The Dynamics of Free-Living Dividing Cell Growth

$\boxed{x \equiv x(t)} \to$ Volume of dividing cells at time t.

The growth rate equation is $\boxed{\dfrac{dx}{dt} = \lambda x}$ $(\lambda > 0)$.

At $\boxed{t = t_0,\ x = x_0} \to$ Initial condition.

$\Rightarrow \boxed{x(t) = x_0 \exp\left[\lambda (t - t_0)\right]}$. Cell doubling happens when $\boxed{x = 2x_0} \Rightarrow$ Doubling time $\boxed{t - t_0 = \frac{\ln 2}{\lambda}}$

Gompertz Law of Tumour Growth

$$\boxed{\frac{dx}{dt} = f(x) = -ax\ln(bx)} \quad \boxed{a, b > 0}.$$

$x(t) \to$ Number of cells in a tumour.

Scale $\boxed{y = x/b^{-1}}$ and $\boxed{T = at}$.

Rescaling:

$$\Rightarrow \boxed{\frac{d\left(\frac{x}{b^{-1}}\right)}{d(at)} = -\left(\frac{x}{b^{-1}}\right)\ln\left(\frac{x}{b^{-1}}\right)} \Rightarrow \boxed{\frac{dy}{dT} = -y\ln y}$$

Integral Solution: Substitute $\boxed{y = e^X} \Rightarrow \boxed{X = \ln y}$

$$\therefore \boxed{\frac{dy}{dT} = e^X \frac{dX}{dT} = y\frac{dX}{dT} = -y\ln y = -yX}$$

$$\Rightarrow \cancel{y}\frac{dX}{dT} = -\cancel{y}X \Rightarrow \boxed{\frac{dX}{dT} = -X}.$$

$$\Rightarrow \boxed{\int\frac{dX}{X} = -\int dT} \Rightarrow \boxed{X = X_0 e^{-T}}$$

X_0 is the integration constant

$\Rightarrow \boxed{\ln y = X_0 e^{-T}} \Rightarrow \boxed{\ln(bx) = X_0 e^{-at}}$

$\Rightarrow \boxed{x = \frac{1}{b} \exp\left(X_0 e^{-at}\right)}$. Exponential of an exponential.

i.) When $\boxed{t \to \infty,\ x \to b^{-1}}$ (limiting ~~value~~ value)

ii.) When $\boxed{t = 0,\ x = x_0}$ (initial value).

$\therefore \boxed{x_0 = \frac{1}{b} \exp(X_0)} \Rightarrow \boxed{e^{X_0} = x_0 b}$ [illegible]

Fixing the unknown $X_0 \Rightarrow \boxed{X_0 = \ln(x_0 b)}$

Since $\boxed{x_0 < b^{-1}}$ (the tumour GROWS from x_0 to b^{-1}).

$\Rightarrow \boxed{\frac{x_0}{b^{-1}} < 1} \Rightarrow \boxed{X_0 = \ln\left(\frac{x_0}{b^{-1}}\right) < 0}$

Hence, $\boxed{x = \frac{1}{b} \exp\left[\ln\left(\frac{x_0}{b^{-1}}\right) e^{-at}\right]}$,

the Gompertz formula for tumour growth, which satisfies over 1000-fold growth.

We differentiate the $x \equiv x(t)$ equation to get.

$$\boxed{\frac{dx}{dt} = \frac{1}{b} \exp\left[\ln\left(\frac{x_0}{b^{-1}}\right) e^{-at}\right] \cdot \ln\left(\frac{x_0}{b^{-1}}\right) e^{-at} \cdot (-a)}$$

Now $\boxed{\ln\left(\frac{x_0}{b^{-1}}\right) < 0} \therefore \boxed{-a \ln\left(\frac{x_0}{b^{-1}}\right) = -a X_0 > 0}$

We write $\boxed{\lambda = -a X_0 > 0}$ to get $\boxed{\frac{dx}{dt} = x \lambda e^{-at}}$.

This equation is in the form $\boxed{\frac{dx}{dt} = f(x,t)}$

The non-autonomous form $\boxed{\frac{dx}{dt} = f(x,t)}$,
can be ~~[illegible]~~ cast in two ways. They are:

i.) $\boxed{\frac{dx}{dt} = \left(\lambda e^{-at}\right)x = \bar{\lambda}(t)\, x} \rightarrow \bar{\lambda}$ depends on t.

ii.) OR $\boxed{\frac{dx}{dt} = \lambda\left(x e^{-at}\right)} \rightarrow \lambda$ is a constant.

First form: $\boxed{\frac{dx}{dt} = \bar{\lambda}(t)\, x}$ (Rate $\propto$ State)

The time scale for tumour generation is

$\boxed{\bar{t} \sim \frac{1}{\bar{\lambda}}}$ (on comparing with $\boxed{t - t_0 = \frac{\ln 2}{\lambda}}$ in free-living and dividing cells)

$\Rightarrow \boxed{\bar{t} \sim \lambda^{-1} e^{at}}$ $\Rightarrow$ As t increases, longer time is taken for the same amount of growth. The cells mature and divide more slowly.

Second form: $\boxed{\frac{dx}{dt} = \lambda\left(x e^{-at}\right)}$. λ is constant and now rate is proportional to a state, ~~[illegible]~~ $\boxed{x e^{-at}}$.

This effective state, contributing to the growth of the tumour, decreases due to necrosis at the core of the tumour, with lower number of living cells.

First form: Growth process slows down. [SUMMARY]

Second form: Number of cells in the growth is lower.