A Simplified Mathematical Model of Tumor Growth *

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28.01.2010

1 INTRODUCTION

1.1 ABSTRACT

A one-dimensional model of tumor tissue growth in which the source of mitotic inhibitor is nonuniformly distributed within the tissue. As a result, stable and unstable regimes of growth become significantly modified from the uniform-source case.

Goals:

• to characterize the transition from stable to unstable tissue growth by a dimensionless number $n$

• to compare the results with the results from the prior paper of Glass

1.2 NOT THAT ABSTRACT

The basic mechanism in this model is that of tissue size regulation via negative feedback from the tissue itself. The tissue produces the agents of negative feedback (tissue-specific, mitotic inhibitor) called chalone. The chalone controls the mitosis. If there is „enough“ chalone in the tissue, then the mitosis will stop and so the growth, otherwise not.

*John A. Adam, Mathematical Biosciences 81:229-244 (1986)
2 The Modell

2.1 Ingredients

- \( t \): time
- \( x \): position
- \( L \): tissue length (\(|x| \leq \frac{L}{2}\))
- \( M_0 \): mitotic rate
- \( D \): chalone diffusion coefficient
- \( P \): chalone production rate
- \( \lambda \): chalone decay rate
- \( C(x, t) \): chalone concentration
- \( \Theta \): critical chalone concentration

\[
S(x) = \begin{cases} 
1 - \frac{2}{L} |x|, & |x| \leq \frac{L}{2} \\
0, & |x| \geq \frac{L}{2}
\end{cases}
\]

2.2 Model Mechanism

The diffusion equation:

\[
\frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2} - \lambda C + PS(x)
\]

(1)

We assume that the tissue growth is regulated by a switch mechanism (chalones):

\[
M = \begin{cases} 
0, & C \geq \Theta \\
M_0, & C < \Theta
\end{cases}
\]

If the chalone concentration \( C = C(x) \) is lower then \( \Theta \) in any point \( x \) in the tissue, then mitosis and subsequent growth will occur. Otherwise the mitosis stops and also the growth.

2.3 The Chalone-Distribution

Is given in evaluated form for \(|x| \leq \frac{L}{2}\) with \( \alpha = \sqrt{\frac{\lambda}{2D}} \) by

\[
C(x) = \frac{2P}{\alpha^3 LD} \left\{ e^{-\frac{x}{L}} \cosh(\alpha|x|) + \alpha \left( \frac{L}{2} - |x| \right) - e^{-\alpha|x|} \right\}
\]

This function decreases monotonically from \( x = 0 \) to \(|x| = \frac{L}{2}\) with the value

\[
C \left( \frac{L}{2} \right) = \frac{P}{\alpha LX} \left( 1 - e^{-\frac{L}{2\alpha}} \right)^2.
\]

(2)
Regimes of Stability and Instability

We define number \( n = \frac{P}{\lambda \Theta} \) and length \( l = \frac{\alpha L_s}{2} \).

Tissue growth will cease, when \( C(x) \geq \Theta \) everywhere in \([-\frac{L_s}{2}, \frac{L_s}{2}]\), that is

\[
C \left( \frac{L_s}{2} \right) \geq \Theta.
\]  

(3)

From (3) we get a convenient determination of the limiting size \( L_s \) of stable tissue:

\[
C \left( \frac{L_s}{2} \right) = \Theta
\]

With equation (2) follows:

\[
\frac{P}{\alpha L_s \lambda} \left\{ 1 - e^{-\frac{\alpha L_s}{2}} \right\}^2 = \Theta
\]

(4)

After rewriting of (4) with \( n \) and \( l \) we get:

\[
\left( 1 - e^{-l} \right)^2 = \frac{l}{n}
\]

(5)

This equation has

- trivial solution \( l = 0 \) for all values of \( n > 0 \)
- one nontrivial solution \( l = 2.4554 \) for \( n_0 = 1.2573 \)
- two nontrivial solutions \( l_1(n) \) and \( l_2(n) \) for \( n > n_0 \)

The nontrivial solutions for \( l \) represent the limiting size \( L_s \).

Returning to inequality (3):

For all \( l \) satisfying

\[
\left( 1 - e^{-l} \right)^2 \geq \frac{l}{n}
\]

the growth is stable and so a limiting size of tissue exists.
For a given $n > n_0$, for example $n = 3$:
The stable tissue zone is the hatched area in the left graph.

$l_1(3)$ and $l_2(3)$ represent the limiting size. This means, if we start with

- length $l < l_1(3)$, then the growth is unstable and the tumor grows until it reaches a stable size
- length $l_1(3) < l < l_2(3)$, then the tumor is stable and won’t grow
- length $l > l_2(3)$, then the growth is unstable and will be unstable for all time

And for $n < n_0$ the tumor growth is always unstable.

The right graph shows the solutions of equation (5) against the corresponding $n$.
It is easy to see, that for a given $n > n_0$ the stable zone is always finite. (Curve A)

The results of Glass are (right graph, curve B):

- for $n < 1$ the tissue growth is unstable
- for $n > 1$ the tissue growth is stable and a limiting size exist
- the stable growth zone is infinite (the area above the curve B is the stable zone)

**Conclusion:**
The results should be taken qualitatively! They indicate that the use of a nonuniformly distributed source provides a more precise and realistic stable zone, which should be considered in more realistic models.