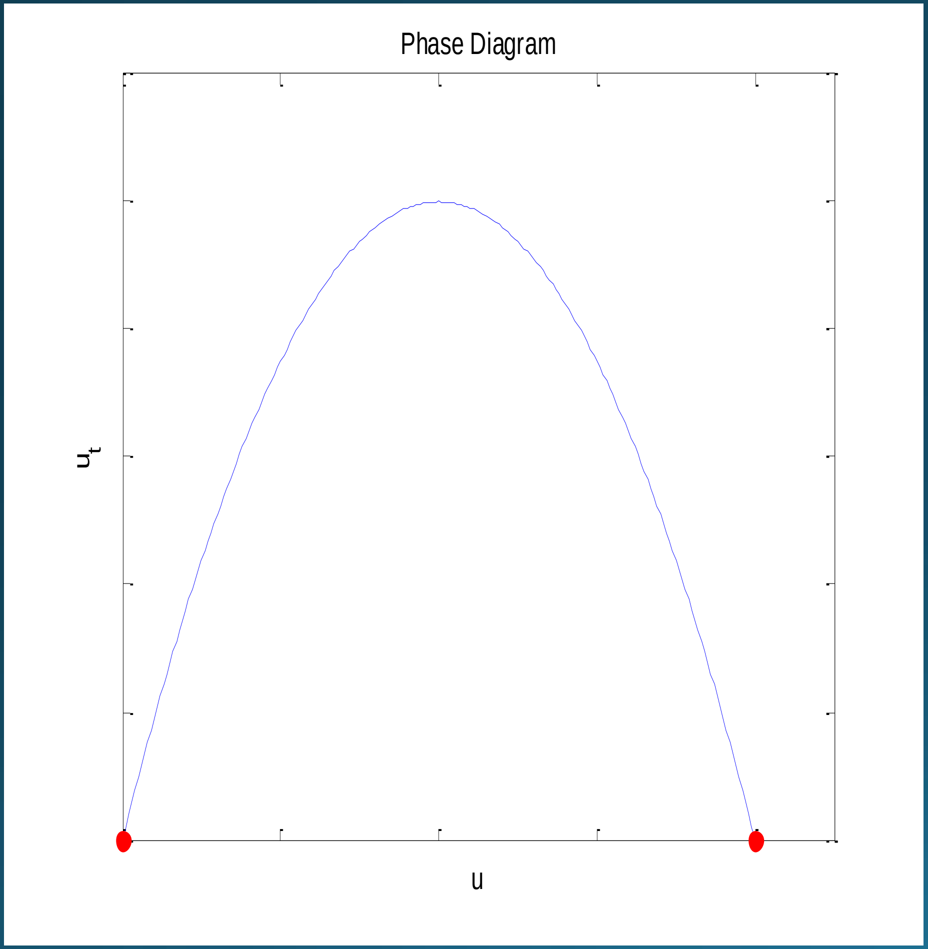
- Originally, the model was

$$\frac{\delta u}{\delta t} = u - \frac{u^3}{3} - v + D\nabla^2 u$$

$$\frac{\delta v}{\delta t} = \varepsilon(u - \beta_0 + K \iint H(u - u_o)\,dxdy)$$

- This model is ***BAD!***
- $\frac{\delta v}{\delta t} > 0$, so the value of v will always increase with respect to time (will not level off).
- u can become negative; this is not plausible.

The Old Model Phase Diagram



$$\frac{\delta u}{\delta t} = u - \frac{u^3}{3} - v$$

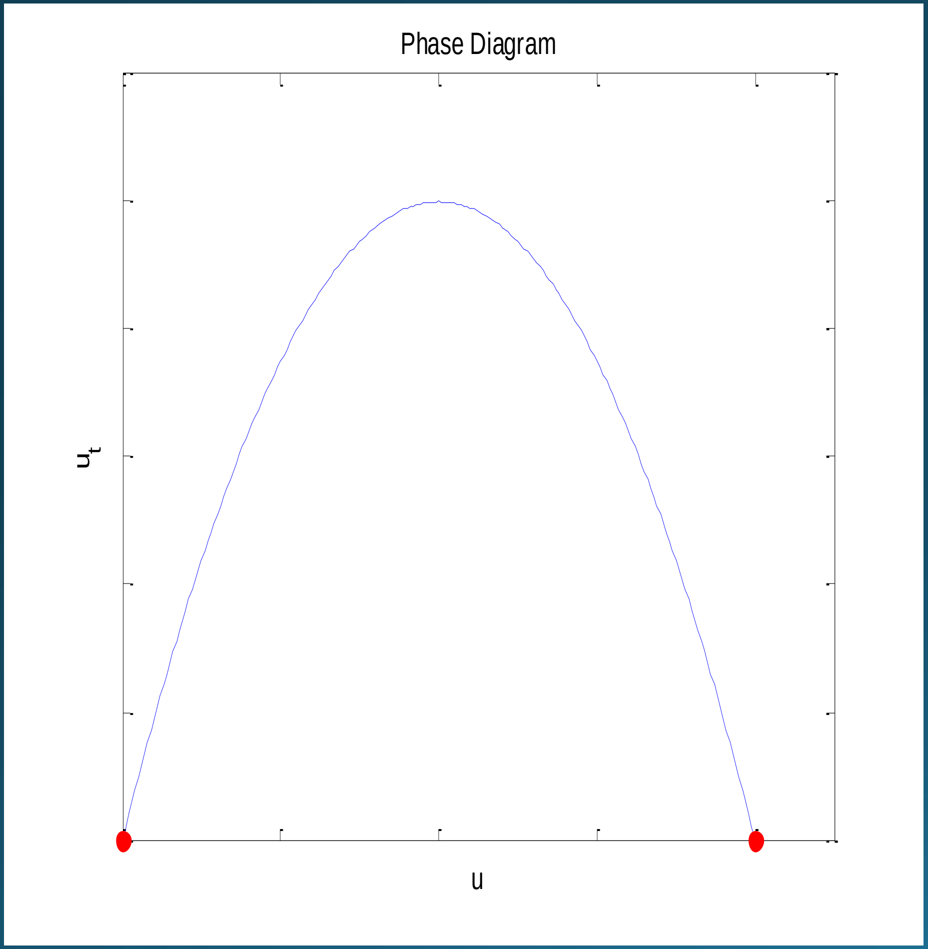
- For the activator equation, we have two transient nodes.
- The two nodes shift depending on the value of v.
- The node on the right needs to be transient; so far so good.
- The node on the left needs to be stationary; this is NOT the case.

The New Model

- $\frac{\delta u}{\delta t} = u\left(\frac{u_{sat}}{1+v} - u\right) + D\nabla^2 u$
- $\frac{\delta v}{\delta t} = \epsilon(u - \alpha v + \beta)$
- $\frac{\delta v}{\delta t}$ now has the $-\alpha v$ term; this allows $\frac{\delta v}{\delta t}$ to go to zero.
- u now more accurately represents the expected behavior of the activator level; it can no longer become negative.

Potential Problems: How accurately does this new model portray the oligemia phase of the spreading depression?

The New Model Phase Diagram



$$\frac{\delta u}{\delta t} = u\left(\frac{u_{sat}}{1+v} - u\right)$$

- The node on the right shifts to the left as v increases, and the node on the left is stationary.
- This yields the desired behavior.

The Inhibitor Equation

- $\frac{\delta v}{\delta t} = \epsilon(u - \alpha v + \beta)$ is solvable.
- Assuming an initial condition of $v(0) = 0$:

$$v(t) = \frac{\beta}{\alpha}(1 - e^{-\epsilon\alpha t}) + \epsilon e^{-\epsilon\alpha t}\int u(t)e^{\epsilon\alpha t}dt$$

- Thus, $v(t)$ has the potential to level out (However, it cannot become negative, which is reasonable).

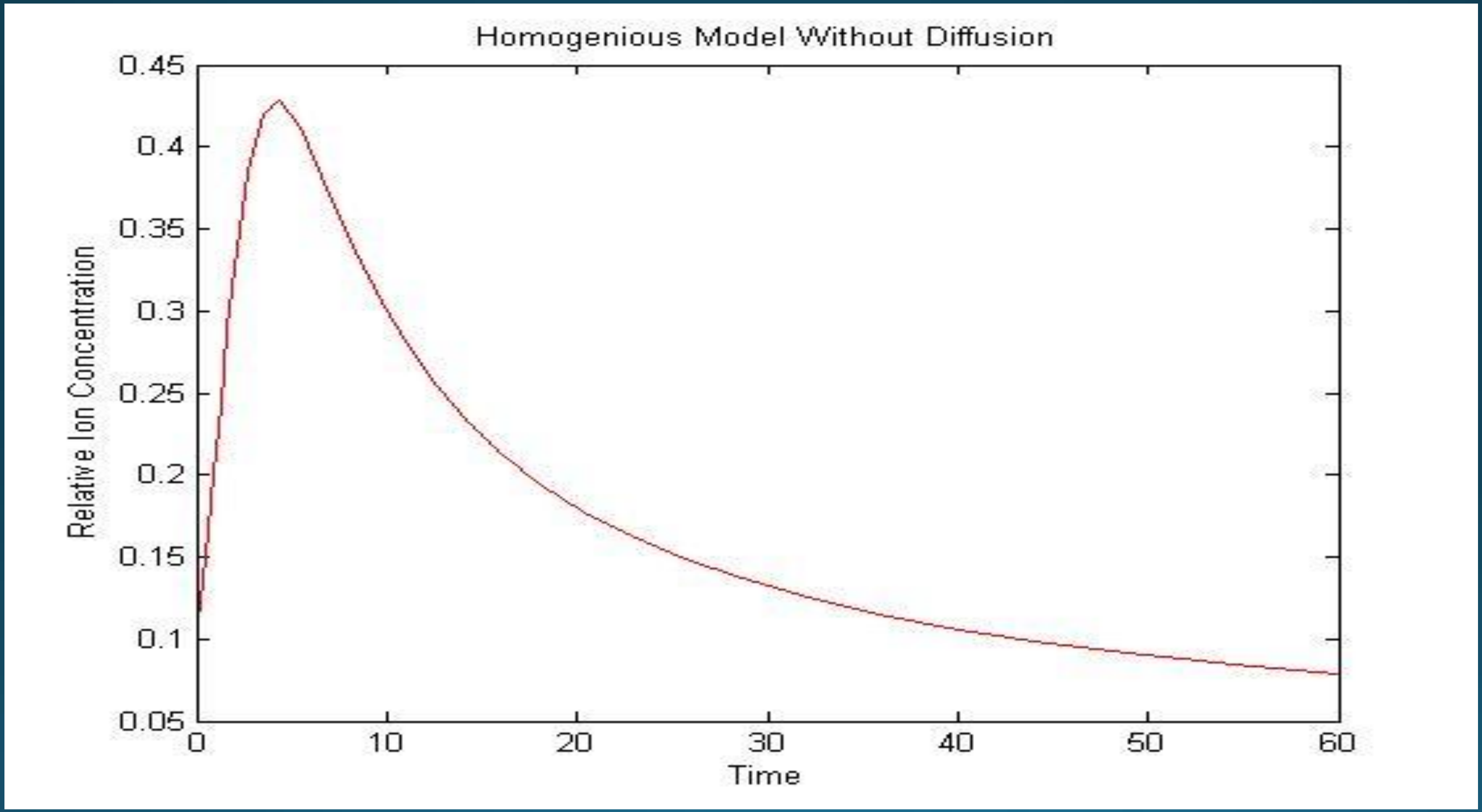
The Activator Equation

- $\frac{\delta u}{\delta t} = u\left(\frac{u_{sat}}{1+v} - u\right) + D\nabla^2 u$
- As is, the activator equation is unsolvable; certain assumptions need to be made.
- If radial symmetry is assumed, the activator equation can be simplified:
- $\frac{\delta u}{\delta t} = u\left(\frac{u_{sat}}{1+v} - u\right) + D\left[\frac{1}{r^2}\frac{\delta}{\delta r}(r^2\frac{\delta u}{\delta r})\right]$

where *r* is the radial distance from the initial starting point of the spreading depression.

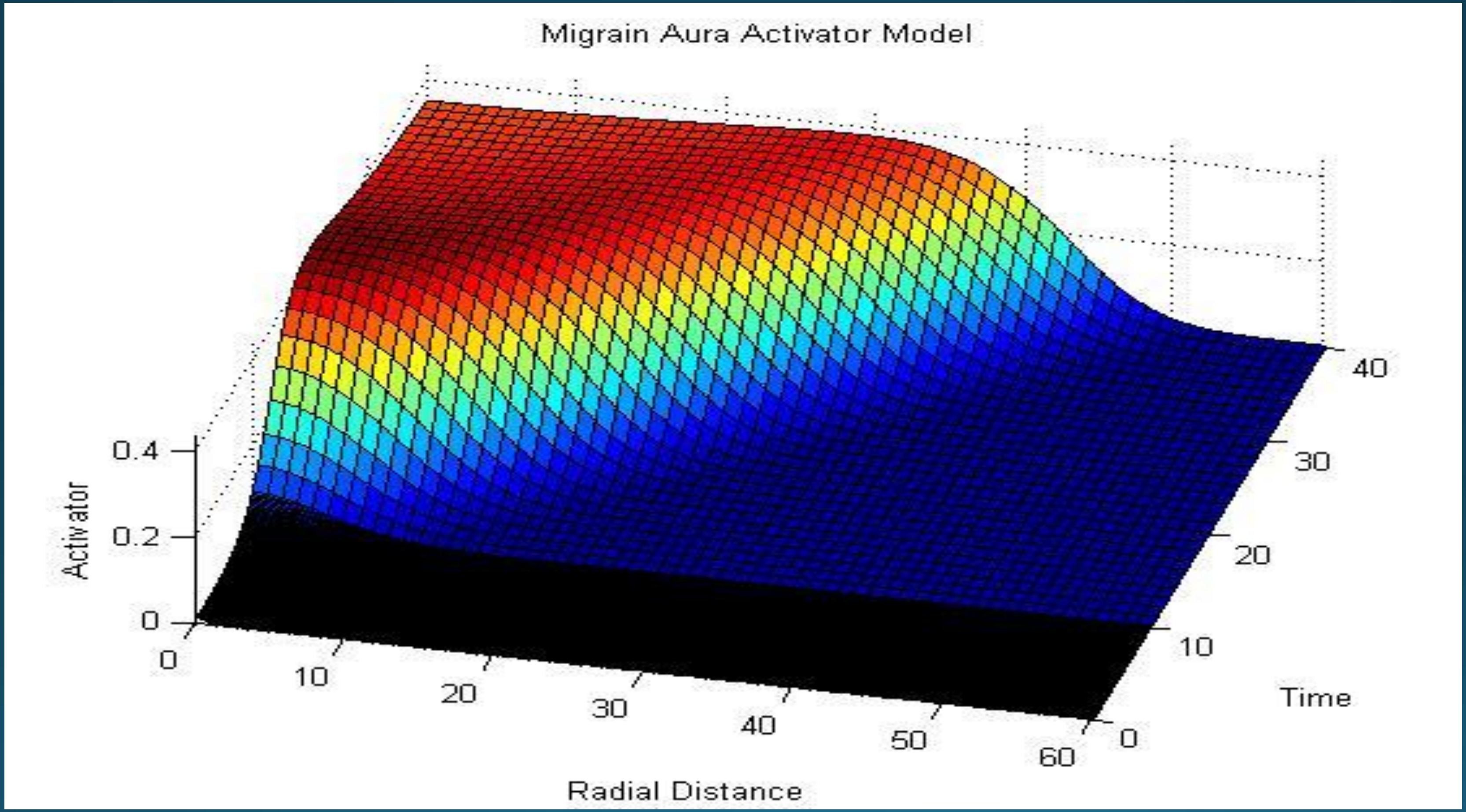
- This modified equation is solvable.

Results



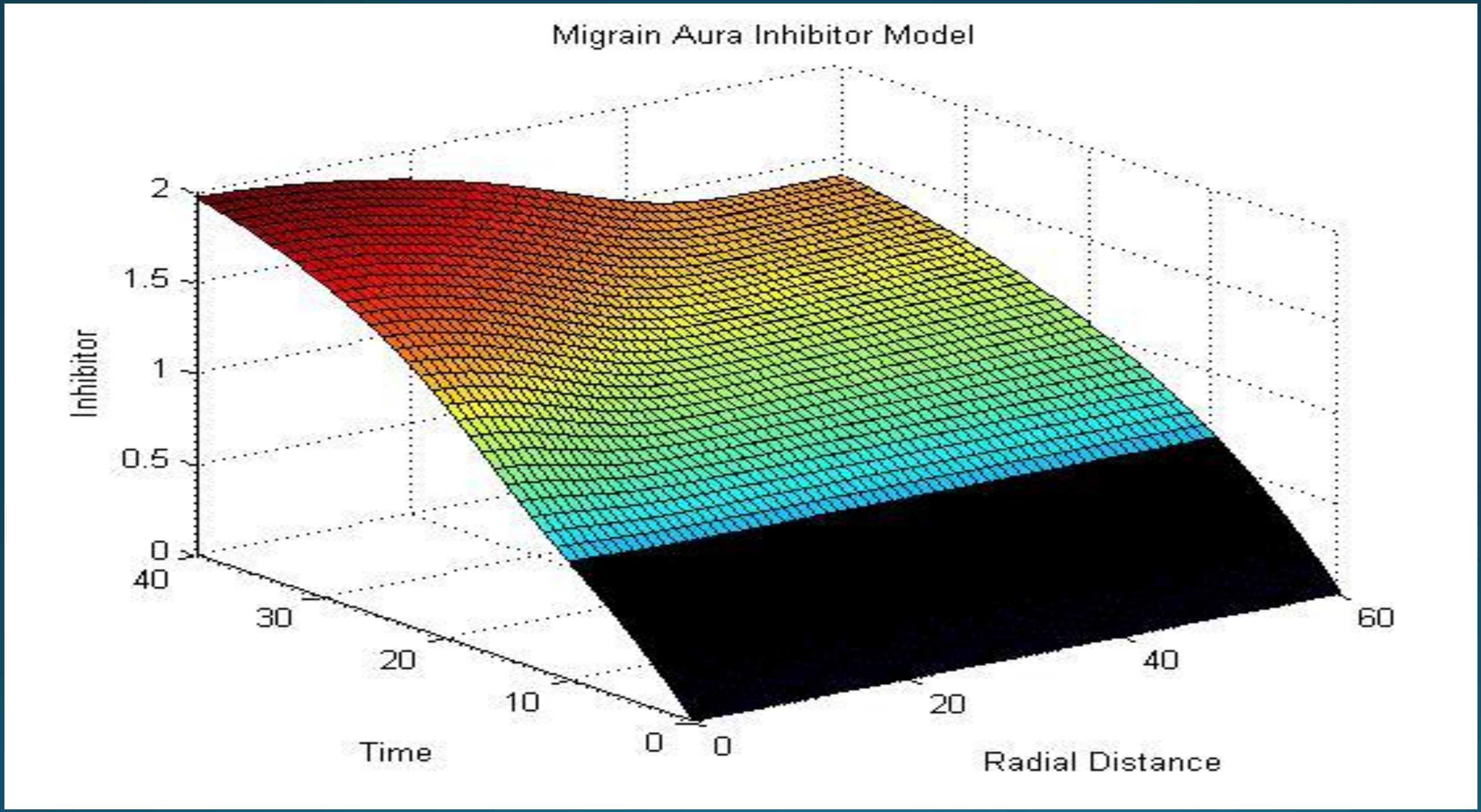
Homogenious Model Without Diffusion
Relative Ion Concentration
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
10
20
30
40
50
60
Time

Results



Migrain Aura Activator Model
Activator
0.4
0.2
0
0
10
20
30
40
50
60
Radial Distance
0
10
20
30
40
Time

Results



Migrain Aura Inhibitor Model
Inhibitor
2
1.5
1
0.5
0
40
30
20
10
0
Time
0
20
40
60
Radial Distance

Future Work

- The current model models the expected behavior of the spreading depression. In the future, more experiments can be done to verify the behavior.
- The model could be modified to account for multiple starting points in the spreading depression.
- The model could be modified so that it no longer assumes a radially symmetric spreading depression wave.

Future Work Cont.

From: Migraine generator network and spreading depression dynamics as neuromodulation targets in episodic migraine

Work Cited

- Markus A. Dahlem · Thomas M. Isele, Transient Localized Wave Patterns and Their Application to Migraine, Journal of Mathematical Neuroscience (2013) 3:7 DOI 10.1186/2190-8567-3-7; 2)
- Markus A. Dahlem, Migraine generator network and spreading depression dynamics as neuromodulation targets in episodic migraine, Chaos: An Interdisciplinary Journal of Nonlinear Science 23, 046101 (2013); doi: 10.1063/1.4813815