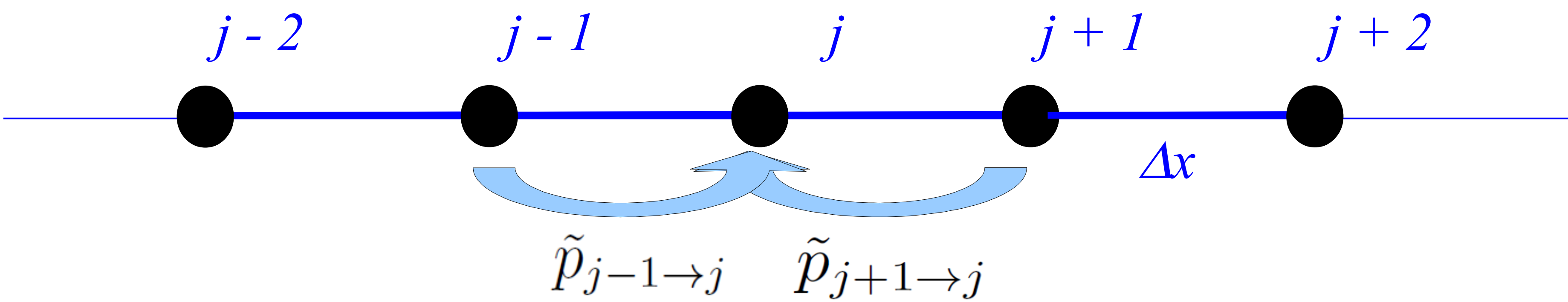
POLITECNICO DI TORINO

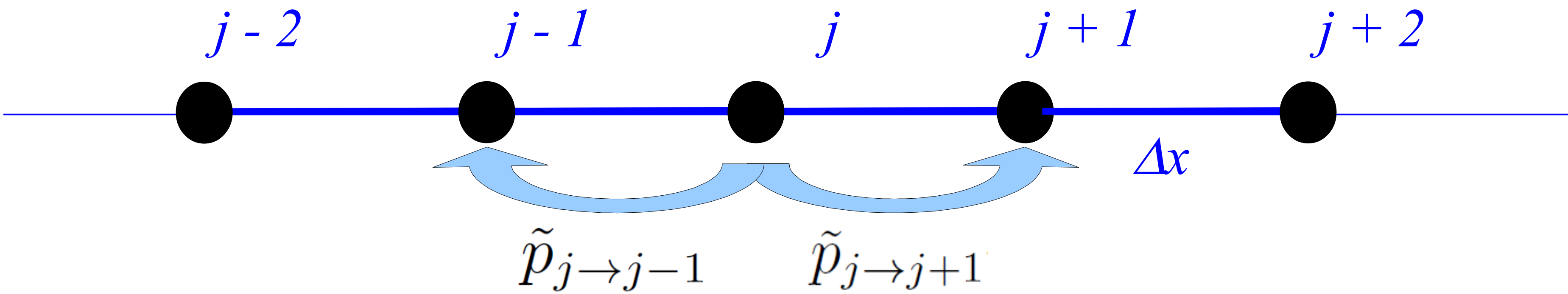
Diffusion

Random walk



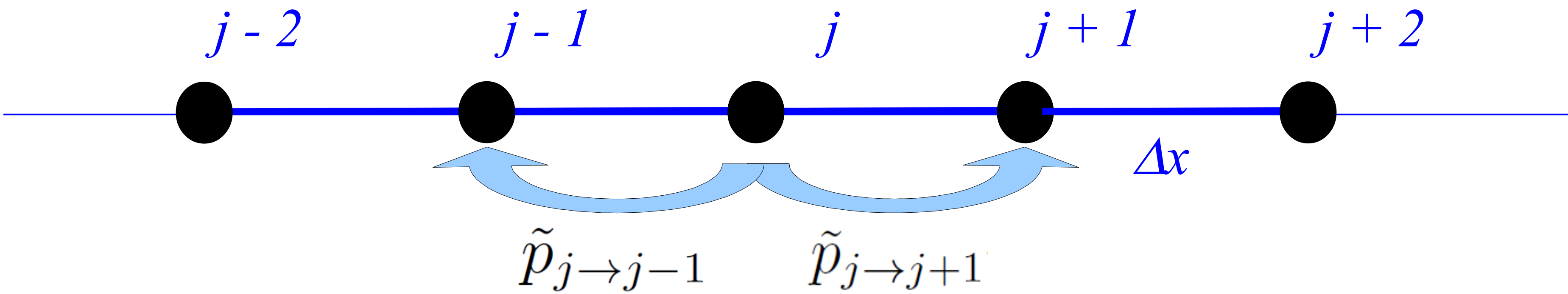
$$u_{i+1,j} = u_{i,j} + \tilde{p}_{j-1\rightarrow j} u_{i,j-1} + \tilde{p}_{j+1\rightarrow j} u_{i,j+1}$$

Random walk



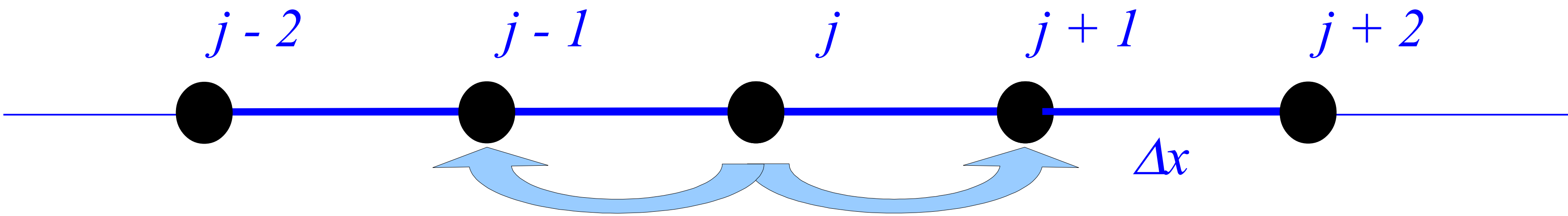
$$u_{i+1,j} = u_{i,j} + \tilde{p}_{j-1\to j}u_{i,j-1} + \tilde{p}_{j+1\to j}u_{i,j+1} - \tilde{p}_{j\to j-1}u_{i,j} - \tilde{p}_{j\to j+1}u_{i,j}$$

Random walk



$$
\begin{aligned}
u_{i+1,j} &= u_{i,j} + \tilde{p}_{j-1\to j}u_{i,j-1} + \tilde{p}_{j+1\to j}u_{i,j+1} - \tilde{p}_{j\to j-1}u_{i,j} - \tilde{p}_{j\to j+1}u_{i,j} \\
&= u_{i,j} + \Delta t[p_{j-1\to j}u_{i,j-1} + p_{j+1\to j}u_{i,j+1} - (p_{j\to j-1} + p_{j\to j+1})u_{i,j}]
\end{aligned}
$$

Random walk



$$\tilde{p}_{j\to j-1} \qquad \tilde{p}_{j\to j+1}$$

$$\begin{aligned} u_{i+1,j} &= u_{i,j} + \tilde{p}_{j-1\to j}u_{i,j-1} + \tilde{p}_{j+1\to j}u_{i,j+1} - \tilde{p}_{j\to j-1}u_{i,j} - \tilde{p}_{j\to j+1}u_{i,j} \\ &= u_{i,j} + \Delta t[p_{j-1\to j}u_{i,j-1} + p_{j+1\to j}u_{i,j+1} - (p_{j\to j-1} + p_{j\to j+1})u_{i,j}] \end{aligned}$$

Per $\Delta t \to 0$

$$\frac{du_j}{dt} = p_{j-1\to j}u_{j-1} + p_{j+1\to j}u_{j+1} - (p_{j\to j-1} + p_{j\to j+1})u_j$$

Constant coefficients

$$\frac{du_j}{dt} = p_{j-1\to j}u_{j-1} + p_{j+1\to j}u_{j+1} - (p_{j\to j-1} + p_{j\to j+1})u_j$$

If $p_{j\to k} = \frac{D}{\Delta x^2}$ ⟺ $\tilde{p}_{j\to k} = \frac{\Delta t}{\Delta x^2}D$

↓

$$\frac{du_j}{dt} = \frac{D}{\Delta x^2}(u_{j-1} - 2u_j + u_{j+1})$$

$\Delta x \to 0$ ⟹

$$\boxed{\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2}}$$

$$u_{j+1} \approx u_j + \frac{\partial u_j}{\partial x}\Delta x + \frac{\partial^2 u_j}{\partial x^2}\frac{\Delta x^2}{2}$$

$$u_{j-1} \approx u_j - \frac{\partial u_j}{\partial x}\Delta x + \frac{\partial^2 u_j}{\partial x^2}\frac{\Delta x^2}{2}$$

Looking here

$$\frac{du_j}{dt} = p_{j-1\to j}u_{j-1} + p_{j+1\to j}u_{j+1} - (p_{j\to j-1} + p_{j\to j+1})u_j$$

If $p_{j\to k} = \frac{D_j}{\Delta x^2}$ ⟷ $\tilde{p}_{j\to k} = \frac{\Delta t}{\Delta x^2}D_j$

↓

$$\frac{du_j}{dt} = \frac{1}{\Delta x^2}(D_{j-1}u_{j-1} - 2D_j u_j + D_{j+1}u_{j+1})$$

↓

$$\boxed{\frac{\partial u}{\partial t} = \frac{\partial^2}{\partial x^2}[D(x)u]}$$

↓

$$\frac{\partial u}{\partial t} - \frac{\partial}{\partial x}[D'(x)u] = \frac{\partial}{\partial x}\left[D(x)\frac{\partial u}{\partial x}\right]$$

POLITECNICO DI TORINO

How can we get the diffusion equation?

$$\frac{du_j}{dt} = p_{j-1\to j}u_{j-1} + p_{j+1\to j}u_{j+1} - (p_{j\to j-1} + p_{j\to j+1})u_j$$

$$? \quad \frac{\partial u}{\partial t} = \nabla \cdot (D\nabla u) \quad ?$$

Looking in the middle

$$\frac{du_j}{dt} = p_{j-1\to j}u_{j-1} + p_{j+1\to j}u_{j+1} - (p_{j\to j-1} + p_{j\to j+1})u_j$$

If $p_{j\to j\pm 1} = \frac{D_{j\pm\frac{1}{2}}}{\Delta x^2}$ ⟷ $\tilde{p}_{j\to j\pm 1} = \frac{\Delta t}{\Delta x^2} D_{j\pm\frac{1}{2}}$

↓

$$\frac{du_j}{dt} = \frac{1}{\Delta x^2}\left[D_{j-\frac{1}{2}}u_{j-1} - \left(D_{j-\frac{1}{2}} + D_{j+\frac{1}{2}}\right)u_j + D_{j+\frac{1}{2}}u_{j+1}\right]$$

$$= \frac{1}{\Delta x^2}\left[D_{j-\frac{1}{2}}(u_{j-1} - u_j) - D_{j+\frac{1}{2}}(u_j - u_{j+1})\right]$$

$$\approx \frac{1}{\Delta x}\left[D_{j+\frac{1}{2}}\frac{\partial u_{j+\frac{1}{2}}}{\partial x} - D_{j-\frac{1}{2}}\frac{\partial u_{j-\frac{1}{2}}}{\partial x}\right]$$

$$\approx \frac{\partial}{\partial x}\left(D_j\frac{\partial u_j}{\partial x}\right)$$

$\Delta x \longrightarrow 0$ ⟶

$$\boxed{\frac{\partial u}{\partial t} = \frac{\partial}{\partial x}\left(D(x)\frac{\partial u}{\partial x}\right)}$$

Looking in the middle

If $p_{j\to j\pm 1} = \frac{D_{j\pm\frac{1}{2}}}{\Delta x^2}$ ⟺ $\tilde{p}_{j\to j\pm 1} = \frac{\Delta t}{\Delta x^2} D_{j\pm\frac{1}{2}}$

⇓

$$D_{j\pm\frac{1}{2}} \approx D_j \pm \frac{\partial D_j}{\partial x}\frac{\Delta x}{2}$$

$$\begin{aligned}\frac{du_j}{dt} &\approx \frac{1}{\Delta x^2}\left[\left(D_j - \frac{1}{2}\frac{\partial D_j}{\partial x}\Delta x\right)\left(u_j - \frac{\partial u_j}{\partial x}\Delta x + \frac{\partial^2 u_j}{\partial x^2}\frac{\Delta x^2}{2}\right) - 2D_j u_j\right.\\ &\quad \left. + \left(D_j + \frac{1}{2}\frac{\partial D_j}{\partial x}\Delta x\right)\left(u_j + \frac{\partial u_j}{\partial x}\Delta x + \frac{\partial^2 u_j}{\partial x^2}\frac{\Delta x^2}{2}\right)\right],\\ &\approx \frac{\partial D_j}{\partial x}\frac{\partial u_j}{\partial x} + D_j\frac{\partial^2 u_j}{\partial x^2},\end{aligned}$$

$\Delta x \to 0$ ⟹

$$\boxed{\frac{\partial u}{\partial t} = \frac{\partial}{\partial x}\left(D(x)\frac{\partial u}{\partial x}\right)}$$

Looking ahead

If $p_{j\to j\pm1} = \dfrac{D_{j\pm1}}{\Delta x^2}$ ⟷ $\tilde{p}_{j\to j\pm1} = \dfrac{\Delta t}{\Delta x^2} D_{j\pm1}$

↓

$$\frac{du_j}{dt} = \frac{1}{\Delta x^2}\left[D_j u_{j-1} - (D_{j-1} + D_{j+1})u_j + D_j u_{j+1}\right]$$

$$D_{j\pm1} = D_j \pm \frac{\partial D_j}{\partial x}\Delta x + \frac{\partial^2 D_j}{\partial x^2}\frac{\Delta x^2}{2}$$

$$D_{j-1} + D_{j-1} \approx 2D_j + \frac{\partial^2 D_j}{\partial x^2}\Delta x^2$$

$$u_{j-1} + u_{j-1} \approx 2u_j + \frac{\partial^2 u_j}{\partial x^2}\Delta x^2$$

Looking ahead

$$\frac{du_j}{dt} \approx \frac{1}{\Delta x^2}\left[D_j\left(2u_j + \frac{\partial^2 u_j}{\partial x^2}\Delta x^2\right) - \left(2D_j + \frac{\partial^2 D_j}{\partial x^2}\Delta x^2\right) u_j\right]$$

$$= D_j \frac{\partial^2 u_j}{\partial x^2} - \frac{\partial^2 D_j}{\partial x^2} u_j$$

$\Delta x \to 0$

$$\frac{\partial u}{\partial t}(x,t) = D(x)\frac{\partial^2 u}{\partial x^2}(x,t) - u(x,t)\frac{\partial^2 D}{\partial x^2}(x)$$

$$\frac{\partial u}{\partial t} + \frac{\partial}{\partial x}\left[D'(x)u\right] = \frac{\partial}{\partial x}\left[D(x)\frac{\partial u}{\partial x}\right]$$

Summary

Looking here

$$\frac{\partial u}{\partial t} = \frac{\partial^2}{\partial x^2}[D(x)u]$$

$$\frac{\partial u}{\partial t} - \frac{\partial}{\partial x}[D'(x)u] = \frac{\partial}{\partial x}\left[D(x)\frac{\partial u}{\partial x}\right]$$

Looking in the middle

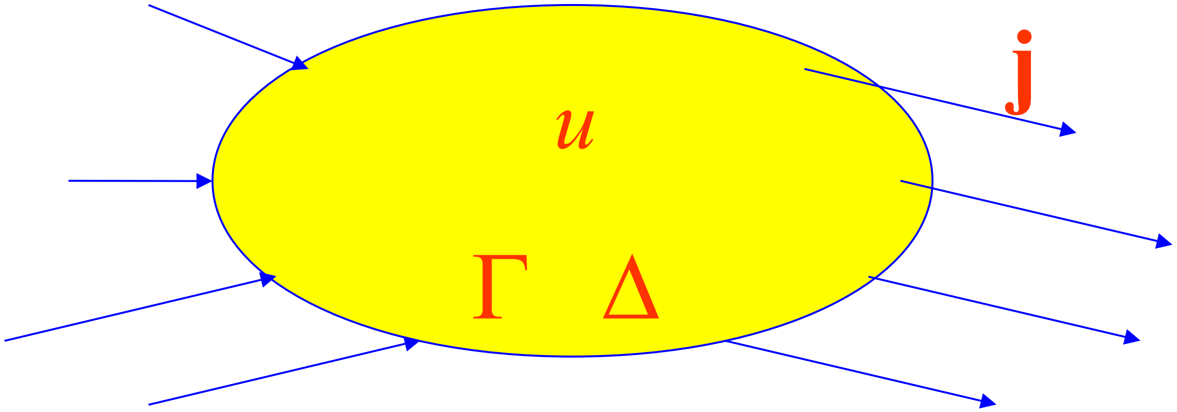
$$\frac{\partial u}{\partial t} = \frac{\partial}{\partial x}\left(D(x)\frac{\partial u}{\partial x}\right)$$

Looking ahead

$$\frac{\partial u}{\partial t}(x,t) = D(x)\frac{\partial^2 u}{\partial x^2}(x,t) - u(x,t)\frac{\partial^2 D}{\partial x^2}(x)$$

$$\frac{\partial u}{\partial t} + \frac{\partial}{\partial x}[D'(x)u] = \frac{\partial}{\partial x}\left[D(x)\frac{\partial u}{\partial x}\right]$$

Diffusion equation



$$M = \int_{\mathcal{V}} u \, dV$$

$$\frac{dM}{dt} = -\int_{\partial\mathcal{V}} \mathbf{j} \cdot \mathbf{n} \, d\Sigma + \int_{\mathcal{V}} (\Gamma - \Delta) \, dV$$

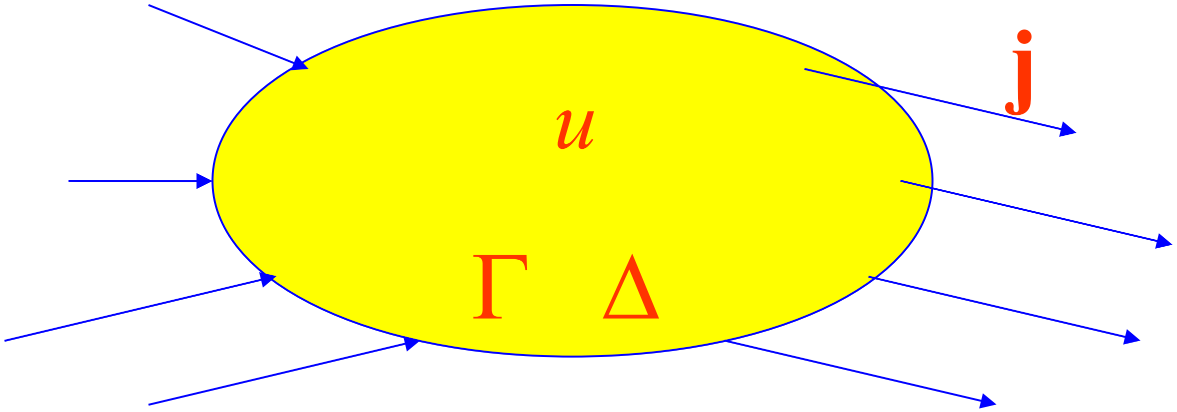
because of influx/outflux

density of cells changes →

$$\frac{\partial u}{\partial t} + \nabla \cdot \mathbf{j} = \Gamma - \Delta$$

because of birth/death

Diffusion equation



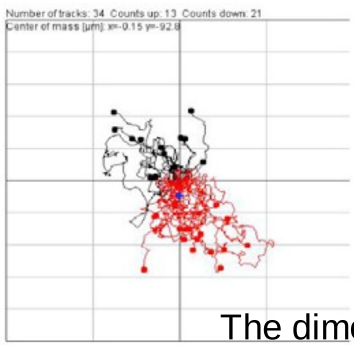
Fick's law $\mathbf{j} = -D\nabla u$ → $\dfrac{\partial u}{\partial t} = \nabla \cdot (D\nabla u)$

If *D* is constant $\dfrac{\partial u}{\partial t} = D\nabla^2 u$

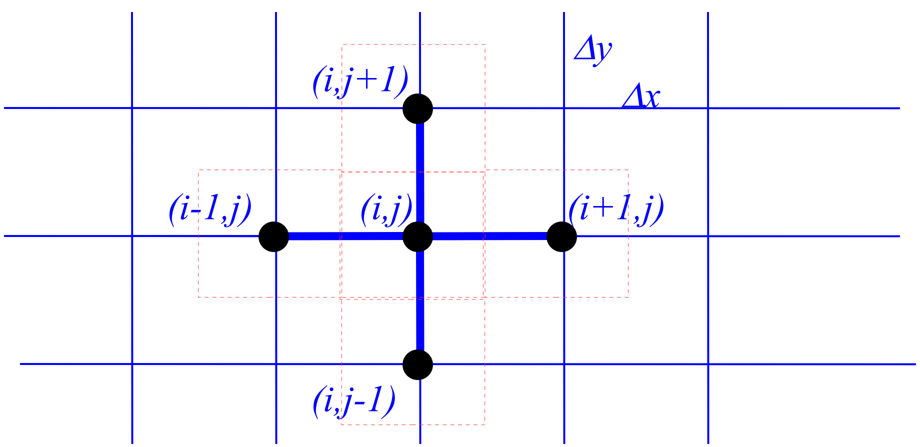
$$\frac{\partial u}{\partial t} = D\left(\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} + \frac{\partial^2 u}{\partial z^2}\right)$$

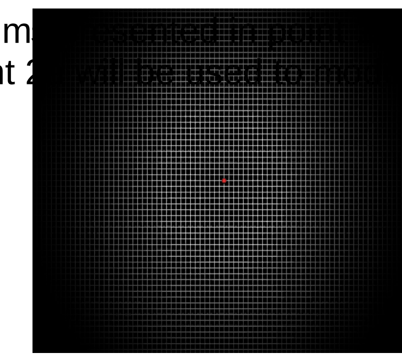
Diffusion equation

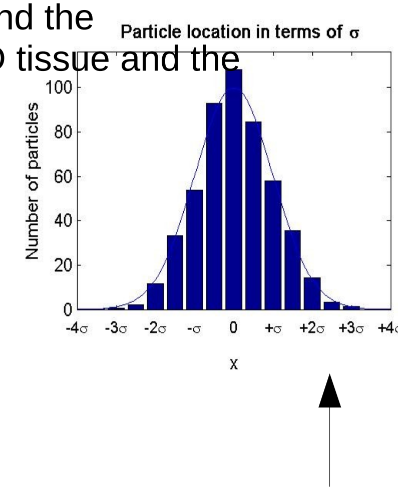
# cells in the node at time *t*	=	# cells in the node at preceding time
	+	# cells coming from neighbours
	–	# cells going to neighbours



The dimensionally coupled system ... a and the computational techniques in point 2 ... 3D tissue and the







Original at
ocw.mit.edu/ans7870/1/1.061/f04/animation/walk2.avi

Reaction-diffusion equation

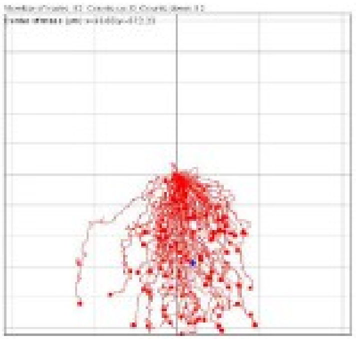
# cells in the node at time *t*		# cells in the node at preceding time
	+	# cells coming from neighbours
	–	# cells going to neighbours
	+	# generated (born) in the node
	–	# degradated (dead) in the node

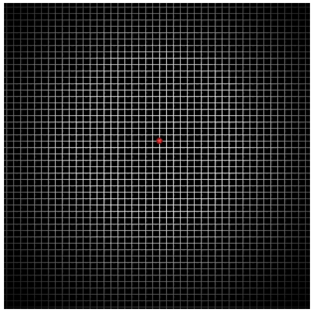
$$\frac{\partial u}{\partial t} = \nabla \cdot (\mathbf{D} \nabla u) + \Gamma - \Delta$$

POLITECNICO DI TORINO

Advection-reaction-diffusion equation

# cells in the node at time t	=	# cells in the node at preceding time
	+	# cells coming from neighbours
	−	# cells going to neighbours
	+	# generated (born) in the node
	−	# degradated (dead) in the node
	−	# advected with velocity **v**





Original at

ocw.mit.edu/ans7870/1/1.061/f04/animation/ch6_cont.avi

$$\frac{\partial u}{\partial t} + \nabla \cdot (u\mathbf{v}) = \nabla \cdot (D \nabla u) + \Gamma - \Delta$$

u changes in time → $\frac{\partial u}{\partial t}$

because it is advected → $\nabla \cdot (u\mathbf{v})$

because diffuses → $\nabla \cdot (D \nabla u)$

because of birth/death → $\Gamma - \Delta$

POLITECNICO DI TORINO

Fundamental solutions

Diffusione in R^n

$$\frac{\partial u}{\partial t} = D\nabla^2 u \qquad u(x,t) = \frac{M}{(4\pi Dt)^{d/2}} \exp\left[-\frac{|\mathbf{x}|^2}{4Dt}\right]$$

Diffusione con crescita

$$\frac{\partial u}{\partial t} = D\nabla^2 u + \gamma u \qquad u(x,t) = \frac{M}{(4\pi Dt)^{d/2}} \exp\left[-\frac{|\mathbf{x}|^2}{4Dt} + \gamma t\right]$$

Convezione-diffusione

$$\frac{\partial u}{\partial t} + \mathbf{v} \cdot \nabla u = D\nabla^2 u$$

$$u(x,t) = \frac{M}{(4\pi Dt)^{d/2}} \exp\left[-\frac{|\mathbf{x} - \mathbf{v}t|^2}{4Dt}\right]$$

Drug efficacy

$$\frac{\partial u}{\partial t} = D\nabla^2 u$$

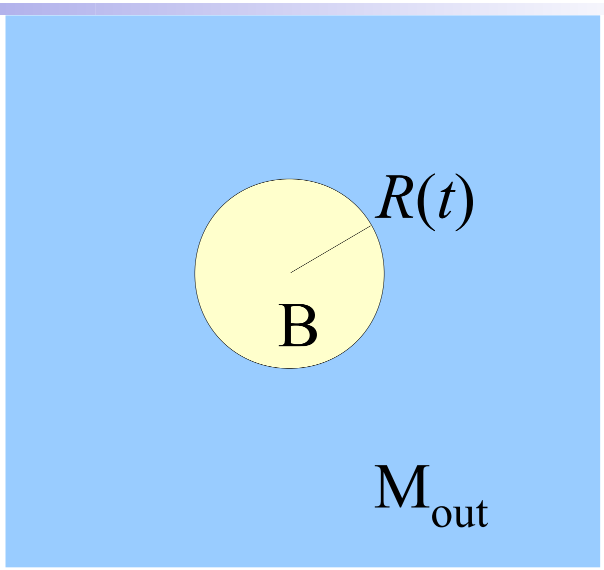
$$u(x,t) = \frac{M}{(4\pi Dt)^{d/2}} \exp\left[-\frac{|\mathbf{x}|^2}{4Dt}\right]$$

When $u > \bar{u}$ in x_0?

Population expansion

$$\frac{\partial u}{\partial t} = D\nabla^2 u$$

$$u(x,t) = \frac{M}{(4\pi D t)^{d/2}} \exp\left[-\frac{|\mathbf{x}|^2}{4Dt}\right]$$



Population expansion with growth

$$\frac{\partial u}{\partial t} = D\nabla^2 u + \gamma u$$

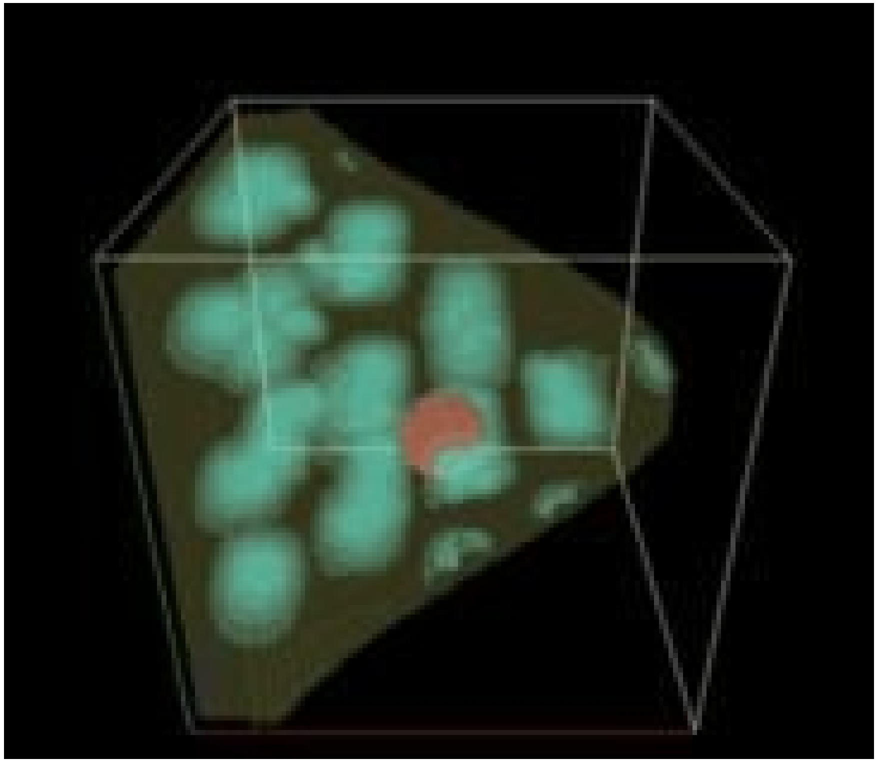
$$u(x,t) = \frac{M}{(4\pi D t)^{d/2}} \exp\left[-\frac{|\mathbf{x}|^2}{4Dt} + \gamma t\right]$$

Diffusion models

rate of change of tumor cell population
= diffusion (motility) of tumor cells
+ net proliferation of tumor cells

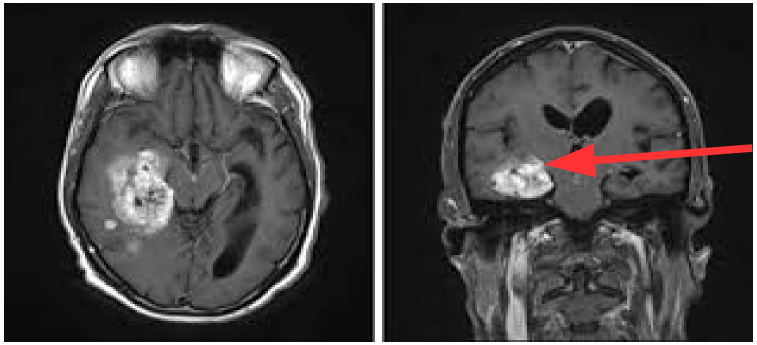
$$\frac{\partial c}{\partial t} = \nabla \cdot (D \nabla c) + \rho c$$

Breast tumour

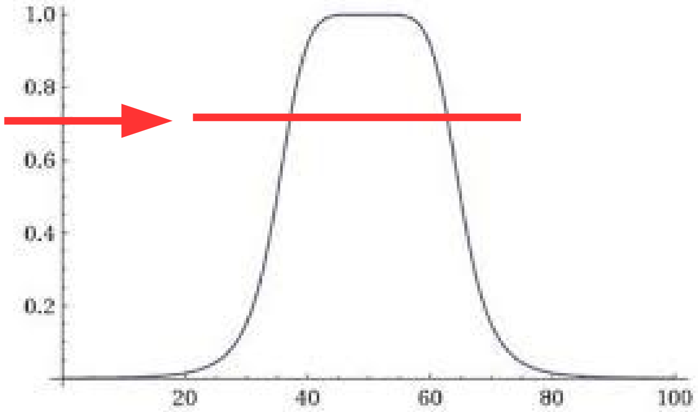


Original at:
www.maths.dundee.ac.uk/mbg/

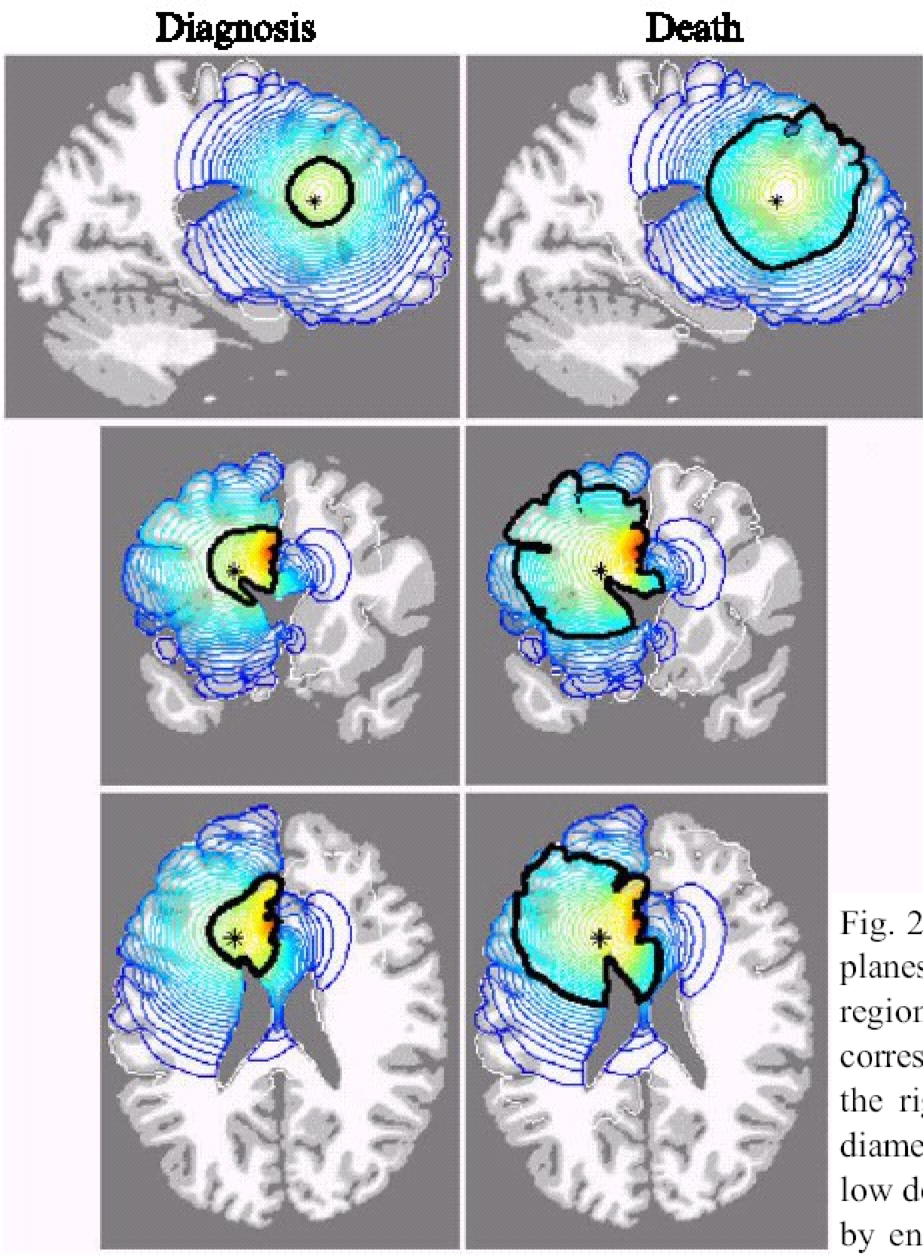
Inverse problems



Detection threshold



$$\frac{\partial c}{\partial t} = \nabla \cdot (D \nabla c) + \rho c$$



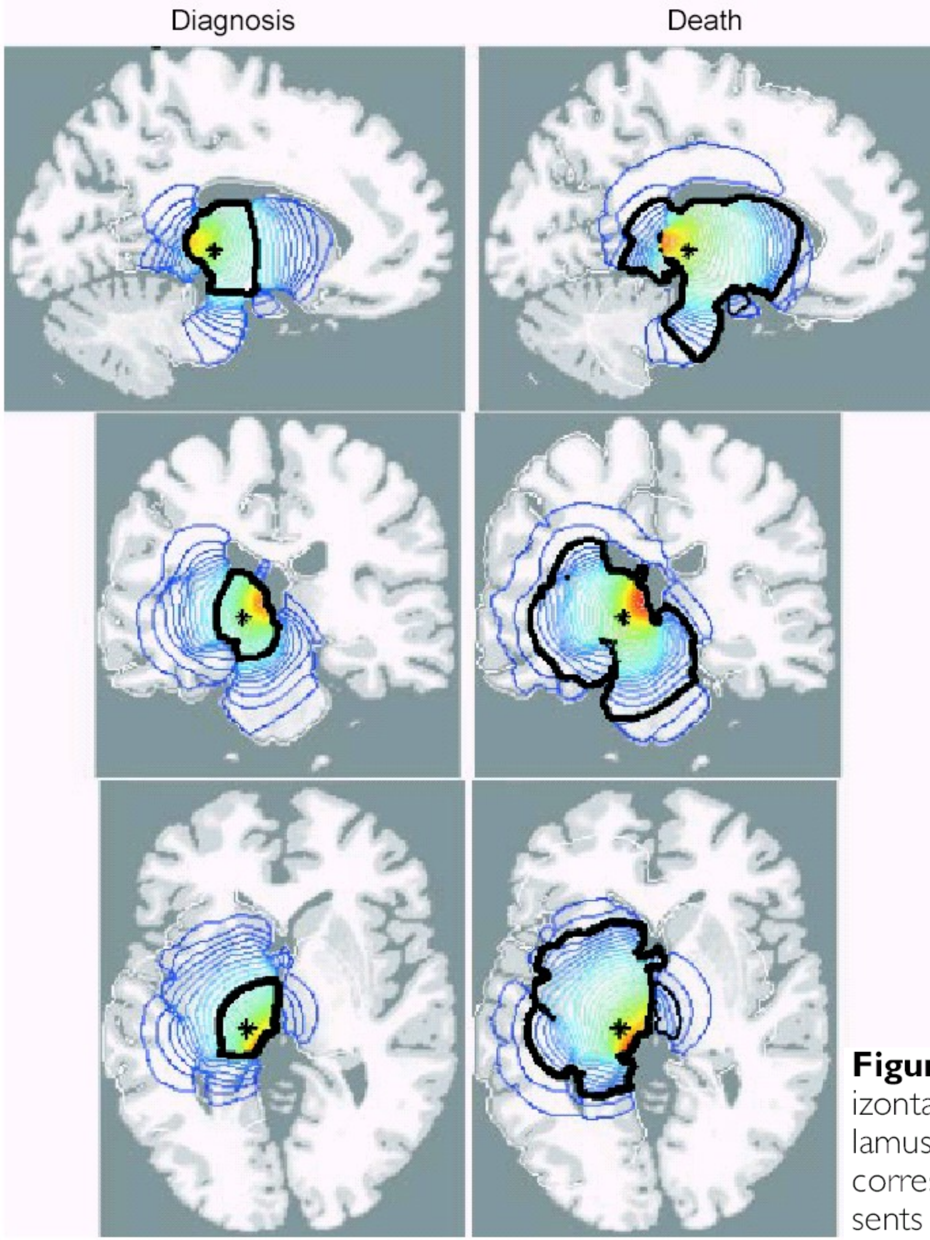
rate of change of tumor cell population
= diffusion (motility) of tumor cells
+ net proliferation of tumor cells

$$\frac{\partial c}{\partial t} = \nabla \cdot (D \nabla c) + \rho c$$

K. Swanson

UW PATHOLOGY

Fig. 2. Sections of a virtual human brain in sagittal, coronal and horizontal planes that intersect at the site of a glioma originating in the superior frontal region denoted by an asterisk (*). The left column of brain sections corresponds to the tumor at diagnosis (3 cm in average diameter) whereas the right column represents the same tumor at death (6 cm in average diameter). Red denotes a high density of tumor cells while blue denotes a low density. A thick black contour defines the edge of the tumor detectable by enhanced MRI. Cell migration was allowed to occur in a truly three-dimensional solid representation of the brain. The elapsed time between diagnosis and death for this virtual glioma is approximately 158 days, about one-fourth of the total history of the tumor. Reprinted from Swanson et al. [22], with the kind permission of Nature Publishing Group.



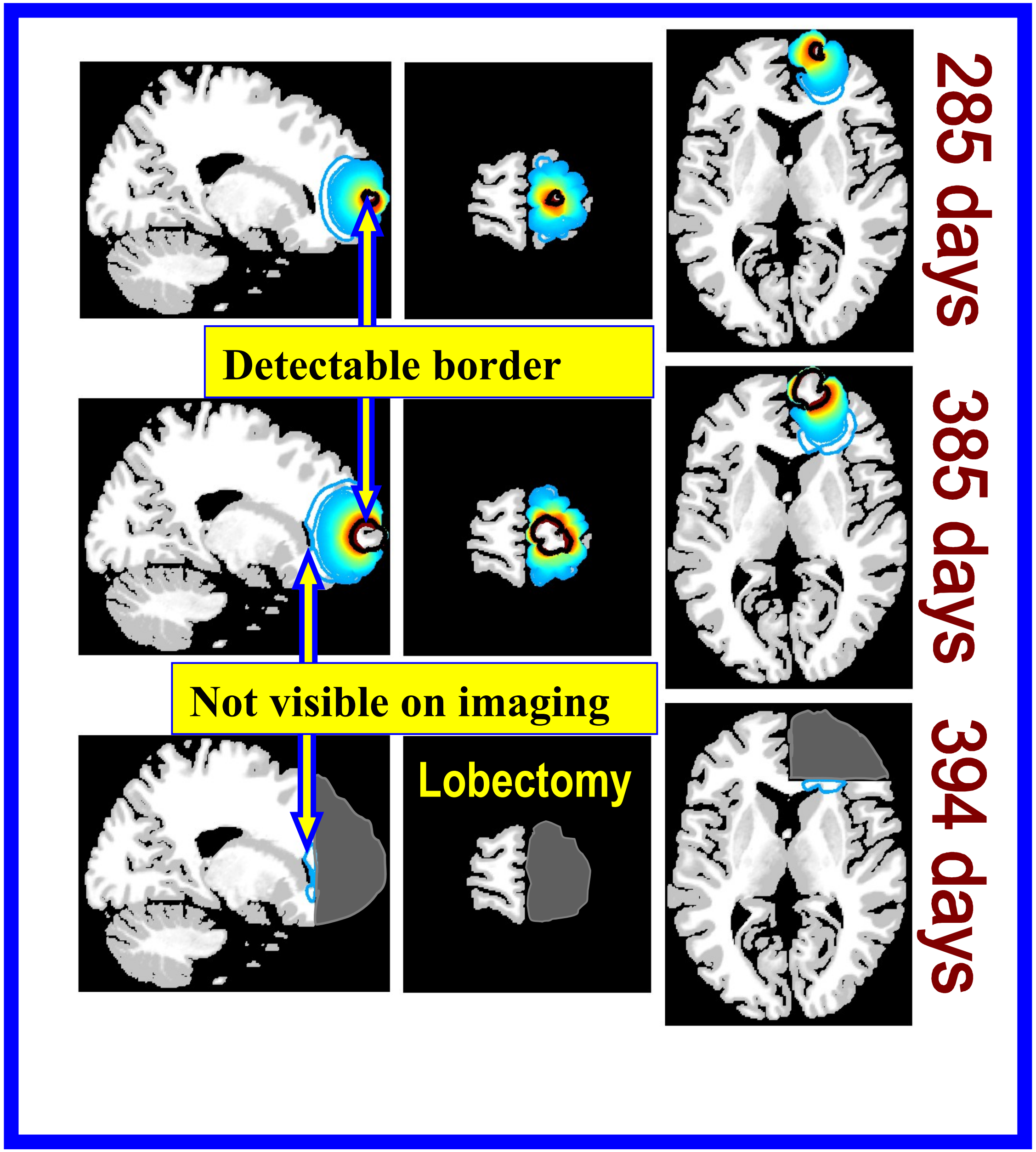
rate of change of tumor cell population
= diffusion (motility) of tumor cells
+ net proliferation of tumor cells

$$\frac{\partial c}{\partial t} = \nabla \cdot (D \nabla c) + \rho c$$

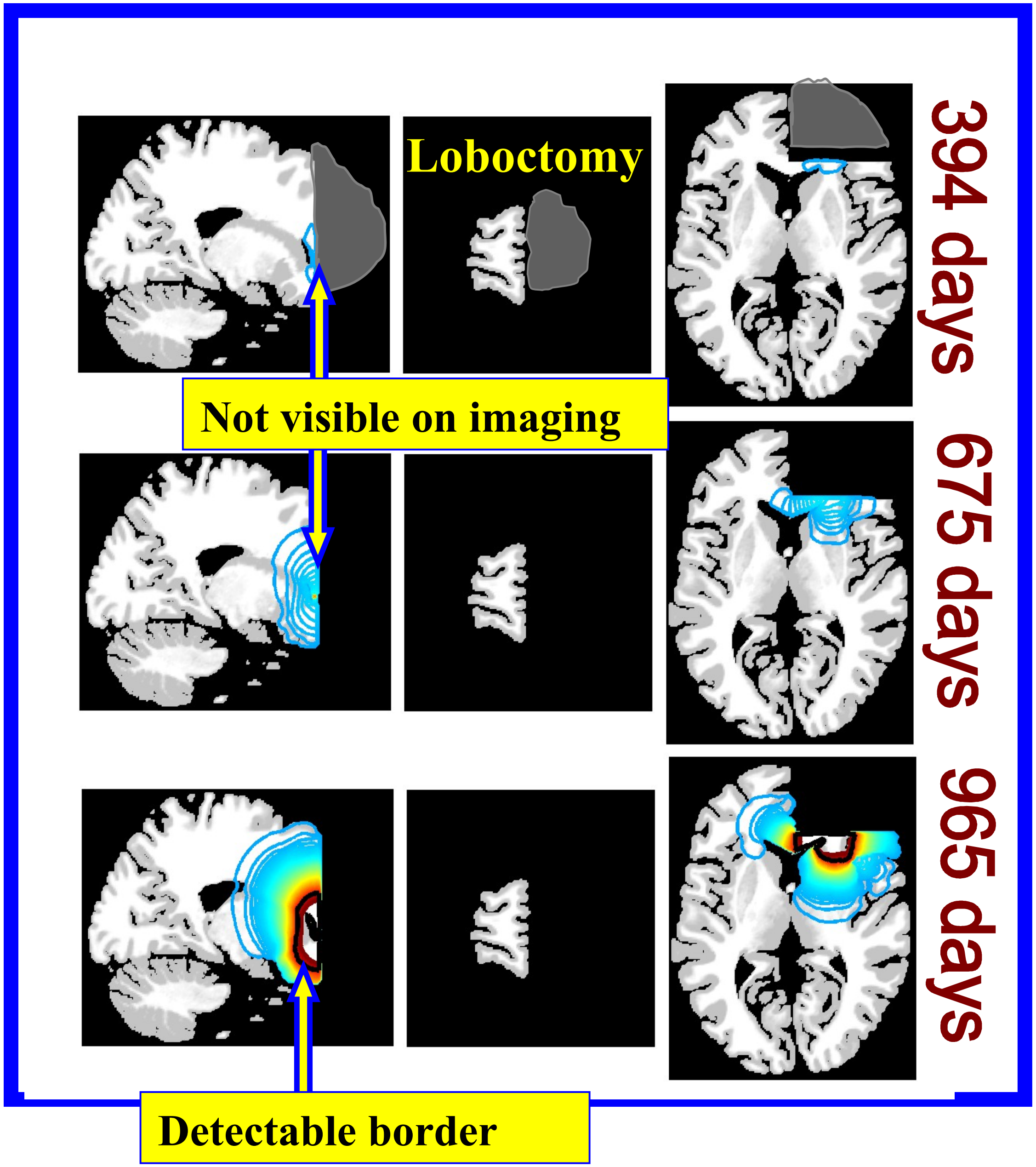
K. Swanson

UW PATHOLOGY

Figure 2 Sections of the virtual human brain in sagittal, coronal and horizontal planes that intersect at the site of the glioma originating in the thalamus denoted by an asterisk (*). The left column of brain sections corresponds to the tumour at diagnosis whereas the right column represents the same tumour at death. Red denotes a high density of tumour cells while blue denotes a low density. A thick black contour defines the edge of the tumour detectable by enhanced CT. Cell migration was allowed to occur in a truly three-dimensional solid representation of the brain. The elapsed time between diagnosis and death for this virtual gliomas is approximately 256 days.



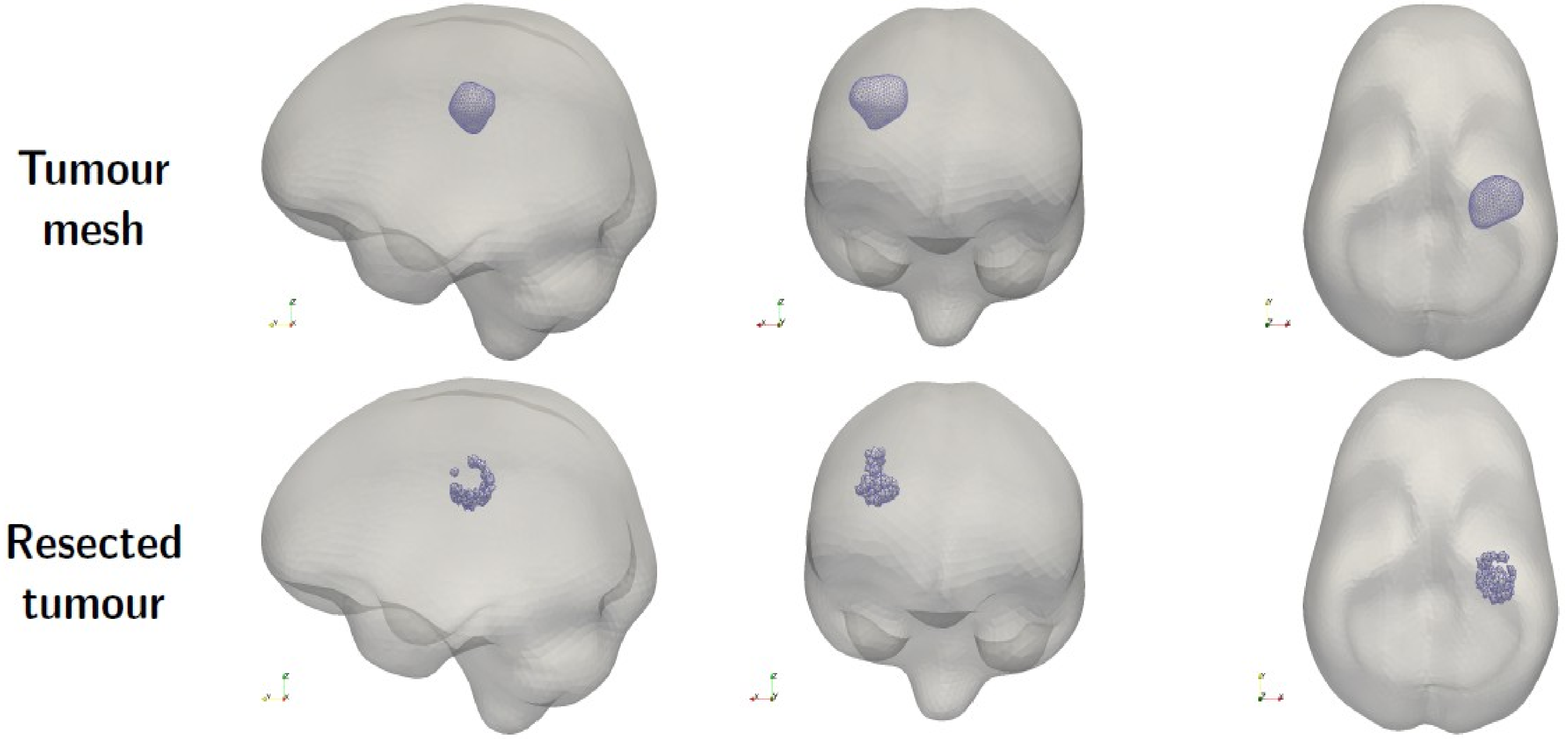
Sagittal, coronal and axial virtual MRIs from a continuous motion picture of the recurrence of a "favorable" glioblastoma (unusually small, 1 cm in diameter, and unusually far forward in frontal polar cortex) following extensive resection of most of the frontal lobe. Thick black contours represent the edge of the gadolinium-enhanced T1-weighted MRI (T1Gd) signal. Red: high glioma cell density; Blue: low density.



Sagittal, coronal and axial virtual MRIs from a continuous motion picture of the recurrence of a “favorable” glioblastoma (unusually small, 1 cm in diameter, and unusually far forward in frontal polar cortex) following extensive resection of most of the frontal lobe. Thick black contours represent the edge of the gadolinium-enhanced T1-weighted MRI (T1Gd) signal. Red: high glioma cell density; Blue: low density.

Control & optimization of chemotherapy

Giverso, Agosti, Ciarletta, Ambrosi, *ZAMM* (2018)



Control & optimization of chemotherapy

Standard Stupp protocol: