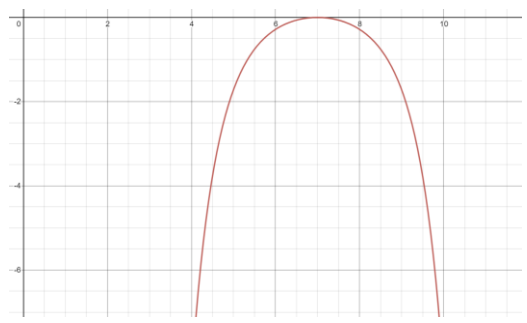
proliferation | carrying capacity limited | matrix limited | diffusion | carrying capacity limited | matrix limited | slower growth/death from non-optimal pH

healthy cells
$$\frac{\partial N_1}{\partial t} = k_1 N_1 \left(1 - \frac{N_1}{\theta_1} - \frac{N_2}{\theta_2}\right)\left(1 - \frac{M}{M_o}\right) + \nabla \cdot \left(D_{N_1}\left(1 - \frac{N_1}{\theta_1} - \frac{N_2}{\theta_2}\right)\left(1 - \frac{M}{M_o}\right)\nabla N_1\right) - f_1(H)N_1$$

tumor cells
$$\frac{\partial N_2}{\partial t} = k_2 N_2 \left(1 - \frac{N_1}{\theta_1} - \frac{N_2}{\theta_2}\right)\left(1 - \frac{M}{M_o}\right) + \nabla \cdot \left(D_{N_2}\left(1 - \frac{N_1}{\theta_1} - \frac{N_2}{\theta_2}\right)\left(1 - \frac{M}{M_o}\right)\nabla N_2\right) - f_2(H)N_2$$



$$f_1(H) = d_1\left(1 - e^{-\left(\frac{H - H_1^{opt}}{H_1^{width}}\right)^2}\right)$$

$$f_2(H) = d_2\left(1 - e^{-\left(\frac{H - H_2^{opt}}{H_2^{width}}\right)^2}\right)$$

optimal pH curve

diffusion | acid production by tumor cells | hydrogen uptake by surrounding tissue | acid-base neutralization

protons
$$\frac{\partial H}{\partial t} = D_H \nabla^2 H + k_{acid} N_2 - d_H(H - H_0) - k_{neut} HB$$

bicarbonate treatment
$$\frac{\partial B}{\partial t} = D_B \nabla^2 B + \cancel{d_B} - k_{neut} HB$$

diffusion | bicarbonate introduction | acid-base neutralization

Use initial conditions to introduce B into system instead

matrix degradation by MMPs

generalized extracellular matrix
$$\frac{\partial M}{\partial t} = -f_{MMP}(H) P M$$

MMP degradation

MMPs
$$\frac{\partial P}{\partial t} = D_P \nabla^2 P + k_P N_2 - d_p P$$

diffusion | MMP production by tumor cells

$$f_{MMP}(H) =$$

pH-dependent MMP activity