Inverse problems for biomedical models of brain tumor evolution

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Motivation

- Brain cancer is one of the most common cancer-types worldwide
- Reconstruction of initial cell density may aid cancer research

Tumor growth model for brain cancer [J. D. Murray, 2002]

Reaction-diffusion formalism describes the evolution of tumor cell density via two biological phenomena – *diffusion* and *proliferation*:

$$\begin{aligned} \partial_t u(x,t) - \operatorname{div}(D(x)\nabla u(x,t)) &= f(u(x,t)) && \text{in } \Omega\times(0,T),\\ D(x)\nabla u(x,t)\cdot n(x) &= 0 && \text{on } \partial\Omega\times(0,T), \end{aligned}$$

where $D(x)$ is a diffusion coefficient, $f(u)$ a proliferation function, $u(x,t)$ a normalized *tumor cell density*, and Ω the brain region.

Direct problem – Prediction (well-posed)

Determine a **future state** of a tumor given its current state, i.e., $u(x,0)$ is known and the model is used to compute $u(x,T)$.

Inverse problem – Source localization (ill-posed)

Determine an **initial state** of a tumor given its current state, i.e., $\psi(x) := u(x,T)$ is known and the model is used to compute $u(x,0)$.

This inverse problem is *ill-posed* since small measurement error may have a profound adverse effect on computational errors.

Main contribution: Solving the inverse problem

We propose an iterative method, where the ill-posed problem is replaced by well-posed problems with multiple regularizing terms.

Sobolev-type cost in non-linear conjugate gradient (NCG)

Given a current state $\psi(x)$ and a set of regularization parameters $m_1, m_2, \mu_1, \mu_2 \geq 0$, one aims to minimize the cost functional

$$\begin{aligned} E(u) = {} & m_1\|u(\cdot,T)-\psi(\cdot)\|^2_{L^2(\Omega)} + m_2\|\nabla u(\cdot,T)-\nabla\psi(\cdot)\|^2_{L^2(\Omega)}\\ & + \mu_1\|u(\cdot,0)\|^2_{L^2(\Omega)} + \mu_2\|\nabla u(\cdot,0)\|^2_{L^2(\Omega)} \end{aligned}$$

Given a guesstimate of initial data $u(x,0)$, the direct problem is solved. Then, the following **well-posed** *adjoint problem* is solved:

$$\begin{aligned} \partial_t\lambda(x,t) + \operatorname{div}(D(x)\nabla\lambda(x,t)) &= f'_u(u(x,t))\lambda(x,t) && \text{in } \Omega\times(0,T),\\ D(x)\nabla\lambda(x,t)\cdot n(x) &= 0 && \text{on } \partial\Omega\times(0,T),\\ \lambda(x,T) &= (m_1+\widetilde{m}_2\Delta)(u(x,T)-\psi(x,T)) && \text{in } \Omega, \end{aligned}$$

The Fréchet derivative of the cost functional is then given by

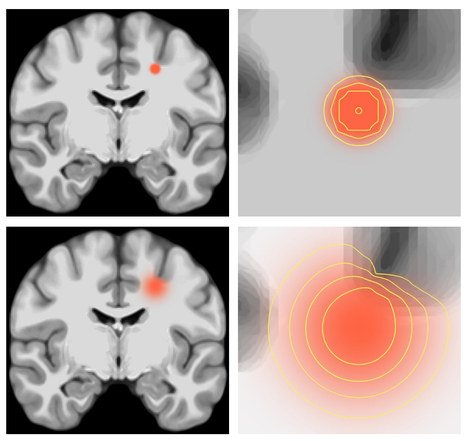
$$E'(u) = \mathcal{S}\big(\lambda(x,0)+\mu_1 u(x,0)\big) + \widetilde{\mu}_2 u(x,0), \qquad x\in\Omega,$$

where the operator $\mathcal{S}$ transforms elements of L^2-dual to Sobolev $W^{1,2}$-dual. The descent direction is obtained by *Fletcher–Reeves* conjugate gradient. The *optimal step-length* for updating the initial data estimate $u(x,0)$ is found by solving a sensitivity problem.

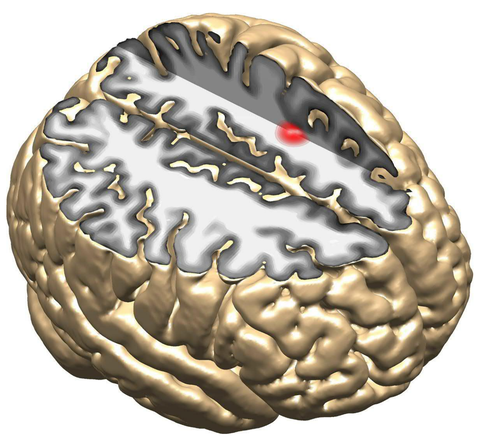
Numerical results

Set-up: Brain region Ω and the diffusion coefficient $D(x)$ were based on segmentation of T1-weighted MR images from BraTS2020 dataset. Proliferation function was logistic, i.e., $f(u) = \rho u(1-u)$.

A tumor with Gaussian cell density was planted at a random position in the white matter, and grown according to the model.

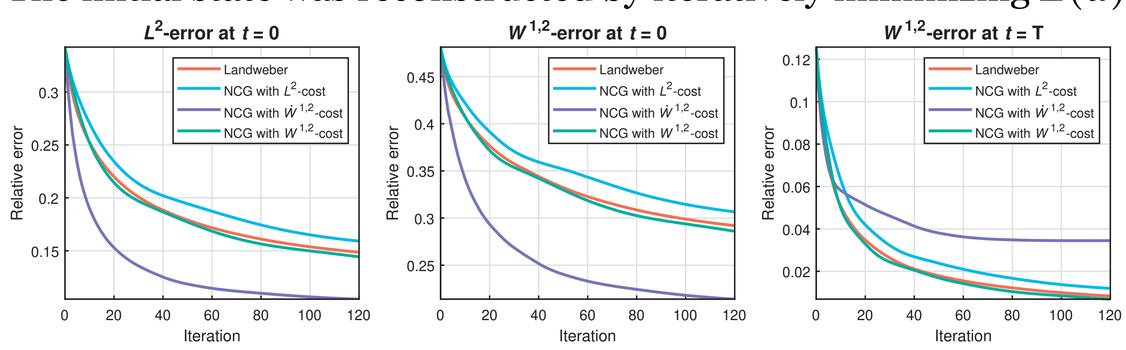


Coronal brain slice
Tumor at $t = 0$ (top) and $t = T$ (bottom)

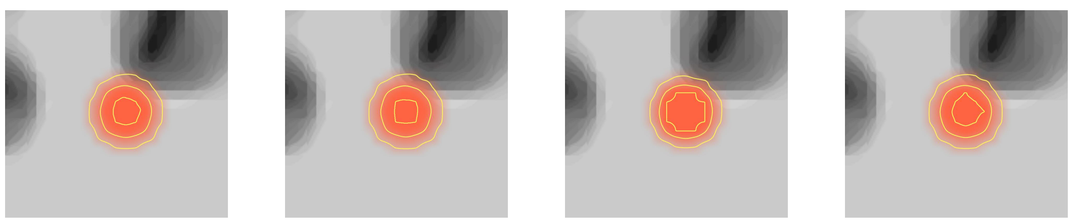


Brain with axial and sagittal slice
Tumor at $t = T$

The initial state was reconstructed by iteratively minimizing $E(u)$.



Various error measurements during the reconstruction process



Landweber | NCG with L^2-cost | NCG with $\dot{W}^{1,2}$-cost | NCG with $W^{1,2}$-cost

Cell density at $t = 0$ as reconstructed for different cost functionals $E(u)$

Conclusion

- Finetuning regularization parameters allows faster convergence, while keeping numerical stability of the solution.
- Simulation with planted tumors shows potential for our approach.

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