Multiscale models for glioma invasion: proliferation and therapy aspects

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Bedlewo, June 2015

Joint work with:

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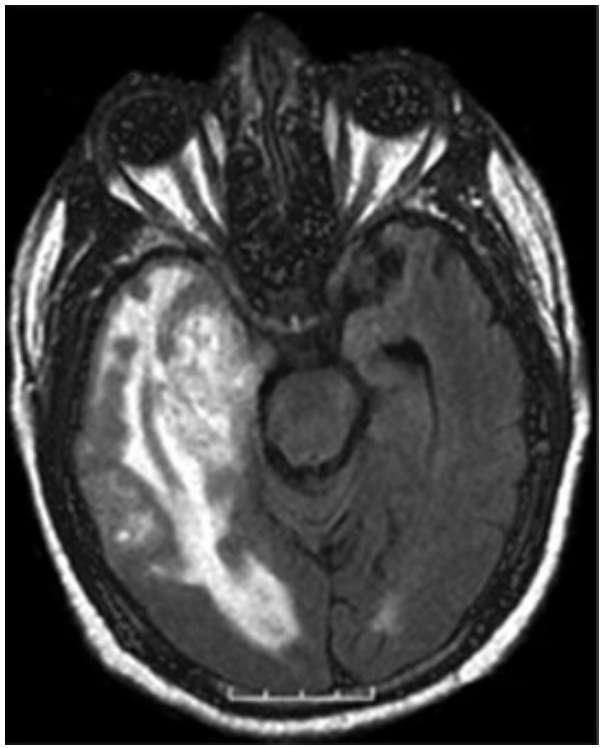
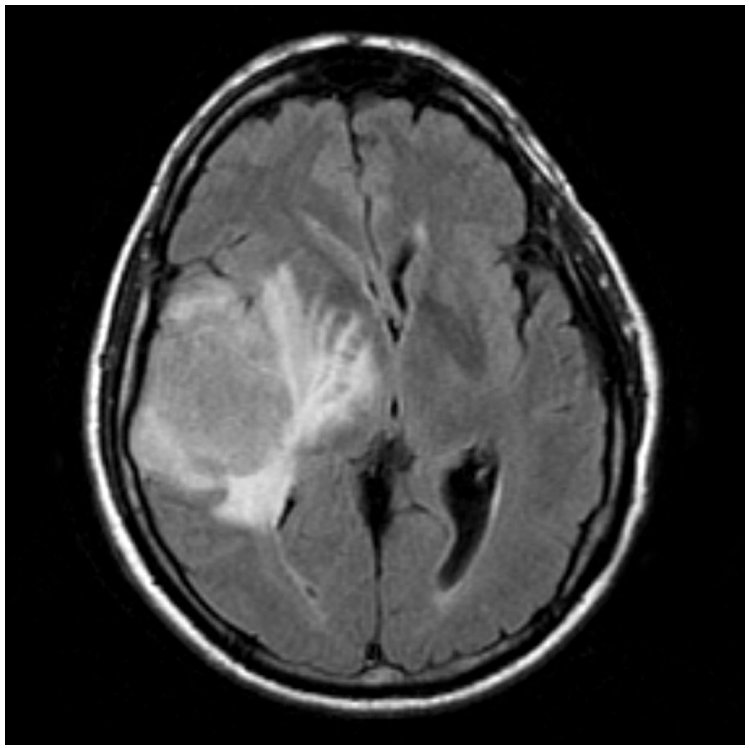
- Katarina Wolf (Radboud Univ. Nijmegen Medical Centre)

Glioblastoma multiforme

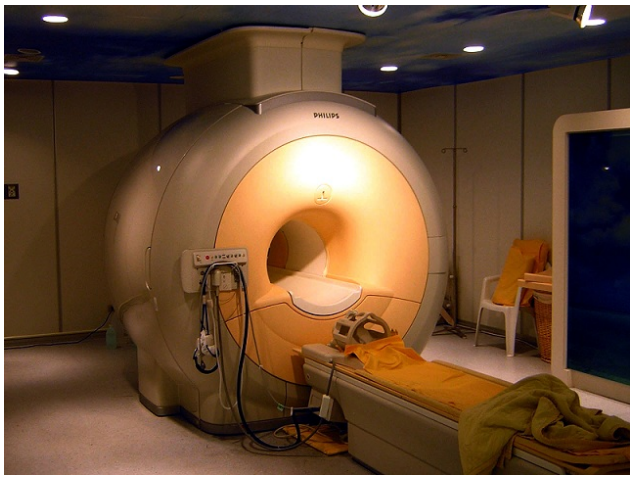




Pictures from radiopedia.org

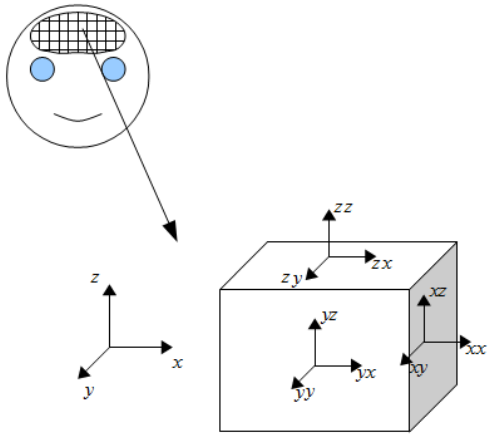
Diffusion tensor imaging

- Variant of diffusion-weighted magnetic resonance imaging, DW-MRI.
- Measures the spatial diffusion of water molecules by MRI per volume element (voxel) .



MRI-device (Philips Chieva 3.0 T)
http://upload.wikimedia.org/

Consider a single voxel:

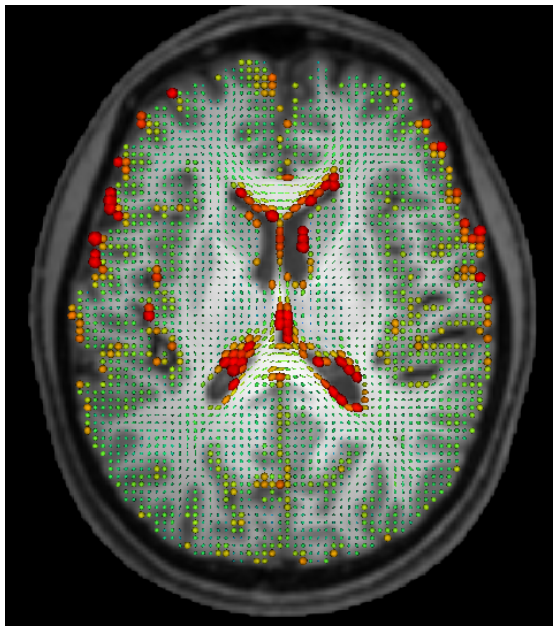


This leads to a diffusion tensor

$$\mathbb{D}(\mathbf{x}) = \begin{pmatrix} d_{xx}(\mathbf{x}) & d_{xy}(\mathbf{x}) & d_{xz}(\mathbf{x}) \\ d_{yx}(\mathbf{x}) & d_{yy}(\mathbf{x}) & d_{yz}(\mathbf{x}) \\ d_{zx}(\mathbf{x}) & d_{zy}(\mathbf{x}) & d_{zz}(\mathbf{x}) \end{pmatrix}$$

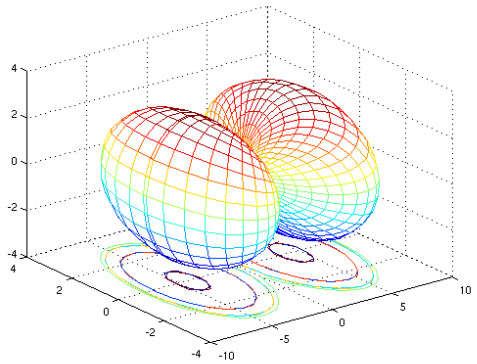
Representation of anisotropic diffusion tensor data

Ellipsoids



$$\frac{\theta_1^2}{\lambda_1}+\frac{\theta_2^2}{\lambda_2}+\frac{\theta_3^2}{\lambda_3}=1$$

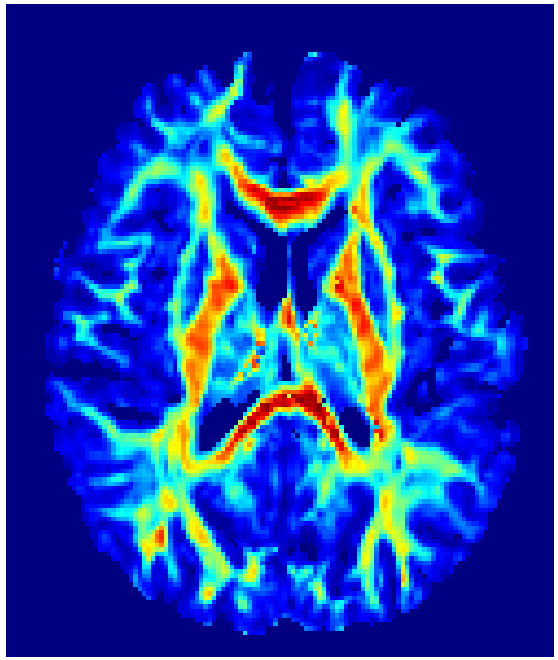
Peanut



$$\mathbb{S}^2 \ni \theta \mapsto \theta^T \mathbb{D} \theta \in \mathbb{R}$$

$$\bar{\lambda}=\frac{1}{3}\sum_{i=1}^{3}\lambda_i$$

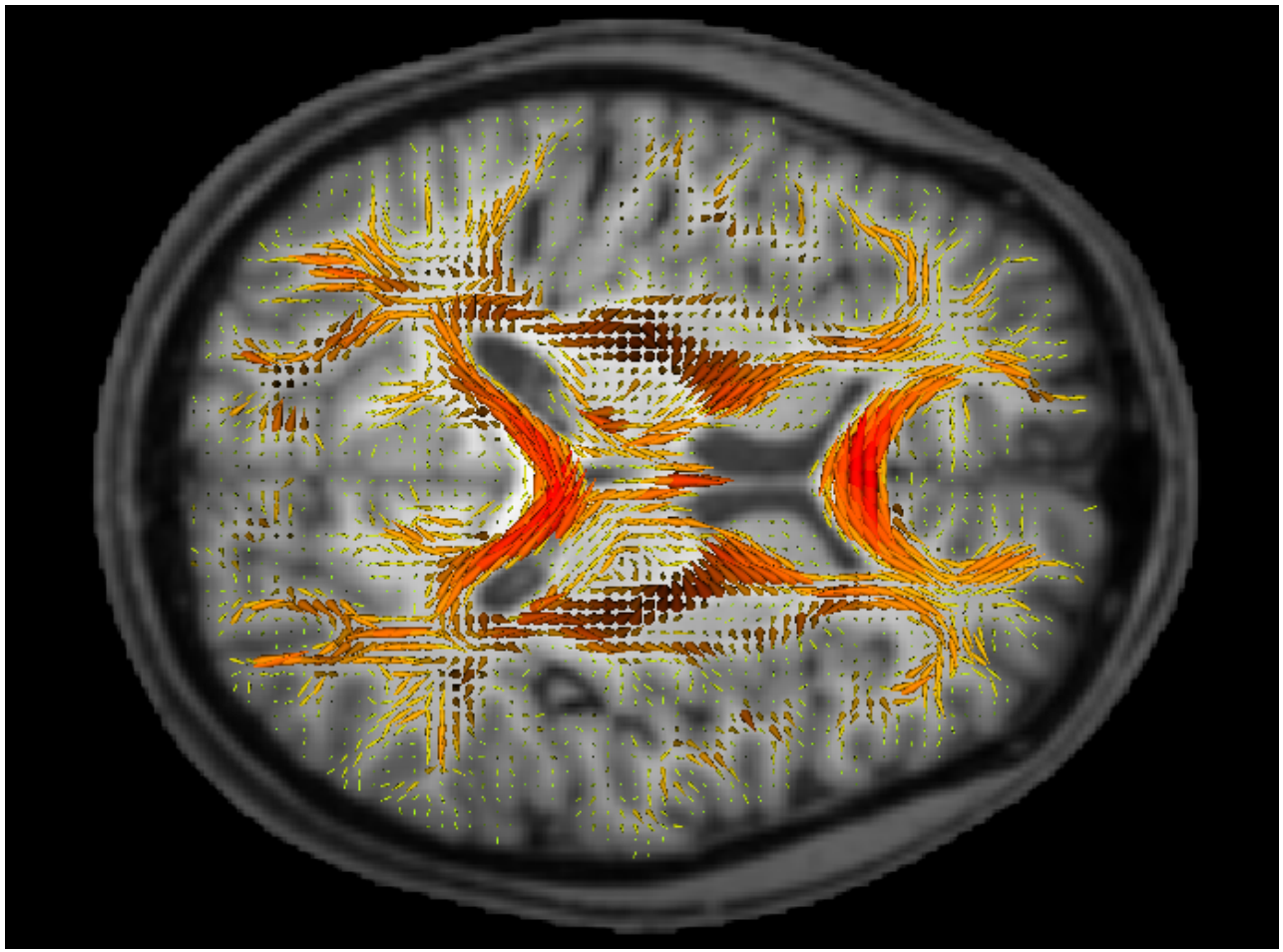
Fractional anisotropy



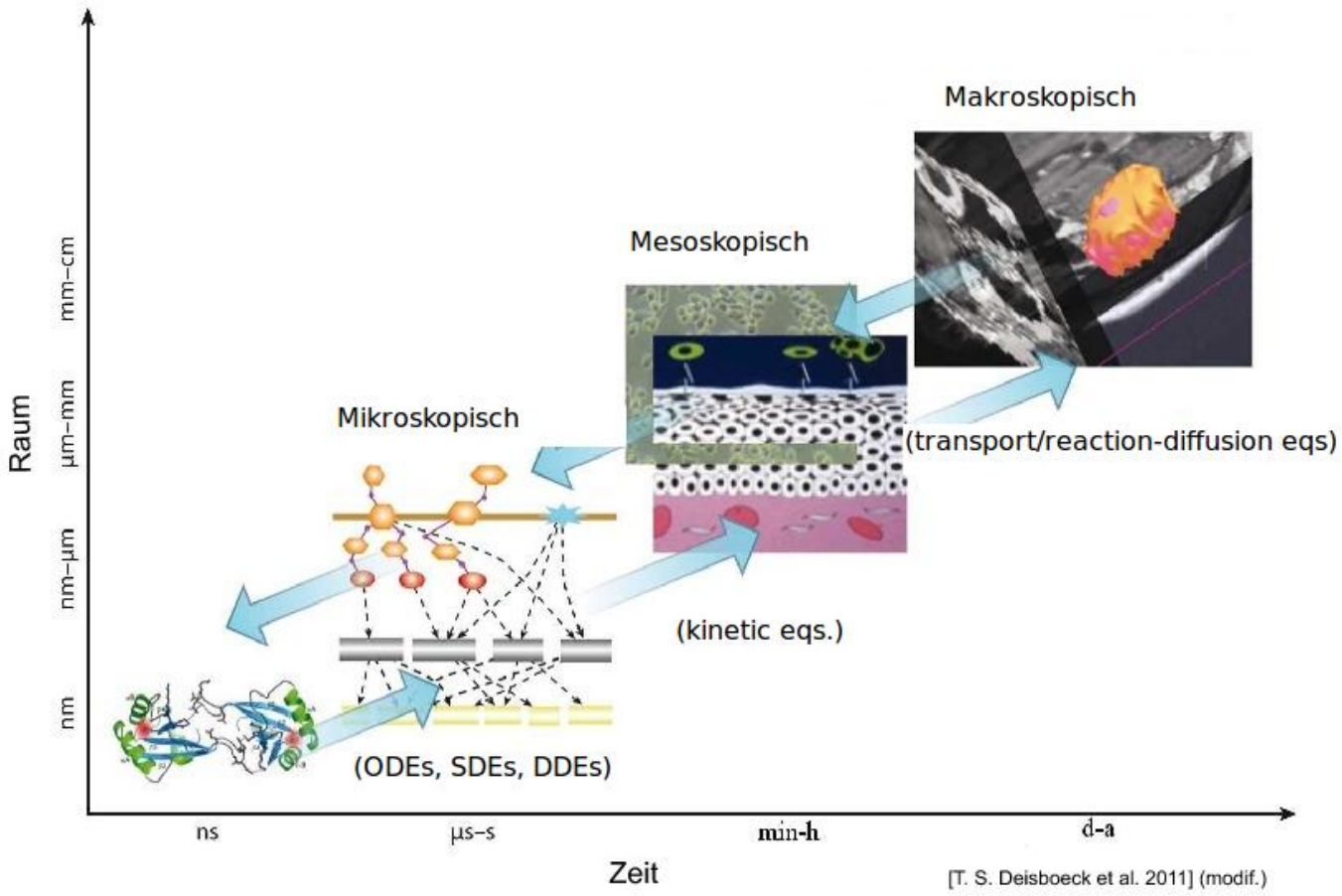
$$FA(\mathbf{x})=\sqrt{\frac{3}{2}}\frac{\sqrt{\sum_{i=1}^{3}(\lambda_i-\bar{\lambda})^2}}{\sqrt{\sum_{i=1}^{3}\lambda_i^2}}$$

Data

Visualization of the main direction of diffusion by a vector pointing in the direction of the tensor's leading eigenvalue



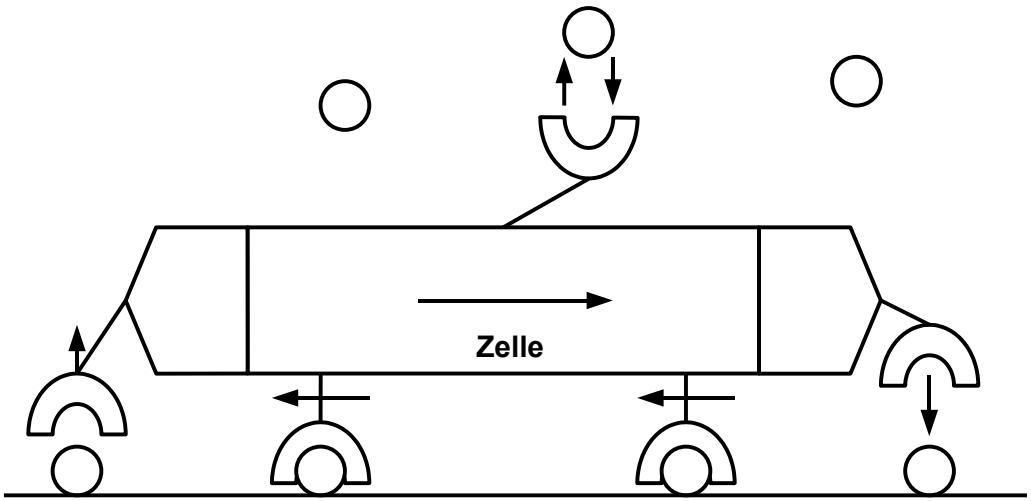
Modeling scales



Goal: multiscale descriptions

Biochemical basis of the microscopic model

- Cells interact with the neighbouring tissue in order to move forward (contact guidance)



- Receptor binding to unsoluble components Q

$$Q + (R_0 - y) \underset{k^-}{\overset{k^+}{\rightleftharpoons}} RQ$$

Notation: $y := RQ$.

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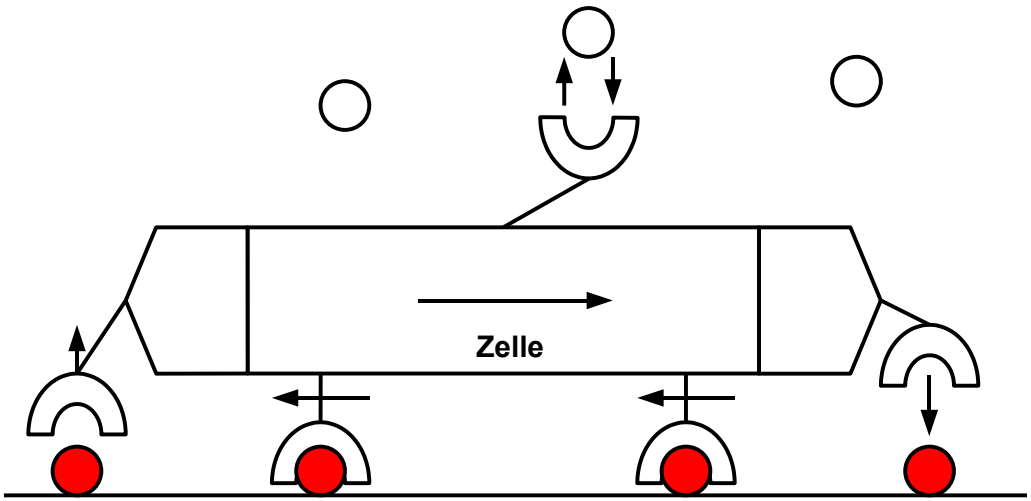

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Individual variables (N cells)

Position	$\mathbf{x}^{(j)} \in \mathbb{R}^n$
Velocity	$\mathbf{v}^{(j)} \in V = s\mathbb{S}^{n-1}$
Receptor state	$\mathbf{y}^{(j)} \in Y \ (j = 1, ..., N).$

- Newton's law (in the absence of reorientations)

$$\frac{d\mathbf{x}^{(j)}}{dt} = \mathbf{v}^{(j)} \ , \ \frac{d\mathbf{v}^{(j)}}{dt} = 0$$

- ODE for receptor dynamics

$$\frac{d\mathbf{y}^{(j)}}{dt} = G(\mathbf{y}^{(j)}, Q(t, \mathbf{x}^{(j)}))$$

Mesoscale involving the microscale

- Goal: derive a kinetic equation for the cell density $p(t, \mathbf{x}, \mathbf{v}, \mathbf{y})$.
- In the absence of reorientations:

$$\frac{\partial p}{\partial t} + \underbrace{\mathbf{v} \cdot \nabla_{\mathbf{x}} p}_{\text{Transport with velocity } \mathbf{v}} + \underbrace{\nabla_{\mathbf{y}} \cdot (\mathbf{G}(\mathbf{y}, Q) p)}_{\text{From receptor dynamics}} = 0$$

- Changes in orientation (and speed) have to be incorporated in the right-hand side.

Micro-meso model: kinetic transport equations

$$\partial_t p + \nabla_{\mathbf{x}} \cdot (\mathbf{v} p) + \partial_y \left(G(y) p \right) = -\lambda(y) p + \lambda(y) \int_V K(\mathbf{x}, \mathbf{v}, \mathbf{v}') p(\mathbf{v}') d\mathbf{v}'$$

with $p(t, \mathbf{x}, \mathbf{v}, y)$ cell density at time t, position $\mathbf{x} \in \mathbb{R}^n$, with velocity $\mathbf{v} \in V \subset \mathbb{R}^n$, and internal state $y \in Y \subseteq [0, R_0]$.

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Subcellular dynamics: $\frac{d}{dt} y(t) = G(y(t), Q(t, \mathbf{x}))$.

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$$\dot{y} = k^+ (R_0 - y) Q - k^- y.$$

Proliferation: Go-or-grow

- Moving cancer cells:

$$\partial_t p + \nabla_{\mathbf{x}} \cdot (\mathbf{v} p) + \partial_y \left(G(y, Q) p \right) = \mathcal{L}[\lambda] p - a(\mathbf{x}) p + \frac{bq}{\omega} r - \ell(N) p$$

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- Non-moving (proliferating) cancer cells:

$$\partial_t r = a(\mathbf{x}) \int_V p d\mathbf{v} - br + g(N) r - \ell(N) r.$$

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- Total cell density (macroscopic):

$$N(t, \mathbf{x}) = \int_V \int_Y p(t, \mathbf{x}, \mathbf{v}, y) dy \, d\mathbf{v} + \int_Y r(t, \mathbf{x}, y) dy$$

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Write the transport equations w.r.t. z and consider the moments w.r.t. z and $\mathbf{v}$. Wanted:

$$M(t,\mathbf{x}) := \iint_{V\times Z} p(t,\mathbf{x},\mathbf{v},z)dzd\mathbf{v}$$

$$w(t,\mathbf{x},\mathbf{v}) := \int_Z r(t,\mathbf{x},\mathbf{v},z)dz$$

to recover the macroscopic cell density $N(t,\mathbf{x})$.

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Then

$$\partial_t N_0 - \nabla \cdot \left(\frac{1}{\lambda_0 + a(\mathbf{x})} \nabla \cdot \left(\frac{b}{a(\mathbf{x}) + b} \mathbb{D}_T(\mathbf{x}) N_0 \right) \right)$$
$$+ \nabla \cdot \left(\frac{\lambda_1}{\lambda_0 + a(\mathbf{x})} \gamma(\mathbf{x}) f'(Q) \frac{b}{a(\mathbf{x}) + b} \mathbb{D}_T(\mathbf{x}) \cdot \nabla Q \; N_0 \right)$$
$$= \frac{a(\mathbf{x})}{a(\mathbf{x}) + b} g(N_0) N_0 - N_0 \ell(N_0),$$

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$$= \frac{a(\mathbf{x})}{a(\mathbf{x}) + b} g(N_0) N_0 - N_0 \ell(N_0),$$

with the tumor diffusion tensor $\mathbb{D}_T(\mathbf{x}) = \frac{1}{\omega} \int_V \mathbf{v}\mathbf{v}^t q(\hat{\mathbf{v}}) \, d\mathbf{v}$.

Effective equations on the macroscale

With the logistic growth choice $g(N_0) = c_g$, $\ell(N_0) = c_\ell N_0$, where $N_0 = \frac{a+b}{b} M_0$, we get

$$\partial_t N_0 - c_D(\mathbf{x})\nabla\nabla\left(\mathbb{D}_T(\mathbf{x})N_0\right) - \lambda_1 c_D(\mathbf{x})\nabla\left(\mathbf{u}(\mathbf{x})N_0\right) = \frac{a}{a+b} c_g N_0 - c_\ell N_0^2,$$

with $c_D(\mathbf{x}) = \frac{b}{(\lambda_0 + a(\mathbf{x}))(a(\mathbf{x})+b)}$ and the drift velocity

$$\mathbf{u}(\mathbf{x}) = \gamma(\mathbf{x}) f'(Q(\mathbf{x}))\mathbb{D}_T(\mathbf{x})\nabla Q,$$

where $\gamma(\mathbf{x}) = (k^+ Q + k^- + \lambda_0 + a)^{-1}$ and $f(Q(\mathbf{x})) = \frac{k^+ Q(\mathbf{x}) R_0}{k^+ Q(\mathbf{x}) + k^-}$.

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Choices of $Q(\mathbf{x})$:

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$$l_c = \sqrt{Dt_c},$$

  with D a diffusion-related coefficient and t_c the characteristic (diffusion) time.

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  Choice of D: $tr(\mathbb{D}_W)$.

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Choice of characteristic time t_c: expected exit time of Brownian motion from a ball with minimal radius surrounding the voxel of length h, hence $t_c = \frac{h^2}{4}$.

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Volume fraction of tissue fibers: $l_c = \sqrt{\frac{h^2 tr(\mathbb{D}_W)}{4 l_1}}$.

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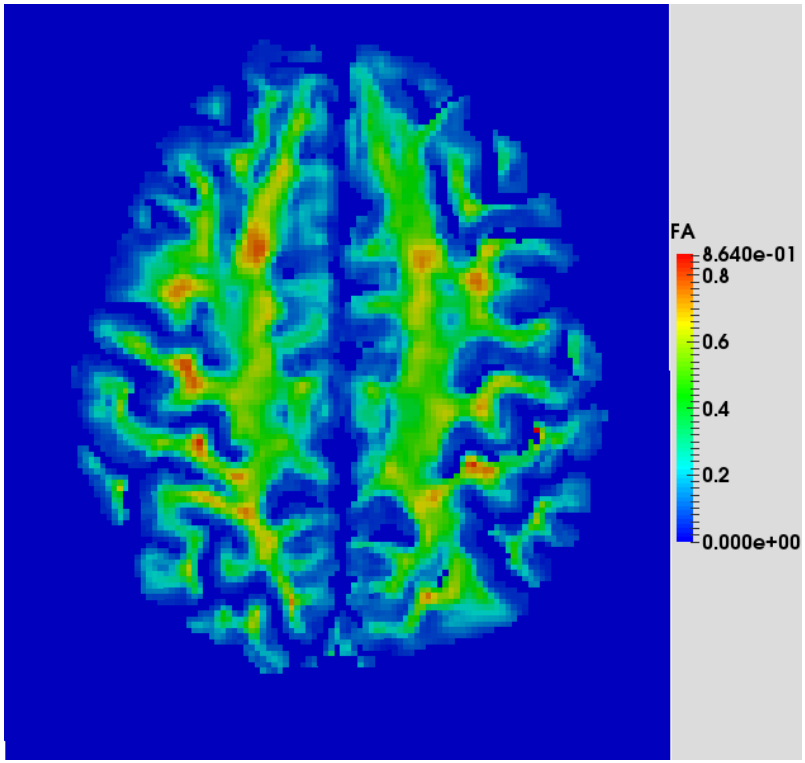
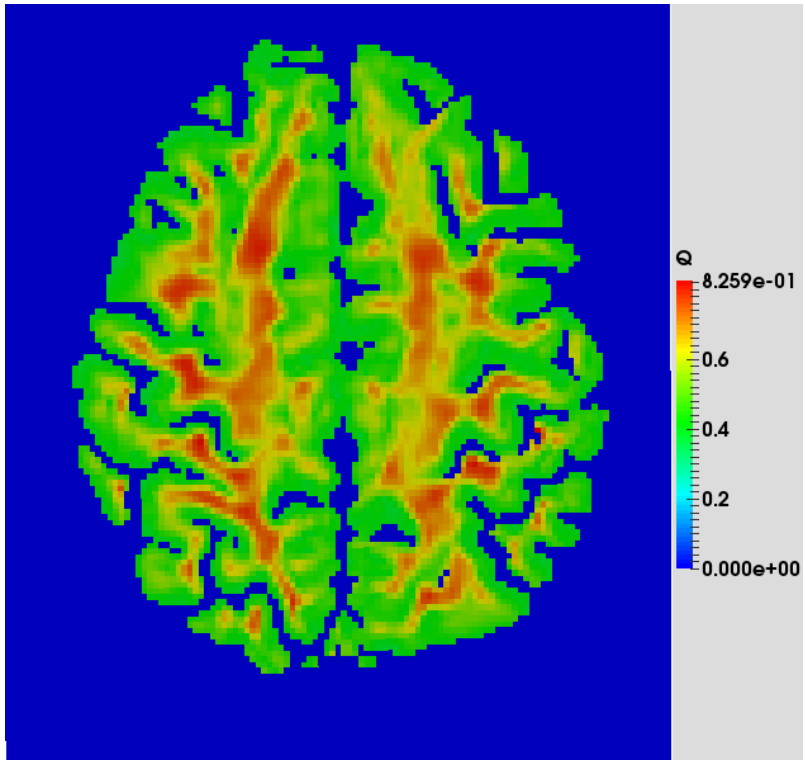
The free volume fraction of one voxel is l_c^3/h^3. So the occupied volume is $Q = 1 - \frac{l_c^3}{h^3}$.

Volume fraction of tissue fibers



FA



Estimated Q

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Choices of $q(\mathbf{x},\theta)$:

- Peanut: $q(\mathbf{x},\theta)=\frac{n}{|\mathbb{S}^{n-1}|\mathrm{tr}\mathbb{D}_W(\mathbf{x})}\theta^t\mathbb{D}_W(\mathbf{x})\theta.$

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  $q(\mathbf{x},\theta)=ODF(\theta):=\int_0^\infty \Pi(r\theta)r^2\,dr$, with $\Pi(r\theta)$:

  displacement probability of a spatial point in spherical coordinates. It can be shown (Aganj et al 2010) that

$$q(\mathbf{x},\theta)=\frac{1}{4\pi|\mathbb{D}_W(\mathbf{x})|\left(\theta^t\mathbb{D}_W(\mathbf{x})^{-1}\theta\right)^{\frac{3}{2}}}$$

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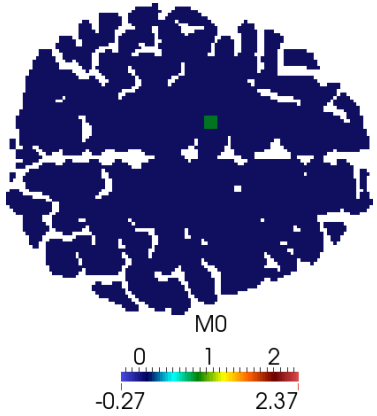
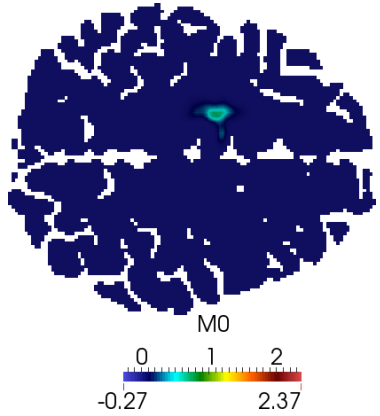
The tumor diffusion tensor can be explicitly computed for each of these choices.

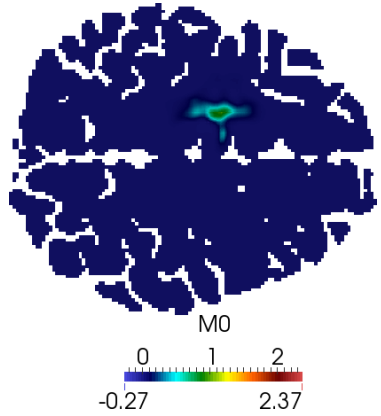
Simulations (with FA and peanut)



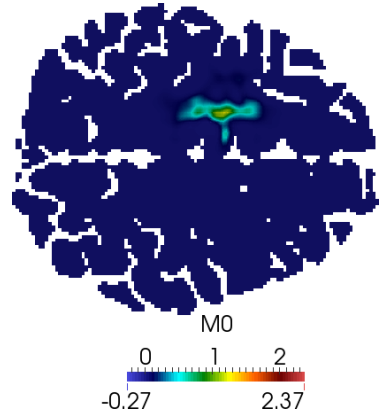
$t = 0$



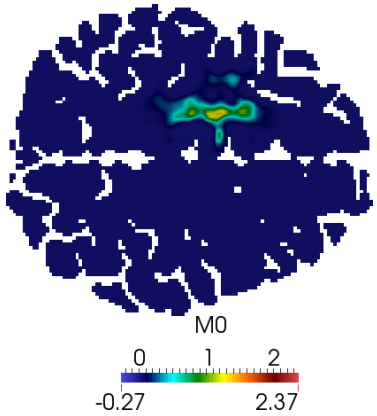
$t = 100 \cdot 10^4 s$



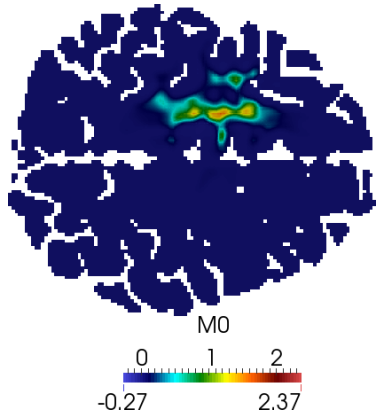
$t = 200 \cdot 10^4 s$



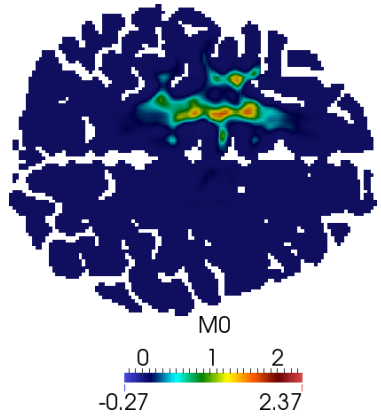
$t = 300 \cdot 10^4 s$



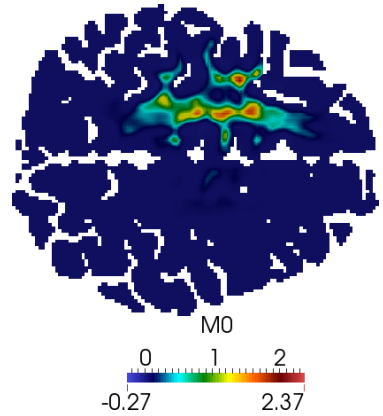
$t = 400 \cdot 10^4 s$



$t = 500 \cdot 10^4 s$



$t = 600 \cdot 10^4 s$



$t = 700 \cdot 10^4 s$

Alternative modeling of proliferation: interactions with tissue

$$\mathcal{P}(p) = \underbrace{\mu(\mathbf{x}, M, \mathbf{v})}_{\text{growth rate}} \int_Z \chi(\mathbf{x}, z, z') p(t, \mathbf{x}, \mathbf{v}, z') Q(\mathbf{x}) \, dz',$$

$$\text{with } M(t, \mathbf{x}) = \int_V \int_Z p(t, \mathbf{x}, \mathbf{v}, z) \, dz \, d\mathbf{v}.$$

Alternative modeling of proliferation: interactions with tissue

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with $M(t, \mathbf{x}) = \int_V \int_Z p(t, \mathbf{x}, \mathbf{v}, z) \, dz \, d\mathbf{v}$.

The kernel χ characterizes the transition from the state z' to the state z during a proliferative action.

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with $M(t, \mathbf{x}) = \int_V \int_Z p(t, \mathbf{x}, \mathbf{v}, z) \, dz \, d\mathbf{v}$.

The kernel χ characterizes the transition from the state z' to the state z during a proliferative action.

Then our kinetic transport equation becomes

$$\partial_t p + \nabla_{\mathbf{x}} \cdot (\mathbf{v} p) - \partial_z (((k^+ Q + k^-) z - f'(Q) \mathbf{v} \cdot \nabla Q) p) = \mathcal{L}[\lambda_0] p - \mathcal{L}[\lambda_1] z p + \mathcal{P}(p).$$

Alternative modeling of proliferation: interactions with tissue

$$\mathcal{P}(p) = \underbrace{\mu(\mathbf{x}, M, \mathbf{v})}_{\text{growth rate}} \int_Z \chi(\mathbf{x}, z, z')p(t, \mathbf{x}, \mathbf{v}, z')Q(\mathbf{x})\ dz',$$

with $M(t, \mathbf{x}) = \int_V \int_Z p(t, \mathbf{x}, \mathbf{v}, z)\ dz\ d\mathbf{v}$.

The kernel χ characterizes the transition from the state z' to the state z during a proliferative action.

Then our kinetic transport equation becomes

$$\partial_t p + \nabla_{\mathbf{x}} \cdot (\mathbf{v}p) - \partial_z(((k^+ Q + k^-)z - f'(Q)\mathbf{v} \cdot \nabla Q)p) = \mathcal{L}[\lambda_0]p - \mathcal{L}[\lambda_1]zp + \mathcal{P}(p).$$

Remark: KTAP by Bellomo assumes cell-cell interactions

$$P_i[p](t, z) = \sum_{h=1}^{n} \sum_{k=1}^{n} \mu_{hk} \iint_{Z \times Z} \chi^i_{hk}(z', z''; z)p_h(t, z')p_k(t, z'')dz'dz''$$

Effective equations on macroscale

Assume μ does not depend on $\mathbf{v}$. Then by doing again a parabolic scaling we get

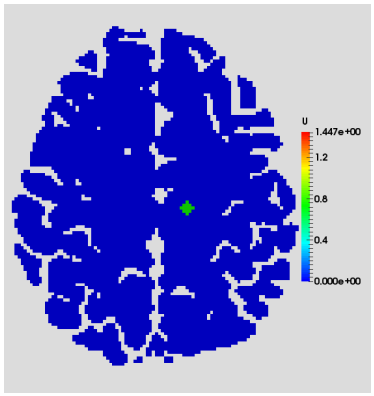
$$\partial_t M_0 - \nabla\nabla : (\mathbb{D}_T M_0) + \nabla\cdot(g(Q(\mathbf{x}))\mathbb{D}_T \nabla Q M_0) = Q(\mathbf{x})\mu(\mathbf{x}, M_0)M_0$$

with the drift velocity

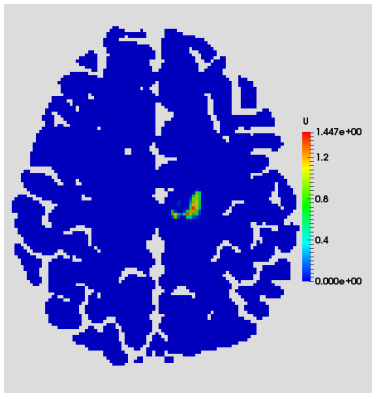
$$\mathbf{u}(\mathbf{x}) = \frac{1}{\lambda_0 \omega}\int_V \mathbf{v}\otimes\mathbf{v}\nabla q\, d\mathbf{v}$$

and the tumor diffusion tensor $\mathbb{D}_T(\mathbf{x}) = \frac{1}{\lambda_0\omega}\int\limits_V q\mathbf{v}\otimes\mathbf{v}\ d\mathbf{v}$.

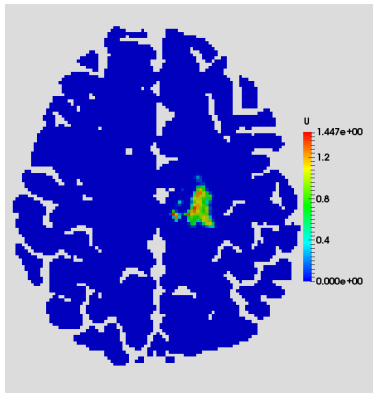
Simulation results (with peanut)



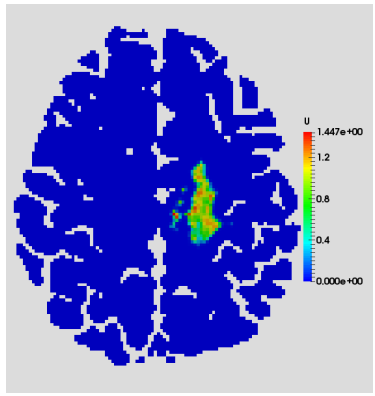
day 0, FA



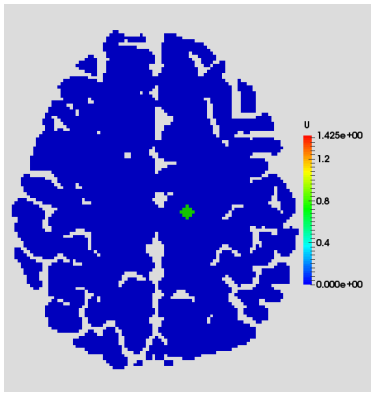
day 200, FA



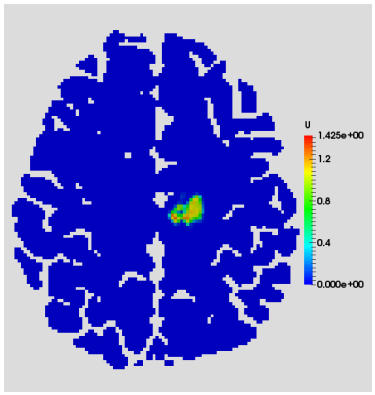
day 400, FA



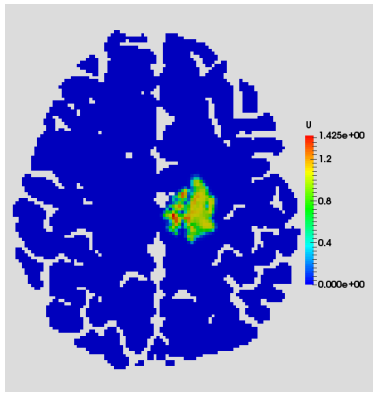
day 600, FA



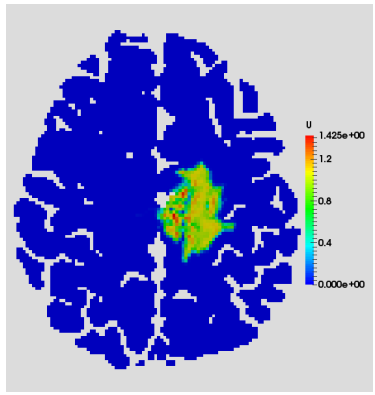
day 0, Q



day 200, Q

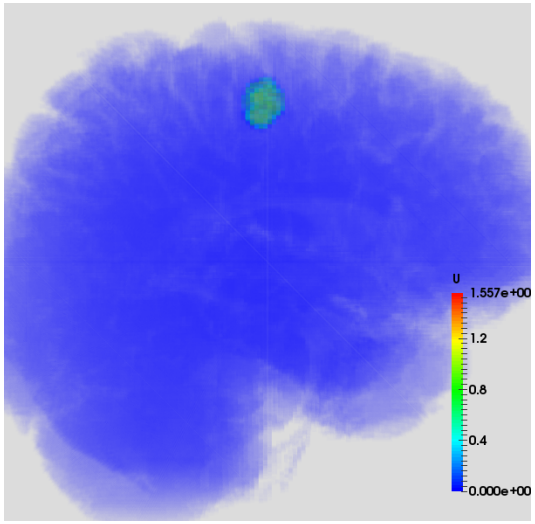


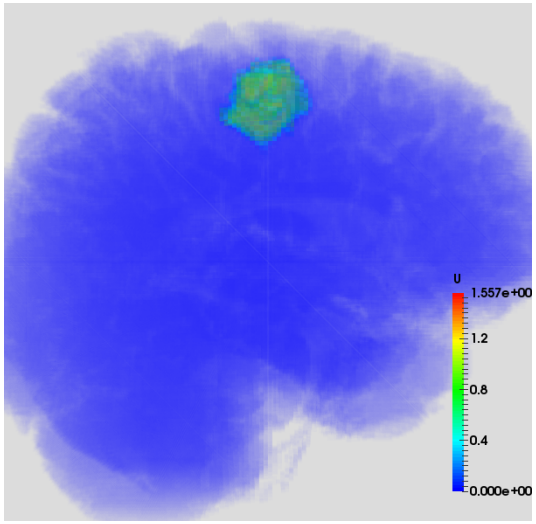
day 400, Q

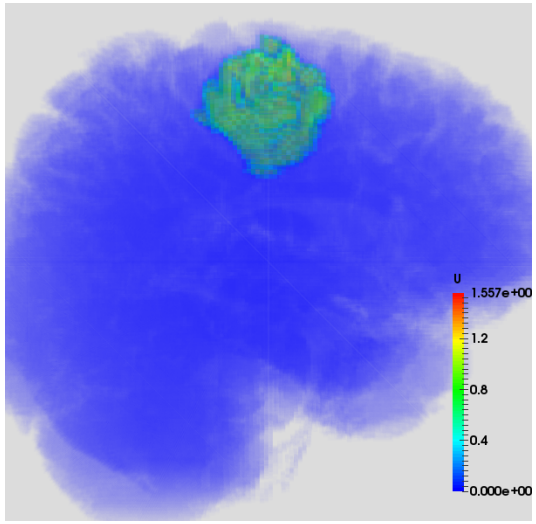


day 600, Q

Simulation results in 3D (with estmated Q and peanut)



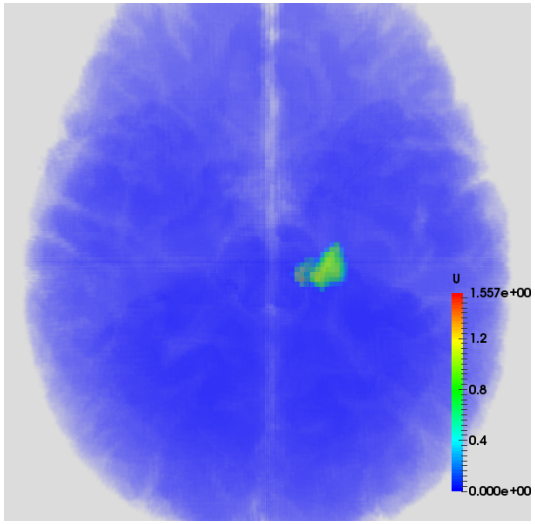


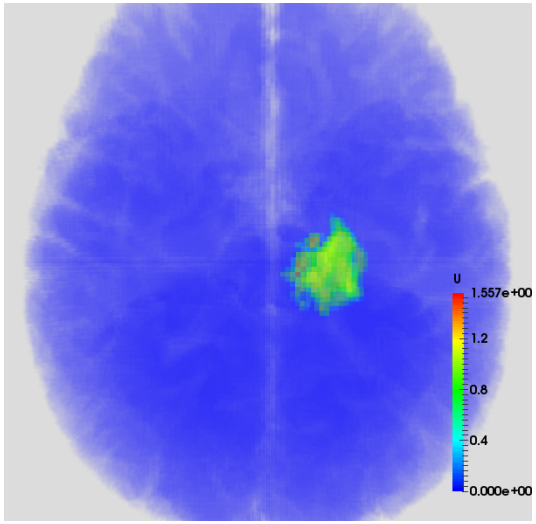


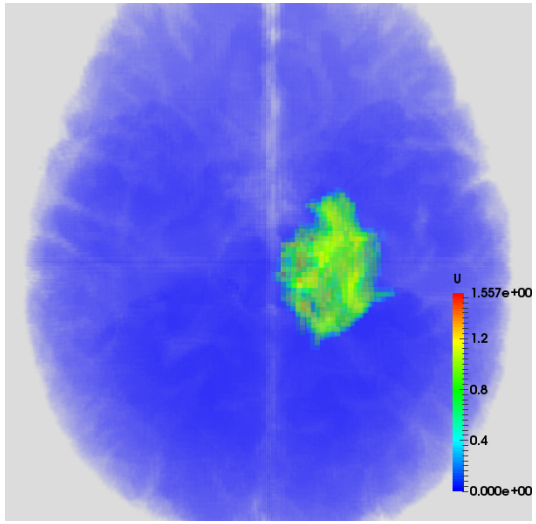
day 200

day 400

day 600

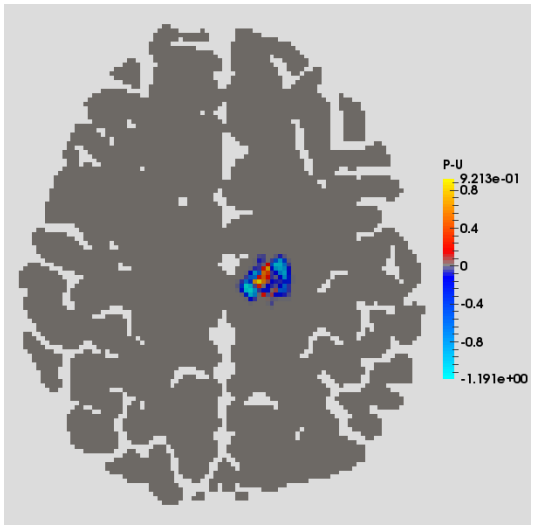




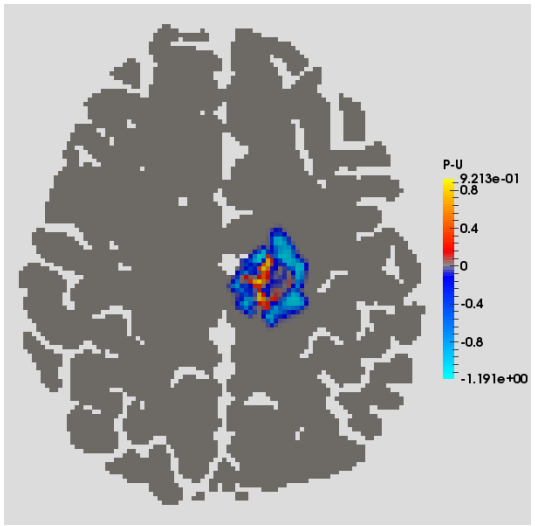


Comparison with a pure macroscopic model

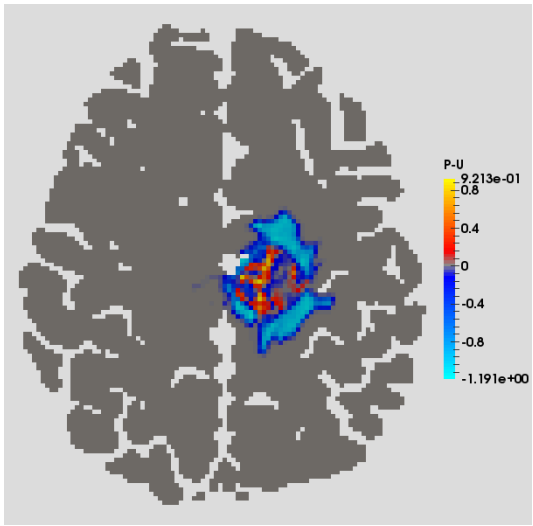
$$\partial_t M_0 - \nabla \cdot (\mathbb{D}_T(\mathbf{x}) \nabla M_0) = Q(\mathbf{x}) \mu(M_0) M_0.$$



day 200, Q



day 400, Q



day 600, Q

Micro-meso model via go-or-grow

$$\partial_t p + \nabla_{\mathbf{x}} \cdot (\mathbf{v} p) + \partial_y \left(G(y, Q, d_c, d_r) p \right)$$
$$= \mathcal{L}[\lambda(y)]p - a(\mathbf{x}, d_c)p + b(\mathbf{x}, d_c)\frac{q(\hat{\mathbf{v}})}{\omega} r - L_1(N, \alpha_1, d_r)p$$

Micro-meso model via go-or-grow

$$\partial_t p + \nabla_{\mathbf{x}} \cdot (\mathbf{v} p) + \partial_y \left(G(y, Q, d_c, d_r) p \right)$$
$$= \mathcal{L}[\lambda(y)]p - a(\mathbf{x}, d_c)p + b(\mathbf{x}, d_c)\frac{q(\hat{\mathbf{v}})}{\omega} r - L_1(N, \alpha_1, d_r)p$$

$$\partial_t r = a(\mathbf{x}, d_c) \int_V p(\mathbf{v}) d\mathbf{v} - b(\mathbf{x}, d_c) r + g(N, d_c) r - L_2(N, \alpha_2, d_r) r$$

Micro-meso model via go-or-grow

$$\partial_t p + \nabla_{\mathbf{x}} \cdot (\mathbf{v} p) + \partial_y \left(G(y, Q, d_c, d_r) p \right)$$
$$= \mathcal{L}[\lambda(y)]p - a(\mathbf{x}, d_c)p + b(\mathbf{x}, d_c)\frac{q(\hat{\mathbf{v}})}{\omega} r - L_1(N, \alpha_1, d_r)p$$

$$\partial_t r = a(\mathbf{x}, d_c) \int_V p(\mathbf{v}) d\mathbf{v} - b(\mathbf{x}, d_c) r + g(N, d_c) r - L_2(N, \alpha_2, d_r) r$$

with $L_I(N, \alpha_I, d_r) := \ell_I(N) + R_I(\alpha_I, d_r)$ $(I = 1, 2)$.

Micro-meso model via go-or-grow

$$\partial_t p + \nabla_{\mathbf{x}} \cdot (\mathbf{v} p) + \partial_y \left(G(y, Q, d_c, d_r) p \right)$$
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$$\partial_t r = a(\mathbf{x}, d_c) \int_V p(\mathbf{v}) d\mathbf{v} - b(\mathbf{x}, d_c) r + g(N, d_c) r - L_2(N, \alpha_2, d_r) r$$

with $L_I(N, \alpha_I, d_r) := \ell_I(N) + R_I(\alpha_I, d_r)$ $(I = 1, 2)$.

$$\dot{y} = G(y, Q, d_c, d_r) = k^+(d_c)(R_0 - y) Q \; S(\alpha_3, d_r) - k^-(d_c) y.$$

Micro-meso model via go-or-grow

$$\partial_t p + \nabla_{\mathbf{x}} \cdot (\mathbf{v} p) + \partial_y \left(G(y, Q, d_c, d_r) p \right)$$
$$= \mathcal{L}[\lambda(y)]p - a(\mathbf{x}, d_c)p + b(\mathbf{x}, d_c)\frac{q(\hat{\mathbf{v}})}{\omega} r - L_1(N, \alpha_1, d_r)p$$

$$\partial_t r = a(\mathbf{x}, d_c) \int_V p(\mathbf{v}) d\mathbf{v} - b(\mathbf{x}, d_c) r + g(N, d_c) r - L_2(N, \alpha_2, d_r) r$$

with $L_I(N, \alpha_I, d_r) := \ell_I(N) + R_I(\alpha_I, d_r)$ $(I = 1, 2)$.

$$\dot{y} = G(y, Q, d_c, d_r) = k^+(d_c)(R_0 - y) Q \; S(\alpha_3, d_r) - k^-(d_c) y.$$

$$R_j(\alpha_j, d_r) = \sum_{i=1}^{\nu} (1 - S(\alpha_j, d_r)) \eta_\delta(t - t_i), \qquad t_i \in \text{radiotherapy},$$

Micro-meso model via go-or-grow

$$\partial_t p + \nabla_{\mathbf{x}} \cdot (\mathbf{v} p) + \partial_y \left(G(y, Q, d_c, d_r) p \right)$$
$$= \mathcal{L}[\lambda(y)]p - a(\mathbf{x}, d_c)p + b(\mathbf{x}, d_c)\frac{q(\hat{\mathbf{v}})}{\omega} r - L_1(N, \alpha_1, d_r)p$$

$$\partial_t r = a(\mathbf{x}, d_c) \int_V p(\mathbf{v}) d\mathbf{v} - b(\mathbf{x}, d_c) r + g(N, d_c) r - L_2(N, \alpha_2, d_r) r$$

with $L_l(N, \alpha_l, d_r) := \ell_l(N) + R_l(\alpha_l, d_r)$ $(l = 1, 2)$.

$$\dot{y} = G(y, Q, d_c, d_r) = k^+(d_c)(R_0 - y) Q \; S(\alpha_3, d_r) - k^-(d_c) y.$$

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supp $\eta_\delta \subset (-\delta, \delta)$, $\delta << 1$, $j = 1, 2, 3$.

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$$\partial_t p + \nabla_{\mathbf{x}} \cdot (\mathbf{v} p) + \partial_y \left(G(y, Q, d_c, d_r) p\right)$$
$$= \mathcal{L}[\lambda(y)]p - a(\mathbf{x}, d_c)p + b(\mathbf{x}, d_c)\frac{q(\hat{\mathbf{v}})}{\omega} r - L_1(N, \alpha_1, d_r)p$$

$$\partial_t r = a(\mathbf{x}, d_c) \int_V p(\mathbf{v}) d\mathbf{v} - b(\mathbf{x}, d_c) r + g(N, d_c) r - L_2(N, \alpha_2, d_r) r$$

with $L_l(N, \alpha_l, d_r) := \ell_l(N) + R_l(\alpha_l, d_r)$ $(l = 1, 2)$.

$$\dot{y} = G(y, Q, d_c, d_r) = k^+(d_c)(R_0 - y) Q\ S(\alpha_3, d_r) - k^-(d_c) y.$$

$$R_j(\alpha_j, d_r) = \sum_{i=1}^{\nu} (1 - S(\alpha_j, d_r)) \eta_\delta(t - t_i), \qquad t_i \in \text{radiotherapy},$$

supp $\eta_\delta \subset (-\delta, \delta)$, $\delta << 1$, $j = 1, 2, 3$.

Survival fractions (LQ model):

$$S(\alpha_j, d_r) = \exp(-\nu(\alpha_j \hat{d}_r + \beta_j \hat{d}_r^2)) = \exp(-\alpha_j d_r (1 + \hat{d}_r / (\alpha_j / \beta_j)))$$

Effective equation on macroscale

Remember $N(t,\mathbf{x}) = \int_V \int_Y p(t,\mathbf{x},\mathbf{v},y)dy\ d\mathbf{v} + \int_Y r(t,\mathbf{x},y)dy.$

Effective equation on macroscale

Remember $N(t,\mathbf{x}) = \int_V \int_Y p(t,\mathbf{x},\mathbf{v},y)dy\ d\mathbf{v} + \int_Y r(t,\mathbf{x},y)dy.$

$$\partial_t N_0 - \nabla\cdot\left(\frac{1}{\lambda_0+a}\nabla\cdot\left(\frac{b}{a+b}\mathbb{D}_T(\mathbf{x})N_0\right)\right)$$
$$+\nabla\cdot\left(\frac{\lambda_1 f'(Q)}{\gamma(\mathbf{x})}\frac{b}{(\lambda_0+a\ )(b\ +a\ )}\mathbb{D}_T(\mathbf{x})\nabla QN_0\right)$$
$$=\left((g(N_0)-L_2(N_0))\frac{a}{a\ +b}-L_1(N_0)\frac{b}{a\ +b}\right)N_0,$$

Effective equation on macroscale

Remember $N(t,\mathbf{x}) = \int_V \int_Y p(t,\mathbf{x},\mathbf{v},y)dy\ d\mathbf{v} + \int_Y r(t,\mathbf{x},y)dy$.

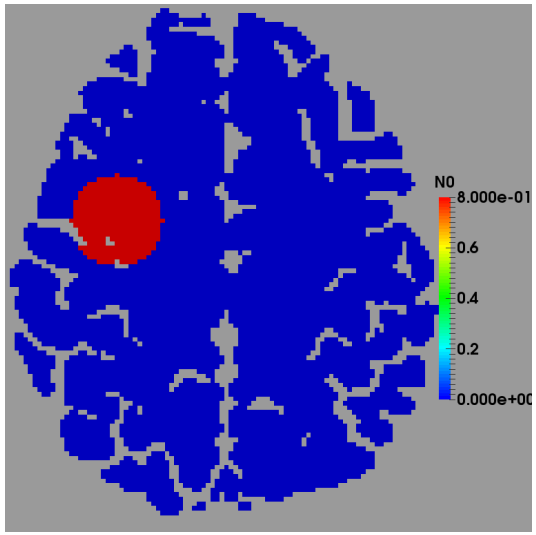
$$\partial_t N_0 - \nabla\cdot\left(\frac{1}{\lambda_0+a}\nabla\cdot\left(\frac{b}{a+b}\mathbb{D}_T(\mathbf{x})N_0\right)\right)$$
$$+\nabla\cdot\left(\frac{\lambda_1 f'(Q)}{\gamma(\mathbf{x})}\frac{b}{(\lambda_0+a\ )(b\ +a\ )}\mathbb{D}_T(\mathbf{x})\nabla QN_0\right)$$
$$=\left((g(N_0)-L_2(N_0))\frac{a}{a\ +b}-L_1(N_0)\frac{b}{a\ +b}\right)N_0,$$

where $\gamma(\mathbf{x}) := k^+QS + k^- + \lambda_0 + a$.

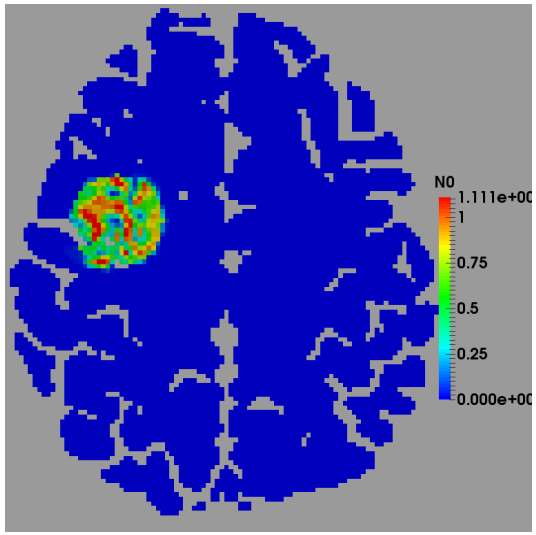
Therapy strategies

- Strategy 1: resection (2 weeks after start), no further therapy.
- Strategy 2: resection (2 weeks after start), followed after 3 weeks by radiotherapy (weekends excluded) for 6 weeks.
- Strategy 3: resection (2 weeks after start), followed after 3 weeks by concurrent chemotherapy and radiotherapy (weekends excluded) for 6 weeks.

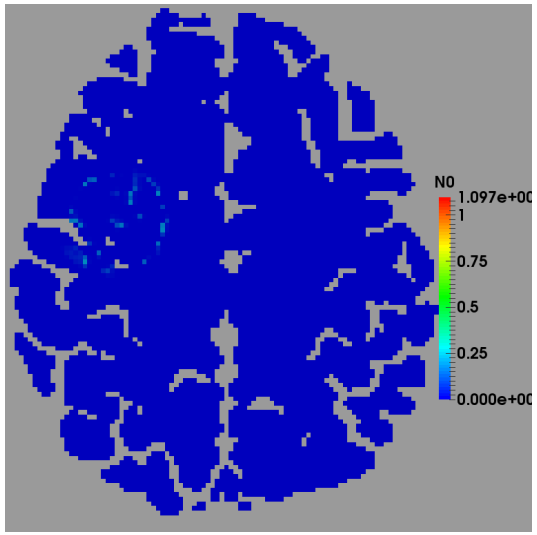
Results



start

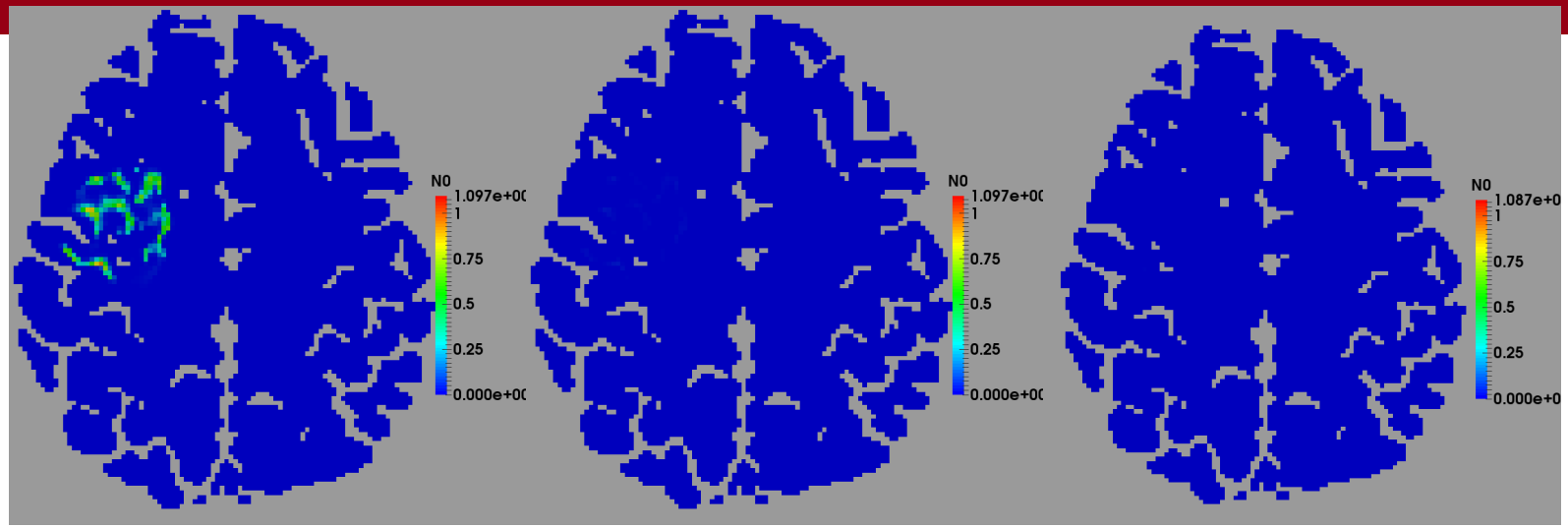


before resection

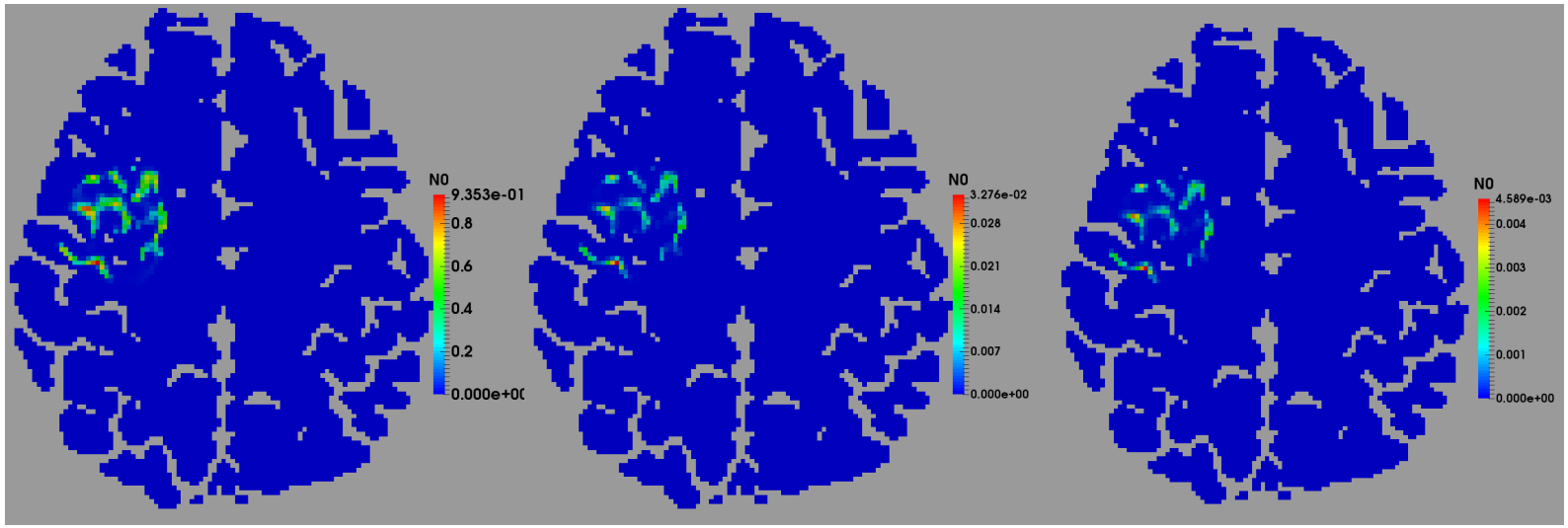


after resection

Results

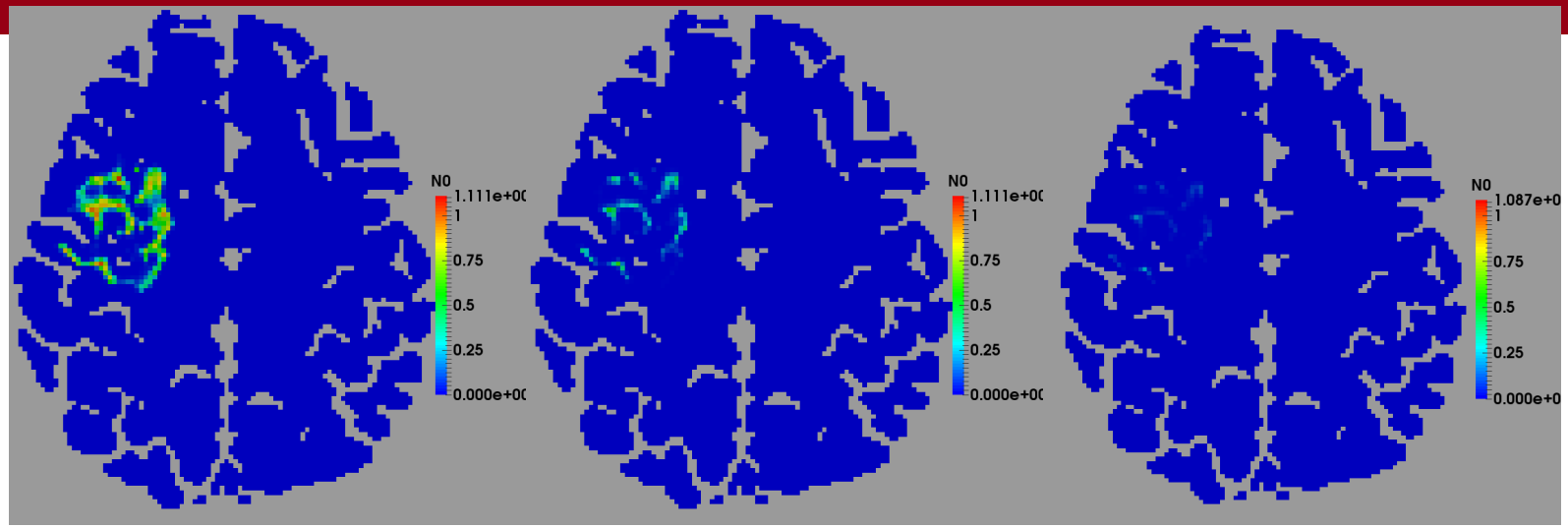


end of therapy

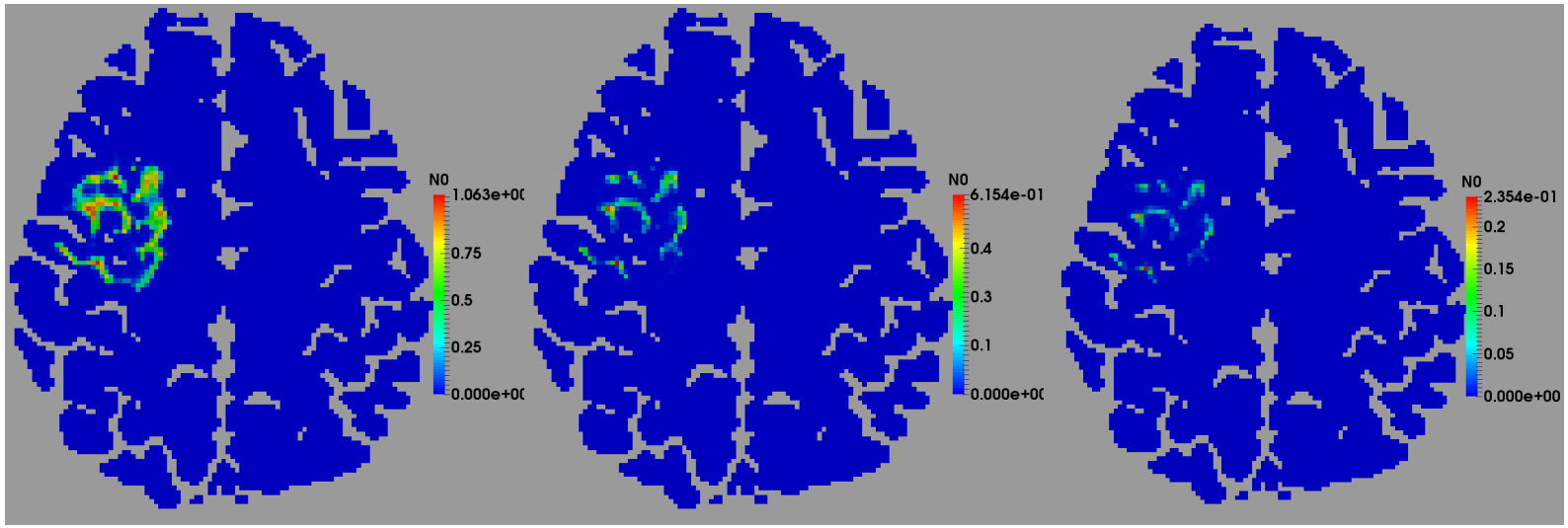


end of therapy, scaled

Results



follow-up after two months



follow-up, scaled

Conclusions and outlook

Multiscale models:

- allow testing the influence of many factors;
- are more difficult to handle numerically and analytically:
  - high dimensionality;
  - different scales both w.r.t. space and time;
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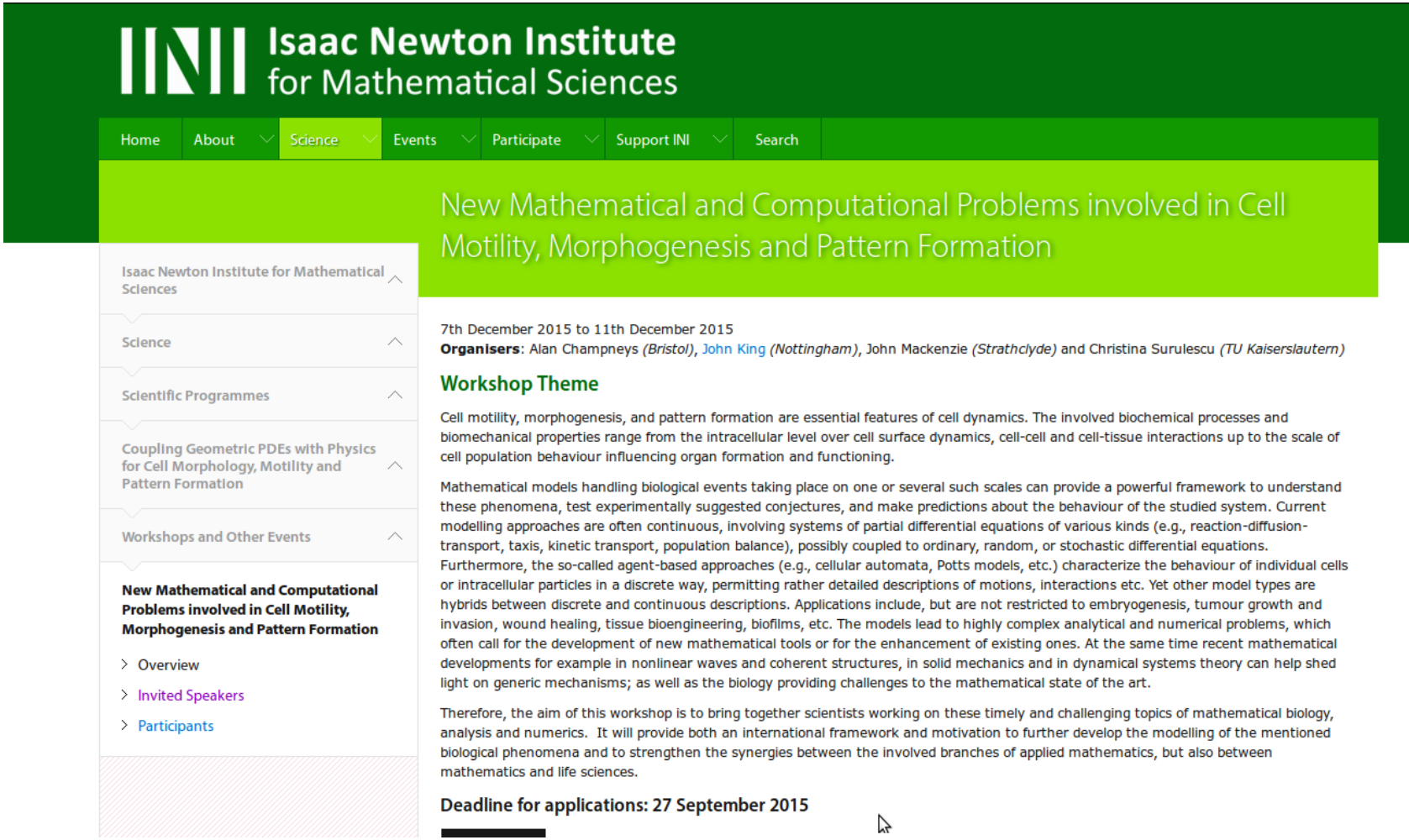
Outlook: tissue degradation, therapy

Meral, Stinner & S. (JCS Multiscale Dyn. 2015) .

FELIX KLEIN ZENTRUM FÜR MATHEMATIK

Upcoming workshop: https://www.newton.ac.uk/event/cgpw04



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New Mathematical and Computational Problems involved in Cell Motility, Morphogenesis and Pattern Formation

Isaac Newton Institute for Mathematical Sciences

Science

Scientific Programmes

Coupling Geometric PDEs with Physics for Cell Morphology, Motility and Pattern Formation

Workshops and Other Events

New Mathematical and Computational Problems involved in Cell Motility, Morphogenesis and Pattern Formation

- Overview
- Invited Speakers
- Participants

7th December 2015 to 11th December 2015

Organisers: Alan Champneys *(Bristol)*, John King *(Nottingham)*, John Mackenzie *(Strathclyde)* and Christina Surulescu *(TU Kaiserslautern)*

Workshop Theme

Cell motility, morphogenesis, and pattern formation are essential features of cell dynamics. The involved biochemical processes and biomechanical properties range from the intracellular level over cell surface dynamics, cell-cell and cell-tissue interactions up to the scale of cell population behaviour influencing organ formation and functioning.

Mathematical models handling biological events taking place on one or several such scales can provide a powerful framework to understand these phenomena, test experimentally suggested conjectures, and make predictions about the behaviour of the studied system. Current modelling approaches are often continuous, involving systems of partial differential equations of various kinds (e.g., reaction-diffusion-transport, taxis, kinetic transport, population balance), possibly coupled to ordinary, random, or stochastic differential equations. Furthermore, the so-called agent-based approaches (e.g., cellular automata, Potts models, etc.) characterize the behaviour of individual cells or intracellular particles in a discrete way, permitting rather detailed descriptions of motions, interactions etc. Yet other model types are hybrids between discrete and continuous descriptions. Applications include, but are not restricted to embryogenesis, tumour growth and invasion, wound healing, tissue bioengineering, biofilms, etc. The models lead to highly complex analytical and numerical problems, which often call for the development of new mathematical tools or for the enhancement of existing ones. At the same time recent mathematical developments for example in nonlinear waves and coherent structures, in solid mechanics and in dynamical systems theory can help shed light on generic mechanisms; as well as the biology providing challenges to the mathematical state of the art.

Therefore, the aim of this workshop is to bring together scientists working on these timely and challenging topics of mathematical biology, analysis and numerics. It will provide both an international framework and motivation to further develop the modelling of the mentioned biological phenomena and to strengthen the synergies between the involved branches of applied mathematics, but also between mathematics and life sciences.

Deadline for applications: 27 September 2015