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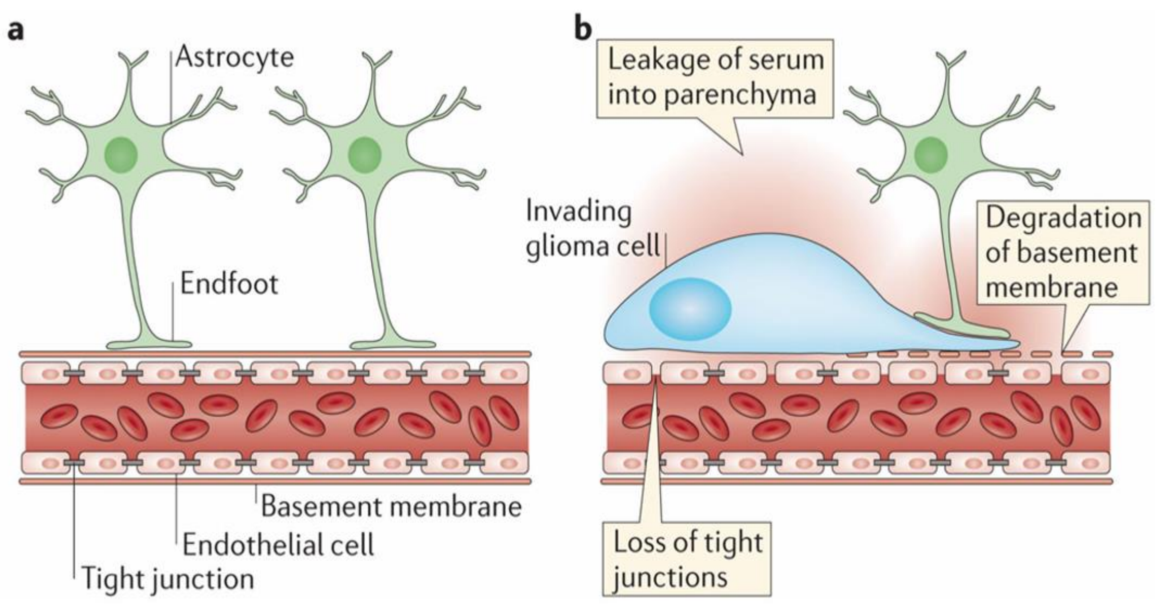
Glioma Infiltration between Astrocytes and Blood Vessels (ODE & PDE)

1. Introduction



Glioma cells migrate along blood vessels, squeezing through narrow spaces between **astrocytic** endfeet and **blood vessels**, while reducing their volume by up to 33%. This **volume regulation** is closely linked to ion channels, particularly involving chloride (Cl-) and calcium (Ca2+) ions. In this study, we focused on the interactions between these ions and how they contribute to volume regulation in glioma cells.

2. ODE Modeling of Ca^{2+} and Cl^{-}

$A(t)$	Area between Glioma and Astrocyte
$Ca(t)$	Ca^{2+} concentration in Glioma cell
$Cl(t)$	Cl^{-} concentration in Glioma cell
$Cl_A(t)$	Cl^{-} concentration in Astrocyte
μ	Ca^{2+} decay rate in Glioma cell
α	Cl^{-} decrease rate
β	Cl^{-} increase rate
K	Ca^{2+} threshold value
M	Maximum of Cl^{-} concentration in Glioma cell
m	Minimum of Cl^{-} concentration in Astrocyte

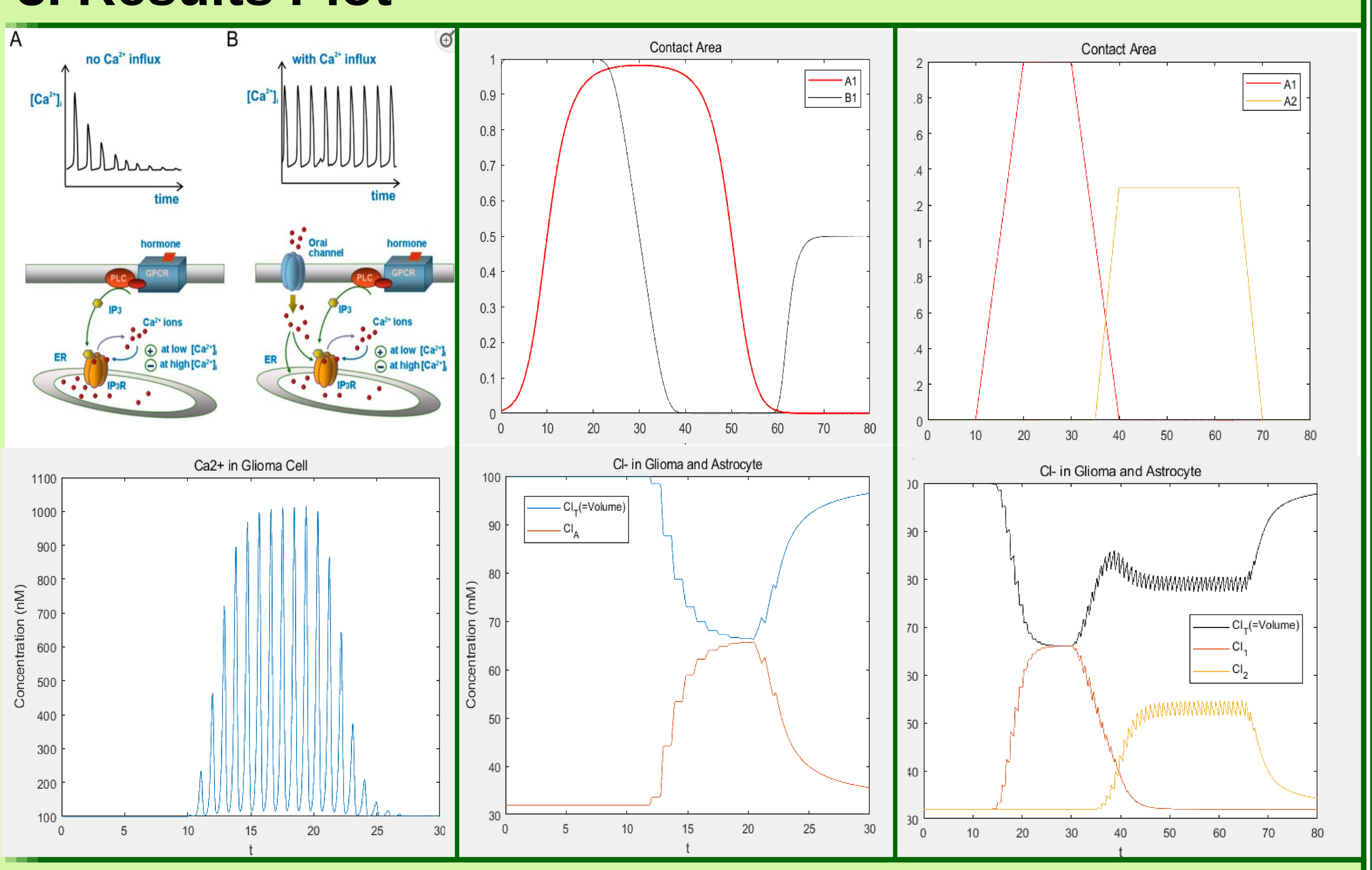
$$\frac{dg(t)}{dt} = A(t) - \mu g(t)$$

$$\frac{dCa(t)}{dt} = g(t)\cdot h(t) \mid h(t): \text{periodic fun. for modeling oscillation.}$$

$$B(t) = \frac{1}{1+e^{-c\frac{dA}{dt}}} \quad \text{sigmoid fun. dependent on the change in } A(t).$$

$$\frac{dCl(t)}{dt} = -\alpha A(t)B(t)\left(\frac{Ca(t)^n}{K^n+Ca(t)^n}\right)\left(Cl(t)-Cl_A(t)\right)$$
$$+\beta A(t)\left(1-B(t)\right)\left(1-\frac{Ca(t)^n}{K^n+Ca(t)^n}\right)\left(1-\frac{Cl(t)}{M}\right)\left(\frac{Cl_A(t)}{m}-1\right)$$

3. Results Plot



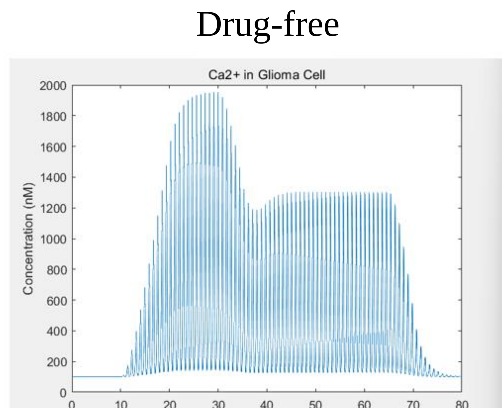
4. Drug Injection

Icatibant : reduces the Ca^{2+} concentration in glioma cell and prevents the switching on of Cl^{-} channel.

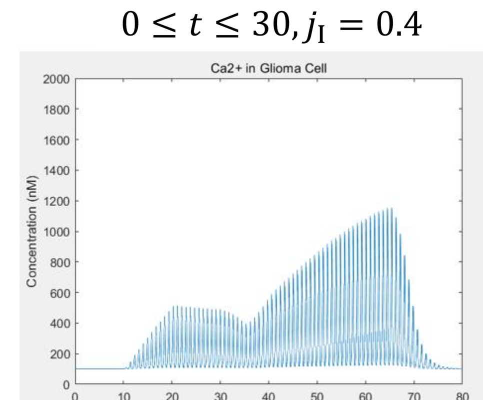
$$\frac{dI}{dt} = j_I(t) - \mu_I I \qquad j: \text{injection}, \ \mu: \text{decay rate}$$

$$\frac{dg(t)}{dt} = A(t) - \mu g(t)(1+I(t))$$

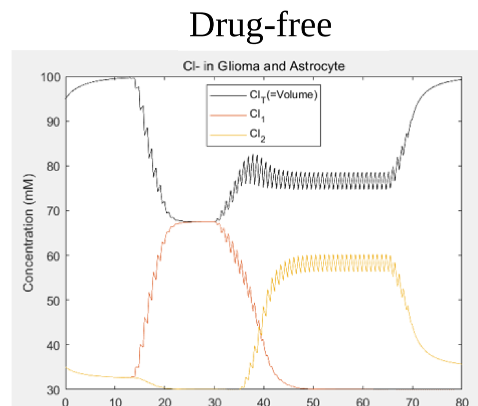
Drug-free



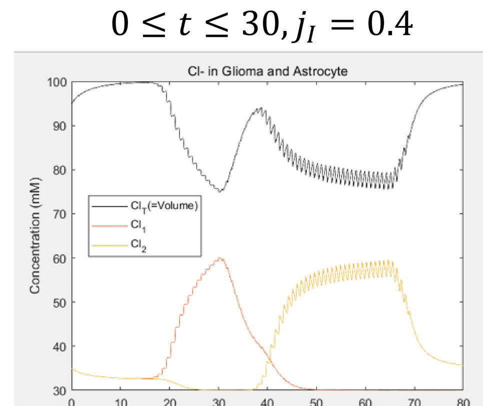
$0 \le t \le 30, j_I = 0.4$



Drug-free



$0 \le t \le 30, j_I = 0.4$

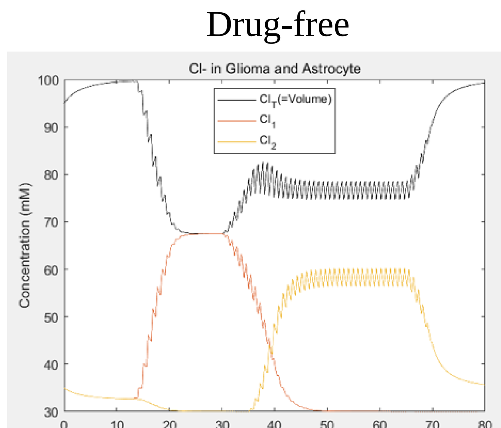


Chlorotoxin : inhibits Cl^{-} channels, reducing the efflux of Cl^{-}.

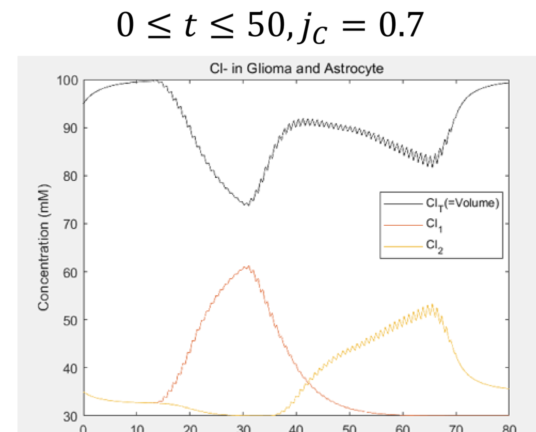
$$\frac{dC}{dt} = j_C(t) - \mu_C C \qquad j: \text{injection}, \ \mu: \text{decay rate}$$

$$\frac{dCl(t)}{dt} = -\frac{\alpha}{1+C(t)}A(t)B(t)\cdot\left(\frac{Ca(t)^n}{K^n+Ca(t)^n}\right)\left(Cl(t)-Cl_A(t)\right)$$
$$+\beta A(t)\left(1-B(t)\right)\left(1-\frac{Ca(t)^n}{K^n+Ca(t)^n}\right)\cdot\left(1-\frac{Cl(t)}{M}\right)\left(\frac{Cl_A(t)}{m}-1\right)$$

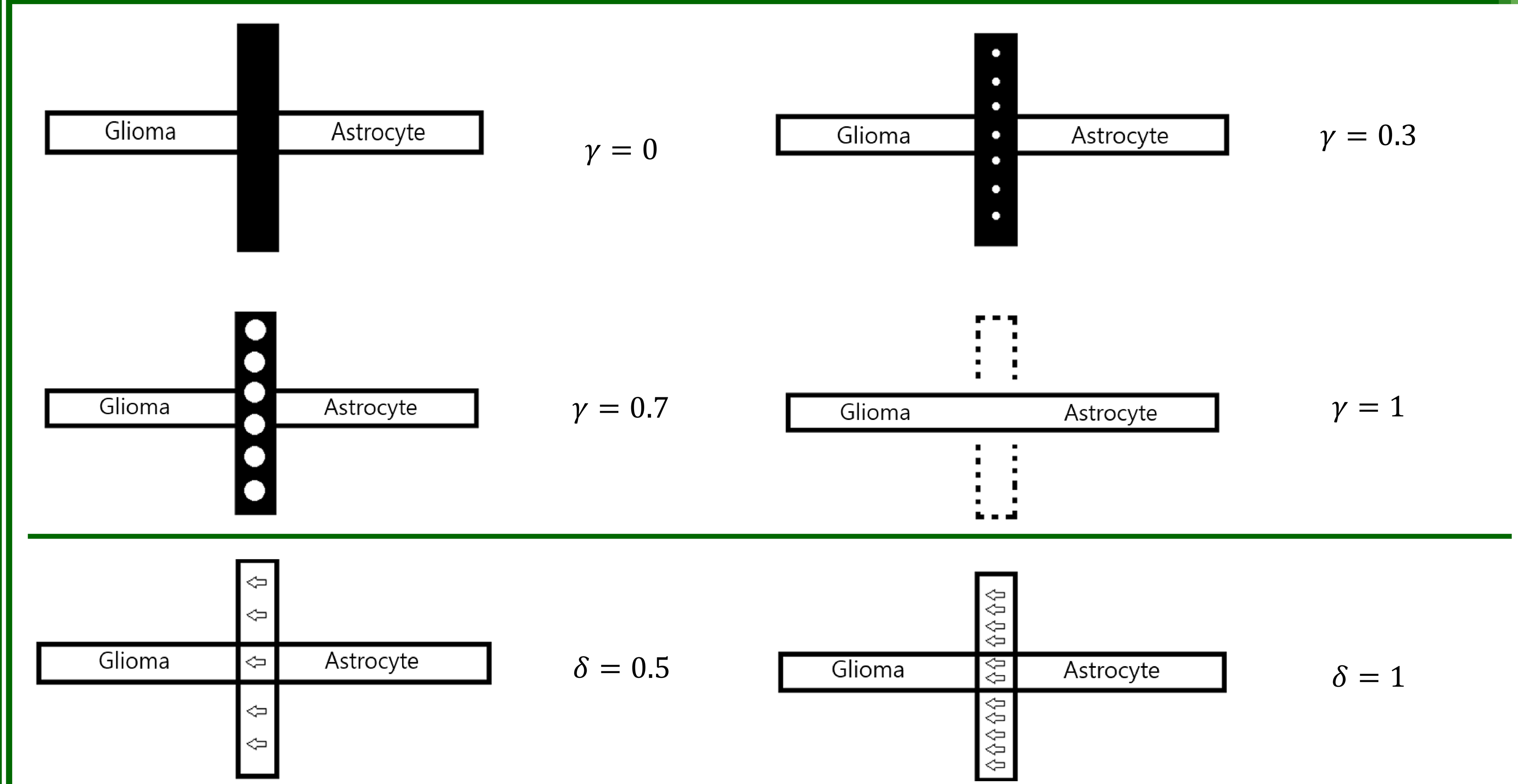
Drug-free



$0 \le t \le 50, j_C = 0.7$



5. Diffusion PDE with Interface Boundary



6. Total Sum Conservation and γ Filter

※Total sum conservation of the diffusion PDE under Neumann boundary condition

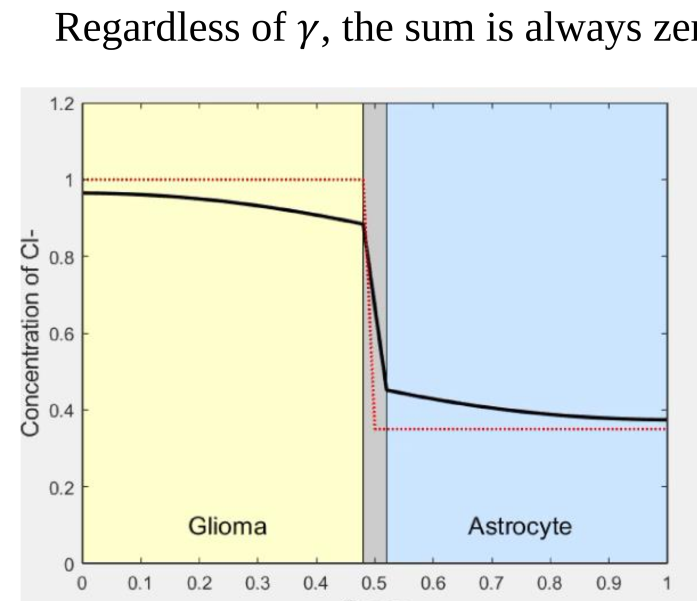
$$u(i+1,1) = u(i,1) + D\frac{dt}{(dx)^2}\left[u(i,2) - 2u(i,1) + \boldsymbol{u(i,1)}\right]$$
$$u(i+1,2) = u(i,2) + D\frac{dt}{(dx)^2}\left[u(i,3) - 2u(i,2) + u(i,1)\right]$$
$$\vdots$$
$$u(i+1,j-1) = u(i,j-1) + D\frac{dt}{(dx)^2}\left[u(i,j) - 2u(i,j-1) + u(i,j-2)\right]$$
$$u(i+1,j) = u(i,j) + D\frac{dt}{(dx)^2}\left[u(i,j+1) - 2u(i,j) + u(i,j-1)\right]$$
$$u(i+1,j+1) = u(i,j+1) + D\frac{dt}{(dx)^2}\left[u(i,j+2) - 2u(i,j+1) + u(i,j)\right]$$
$$\vdots$$
$$u(i+1,N-1) = u(i,N-1) + D\frac{dt}{(dx)^2}\left[u(i,N) - 2u(i,N-1) + u(i,N-2)\right]$$
$$+\quad u(i+1,N) = u(i,N) + D\frac{dt}{(dx)^2}\left[\boldsymbol{u(i,N)} - 2u(i,N) + u(i,N-1)\right]$$

$$S(i+1) = S(i) + \boldsymbol{0} \quad \text{Total sum does not change!}$$

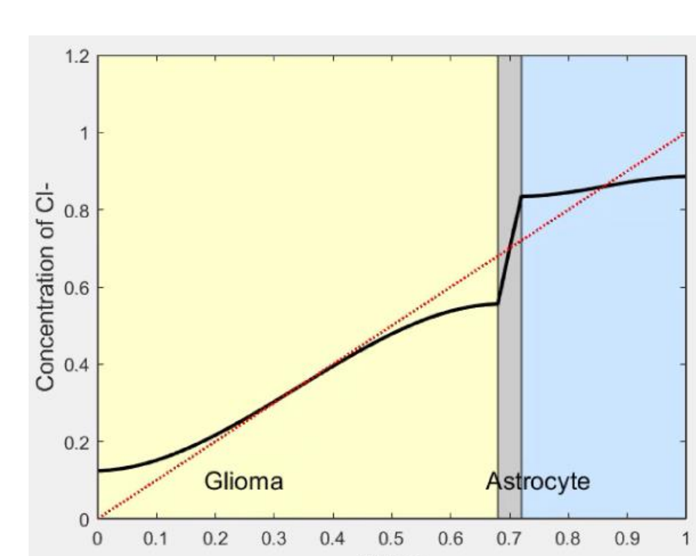
※ Linear interpolation of γ filter

$$\vdots$$
$$[u(i,j^*-1) - 2u(i,j^*-2) + u(i,j^*-3)]$$
$$[\boldsymbol{\gamma\cdot u(i,j^*) - (1+\gamma)\cdot u(i,j^*-1)} + u(i,j^*-2)]$$
$$j^*\text{th row} \cdots \quad \boldsymbol{\gamma}\cdot[u(i,j^*+1) - 2u(i,j^*) + u(i,j^*-1)] \quad \cdots \text{location of the filter}$$
$$[u(i,j^*+2) \boldsymbol{- (1+\gamma)\cdot u(i,j^*+1) + \gamma\cdot u(i,j^*)}]$$
$$[u(i,j^*+3) - 2u(i,j^*+2) + u(i,j^*+1)]$$
$$\vdots$$

$\gamma = 0$ makes two separable Neumann interface boundary
$\gamma = 1$ makes one continuous compartment(No interface boundary)
Regardless of γ, the sum is always zero.



$\gamma = 0.1$
Filter : 0.5
Red line : Initial condition.



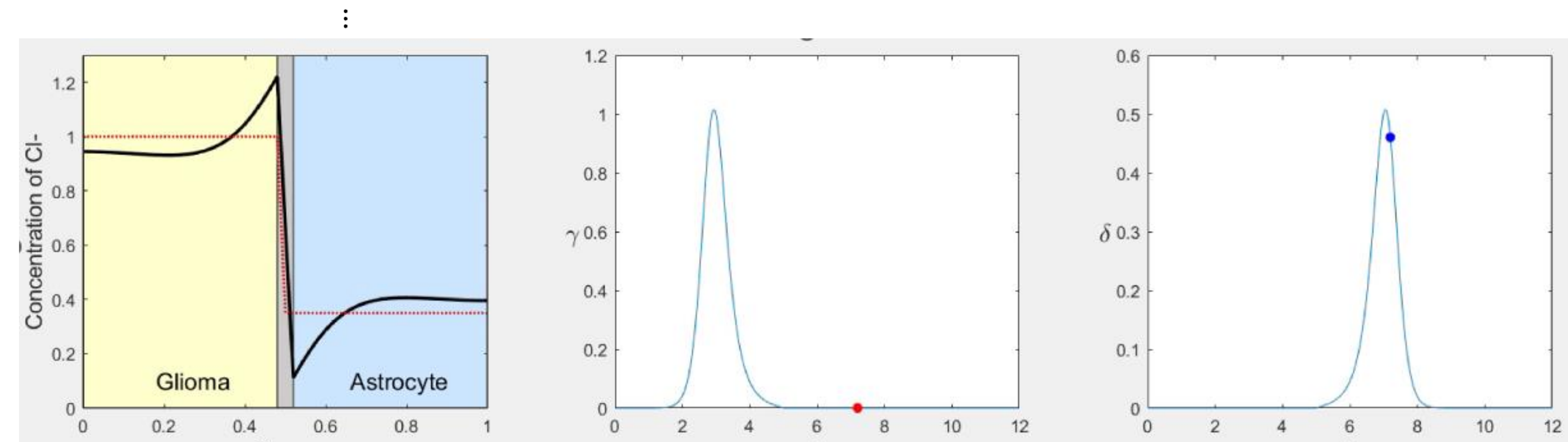
$\gamma = 0$
Filter : 0.7
Red line : Initial condition.

7. γ and δ Filter

$$\vdots$$
$$[u(i,j^*-1) - 2u(i,j^*-2) + u(i,j^*-3)]$$
$$[\boldsymbol{\delta\cdot 2u(i,j^*) - (1+\delta)\cdot u(i,j^*-1)} + u(i,j^*-2)]$$
$$\boldsymbol{\delta}\cdot[u(i,j^*+1) - 2u(i,j^*) + u(i,j^*-1)]$$
$$[u(i,j^*+2) \boldsymbol{- (\delta+1)\cdot u(i,j^*+1)}]$$
$$[u(i,j^*+3) - 2u(i,j^*+2) + u(i,j^*+1)]$$
$$\vdots$$

※ Linear interpolation of δ filter

$\delta = 0$ makes two separable Neumann interface boundary
$\delta = 1$ shifts $u(i,j)$ from the right adjacent index to the left.
Regardless of δ, the total sum is always zero.



8. References

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