Numerical Simulation of Cortical Spreading Depression on a Real Brain Geometry

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Introduction

- migraine is a common disorder where 20% of the patients also suffer from migraine aura preceding the typical headache [1]
- several studies suggest that cortical spreading depressions (CSD) underlay migraine and can help to understand the phenomenon of the visual aura [2]
- CSD is a propagating depolarisation wave that starts from the visual cortex and is followed by a wave of inhibition
- the depolarisation wave requires about 20 minutes to spread over the whole cortex [3]
- the geometry of the cortex is highly individual, and is anticipated to impact the propagation of the depolarisation wave

Aim: simulate the propagation of CSD on a real cortical geometry

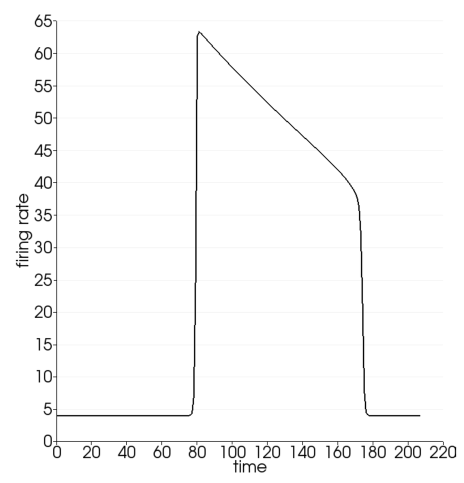
The Excitability Model

- we derive a mean field model for the neuron firing rate, inspired by a variant of the FitzHugh-Nagumo model [4] for excitable media
- the Rogers-McCulloch variant of the FitzHugh-Nagumo model describes the all-or-nothing response of an excitable cell in a simplified manner [5]:

$$\frac{\partial u}{\partial t}(t) = -(I_{ion}(u,w) - I_{st})$$

$$I_{ion}(u,w) = Gu\left(1 - \frac{u}{u_{th}}\right)\left(1 - \frac{u}{u_p}\right) + \eta_1 uw$$

$$\frac{\partial w}{\partial t}(t) = \eta_2\left(\frac{u}{u_p} - \eta_3 w(t)\right)$$



where $u(t)$ is the potential at time $t \geq 0$, $w(t)$ is a recovery variable, I_{ion} is the ionic current, I_{st} is the stimulus, u_{th} and u_p are threshold and peak values for u, while η_1, η_2, η_3 and G are parameters that can be tuned to match the physiological firing rates of resting (4Hz) and excited (60 Hz) cortical neuron during CSD

The Spatial Model

- the propagation of the excitation in space is described by a parabolic reaction-diffusion equation

$$\frac{\partial u}{\partial t}(x,t) = -(I_{ion}(u,w) - I_{st}) + div(D\nabla u)$$

where $D \in \mathbb{R}^{2\times 2}$ is the diffusion tensor, possibly anisotropic
- for all points x in the computational domain, the above equation is coupled with the ODE describing the evaluation of the recovery variable $w(t)$, resulting in a coupled PDE-ODE system

Finite Dimensional Approximation

- time discretisation: finite differences $\frac{\partial u}{\partial t}(t^{n+1}) \sim \frac{u^{n+1} - u^n}{\Delta t}$
- space discretisation: $\mathbb{P}_1$ finite elements
- time advancing scheme: IMEX (implicit/explicit)

From t^n to t^{n+1} :

update: $w^{n+1} = \frac{1}{\eta_3 u_p}u^n + \left(w^n - \frac{1}{\eta_3 u_p}\right)\exp(-\eta_2\eta_3\Delta t)$

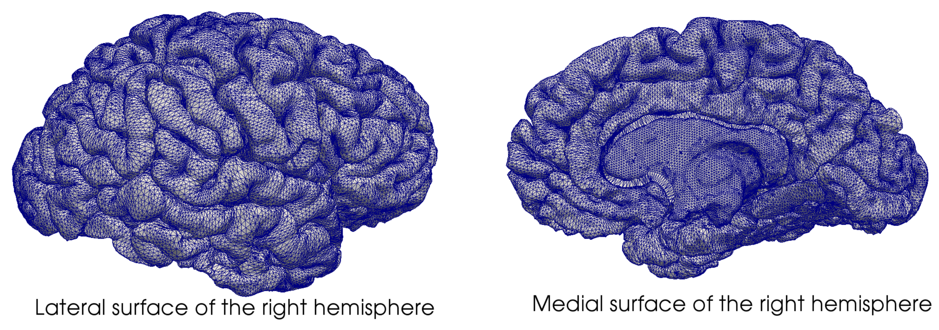
update: $I_{ion}^{n+1} = I_{ion}(u^n, w^{n+1})$

solve: $Au^{n+1} = Mu^n - \Delta t M I_{ion}^{n+1}$

where $A := M + \Delta t S$, while M and S are the finite elements mass and stiffness matrices

The Geometry

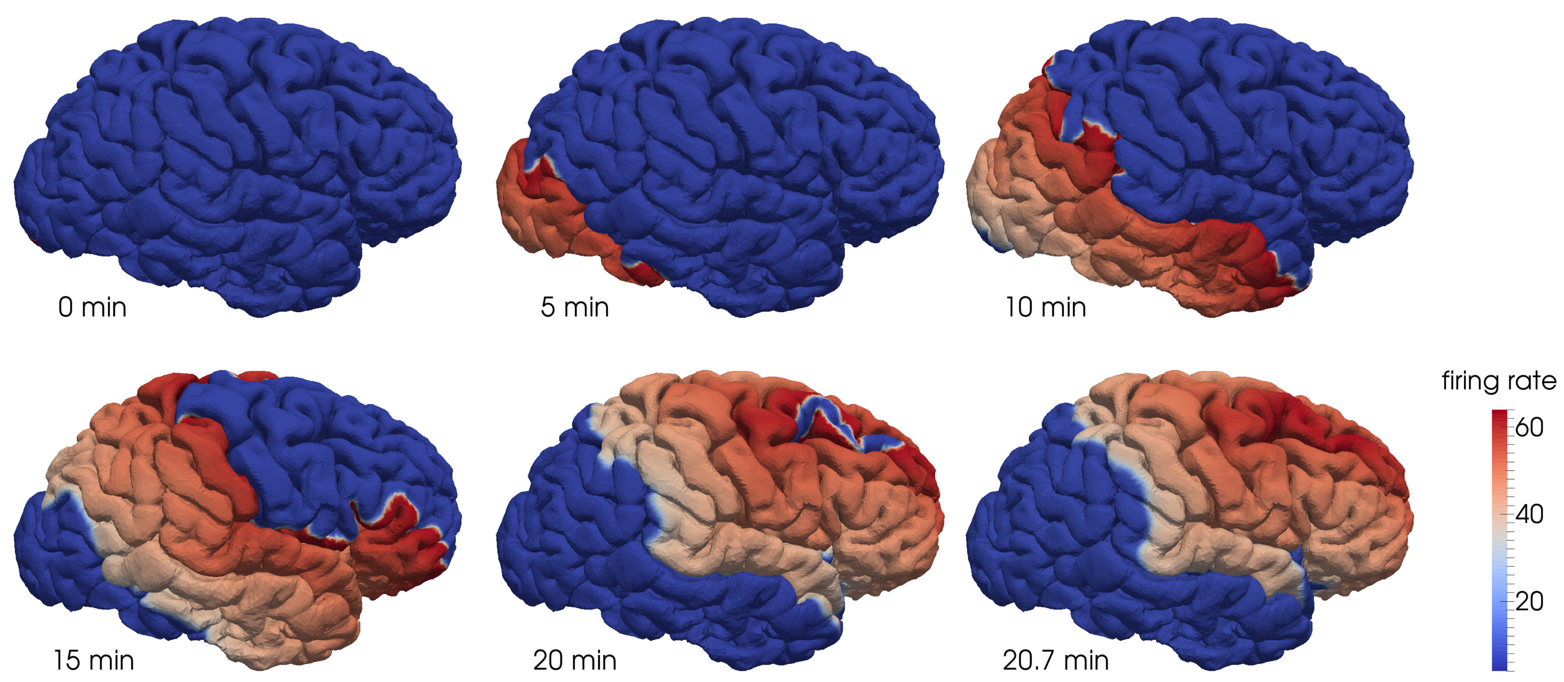
- the computational domain is a cortex reconstructed from MRI images provided by BioCruces Health Research Institute, Barakaldo, Spain and triangulated



- the computational grid features 140.208 nodes and 280.412 triangles

Preliminary Numerical Results

- we use a self-developed Matlab® code
- the time step is $\Delta t = 0.01$ min, and the diffusion tensor is isotropic $D = 0.5 \cdot Id$
- the stimulus current is neglected ($I_{st} = 0$) and no boundary conditions are necessary as the domain is a 2D closed surface
- the initial condition is given by an excited region in the visual cortex
- the simulation is run until the CSD wave has propagated across the whole cortex



Conclusion and open problems

- a first simulation of the propagation of CSD on a real geometry has been performed
- the accuracy of the results will improve by using information from Diffusion Tensor Imaging, which describe the diffusion in every voxel of the brain (in progress)
- the parameters have been empirically tuned to match the expected propagation time of around 20 minutes
- a further study is needed to have patient-specific parameter estimations

References

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