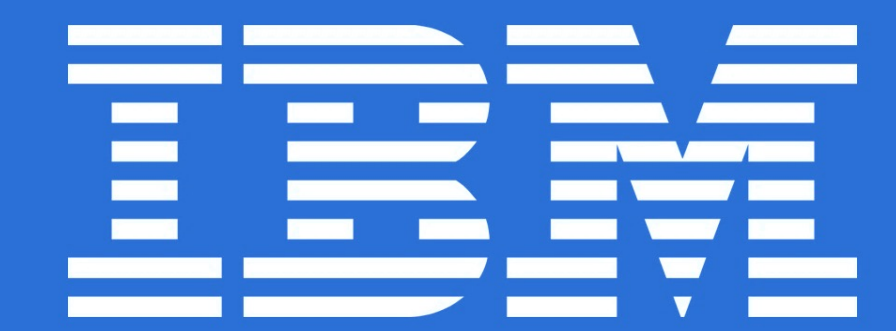# Modeling Cortical Spreading Depression (CSD)

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Introduction

Cortical spreading depression (CSD) is an electrical silent wave across all over the cerebral cortex and impairs some cortical activities. This cortical transmission inhibition is hypothesized to be strongly correlated with a number of neurological disorders. In addition to a series of animal and human brain photographic imaging (PET) studies, recent functional magnetic resonance imaging (functional MRI) and brain magnetic (magnetoencephalography) studies also support this hypothesis.

The precise physiological events involved in CSD are not totally understood, however the most generally accepted hypothesis is that the exceed releases of ionic species such as potassium (K^+) and neurotransmitters, possibly glutamate, is a key event. Here, we describe a reaction-diffusion model in three-dimensional space and study the change in extracellular potassium.

Simulation Method

The Finite Difference method was implemented in Python (IPython) to simulate the diffusion equation (Fick's law) of potassium in CSD model. The equation is

$$\frac{\partial K}{\partial t} = D\nabla^2 K + f(K)$$

where K is the concentration of potassium in location (x,y,z), ∇^2 is Laplacian operator, D is the coefficient of potassium diffusion and $f(K)$ represents the local dynamics of extracellular potassium.

Simulation Condition

Without loss of generality, we take 50x50x50 mesh cube to simulate CSD model, and each grid cell is *0.025mm* x *0.025mm* x *0.025mm*. Initially, we let the potassium concentration of all elements start with 0.03, set each time step to 0.0025 min. and do 2000 ticks (iterations) in our experiment. To simulate the cell channel opening, we locate the channel at the center of the cube, assume the channel is the circle with radius *0.025 mm ~ 0.125 mm* and clamp the center value using a value between 0.5~1.0.
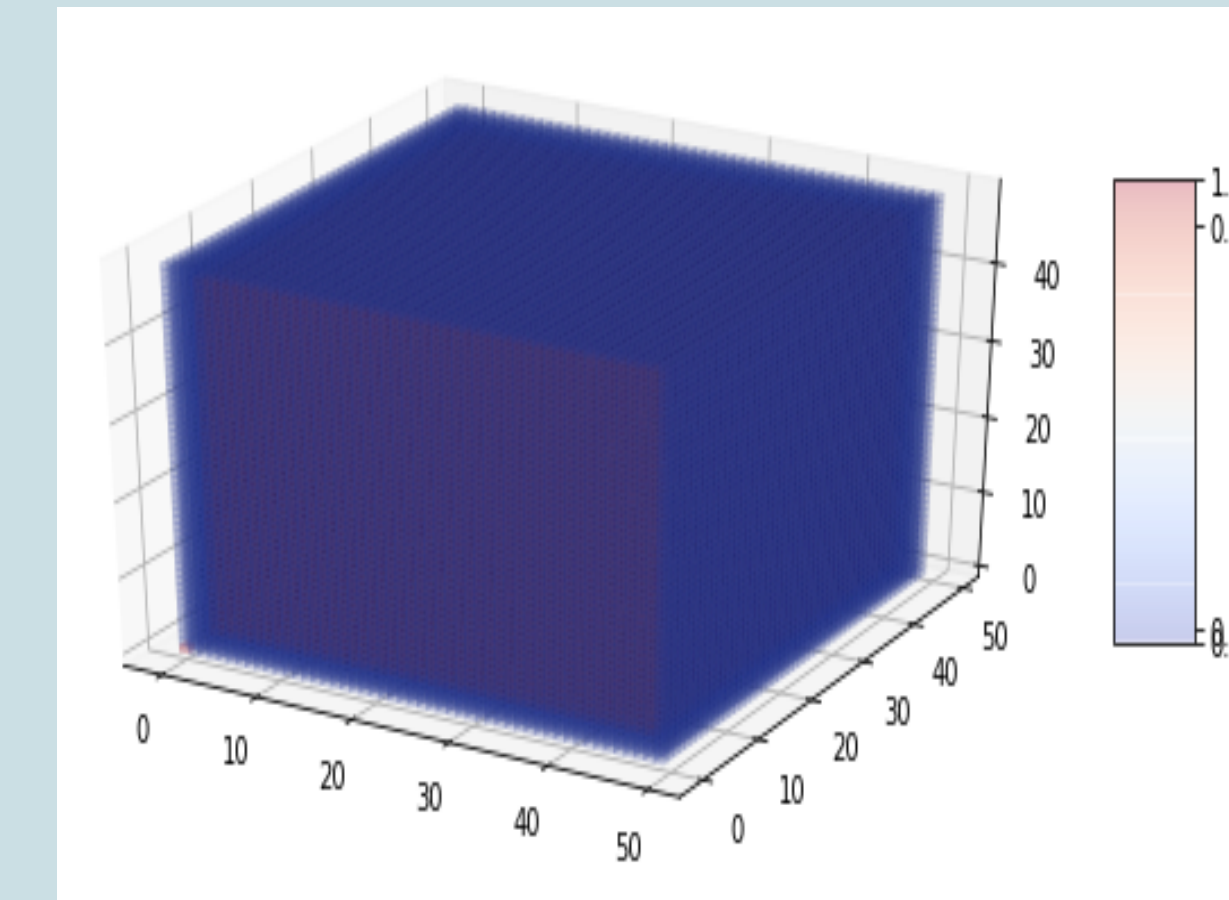

Figure 1: The representation for 50x50x50 mesh cube, with the center is where the source of exceeding K^+ release
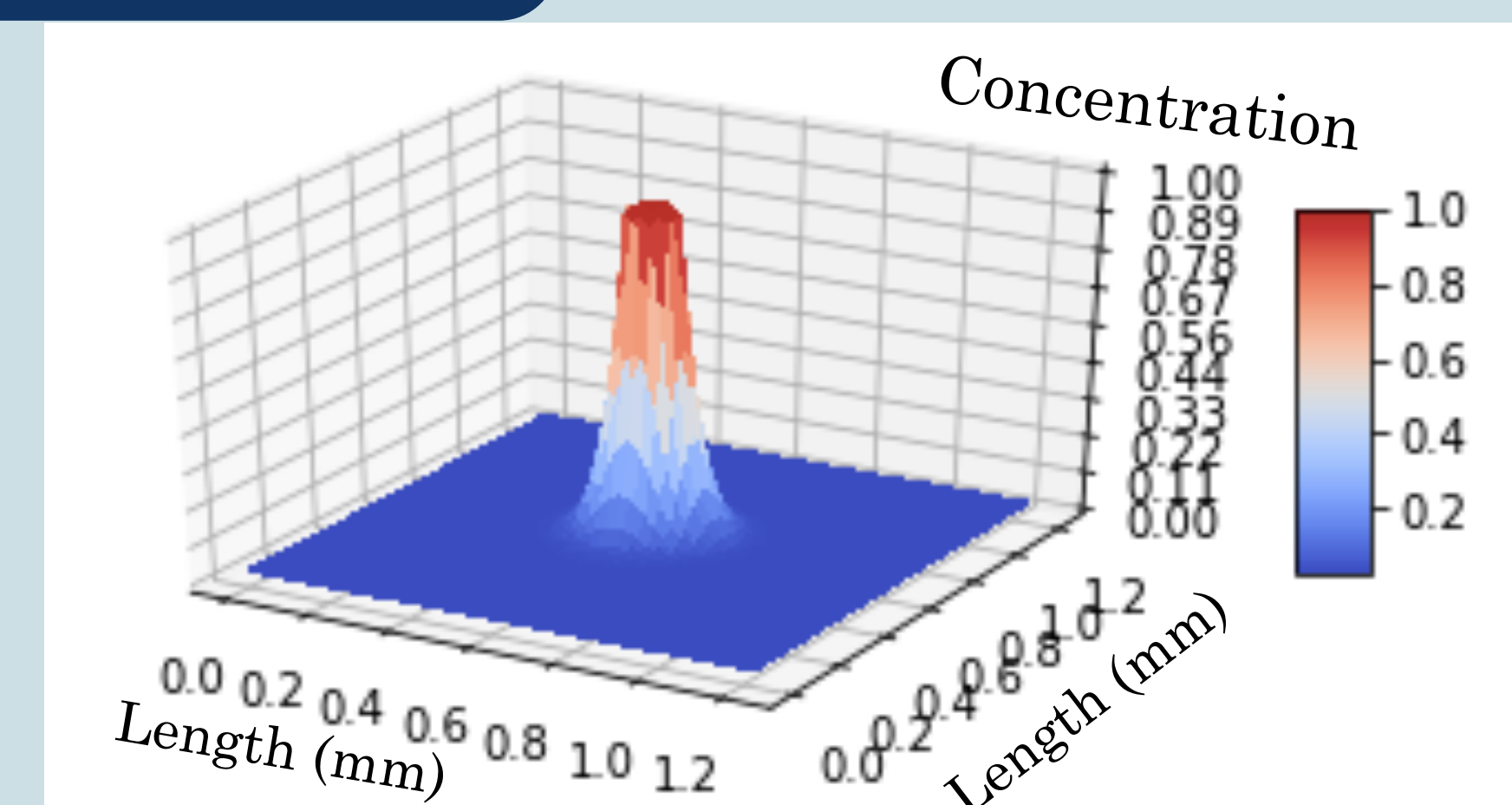
Results

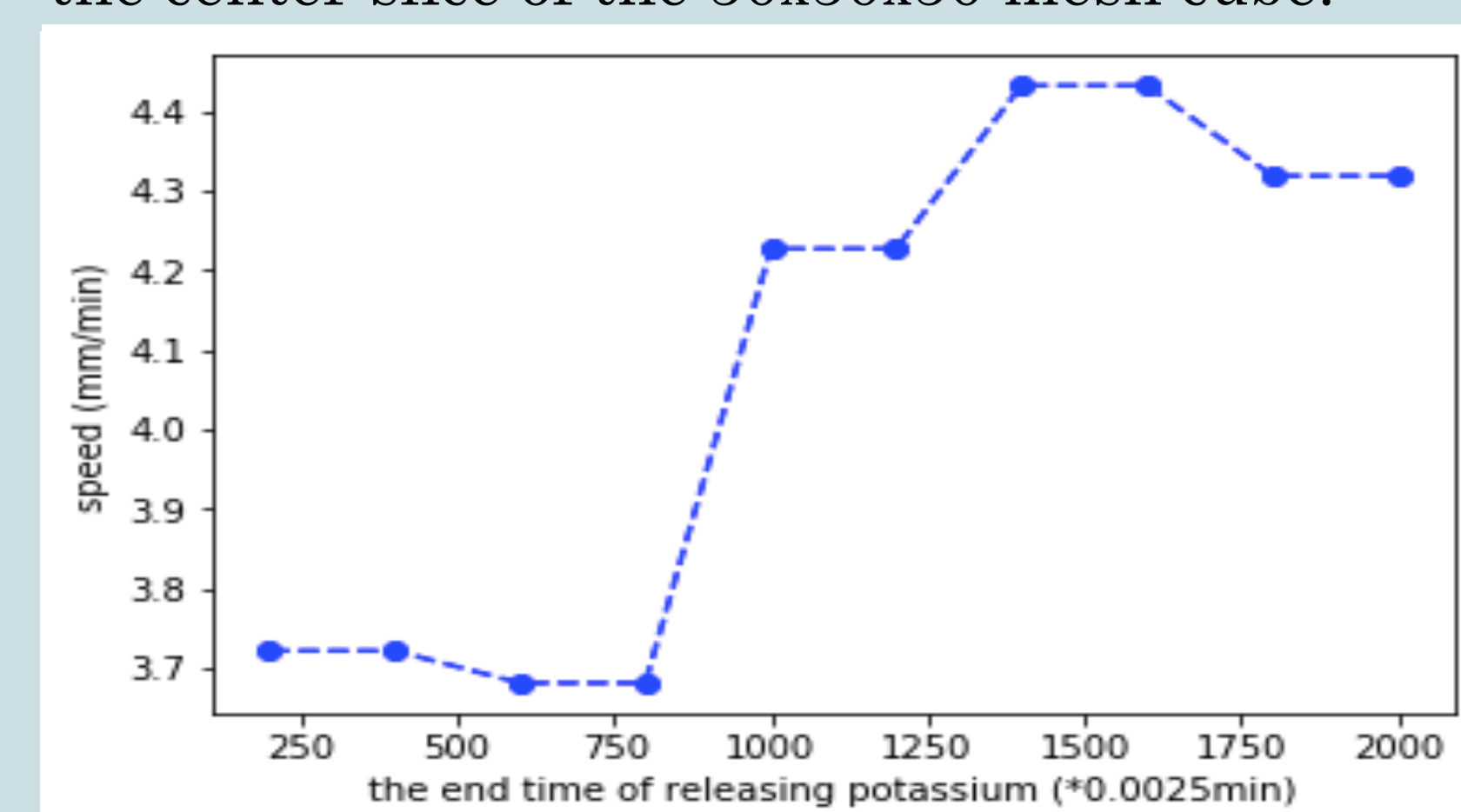**Figure 2:** The concentration of the potassium in the center slice of the 50x50x50 mesh cube.

In this simulation, we focused on the diffusion of potassium ions in the brain and the rate of diffusion. The 3D mesh cube is used to represent the effect on the neighboring area when the ion channel is turned on. In Fig. 2, we present the situation after 0.05 minutes of opening the ion channel. The position of Fig. 2 is in the center slice of the mesh cube, and we raise the value of the center circle to simulate the channel release ion, and also fix the radius of the circle to 0.075mm.
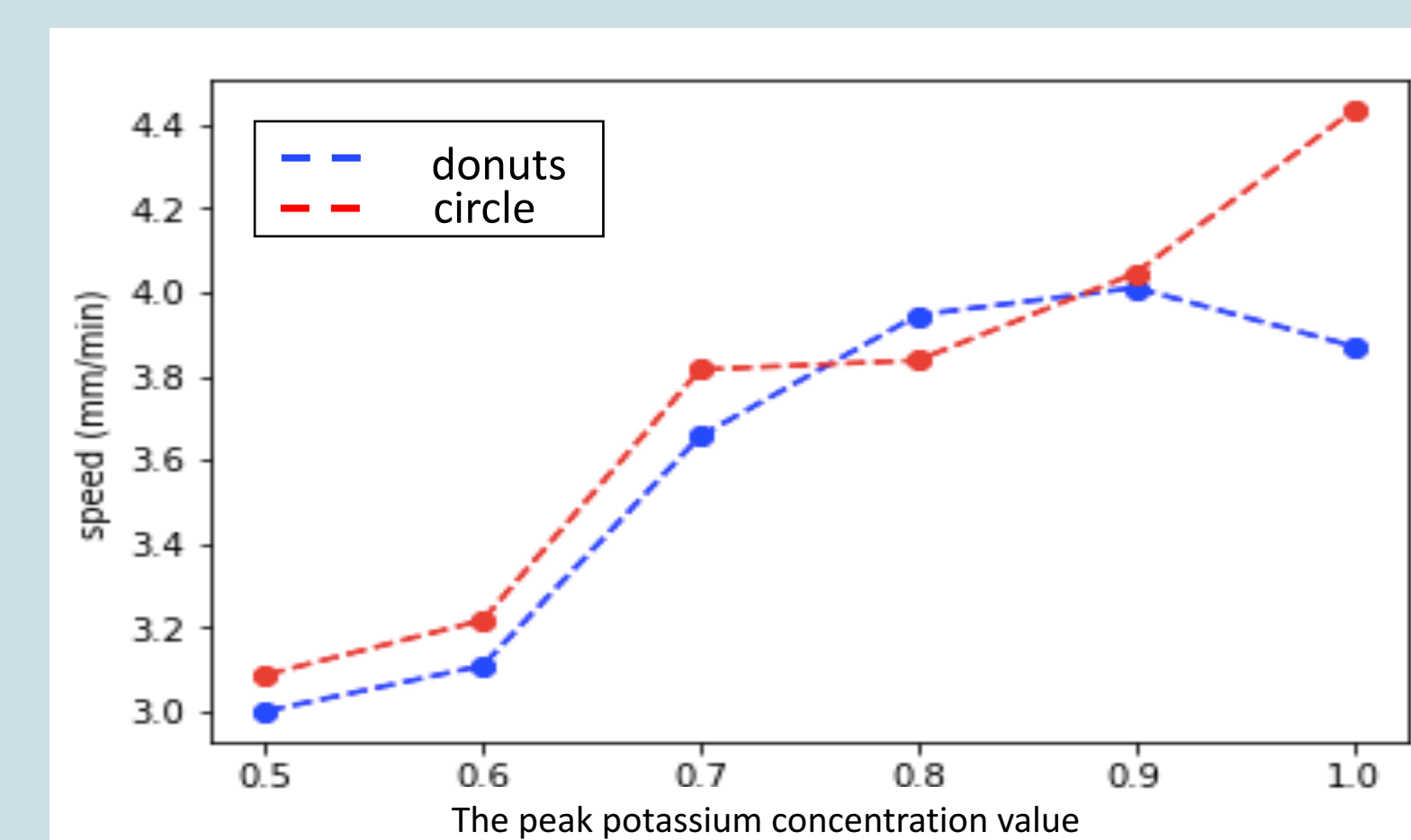

Figure 3: The relationship between the different time interval of releasing potassium and speed.

Figure 4: The relationship between the amount of released potassium concentration and diffusion speed.
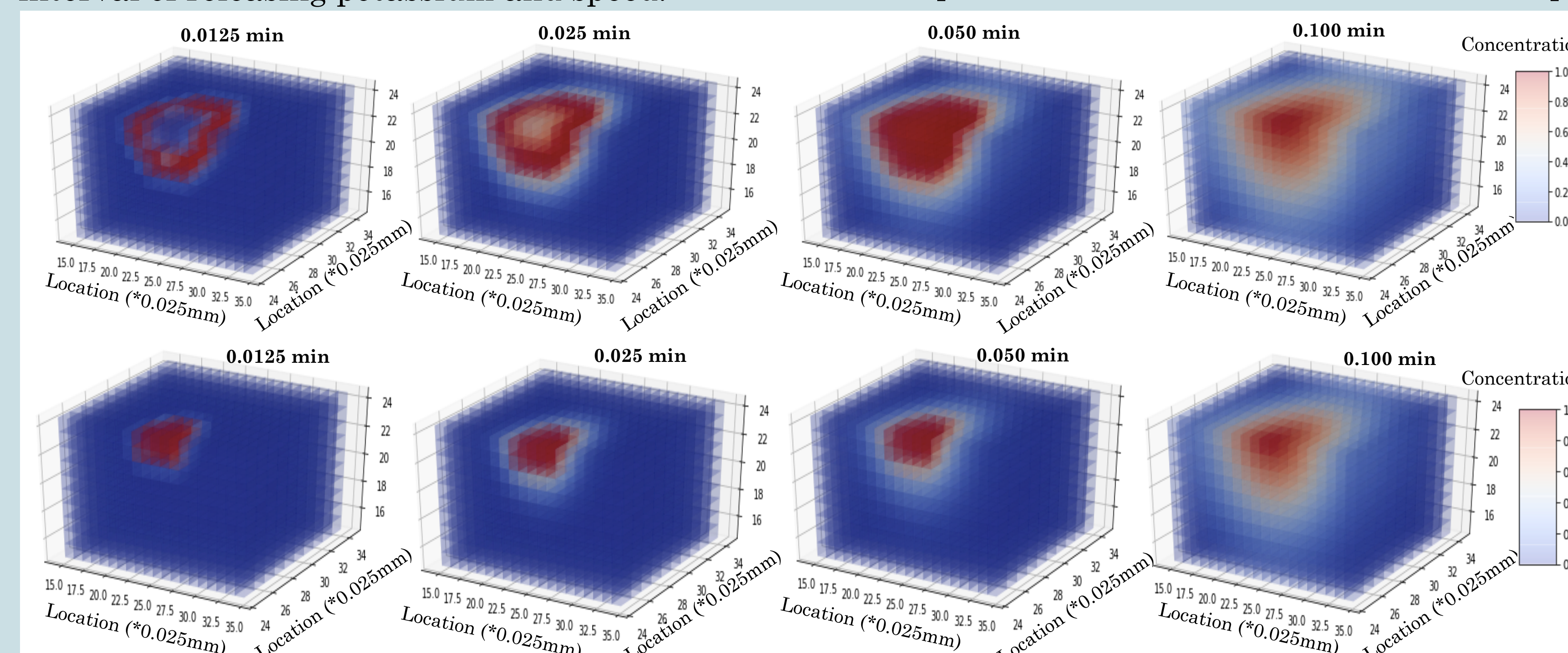

Figure 5: Modeling the effect of potassium release from brain source of different shapes: Diffusion situation, above one is increasing with donuts shape and below one is increasing with circle shape.

Results

In Fig. 3, the model suggests there is a critical threshold for modifying the wave speed. Importantly, there is a non-linear relationship between the wave speed and the intensities of potassium elevation. The speed of the diffusion wave will keep raising, if the cell channel continues opening.
The potassium level being used in the model is an abstract representation of changes in potassium from a baseline value, and because of that it can be rescaled to reflect the change at the physiological range.

In Fig. 4, two different shapes of the sources both generate a non-linear relationship between the level of K^+ and the wave speed. However, at a strong elevation, one form can provide a stronger change in wave speed than the other.

Future work

Based on the experience this preliminary simulation, I will try to transfer this diffusion ipython code to IBM's Neural Tissue Simulator, so that the CSD model can be used in the analysis of neurological disorders.

References

[1] James A. Reggia & David Montgomery, *Modeling Cortical Spreading Depression*
[2] H. Kager,1 W. J. Wadman1& G. G. Somjen, *Conditions for the Triggering of Spreading Depression Studied With Computer Simulations*