Wave Patterns and Their Application to Migraines

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Overview

- Background on migraines/Clinical Symptoms
- Physiological Phenomena in Migraines
- Model
- Conclusions & Future Work

Background

- Migraine
  - Recurrent in many individuals
  - 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)

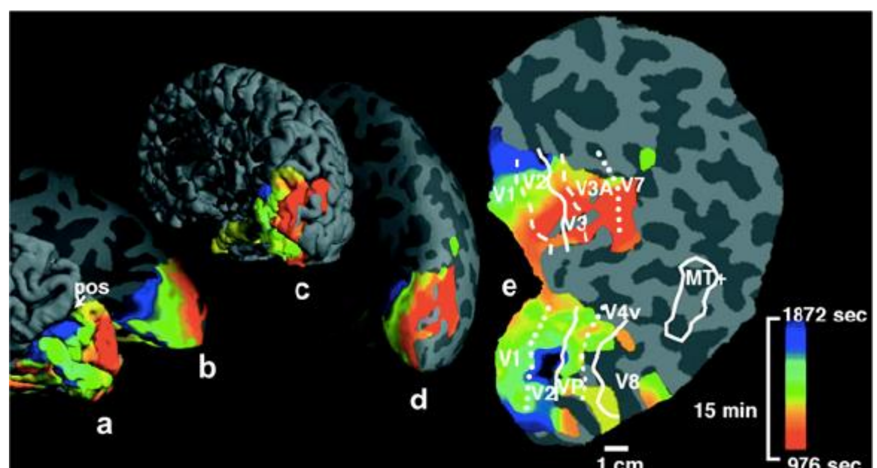
Migraines with Aura (MA)

- In addition to headache:
  - Neurologic symptoms (aura)-rarely exclusive
  - Symptoms include visual hallucinations
  - Caused by Spreading Depression (SD)
- If SD occurs in MO physiological phenomena remain clinically silent
  - Neurological symptoms must last less than 5 min.
- Aura is usually, before the headache phase and lasts usually less than one hour.
- Because of short duration of time:
  - Noninvasive imaging is difficult if SD stays silent (clinical symptoms not present).

Spreading Depression (SD)

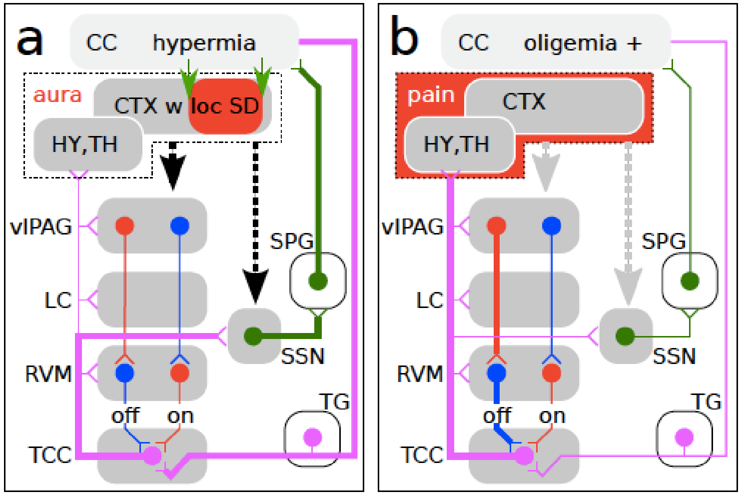
- A massive but temporary perturbation of ion homeostasis due to seizure-like discharges of neurons.

- Cause the neurological migraine aura symptoms, like visual hallucinations



Spreading Depression Facts

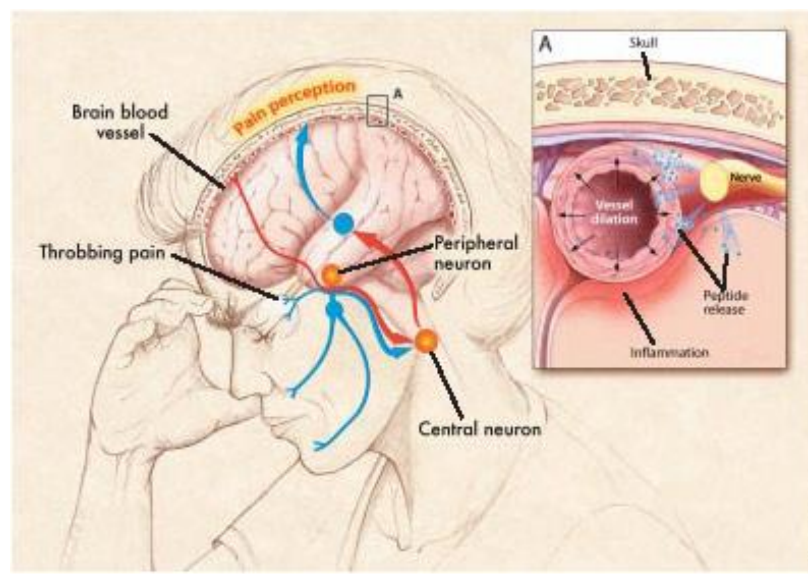
- Difficulty to measure
- Hyperemia
  - Increase in blood flow
  - 2 minutes
- Oligemia
  - Decrease in blood flow
  - 2 hour
- Activator– concentration of potassium ions
- Inhibitor– body's response to change in concentration of potassium ions



Neurons

- The neurons beyond the area
  - a high-frequency of activity
  - “increased synaptic noise”

- The neurons at the edge of the area
  - undergo seizure-like discharging



Electrical Signal Transmission

- The hyperemia in the surrounding areas outside the areas affected by SD can cause the estimated area affected by SD to be overestimated when measured.
- The hyperemia in the neurons not affected by SD can cause the neurons to be less susceptible to SD.

Variable Define

- $u \equiv$ activator (i.e.– $[K^+]_e$)
- $v \equiv$ inhibitor the body
- $D \equiv$ the diffusion coefficient
- $\epsilon \equiv$ time scale separation
  $\beta \equiv$ threshold
- $K \equiv$ mean field coupling
- $H \equiv$ Heaviside step function
- $H(x) = \begin{cases} x < 0 \Rightarrow 0 \\ x = 0 \Rightarrow 0.5 \\ x > 0 \Rightarrow 1 \end{cases}$

Formula Analysis

- $\frac{\delta u}{\delta t} = u - \frac{1}{3}u^3 - v + D\left(\frac{\delta^2 u}{\delta x^2} + \frac{\delta^2 u}{\delta y^2}\right)$
- $\frac{\delta v}{\delta t} = \varepsilon(u + \beta + K \iint H(u - u_0)dxdy)$

Formula Analysis

- Suppose we define c_x as the velocity of the spreading depression in the x direction and c_y as the velocity of the spreading depression in the y direction. We can simply the equations by introducing a variable τ:
- $\tau = t + \frac{1}{c_x} x + \frac{1}{c_y} y$

Formula Analysis

- This yields the following result:
- $\frac{\delta u}{\delta \tau} = u - \frac{1}{3}u^3 - v + 2D\left(c_x^2 + c_y^2\right)\frac{\delta^2 u}{\delta \tau^2}$
- $\frac{\delta v}{\delta \tau} = \varepsilon\left(u + \beta + K\frac{1}{c_x}\frac{1}{c_y}\iint H(u - u_0)d\tau d\tau\right)$

Formula Analysis

The value of ϵ is really small (on the order of 10^{-2}), which means that for small values of τ, $\frac{\delta v}{\delta \tau} = 0$. This yields the following result:

- $\frac{\delta u}{\delta \tau} \approx u - \frac{1}{3}u^3 + \frac{1}{\alpha}\frac{\delta^2 u}{\delta \tau^2} \left(for\ \tau < \frac{1}{\varepsilon}, \frac{1}{\alpha} = 2D\left(c_x^2 + c_y^2\right)\right)$
- $\Rightarrow \frac{\delta^2 u}{\delta \tau^2} = \alpha\left(\frac{\delta u}{\delta \tau} + u\left(\frac{1}{3}u^2 - 1\right)\right)$

Formula Analysis

Let $\frac{\delta u}{\delta \tau} = w$:

- $\frac{\delta}{\delta \tau}\begin{bmatrix} u \\ w \end{bmatrix} = \begin{bmatrix} w \\ \alpha\left(w + \frac{1}{3}u^3 - u\right) \end{bmatrix}$

Formula Analysis

- Thus, the stationary points of this model are at $P_1 = (0,0)$, $P_2 = \left(\sqrt[3]{3}, 0\right)$, $P_3 = \left(-\sqrt[3]{3}, 0\right)$.
- The system has the following Jacobian:
- $J(u, w) = \begin{bmatrix} 0 & 1 \\ \alpha(u^2 - 1) & \alpha \end{bmatrix}$

Formula Analysis

- $J(0,0) = \begin{bmatrix} 0 & 1 \\ -\alpha & \alpha \end{bmatrix} \Rightarrow \lambda_{1,2} = \frac{\alpha}{2} \pm \frac{\sqrt{\alpha^2 - 4\alpha}}{2}$
- P_1 is an unstable node.

Formula Analysis

- $J(\sqrt[3]{3}, 0) = \begin{bmatrix} 0 & 1 \\ \alpha\left(\left(\sqrt[3]{3}\right)^2 - 1\right) & \alpha \end{bmatrix} \Rightarrow \lambda_{1,2} = \frac{\alpha}{2} \pm \frac{\sqrt{\alpha^2 - 4\alpha\left(\left(\sqrt[3]{3}\right)^2 + 1\right)}}{2}$
- P_2 is an unstable node.

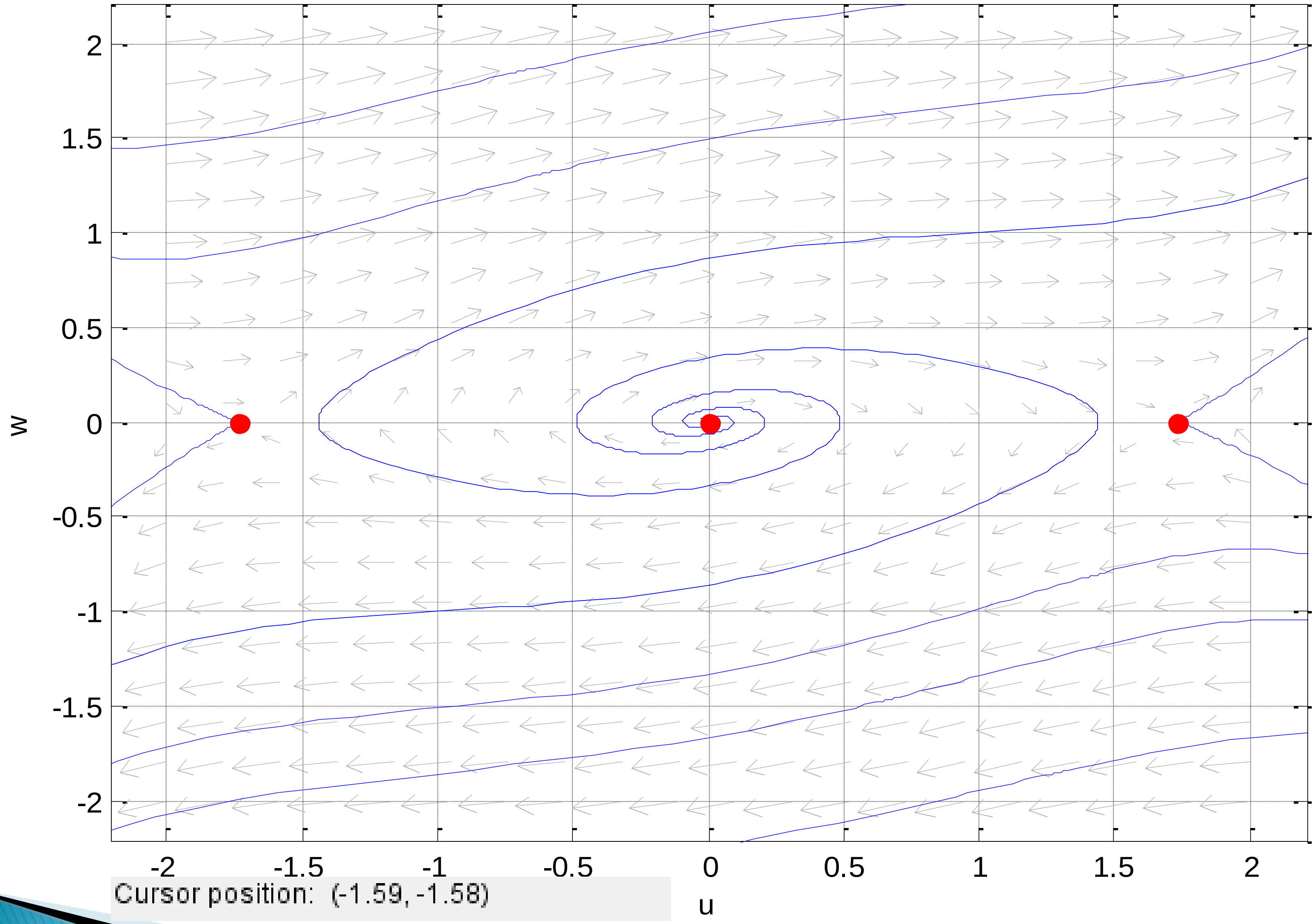
Formula Analysis

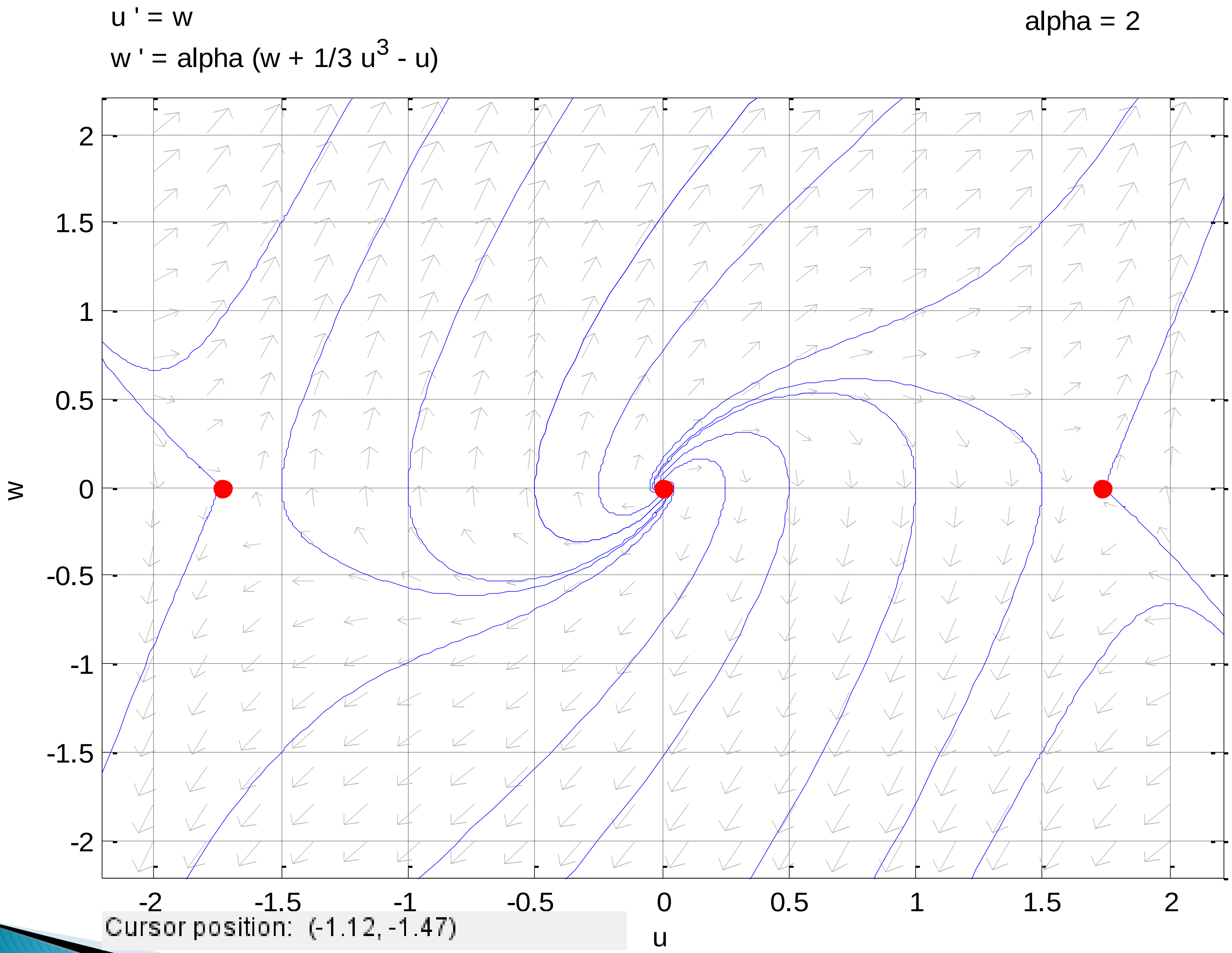
- $J\left(-\sqrt[3]{3},0\right)=\begin{bmatrix}0 & 1\\ \alpha\left(\left(-\sqrt[3]{3}\right)^2-1\right) & \alpha\end{bmatrix}\Rightarrow\lambda_{1,2}=\frac{\alpha}{2}\pm\frac{\sqrt{\alpha^2-4\alpha\left(\left(-\sqrt[3]{3}\right)^2+1\right)}}{2}$
- P_3 is an unstable node.

$u' = w$

$w' = \text{alpha}\,(w + 1/3\, u^3 - u)$

alpha = 1/4



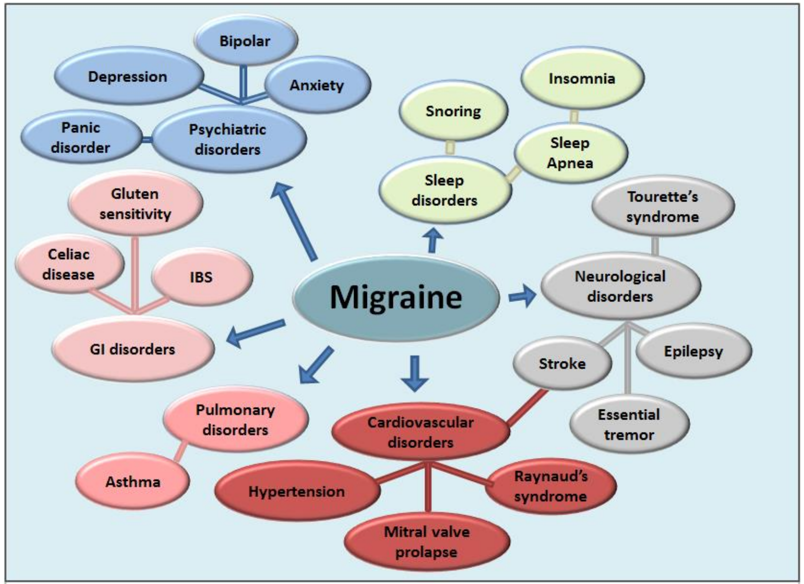

u ' = w
w ' = alpha (w + 1/3 u^3 - u)
alpha = 2
2
1.5
1
0.5
0
-0.5
-1
-1.5
-2
w
-2
-1.5
-1
-0.5
0
0.5
1
1.5
2
u
Cursor position: (-1.12, -1.47)

Conclusions

- Many theories to cause of migraines
- These papers investigate SD
- Further development of model with more clinical studies needed

Future Work

- Consider 1: Epsilon not small–is significant
- Consider 2: Analyze behavior of velocity of spreading depression in x or y (or behavior of c1 and c2 according to equations)



Migraine Comorbidities

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 View online: http://dx.doi.org/10.1063/1.4813815