Numerical Simulation of Cortical Spreading Depression on a Real Brain Geometry

Julia M. Kroos\textsuperscript{a}, Sebastiano Stramaglia\textsuperscript{b}, Jesus M. Cortes\textsuperscript{c} and Luca Gerardo-Giorda\textsuperscript{a}

\textsuperscript{a} BCAM - Basque Center for Applied Mathematics, Bilbao, Spain, \textsuperscript{b} Center of Innovative Technologies for Signal Detection and Processing TIERES, Dipartimento di Fisica, Universita di Bari, Italy, \textsuperscript{c} Computational Neuroimaging Lab, BioCruces Health Research Institute, Cruces University Hospital, Barakaldo, Spain

Introduction

- migraine is a common disorder where 20\% of the patients also suffer from migraine aura preceding the typical headache
- several studies suggest that cortical spreading depressions (CSD) underlay migraine and can help to understand the phenomenon of the visual aura
- 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
- the geometry of the cortex is highly individual, and is anticipated to impact the propagation of the depolarisation wave

The Excitability Model

- we derive a mean field model for the neuron firing rate, inspired by a variant of the FitzHugh-Nagumo model \cite{fitzhugh1961} 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 \cite{rogers1994}

\[
\begin{align*}
\frac{dU}{dt}(t, x) &= -(I_{ion}(w, u) - I_d) \\
I_{ion}(w, u) &= Gw \left(1 - \frac{u}{u_\text{th}}\right) \left(1 - \frac{u}{u_p}\right) + \eta_1 w \\
\frac{d\eta}{dt}(t, x) &= \eta_2 \left(1 - \eta_3/(t)\right)
\end{align*}
\]

where \(u(t)\) is the potential at time \(t \geq 0\), \(w(t)\) is a recovery variable, \(I_{ion}(w, u)\) is the ionic current, \(I_d\) is the stimulus, \(w_{\text{th}}\) and \(w_p\) are threshold and peak values for \(w\), while \(\eta_1, \eta_2, \eta_3\) and \(G\) are parameters that can be tuned to match the physiological firing rates of resting (45 Hz) and excited (60 Hz) cortical neurons during CSD

The Spatial Model

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

\[
\frac{dU}{dt}(x, t) = -[I_{ion}(w, u) - I_d] + div(D\nabla w)
\]

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 evolution of the recovery variable \(w(t)\), resulting in a coupled PDE-ODE system

Finite Dimensional Approximation

- time discretisation: finite differences \(\frac{dU^{n+1}}{dt} = \frac{-U^n + I_{ion}(w^n, u^n) + \eta_1 w^n}{\Delta t}\)
- space discretisation: \(p\) finite elements
- time advancing scheme: IMEX (implicit/explicit)

\[
\begin{align*}
\text{update: } & w^{n+1} = \frac{1}{\Delta t} \left[ \frac{U^n - I_{ion}(w^n, u^n)}{\Delta t} \exp(-\eta_2/\Delta t) \right] \\
\text{update: } & \eta_1^{n+1} = \eta_1^n - \eta_3 \left(1 - \eta_3\right) \Delta t \\
\text{solve: } & A \mathbf{u}^{n+1} = M \mathbf{u}^n - \Delta t M \mathbf{u}^n
\end{align*}
\]

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

Preliminary Numerical Results

- we use a self-developed Matlab\textsuperscript{\textcopyright} code
- the time step is \(\Delta t = 0.01\) min, and the diffusion tensor is isotropic \(D = 0.5 \cdot I_d\)
- the stimulus current is neglected (\(I_d = 0\)) 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