THEORETICAL MODEL OF CANCER GROWTH

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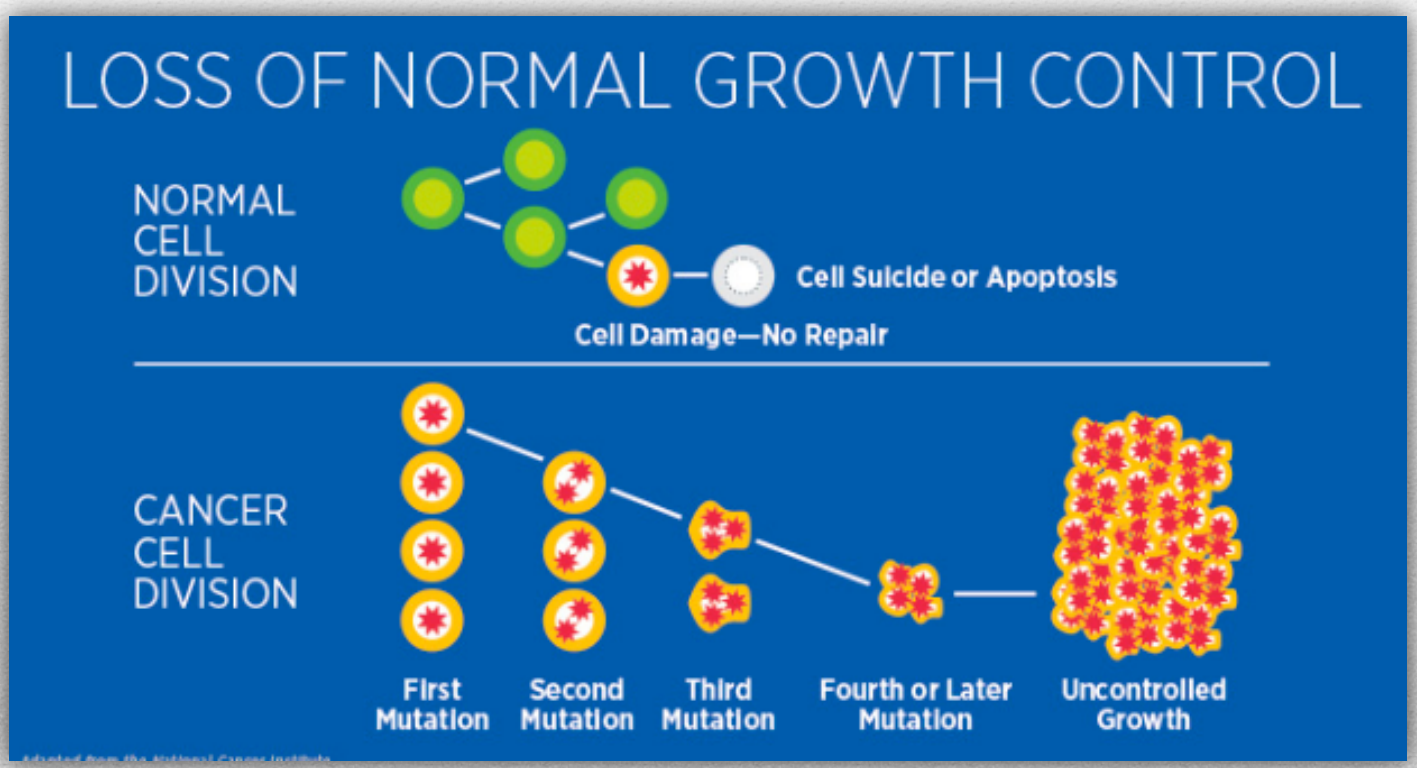
MATH 441
SPRING 2016

What is cancer?

Cancer: is when abnormal cells divide in an uncontrolled way that pushes aside the healthy host cells around them.



Model of the cancer growth

- Interaction :
  - tumor
  - healthy host
  - and immune effector
- Assumption : tumor and healthy cells grow in a logistic manner r, k
- Competition: Lotka-Volterra equations

* The thirds equation: Michaelis-Menten law and rate of death d_3

3d Dynamical system

T- tumor cells
H- healthy host cells
E- effector immune cells

r_i – growth rate (i=1-3)
k_i – carrying capacity
a_{ij}- competitions terms ($i \neq j$ and i,j=1-3)
*d_3- rate of death for immune cells

$$\dot{T} = r_1 T(1 - \frac{T}{k_1}) - a_{12}TH - a_{13}TE$$

$$\dot{H} = r_2 H(1 - \frac{H}{k_2}) - a_{21}HT$$

$$\dot{E} = r_3 \frac{ET}{T + k_3} - a_{31}ET - d_3 E$$

Non-dimensional form:

$r_2 = 1.2$	$r_3 = 1.291$	$a_{12} = 0.5$	$a_{21} = 4.8$	$a_{13} = 1.2$	$a_{31} = 1.1$	$k_3 = 0.3$	$d_3 = 0.1$

$$\dot{x} = x(1-x) - a_{12}xy - a_{13}xz$$

$$\dot{y} = r_2 y(1-y) - a_{21}xy$$

$$\dot{z} = r_3\left(\frac{xz}{x+k_3}\right) - a_{31}xz - d_3 z$$

$$\Rightarrow$$

$$0 = x(1-x) - a_{12}xy - a_{13}xz$$

$$0 = r_2 y(1-y) - a_{21}xy$$

$$0 = r_3\left(\frac{xz}{x+k_3}\right) - a_{31}xz - d_3 z$$

Polynomial form: third eqn of the system

$$0 = r_3\left(\frac{xz}{x+k_3}\right) - a_{31}xz - d_3z$$

$$0 = r_3\left(\frac{xz}{x+k_3}\right) - a_{31}xz - d_3z$$

$$(a_{31}xz + d_3z)(x+k_3) = r_3xz$$

$$a_{31}zx^2 + a_{13}k_3xz + d_3xz + k_3d_3 = r_3xz$$

$$0 = r_3xz - a_{31}zx^2 - a_{13}k_3xz - d_3xz - k_3d_3$$

$$0 = z((r_3 - a_{13}k_3 - d_3)x - a_{31}zx^2 - k_3d_3)$$

Equilibrium points and stability:

- To find the equilibrium points: there are 6 (**x***)

$$F = x(1-x) - 0.5xy - 1.2xz = 0$$

$$G = 1.2y(1-y) - 4.8xy = 0$$

$$L = z(-1.1x^2 + 0.831x - 0.03) = 0$$

$\mathbf{x_1}$ *= (0,0,0)
$\mathbf{x_2}$ *= (0,1,0)
$\mathbf{x_3}$ *= (1,0,0)
$\mathbf{x_4}$ *= (0.75,0,0.21)
$\mathbf{x_5}$ *= (0.04,0,0.8)
$\mathbf{x_6}$ *= (0.04,0.85,0.45)

```
% finding the critical points of the system
syms x y z
[solx,soly,solz]= solve([x-x^2-0.5*x*y-1.2*x*z==0, 1.2*y-1.2*y^2-4.8*x*y==0,
((1.291*x*z)/(x+0.3)- 1.1*z*x-0.1*z)==0],[x,y,z]);
```

Partial Derivatives:

$$Fx = 1 - 0.5y - 1.2z$$
$$Fy = -0.5x$$
$$Fz = -1.2x$$

$$Gx = -4.8y$$
$$Gy = 1.2 - 2.4y - 4.8x$$
$$Gz = 0$$

$$Lx = z(\frac{0.3873}{x+0.3} - 1,1)$$
$$Ly = 0$$
$$Lz = x(\frac{1.291}{x+0.3} - 1.1) - 0.1$$

$$J(\bar{X}) = \begin{pmatrix} 1 - 0.5y - 1.2z & -0.5x & -1.2x \\ -4.8y & 1.2 - 2.4y - 4.8x & 0 \\ z(\frac{0.3873}{x+0.3} - 1,1) & 0 & x(\frac{1.291}{x+0.3} - 1.1) - 0.1 \end{pmatrix}$$

To find eigenvalues : Matlab: [v,e]=eig(A)

Equilibrium	Stability
$\mathbf{x}_1^* = (0,0,0)$	saddle
$\mathbf{x}_2^* = (0,1,0)$	saddle
$\mathbf{x}_3^* = (1,0,0)$	stable (tumor equilibrium)
$\mathbf{x}_4^* = (0.75,0,0.21)$	saddle
$\mathbf{x}_5^* = (0.04,0,0.8)$	stable spiral
$\mathbf{x}_6^* = (0.04,0.85,0.45)$	unstable spiral

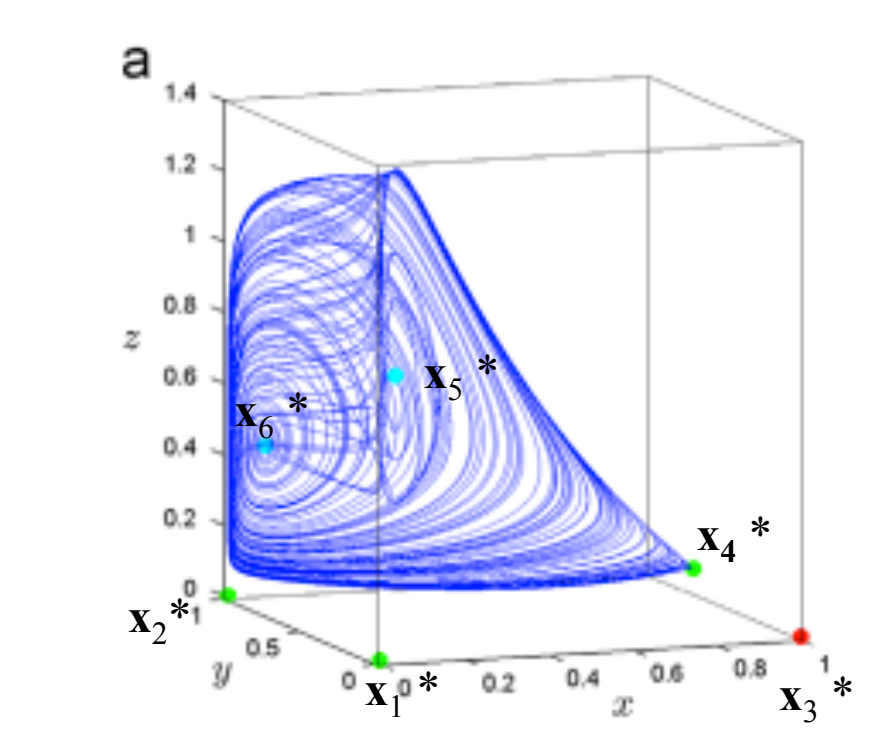
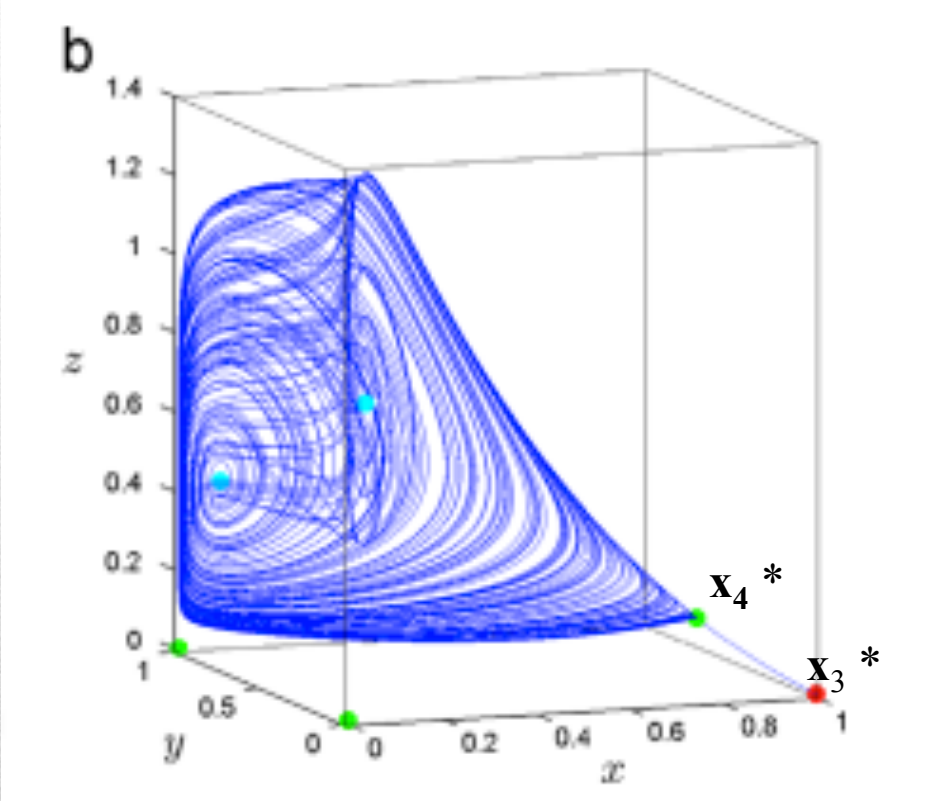


Figure1. the system has two attractors (one stronger than the other one).

Transient Chaos & Boundary Crisis :

- Sensitive to initial condition
- examine global bifurcation
  - $r_3^c = 1.2909$
  - Transient chaos in the system
  - Destruction of chaotic attractor
  - Trajectories converge to stable tumor point (which is the other attractor).



References:

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