Effect on tumor growth in systems of two different types of tumor-associated neutrophils: A mathematical model

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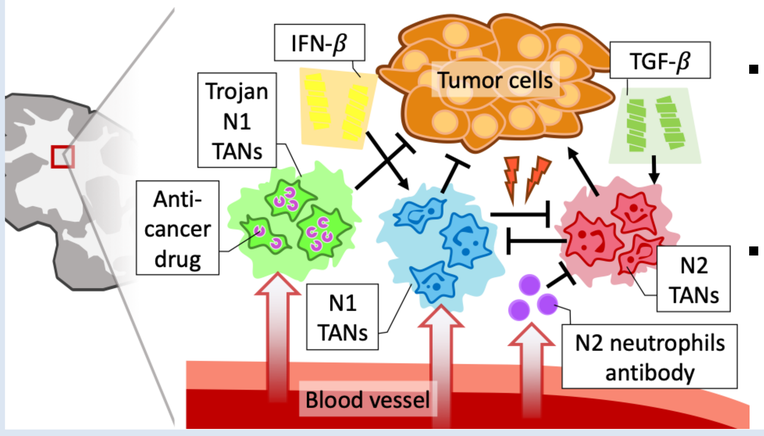
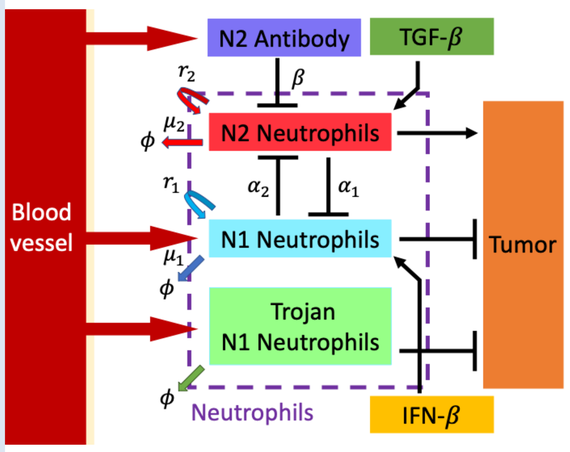
1. Introduction



- Understanding elements of tumor microenvironment (TME) is essential for modeling tumor growth.
- We focused on tumor-associated neutrophils (TANs) which have dual effects on tumor according to their phenotype: anti-tumor (N1) and pro-tumor (N2) effect.
- We adopt a hybrid approach including partial differential equation (PDE) results and cellular automata (CA) to simulate cancer therapy on human brain structure.

2. Mathematical model



$$\frac{\partial N_1}{\partial t} = D_{N_1}\Delta N_1 + r_1 N_1\left(1-\frac{N_1}{w_1 S + K_1}\right) - \alpha_1 N_1 N_2 - \mu_1 N_1$$

$$\frac{\partial N_2}{\partial t} = D_{N_2}\Delta N_2 + r_2 N_2\left(1-\frac{N_2}{w_2 G + K_2}\right) - \alpha_2 N_2 N_1 - \mu_2 N_2 - \beta N_2 A$$

$$\frac{\partial A}{\partial t} = D_A \Delta A + \lambda_A I_A - \mu_A A$$

$$\frac{\partial S}{\partial t} = D_S \Delta S + \lambda_S I_S - \mu_S S$$

$$\frac{\partial G}{\partial t} = D_G \Delta G + \lambda_G I_G - \mu_G G$$

$$\frac{\partial n}{\partial t} = D_n \Delta n + r\left(1 + r_N \frac{{N_2}^2}{k^2 + {N_2}^2}\right) n\left(1-\frac{n}{n_0}\right) - \mu_n N_1 n$$

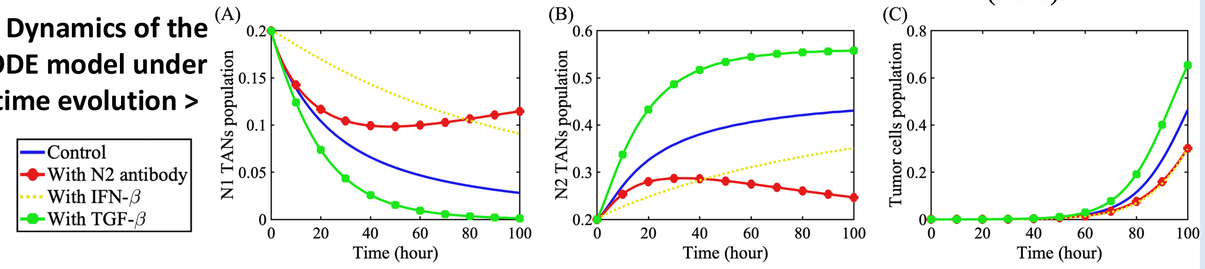
※ Trojan N1 is included in the hybrid approach section

N_1	N1 neutrophils	A	N2 neutrophils antibody
N_2	N2 neutrophils	S	IFN-β
n	Tumor cells	G	TGF-β

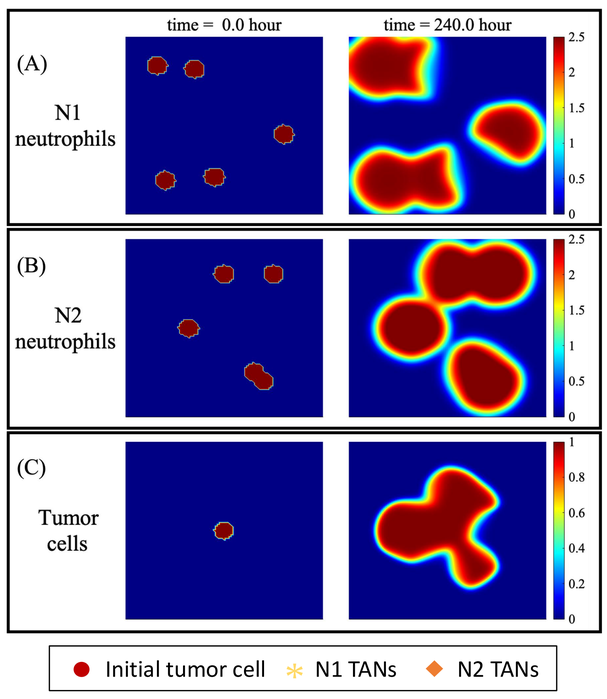
3. ODE & PDE results

※ We obtain results from numerical methods using MATLAB ode45 (ODE) and Euler forward method with central difference (PDE).

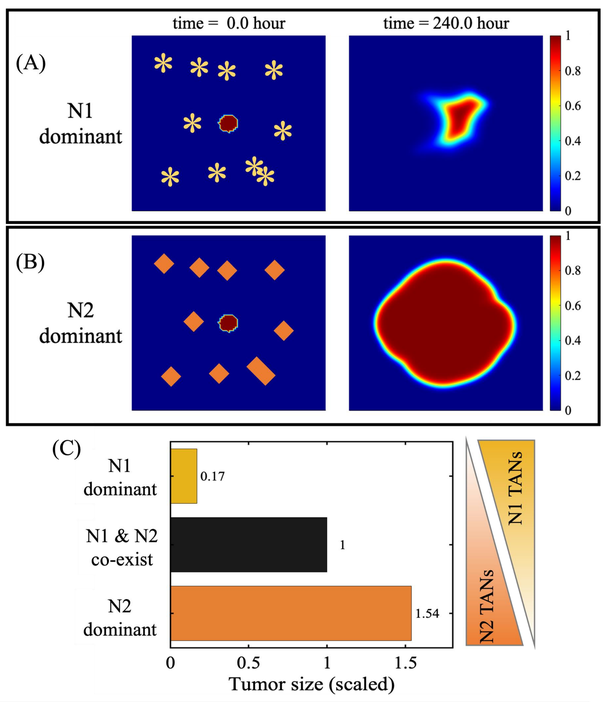
< Dynamics of the ODE model under time evolution >



< Diffusion portraits from PDE mode l>

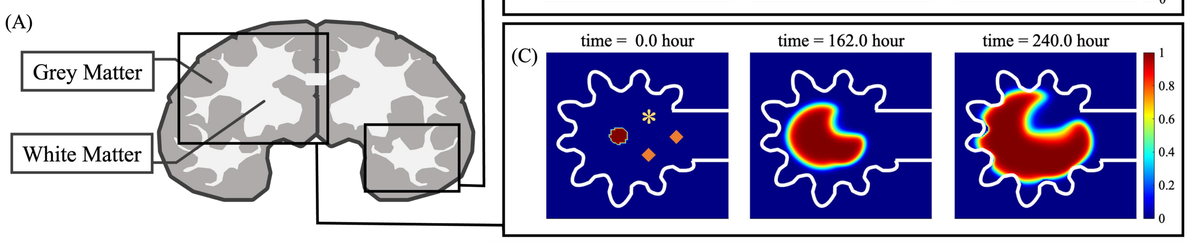


< Tumor growth under varied initial conditions >



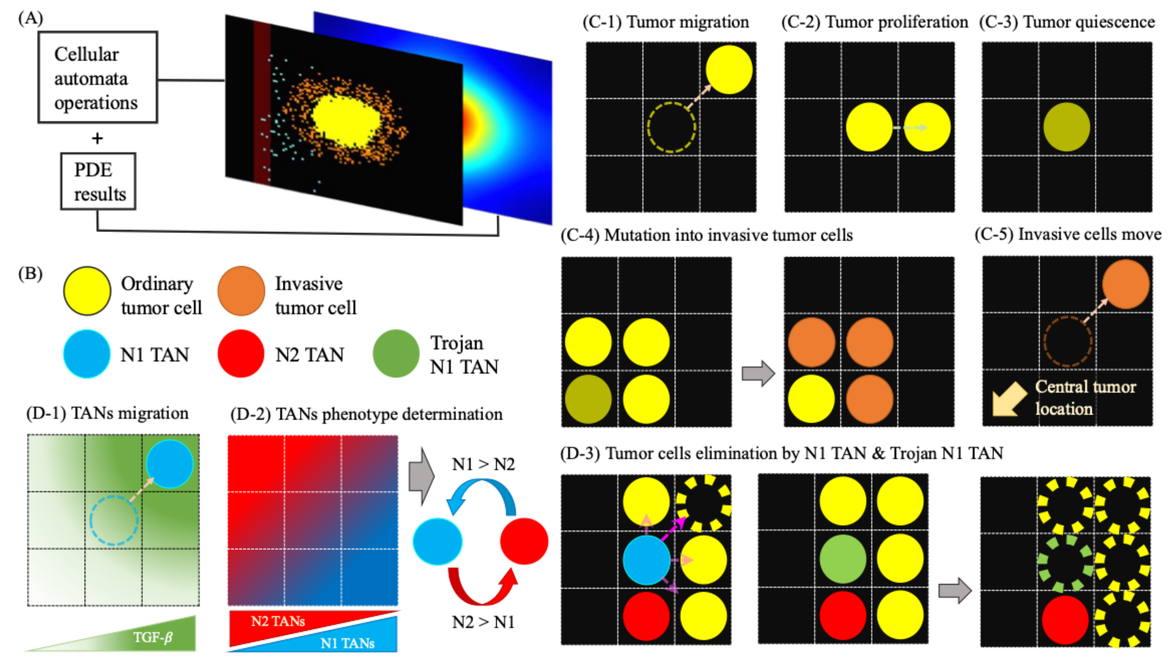
< Tumor growth on human brain tissue with dual diffusion properties >

※ We assume diffusion rate in grey matter is 10^{-6} time of that in white matter.

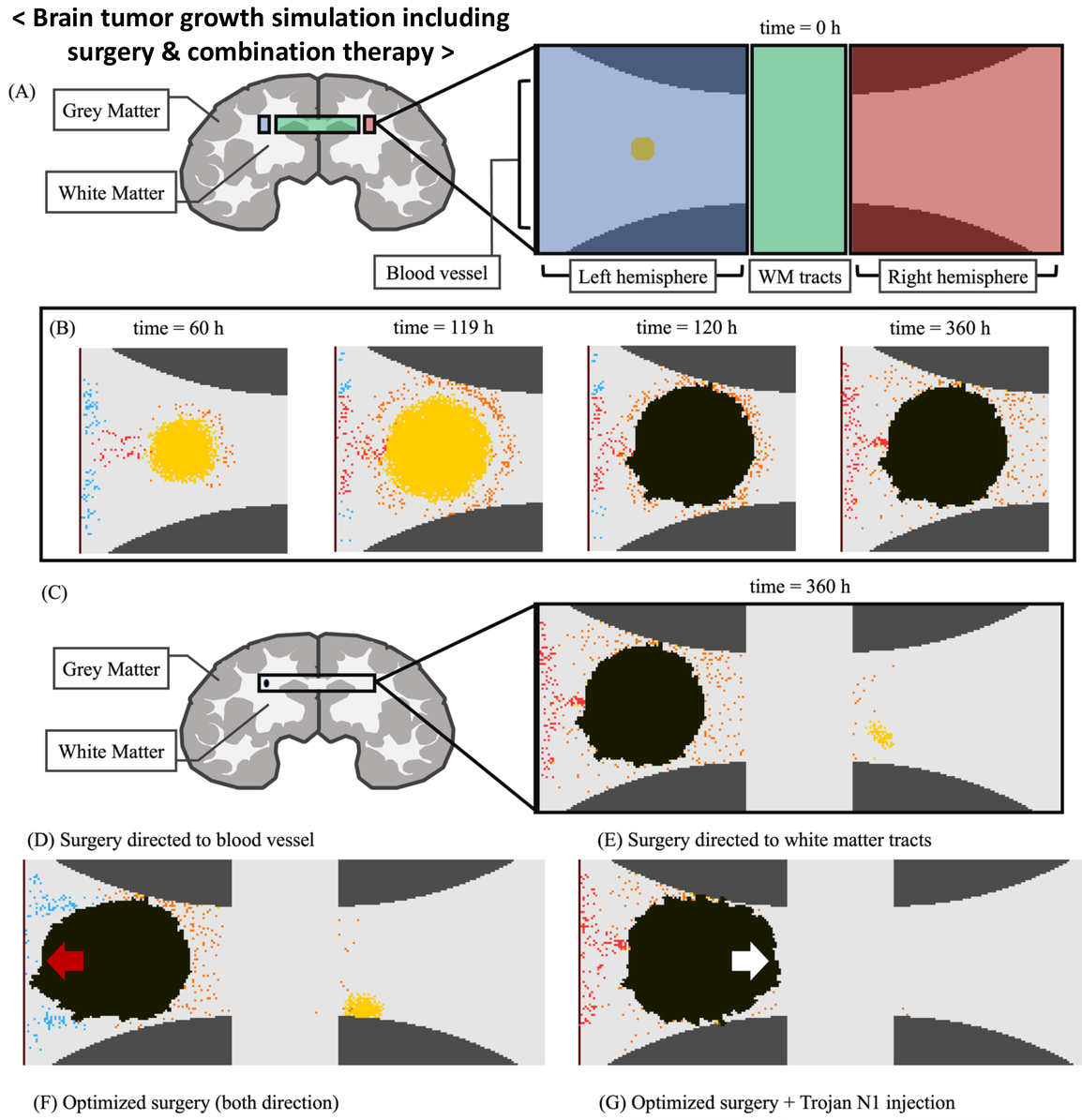


4. Hybrid approach

< Hybrid model introduction & CA rule mechanics >



< Brain tumor growth simulation including surgery & combination therapy >



5. Discussion

- Maintaining N1 TANs domination against N2 TANs is the key of therapeutic approach when utilizing TANs as a cancer treatment agent based on the modeling results.
- To construct a treatment simulation established from the model, considering additional methods with adequate assumptions enables us to enhance the result's accuracy and reliability.
- Using N1 TANs as a nanocarrier can resolve the tumor recurrence problem after surgery on brain tumor which is originated from the invasive tumor cell's high tendency.

6. References

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