

# Notes from ISMCO 2010 Proceedings

## Math & Comp Oncology

### Population Modeling of Tumour Growth

Curves : Reduced Gompertz &  
Tumor Age Prediction

#### Analysis of 3 models:

- (A) Exponential
- (B) Logistic
- (C) Gompertz

Analysis within  
non-linear mixed-effects  
modelling

The growth is not exponential and the growth deceleration can be captured by Gompertz:

$$V(t) = V_0 \cdot e^{\frac{\alpha}{\beta} (1 - e^{-\beta t})}$$

↑  
initial  
tumor  
size  
at  $t=0$

The exponential model:

$$V_E(t, \alpha) = V_0 \cdot e^{\alpha t}$$

The logistic model :

$$V_L(t, \alpha, K) = \frac{V_0 K}{V_0 + (K-V_0)e^{-\alpha t}}$$

K - carrying capacity  
parameter

Gompertz model:

$$\left\{ \begin{array}{l} \frac{dV_G}{dt} = \left( \alpha - \beta \cdot \log \left( \frac{V_G}{V_0} \right) \right) V_G \\ V_G(t=0) = V_0 \end{array} \right.$$

$\alpha$  = growth rate at injection volume  $V_0$

$\beta$  = exponential decay rate

Yet the Gompertz model doesn't assume the correlation among its parameters  $\alpha$  and  $\beta$

So we consider:

$$\alpha^i = k \cdot \beta^i + c$$

$\uparrow$   
characteristic  
constant  
of tumor  
growth

$\rightarrow$  mixed effects

$$\frac{dV_R}{dt} = \beta^i K - \beta^i \log \left( \frac{V_R}{V_0} \right)$$

$i = 1, 2, \dots, N$

$$V_R(t, \beta, k)$$

$K$  can be associated with the carrying capacity  $K = V_0 \cdot e^K$

$V_0$  - initial tumor volume

Reduction of nr. of degrees of freedom in Gompertz model to increase parameter identification and a simpler model.

# Notes on mathematical & computational anatomy

## Cancer Modeling Basics

Cancer dynamics: \* uncontrolled cell growth  
Keywords \* uncontrolled cell proliferation  
\* loss of tissue homeostasis



neoplasia

(new, abnormal growth of tissue)

Malignancy of a tumor is given by:

1. the ability to invade surrounding tissue
2. the ability to spawn new tumors elsewhere  
in the body (metastasis)

Two directions of modeling:

1. Oncogenesis = the process through which a tumor arises
2. malignant neoplasia (carcinogenesis)
  - how tumors grow
  - = how tumors invade
  - = how tumors metastasize

Two basic studies on general growth equations:

1. Gompertz Law / Gompertz growth (1825)
2. von Bertalanffy (1957)

## Von Bertalanffy growth model

- "Why does a tumour grow at all, and why, after a certain time, does its growth come to a stop?"
- model inspired by metabolic processes (e.g. pulse rate, basal metabolic rate etc.)
- the model starts with the conservation equation: growth equals "births" (cell proliferation) minus "deaths" (cell necrosis or apoptosis)
- the growth in mass ( $W(t)$ ) is:

$$\frac{dW}{dt} = \underbrace{\alpha \cdot W^\lambda}_{\text{proliferation}} - \underbrace{\beta \cdot W^\mu}_{\text{apoptosis}}$$

(generalized (two-parameter) von Bertalanffy)

### Variations:

- A. if we set  $\lambda = \mu = 1$  we have the exponential model

$$\frac{dW}{dt} = \underbrace{(\alpha - \beta)}_{\substack{\text{birth rate} \\ \text{apoptosis rate}}} \cdot W$$

per capita

model exponential growth / decay depending on the sign of  $(\alpha - \beta)$

- B. if we let  $\lambda = 1$  and  $\mu = 2$  we recover the logistic model of Verhulst:

$$\frac{dW}{dt} = \underbrace{\alpha W}_{\text{growth rate}} - \underbrace{\beta W^2}_{\text{density dependent apoptosis}} = \alpha W \left(1 - \frac{W}{K}\right)$$

$K = \frac{\alpha}{\beta}$  carrying capacity

C. In most physiologically relevant situations death (apoptosis) processes are proportional to the mass so the model becomes:

$$\frac{dW}{dt} = \alpha \cdot W^2 - \beta \cdot W$$

which for initial condition  $W(0) = W_0$  has the solution:

$$W(t) = \left( \frac{\alpha}{\beta} - \left[ \frac{\alpha}{\beta} - W_0 \right] e^{-(1-\lambda)\beta t} \right)^{\frac{1}{\lambda-1}}$$

$$\lambda \neq 1$$

D. Assuming that proliferation rate scales with body surface area the "classical" von Bertalanffy model is:

$$\frac{dW}{dt} = \alpha \cdot W^{\frac{2}{3}} - \beta \cdot W$$

$$\alpha W^{\frac{2}{3}}$$

$\Rightarrow$  describes an avascular tumor in which proliferation is nutrient limited and only cells close to the surface have sufficient nutrient to divide

$$\beta W$$

$\Rightarrow$  describes that regardless of depth (nutrient content) cell death (apoptosis) is constant.