A Mathematical Model of Basal Cell Carcinoma

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Assumptions

- Proliferation rate of tumor cells depends on the availability of nutrients

- Nutrients are consumed by active tumor cells

- Cell diffusion coefficient expressing tumor cell movements increases with the cell density and the nutrient availability

The Model

$$\frac{\partial n}{\partial t} = \nabla^2 n - nc$$

$$\frac{\partial c}{\partial t} = \nabla(\sigma nc\nabla c) + nc$$

- n(x,y,t) represents the nutrient concentration
- c(x,y,t) represents the density of tumor cells
- σ is the cell motility coefficient (taken to be constant)

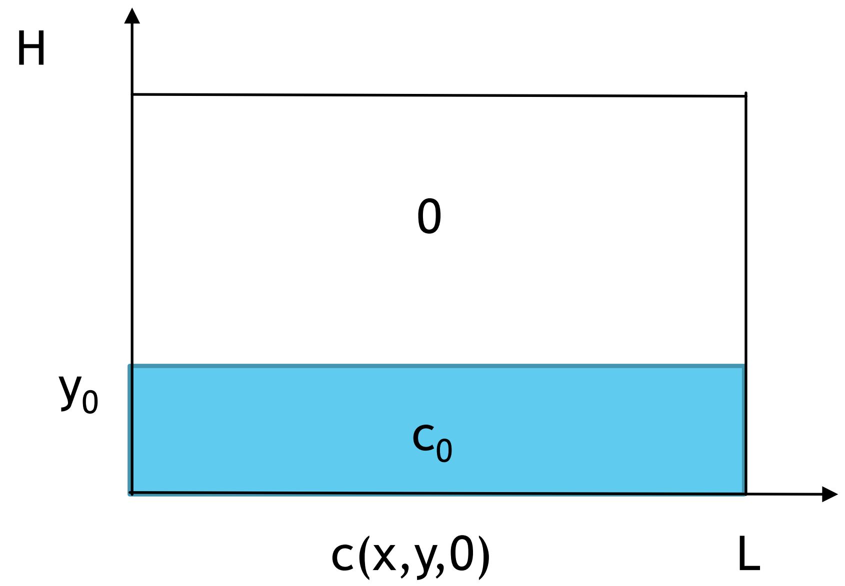
Initial and Boundary Conditions

- $c(x,y,0) = \begin{cases} c_0, & for\ 0 \le y \le y_0 \\ 0, & for\ y_0 < y \le H \end{cases}$
- $n(x,y,0) = n_0,\ for\ 0 < x < L\ and\ 0 < y < H$

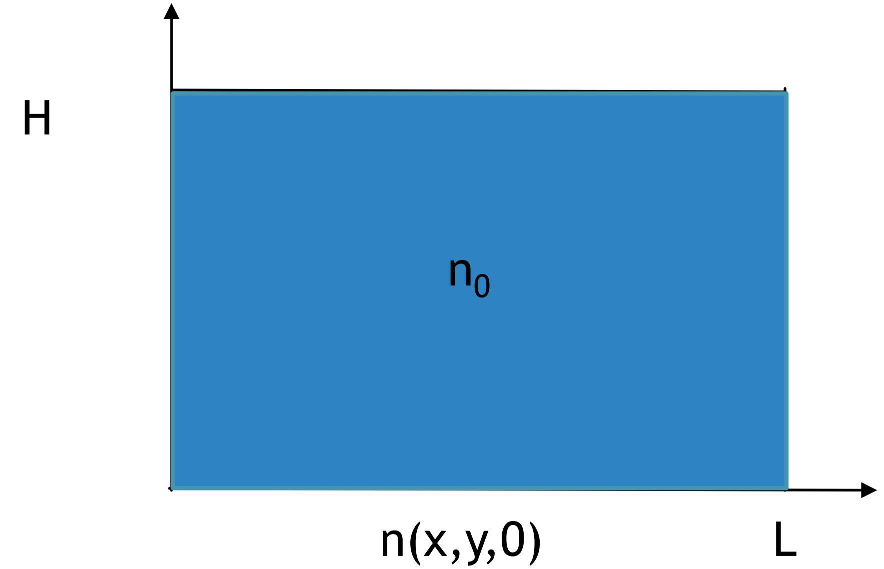
- $n(x,H,t) = n_o,\ for\ 0 < x < L$
- $\frac{\partial}{\partial y} n(x,0,t) = \frac{\partial}{\partial y} c(x,0,t) = \frac{\partial}{\partial y} c(x,H,t) = 0,\ for\ 0 < x < L$
- $\frac{\partial}{\partial x} n(0,y,t) = \frac{\partial}{\partial x} c(0,y,t) = \frac{\partial}{\partial x} n(L,y,t) = \frac{\partial}{\partial x} c(L,y,t) = 0,$

  $for\ 0 < y < H$

Initial tumor cell density



Initial nutrient concentration



1-D Equilibrium States

$$\frac{\partial n}{\partial t} = \frac{\partial^2 n}{\partial x^2} - nc$$

$$\frac{\partial c}{\partial t} = \sigma nc \frac{\partial^2 c}{\partial x^2} + \sigma n \left(\frac{\partial c}{\partial x}\right)^2 + \sigma c \frac{\partial n}{\partial x}\frac{\partial c}{\partial x} + nc$$

- $Any\ n_0, c_0 \in \mathbb{R}\ such\ that\ n_0 c_0 = 0\ are\ constant\ solutions$
- Equilibrium states are not stable!

1-D Finite Difference Method

$$Let\ x_i = i\Delta x, \qquad for\ i = 0, \dots, I$$
$$and\ t_k = k\Delta t, \qquad for\ t = 0, \dots, K$$

$$\frac{\partial n}{\partial t} = \frac{\partial^2 n}{\partial x^2} - nc$$

$$\frac{n_i^{k+1} - n_i^k}{\Delta t} = \frac{n_{i+1}^k - 2n_i^k + n_{i-1}^k}{(\Delta x)^2} - n_i^k c_i^k$$

$$i = 1, \dots, I - 1 \quad and\ k = 0, \dots, K - 1$$

1-D Finite Difference Method

$$\frac{\partial c}{\partial t} = \sigma n c \frac{\partial^2 c}{\partial x^2} + \sigma n \left(\frac{\partial c}{\partial x}\right)^2 + \sigma c \frac{\partial n}{\partial x}\frac{\partial c}{\partial x} + nc$$

$$\frac{c_i^{k+1} - c_i^k}{\Delta t} = \sigma n_i^k c_i^k \left(\frac{c_{i+1}^k - 2c_i^k + c_{i-1}^k}{(\Delta x)^2}\right) + \sigma n_i^k \left(\frac{c_{i+1}^k - c_{i-1}^k}{2\Delta x}\right)^2$$

$$+\sigma c_i^k \left(\frac{n_{i+1}^k - n_{i-1}^k}{2\Delta x}\right)\left(\frac{c_{i+1}^k - c_{i-1}^k}{2\Delta x}\right) + n_i^k c_i^k$$

$$i = 1, \dots, I-1 \quad and\ k = 0, \dots, K-1$$

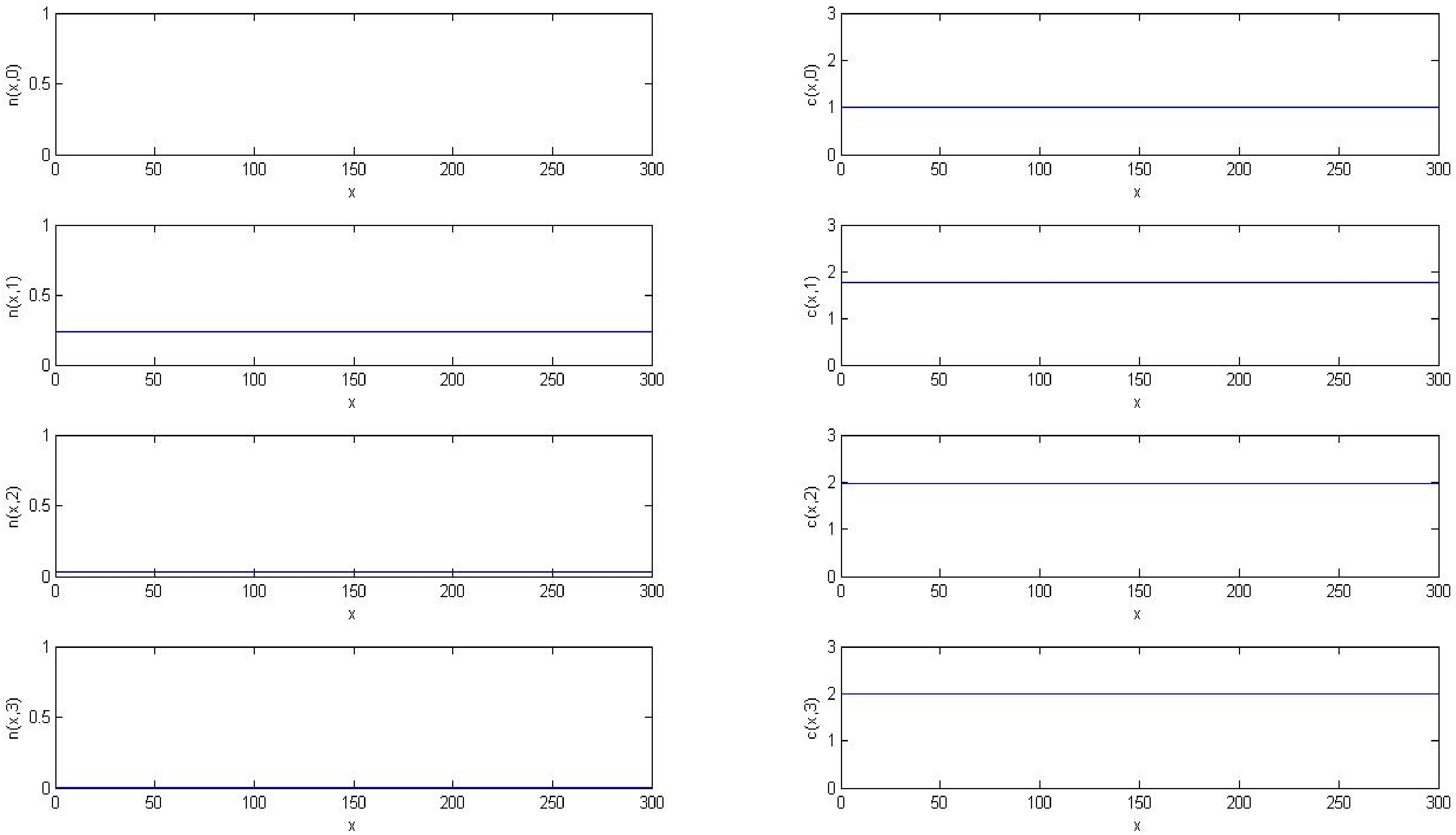
Simulation 1 (x-direction)

$$n_0 = 1 \; and \; c_0 = 1,$$

$$\sigma = 1$$

$$L = 300$$

$$\Delta t = 0.02, \qquad \Delta x = 0.5$$



n(x,0)
c(x,0)
n(x,1)
c(x,1)
n(x,2)
c(x,2)
n(x,3)
c(x,3)
x

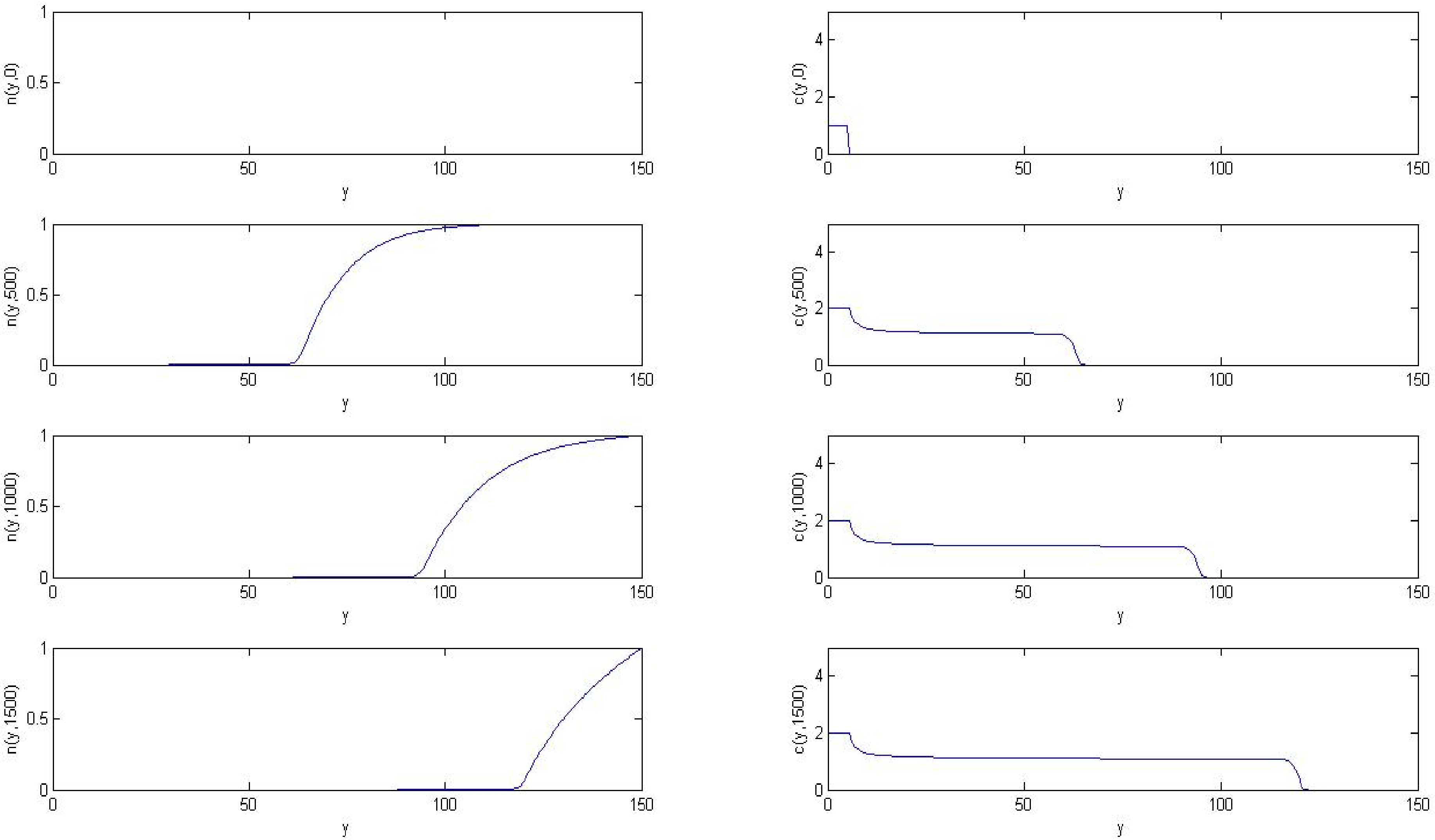
Simulation 2 (y-direction)

$$n_0 = 1 \ \ and \ \ c_0 = 1,$$

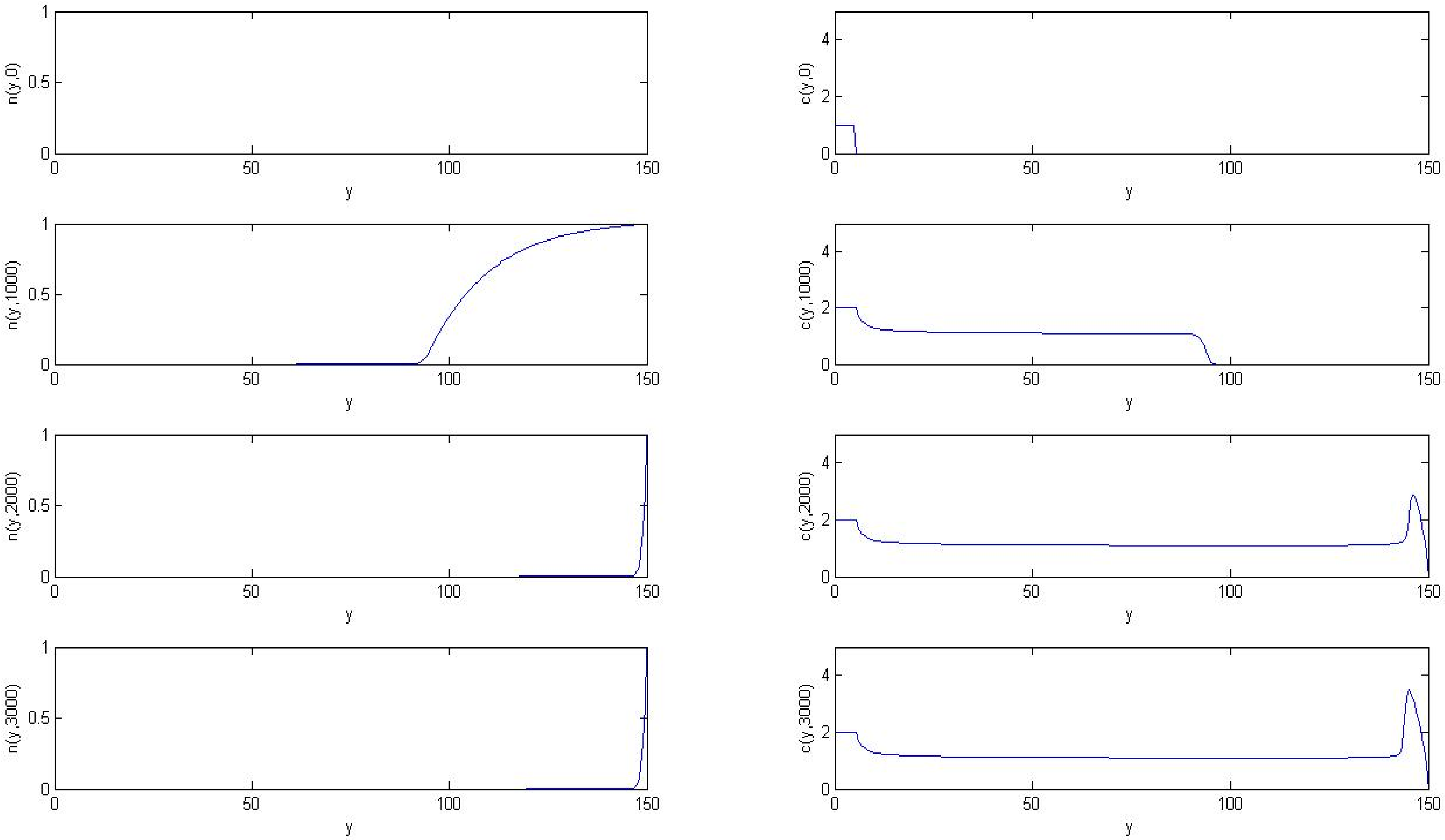
$$\sigma = 1$$

$$y_0 = 5, \qquad H = 150$$

$$\Delta t = 0.02, \qquad \Delta y = 0.5$$



n(y,0)
c(y,0)
n(y,500)
c(y,500)
n(y,1000)
c(y,1000)
n(y,1500)
c(y,1500)
y


n(y,0)
c(y,0)
n(y,1000)
c(y,1000)
n(y,2000)
c(y,2000)
n(y,3000)
c(y,3000)
y

2-D System

$$\frac{\partial n}{\partial t} = \frac{\partial^2 n}{\partial x^2} + \frac{\partial^2 n}{\partial y^2} - nc$$

$$\frac{\partial c}{\partial t} = \sigma nc \frac{\partial^2 c}{\partial x^2} + \sigma\left(n\frac{\partial c}{\partial x} + c\frac{\partial n}{\partial x}\right)\frac{\partial c}{\partial x}$$
$$+\sigma nc \frac{\partial^2 c}{\partial y^2} + \sigma\left(n\frac{\partial c}{\partial y} + c\frac{\partial n}{\partial y}\right)\frac{\partial c}{\partial y} + nc$$

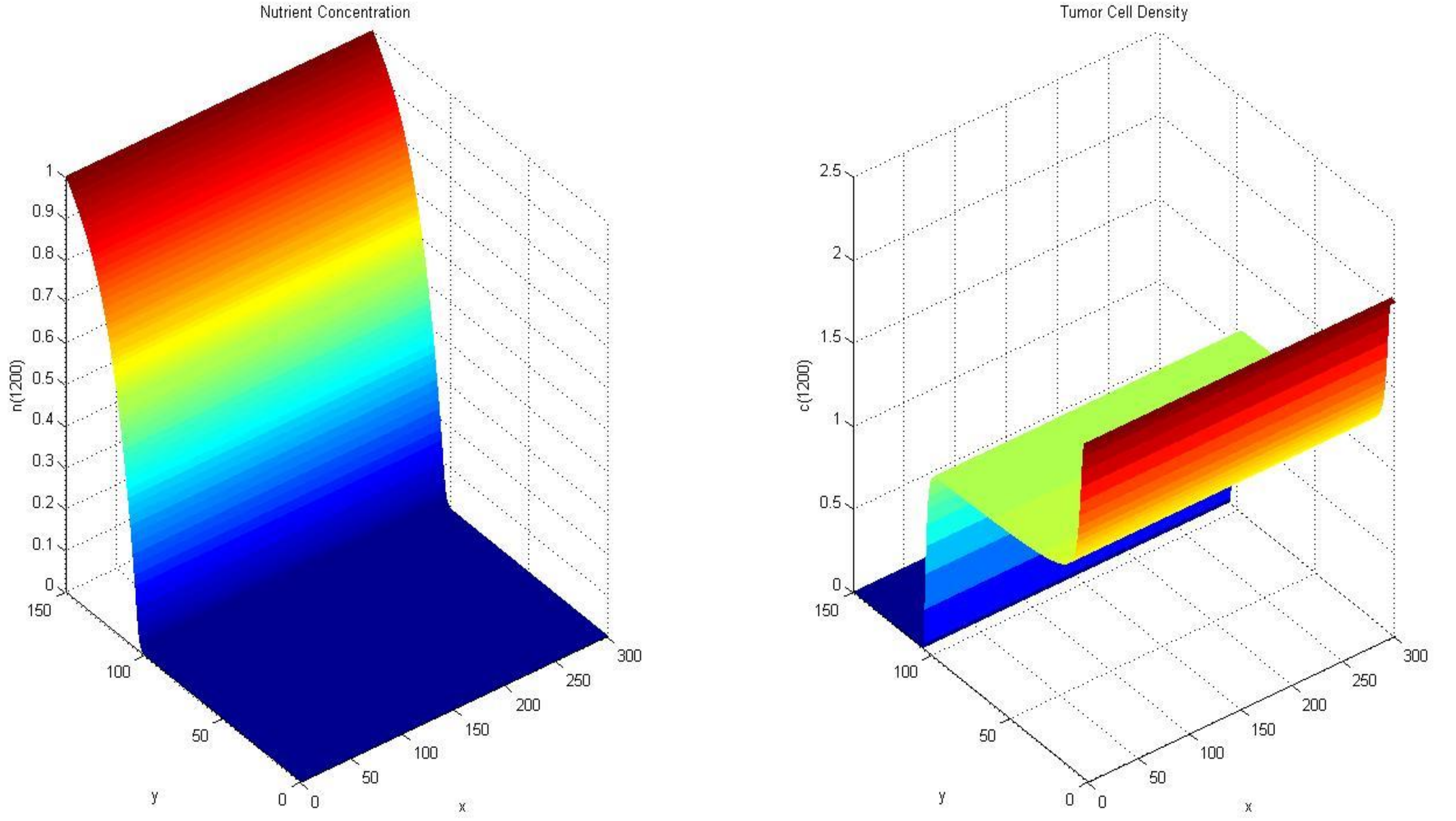
2-D Simulation

$$n_0 = 1 \;\; and \;\; c_0 = 1,$$

$$\sigma = 1$$

$$L = 300, \qquad y_0 = 5, \qquad H = 150$$

$$\Delta t = 0.012, \qquad \Delta x = \Delta y = 0.5$$



Nutrient Concentration
n(1200)
x
y
Tumor Cell Density
c(1200)
x
y

Conclusion

More data is needed to make this model useful!

Future goals:

Simulation using a finite element method

3-D simulation

References

- Tohya S, Mochizuki A, Imayama S. On Rugged Shape of Skin Tumor (Basal Cell Carcinoma). J Theor Biol. 1998;194:65-78.

- Eikenberry, Steffen, Craig Thalhauser, and Yang Kuang. "Tumor-Immune Interaction, Surgical Treatment, and Cancer Recurrence in a Mathematical Model of Melanoma." Ed. Carl T. Bergstrom. *PLoS Computational Biology* 5.4 (2009): e1000362. *PMC*. Web. 4 Mar. 2015.

Reminder for us all…

Always wear sunscreen!