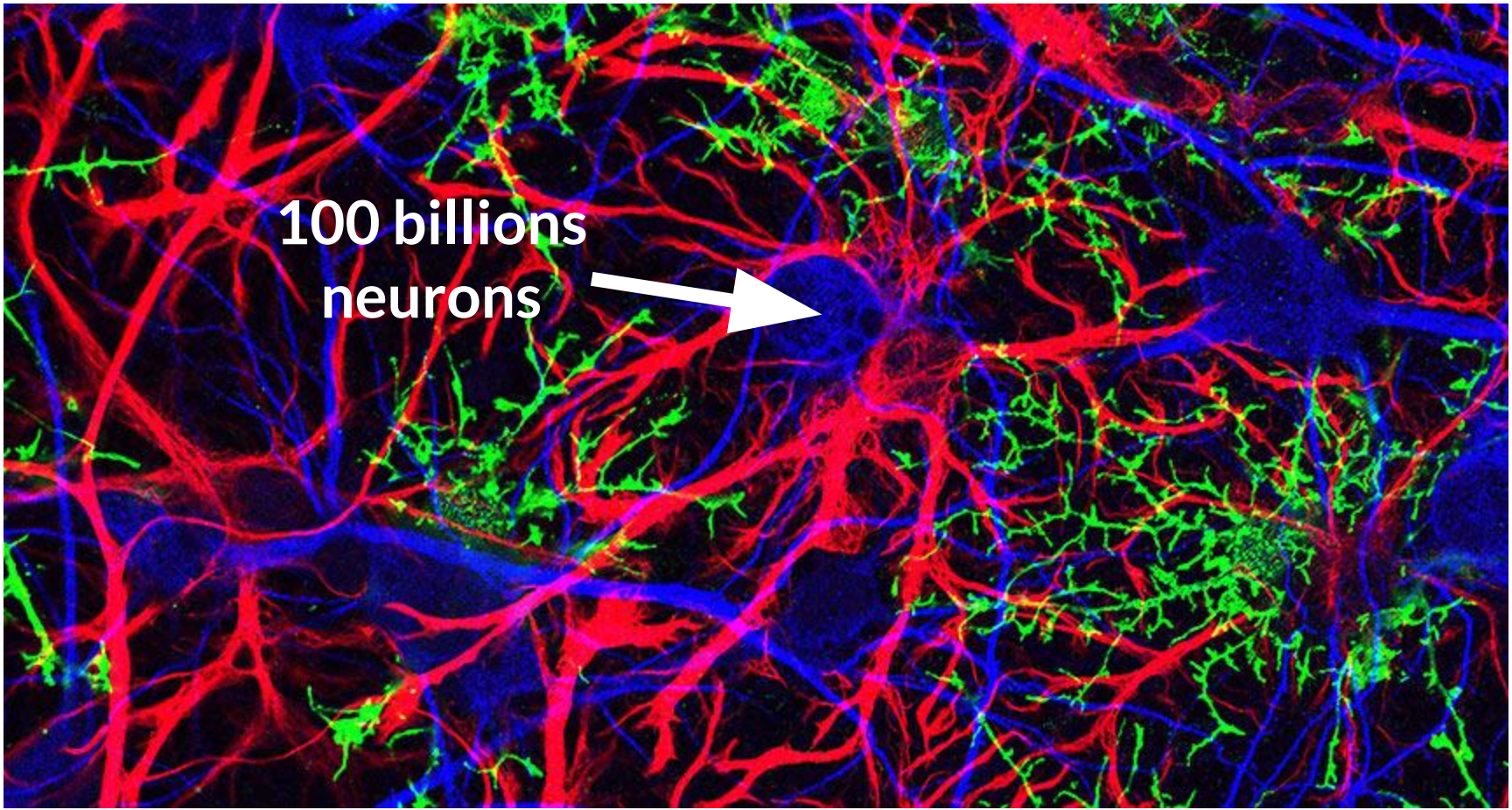
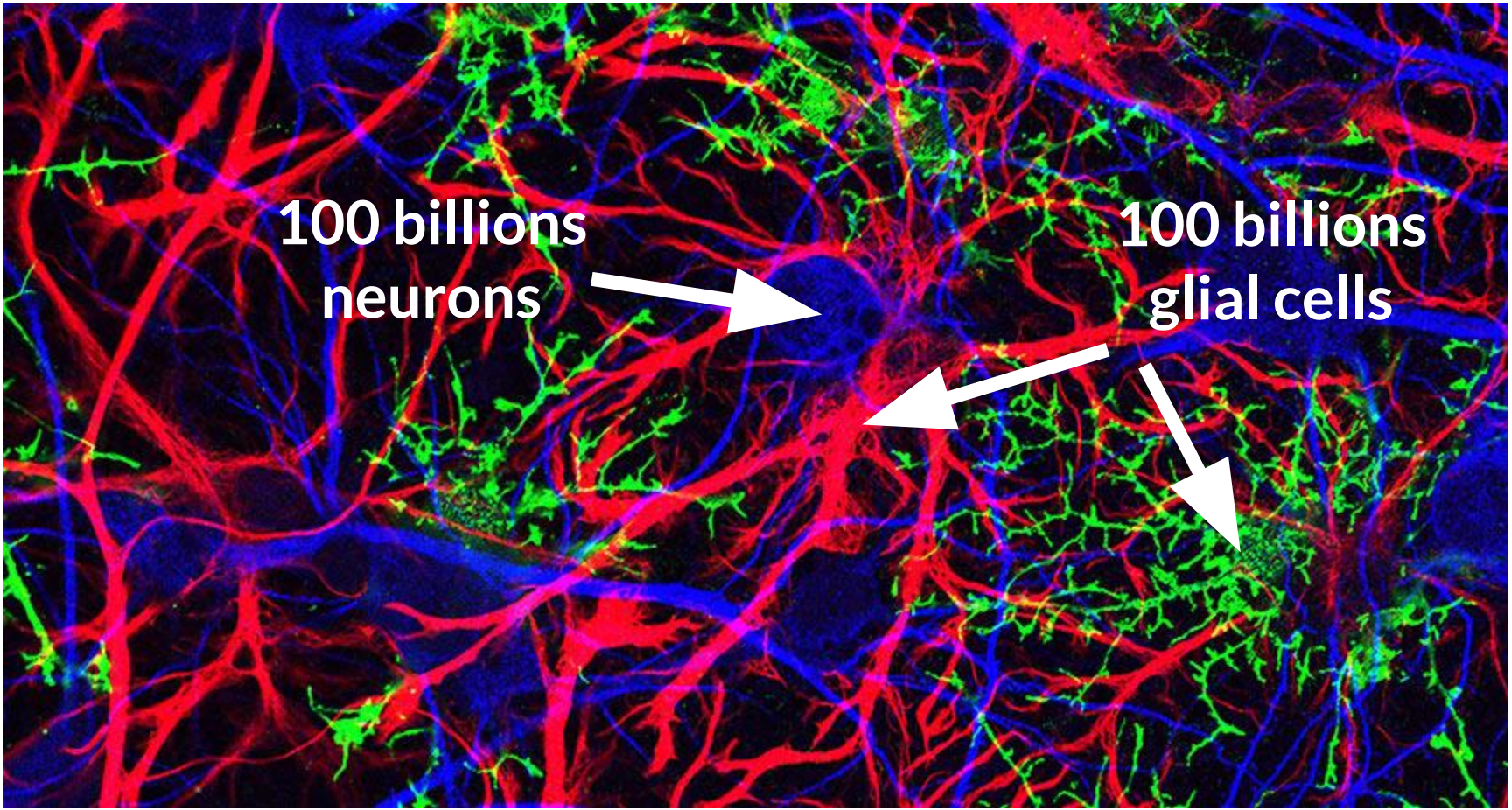
Mathematical modelling of glials - the “forgotten brain cell”

08.10.2019

Ada Johanne Ellingsrud • ada@simula.no


100 billions
neurons


100 billions
neurons
100 billions
glial cells

by Buck Institute

FEBRUARY 12, 2019 . PRESS RELEASE

Intervening in glial cells protects neurons in Parkinson's model

Buck researchers identify crosstalk between dopaminergic neurons and glial cells in fruit flies providing a potential new target for preventative treatment.

by Buck Institute

FEBRUARY 12, 2019 . PRESS RELEASE

Intervening in glial cells protects neurons in Parkinson's model

Buck researchers identify crosstalk between dopaminergic neurons and glial cells in fruit flies providing a potential new target for preventative treatment.

Scientists identify glial cells as important factor in development of schizophrenia

The disease could develop due to damage to on a particular type of brain cell.

Kristian Sjøgren

PUBLISERT Torsdag 05. oktober 2017 - 06:25

by Buck Institute

FEBRUARY 12, 2019 . PRESS RELEASE

Intervening in glial cells protects neurons in Parkinson's model

Buck researchers identify crosstalk between dopaminergic neurons and glial cells in fruit flies providing a potential new target for preventative treatment.

Scientists identify glial cells as important factor in development of schizophrenia

The disease could develop due to damage to on a particular type of brain cell.

Kristian Sjøgren

PUBLISERT Torsdag 05. oktober 2017 - 06:25

Curr Alzheimer Res. 2016;13(8):894-911.

Glial Cells - The Key Elements of Alzheimer´s Disease.

Dzamba D, Harantova L, Butenko O, Anderova M[1].

Author information

1 Department of Cellular Neurophysiology, Institute of Experimental Medicine, AS CR, Videnska 1083, 142 00 Prague 4, Czech Republic. anderova@biomed.cas.cz.

by Buck Institute

FEBRUARY 12, 2019 . PRESS RELEASE

Intervening in glial cells protects neurons in Parkinson's model

Buck researchers identify crosstalk between dopaminergic neurons and glial cells in fruit flies providing a potential new target for preventative treatment.

ARTICLE

Glial Cells—A New Target for Chronic Pain Treatment

Neurology Reviews. 2009 March;17(3):1, 21

NEUROLOGY REVIEWS

Scientists identify glial cells as important factor in development of schizophrenia

The disease could develop due to damage to on a particular type of brain cell.

Kristian Sjøgren

PUBLISERT Torsdag 05. oktober 2017 - 06:25

Curr Alzheimer Res. 2016;13(8):894-911.

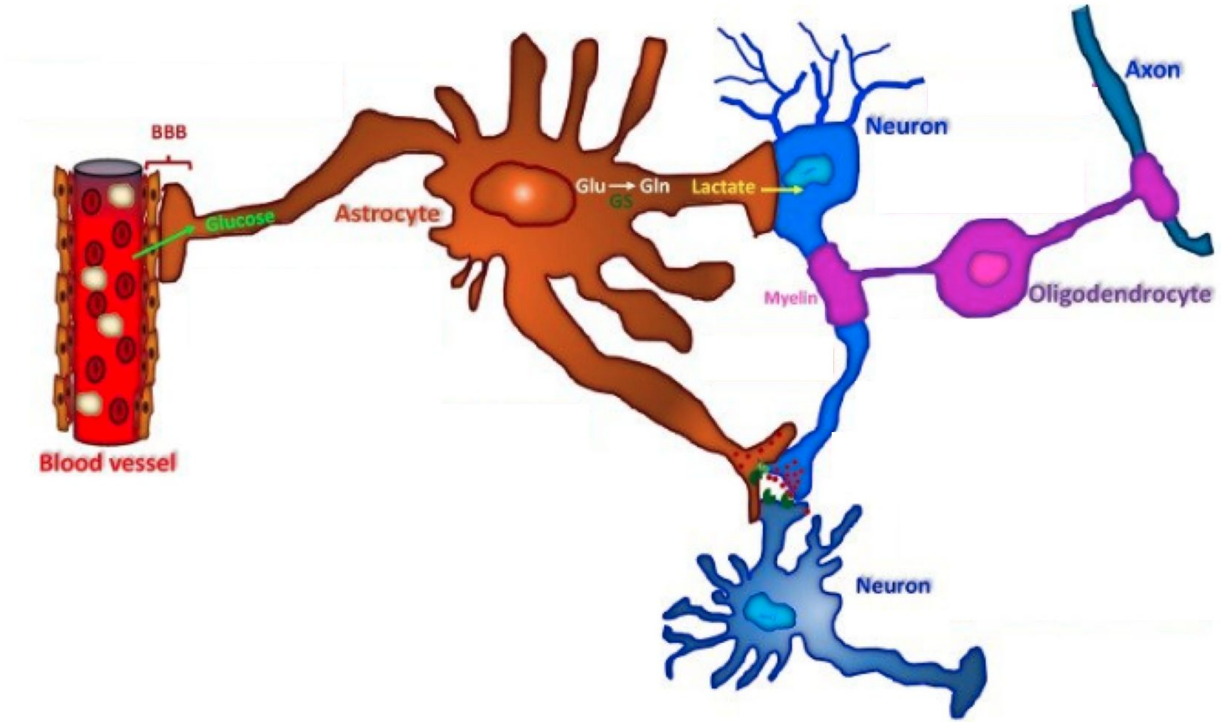
Glial Cells - The Key Elements of Alzheimer´s Disease.

Dzamba D, Harantova L, Butenko O, Anderova M[1].

Author information

1 Department of Cellular Neurophysiology, Institute of Experimental Medicine, AS CR, Videnska 1083, 142 00 Prague 4, Czech Republic. anderova@biomed.cas.cz.

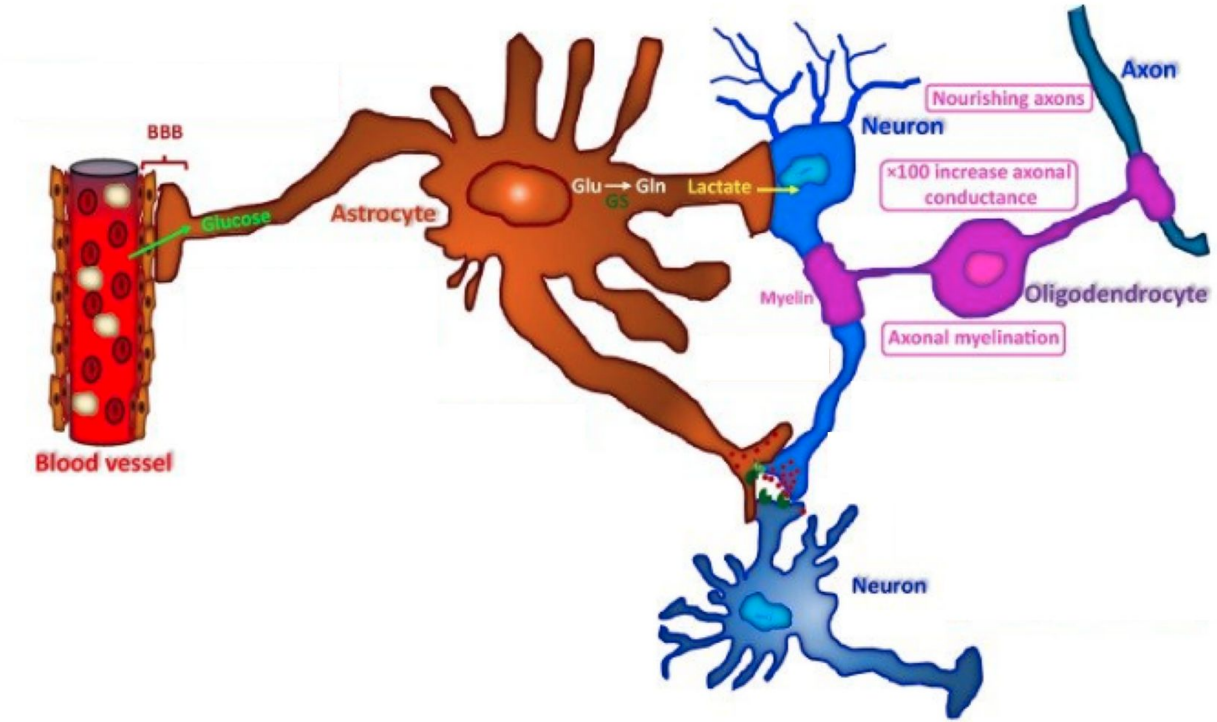
Glials are crucial to the wellbeing of neurons



[Kaminsky et al, 2016]

Glials are crucial to the wellbeing of neurons

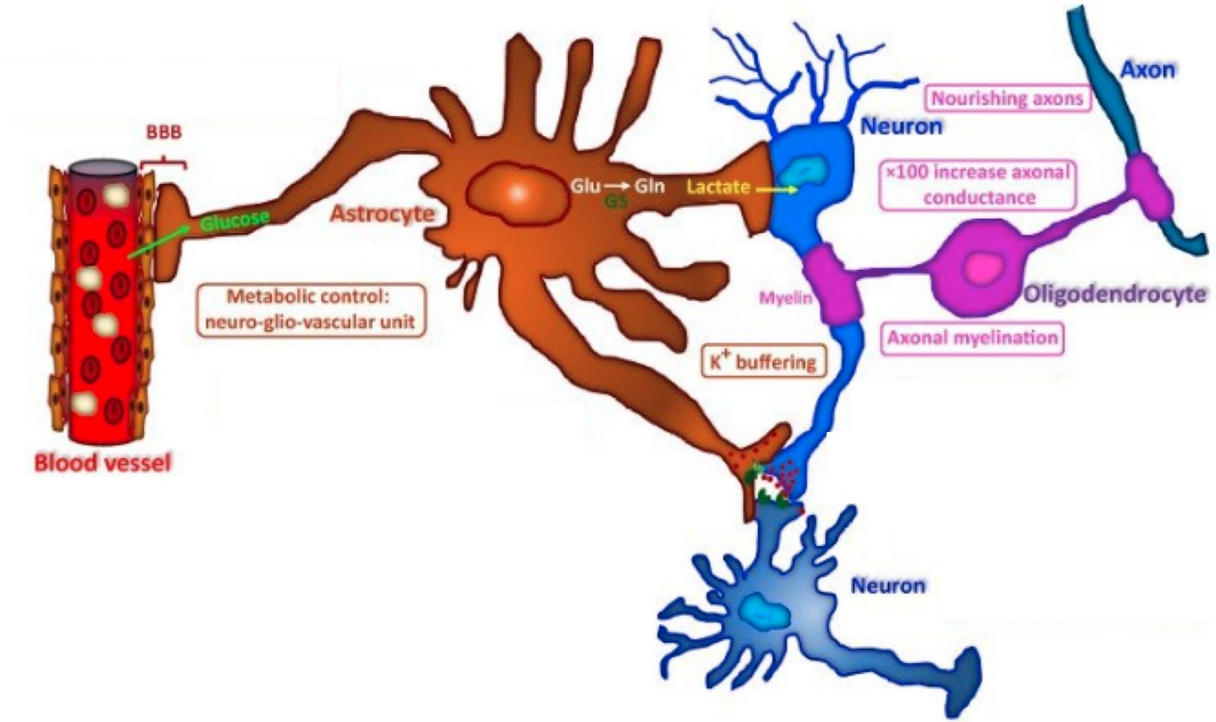
Help neurons send electrical signals efficiently



[Kaminsky et al, 2016]

Glials are crucial to the wellbeing of neurons

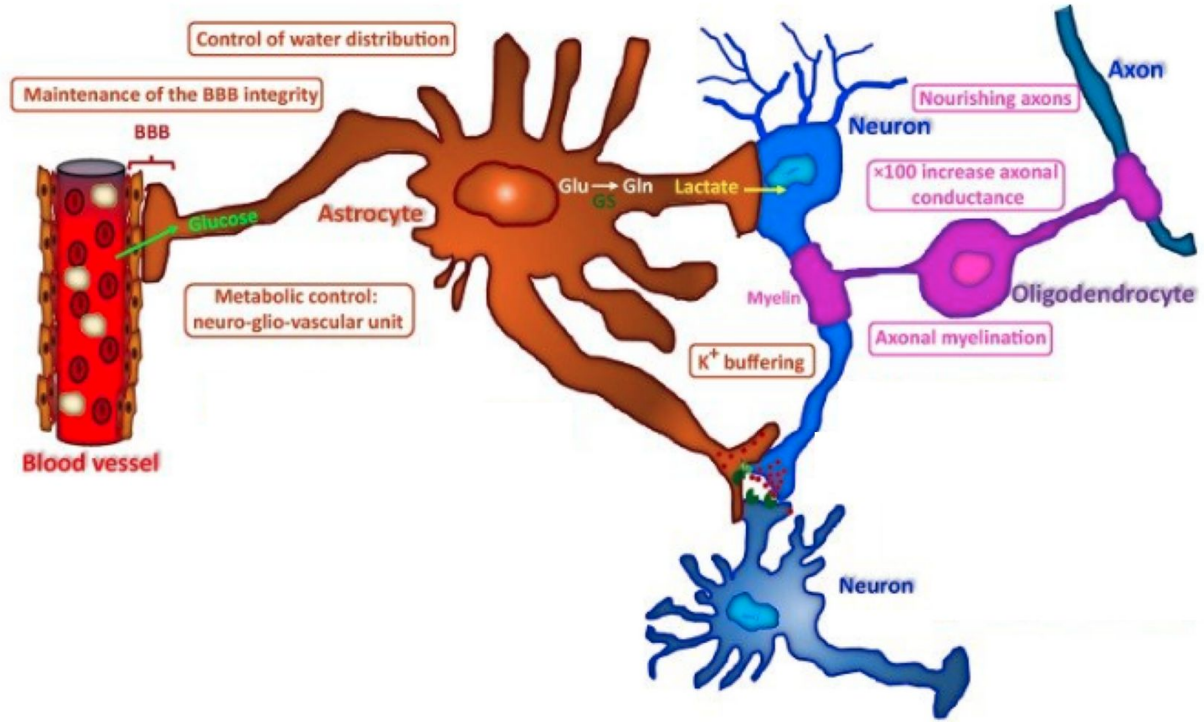
Keep the environment between the neurons clean



[Kaminsky et al, 2016]

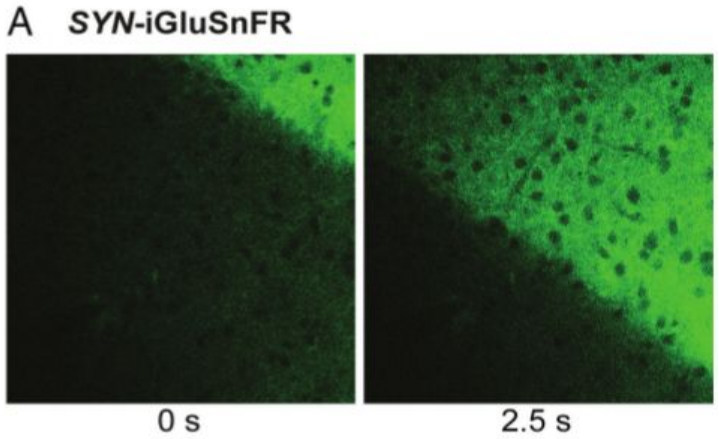
Glials are crucial to the wellbeing of neurons

Control water distribution in the brain tissue



[Kaminsky et al, 2016]

Traditional medical techniques struggle to give insight



[Enger et al, 2015]

A computational lab

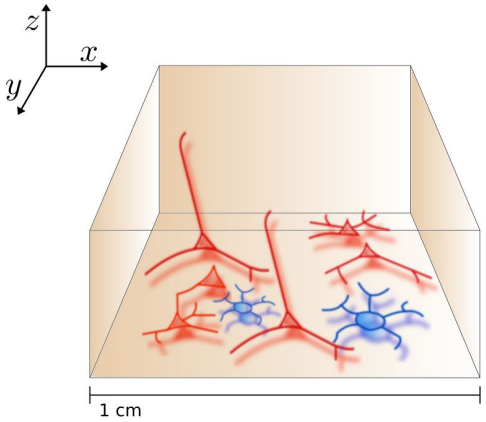
A computational lab

Electrodiffusion

How ions and molecules moves inside and outside cells to affect the electrical properties of the tissue

A computational lab

The mathematical model represents electrodiffusion processes in the brain tissue



Tissue model (PDEs)

- PDEs

Cell model (ODEs)

- ODEs and algebraic expressions

$$\alpha_n, [\mathrm{Na}^+]_n, [\mathrm{K}^+]_n, [\mathrm{Cl}^-]_n, \phi_n$$

$\gamma_n w_n$ ↓ $\gamma_n J_n$ ↓

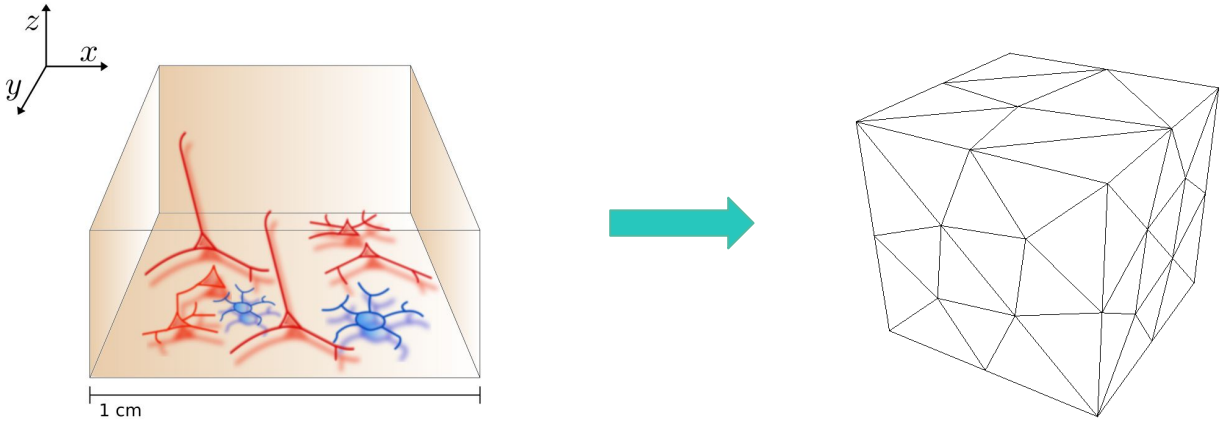
$$\alpha_e, [\mathrm{Na}^+]_e, [\mathrm{K}^+]_e, [\mathrm{Cl}^-]_e, \phi_e$$

$\gamma_g w_g$ ↑ $\gamma_g J_g$ ↑

$$\alpha_g, [\mathrm{Na}^+]_g, [\mathrm{K}^+]_g, [\mathrm{Cl}^-]_g, \phi_g$$

A computational lab

The equations are discretized such that they can be represented on the mesh



A computational lab

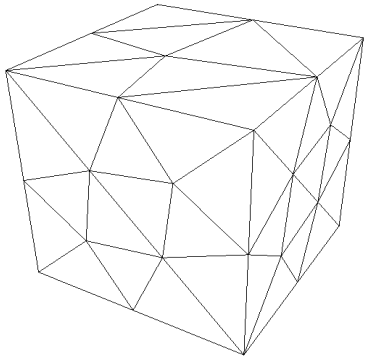
The discrete equations are solved using the finite element method

```
def ODE_solver(self):
    """ Create PointIntegralSolver for solving membrane ODEs """
    # split function for unknown PDE solution in previous time step
    phi_N_ = split(self.w_)[11]
    phi_E_ = split(self.w_)[13]
    # membrane potential for neuron in previous time step
    phi_NE_ = phi_N_ - phi_E_

    # trial and test functions
    s = split(self.ss)
    q = split(TestFunction(self.S))
    # get rhs of ODE system
    F = self.problem.F
    F_exprs = F(phi_NE_, s, self.problem.t)
    F_exprs_q = ufl.zero()

    for i, expr_i in enumerate(F_exprs.ufl_operands):
        F_exprs_q += expr_i*q[i]
    rhs = F_exprs_q*dP()

    # create ODE scheme
    Scheme = eval("BackwardEuler")
    scheme = Scheme(rhs, self.ss, self.problem.t)
    # create ODE solver
    self.pi_solver = PointIntegralSolver(scheme)

    return
```

A computational lab

The computational solver is verified by comparing results to experimental data

Computational model

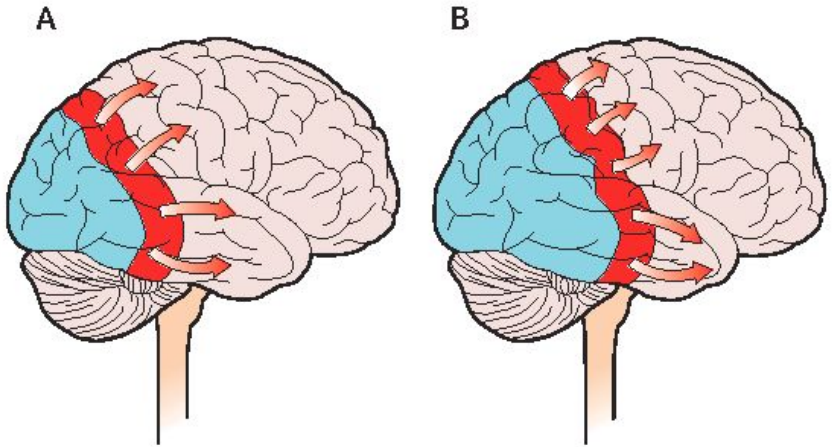


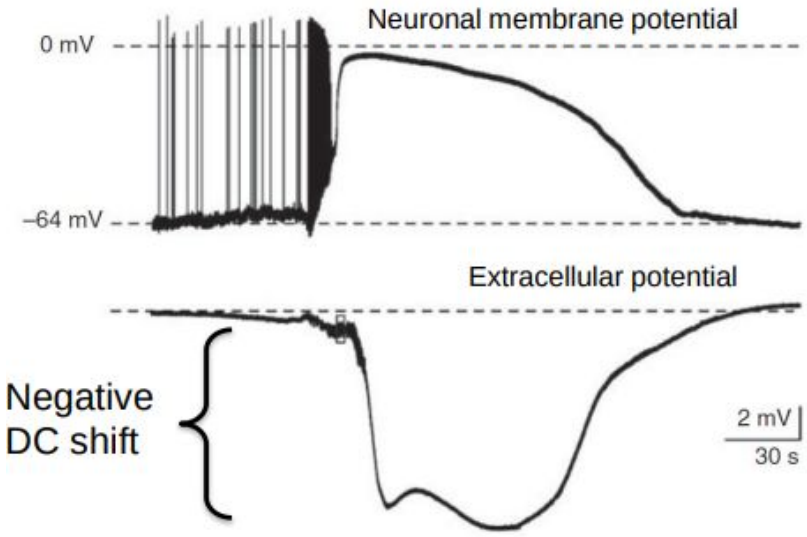
Experimentalists (lab)

Role of glial cells in spreading depression

Spreading depression

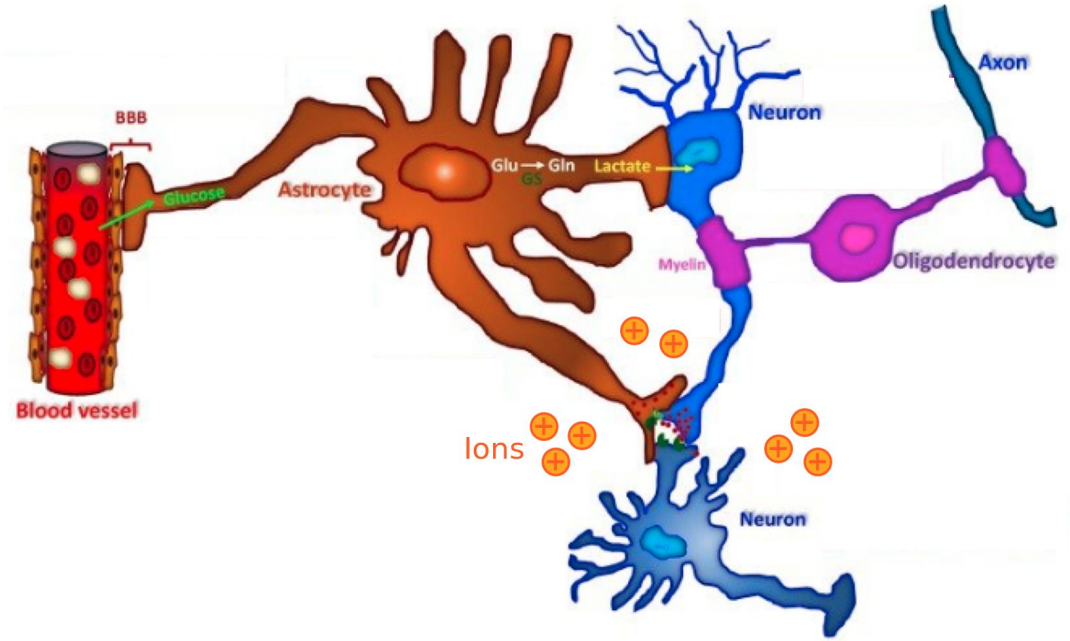
Spreading depression is a wave of rapid depolarization of the brain tissue.





[Ghadiri et al. 2012]

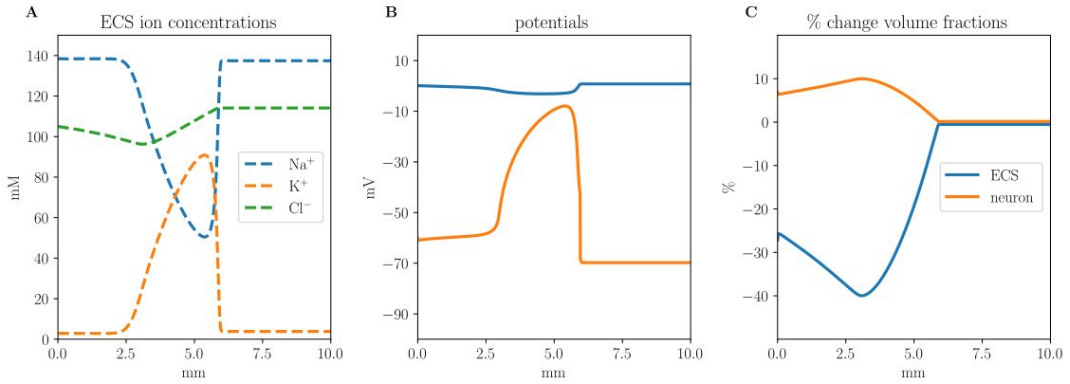
During spreading depression, ions accumulated in the extracellular space



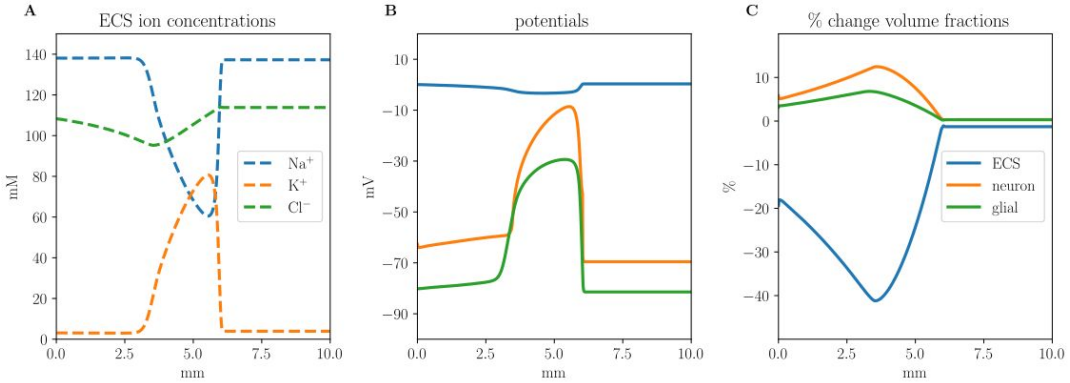
Can glial cells act as a buffer to keep the extracellular space clean?

[Kaminsky et al, 2016]

Can glial cells act as a buffer to keep the space between the cells clean?

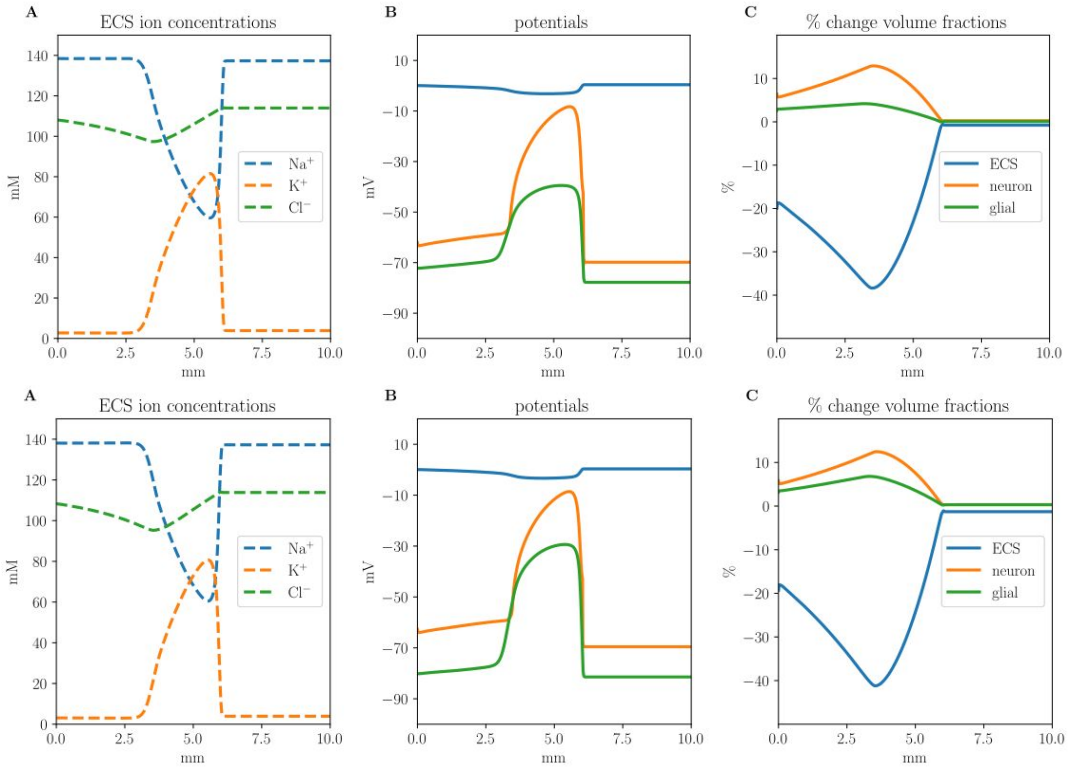


No glial



With glial

What is the effect of blocking the KIR channel?



Block KIR

Open KIR

Mathematical modelling will not replace medical experiments but, ..

- .. it is a promising tool to provide new insight where traditional medical techniques fail
- .. can be used to test hypothesis in a flexible and efficient manner

simula

UiO :

This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme under grant agreement 714892"

Thank you!

08.10.2019

Ada Johanne Ellingsrud •
ada@simula.no