

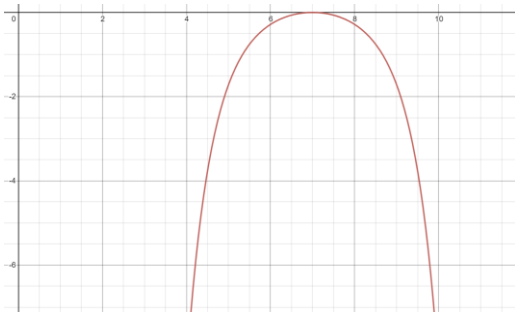
proliferation carrying capacity is lowered by presents of matrix

diffusion limited by presence of matrix

slower growth/death from non-optimal pH

healthy cells $\frac{\partial N_1}{\partial t} = k_1 N_1 \left(1 - \frac{N_1}{\theta_1 - \alpha_1 M} - \frac{N_2}{\theta_2 - \alpha_2 M} \right) + \nabla \cdot \left(D_{N_1} \left(1 - \frac{N_1}{\theta_1 - \alpha_1 M} - \frac{N_2}{\theta_2 - \alpha_2 M} \right) \nabla N_1 \right) - f_1(H) N_1$

tumor cells $\frac{\partial N_2}{\partial t} = k_2 N_2 \left(1 - \frac{N_1}{\theta_1 - \alpha_1 M} - \frac{N_2}{\theta_2 - \alpha_2 M} \right) + \nabla \cdot \left(D_{N_2} \left(1 - \frac{N_1}{\theta_1 - \alpha_1 M} - \frac{N_2}{\theta_2 - \alpha_2 M} \right) \nabla N_2 \right) - f_2(H) N_2$



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

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

optimal pH curve

generalized extracellular matrix

matrix degradation by MMPs

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

protons

diffusion

acid production by tumor cells

hydrogen uptake by surrounding tissue

acid-base neutralization

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

bicarbonate treatment

diffusion

acid-base neutralization

bicarbonate introduction

$$\frac{\partial B}{\partial t} = D_B \nabla^2 B + \cancel{\alpha_B} - k_{neut} H B$$

Use initial conditions to introduce B into system instead

MMPs

diffusion

MMP production by tumor cells

MMP degradation

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

$f_{MMP}(H) =$

pH-dependent MMP activity

