The Richards family of growth functions: theory, statistical models, Bayesian inference & example

Contents

Generalities on GF

A great deal of diversity in

- Growth models
  - Empirical, phenomenogical vs mechanistic
  - Levels of organization: molecule, cell, tissue, organ, individual, group
- Mathematical equations
  - Formulae: (>40) from Bertalanffy to West Brown-Enquist via
    (Blumberg, Brody, Chapman, Jolicoeur, Korf, Lotka, Monod, Savageau, Schnute, Teissier, Tjorve, Weibul)
  - Discrete vs Continuous
  - Function, differential equation
  - Deterministic vs stochastic
  - Objective : causal vs predictive
- Domains of interest
  - Research works (math, chemistry, biology, pkpd, demography, ecology, biomechanics)
  - Applications in different areas (agriculture, medicine, pharmacy, economics, technology)

Features of GF presented here

- Monotone increasing positive functions up to a max size
  (carrying capacity*; mature size or weight)
- S-Shaped
- Interest in rates of growth
  - Absolute: dy/dt & Specific (or relative): $\frac{dy}{ydt}$
  - Acceleration : d^2y/dt^2
  - Inflection time and size
- Autonomous ODE
  - The system reacts to its state variables not directly to time per se
    $\frac{dy}{dt} = h(y) \text{ not } \tilde{h}(y,t)$
  - Easier integration
  - Solution translation invariant wrt time
  - If $y_1(t)$ solution with $y_1(t=0) = y_0$ then
    $y_2(t) = y_1(t-t_0)$ also sol & $y_2(t_0) = y_1(0) = y_0$

*(capacité de charge)

Mitscherlich (1794-1863)

Mitscherlich E.A. (1909). Das Gesetz des Minimums und das Gesetz des abnehmenden Bodenertrags, Landwirtschaftliche Jahrbücher 38, 537-552

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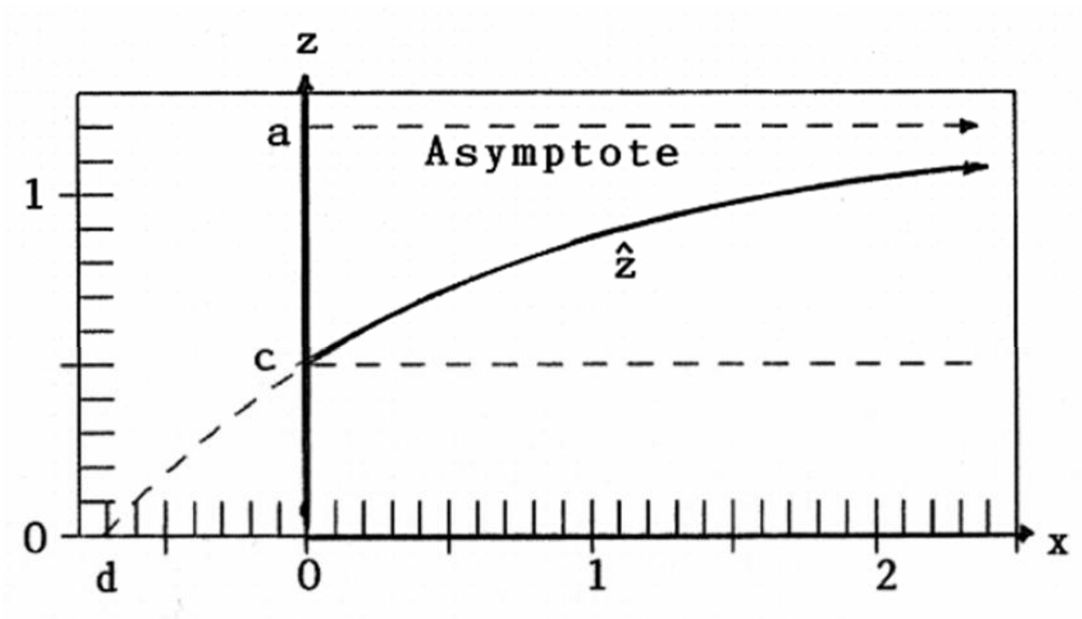


Figure 1: Crop-yield $\hat{z}(x)$ as function of one fertilizer x

The Mitscherlich function

1) Named after Eilhard Mitscherlich (1794-1863) and his 1909 paper

Famous German chemist, prof at U of Gottingen, Heidelberg and eventually Berlin

Known also as **Monomolecular,** Negative or Confined Exponential

2) Applied at start by **Brody** (1925) for animal body & **Gregory** (1928) for leave area growth

Linked to the law of diminishing returns (Turgot, Liebig, Ricardo) in economics, agronomy, etc…

Use in models of many areas of agronomy, forestry, geography, sociology.

Analytical framework for technology transfer

3) Objective: Attenuation of the slope of the Malthus exponential growth function

$\frac{dy}{dt} = Ky \Rightarrow y = y_0 \exp(Kt)$ to take into account limitations of growth by relating growth rate not in proportion of absolute growth itself but to its remaining part

The Mitscherlich function: pilot model

Reaction between 2 chemical species A & B: $A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} B$

with $[A]+[B]=C\ (cst)$. Letting $[B]=y$ so that $[A]=C-y$

$$\frac{dy}{dt}=k_1[A]-k_2[B]=k_1(C-y)-k_2y=k_1C-(k_1+k_2)y$$

At equilibrium $y'=0 \Rightarrow k_1C=(k_1+k_2)y^{\#}$, $\boxed{\frac{dy}{dt}=(k_1+k_2)(y^{\#}-y)}$

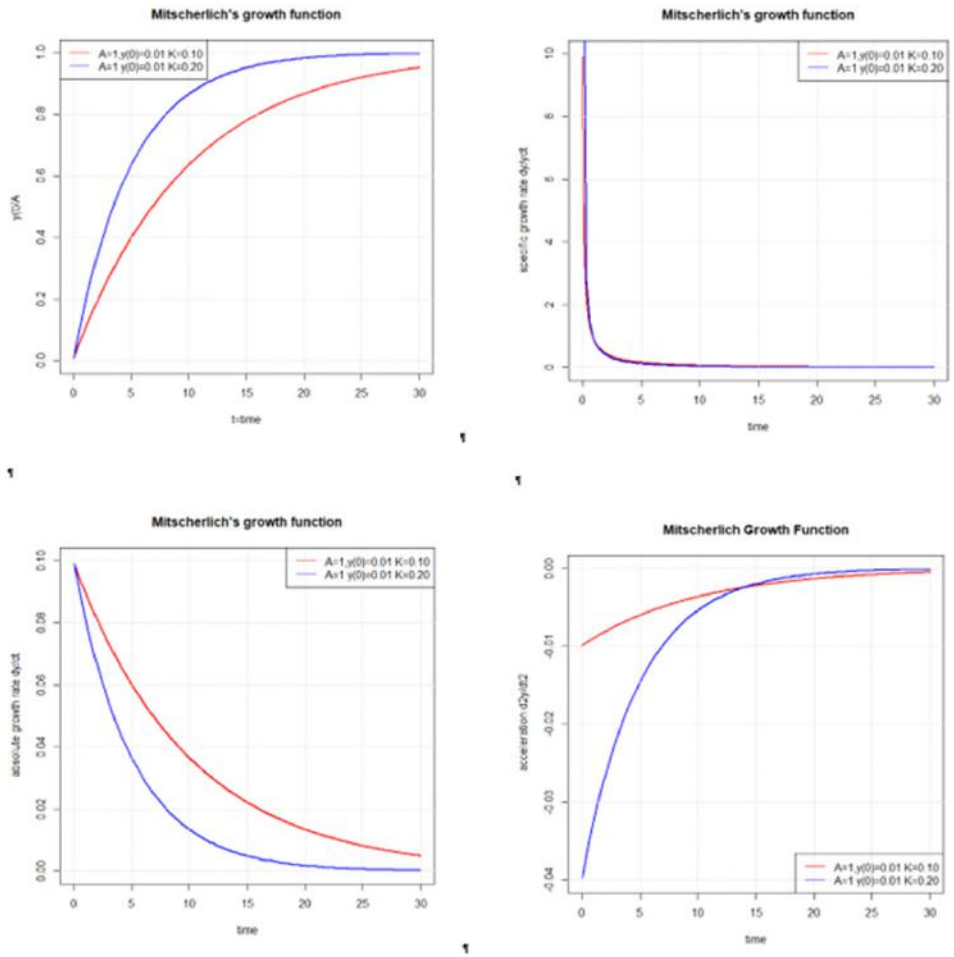
$$\frac{d(y^{\#}-y)}{y^{\#}-y}=-(k_1+k_2)dt \Rightarrow \ln(y^{\#}-y)=\ln\left(y^{\#}-\underbrace{y_0}_{0}\right)-(k_1+k_2)(t-\underbrace{t_0}_{0})$$

$$y^{\#}-y=y^{\#}\exp[-(k_1+k_2)t] \qquad \boxed{y=\underbrace{y^{\#}}_{"A"}\left[1-\exp\left[-\left(\underbrace{k_1+k_2}_{"K"}\right)t\right]\right]}$$

The Mitscherlich function/ G-rates

- Growth rate ODE: $\boxed{dy/dt = K\left(A - y\right)}$
- Integrated as: $\boxed{y = A\left[1 - B\exp(-Kt)\right]}$, $B = 1 - (y_0 / A)$
- $\ln\left(1 - \dfrac{y}{A}\right) = \ln(B) - Kt$
- Acceleration: $\boxed{d^2y/dt^2 = -AK^2B\exp(-Kt)}$ <0
- No inflection point
- Specific growth rate: $\boxed{\dfrac{1}{y}\dfrac{dy}{dt} = K\left(\dfrac{A}{y} - 1\right)}$
- Exponential decay of growth rate with time

The Mitscherlich function: Figures



Pierre-François Verhulst (1804-1849)

Logistic/ growth under substrate limitations

Substrate dependency

1) $\dfrac{dy}{dt} = \mu(S) = \mu S y$ (Deschamps, 1902)

2) $\dfrac{dS}{dy} = -\rho^{-1} = Cst$ resulting from $dy \propto dS$

From (2) $S - \underbrace{S_{\max}}_{0} = -\rho^{-1}(y - \underbrace{y_{\max}}_{A})$

$$\frac{dy}{dt} = -\mu\rho^{-1} y\left(y - A\right) = A\mu\rho^{-1} y\left(1 - y / A\right)$$

$K = A\mu\rho^{-1}$, then $\boxed{\dfrac{dy}{dt} = Ky\left(1 - \dfrac{y}{A}\right)}$

Ex: Bacterial growth: cf thèse de Monod (1941)

$\mu(S)$ replaced by $\mu_{\max} S / (K_h + S)$ (logistic for S small)

Verhults' Logistic for Human Population Growth

1-Limitations to Malthus exponential growth function

2- Verhust's formulation (1838, 1842)

$\frac{dp}{dt} = mp - \varphi(p)$ $\varphi(p)$ unknown function of population size (p), taken as np^2

2-Growth rate per capita of a population results from the balance between natality: $\eta = \eta_0 - \eta_1 N$ and mortality: $\mu = \mu_0 + \mu_1 N$ so that

$$\frac{dN}{Ndt} = \eta - \mu = (\eta_0 - \mu_0) - (\eta_1 + \mu_1)N = a - bN$$

$$\boxed{\frac{dN}{dt} = aN\left[1 - (N / N_*)\right]}$$

where $N_* = a / b$ for which absolute & specific growth rates are nil and a maximum of population size if $N_0 = N(t = 0) < N_*$, known as "Carrying Capacity"; b being known as the crowding coefficient.

Verhults' Logistic for Human Population Growth

Coming back to the ODE $\boxed{\dfrac{dN}{Ndt} = a\left[1-(N/N_*)\right]}$

Letting $P = N/N_*$ the scaled population size, the ODE becomes $\dfrac{dP}{dt} = aP(1-P)$,

Integrated as: $\boxed{N = \dfrac{N_*}{1+\left[(N_*/N_0)-1\right]\exp(-at)}}$

$N = N_*$ upper asymptote and $N = 0$ lower asymptote, N sigmoid

Inflection point at $N_I / N_* = 1/2$ for $t_I = \ln\left[(N_*/N_0)-1\right]/a$

Verhults' Logistic: summary

- Growth rate ODE $\boxed{\frac{dy}{dt} = Ky\left(1 - \frac{y}{A}\right)}$
- Integrated as: $\boxed{y = \frac{A}{1 + B\exp(-Kt)}}$ $B = \left(A / y_0\right) - 1$
- Plot of $\ln[(A / y) - 1]$ against time: $\boxed{\ln\left(\frac{A}{y} - 1\right) = \ln B - Kt}$
- Acceleration: $\boxed{y'' = Ky'\left(1 - 2\frac{y}{A}\right)}$ Inflection at $y(t_I) = A / 2$
- Specific growth rate: $\boxed{\frac{1}{y}\frac{dy}{dt} = K\left(1 - \frac{y}{A}\right)}$

Epilogue

-Verhulst dismissed his logistic model in a 2nd communication to the Belgian Royal Society (May 15, 1846 published in 1847) by switching from $\frac{dN}{Ndt}=a\frac{N_*-N}{\boxed{N_*}}$ to

$\frac{dN}{Ndt}=a\frac{N_*-N}{\boxed{N}}$ ie from Logistic to Mitscherlich due to more satisfying predictions of

$N_* = 6.58$ to 9.44 M (Mawhin, 2020, Bacaer, 2008)

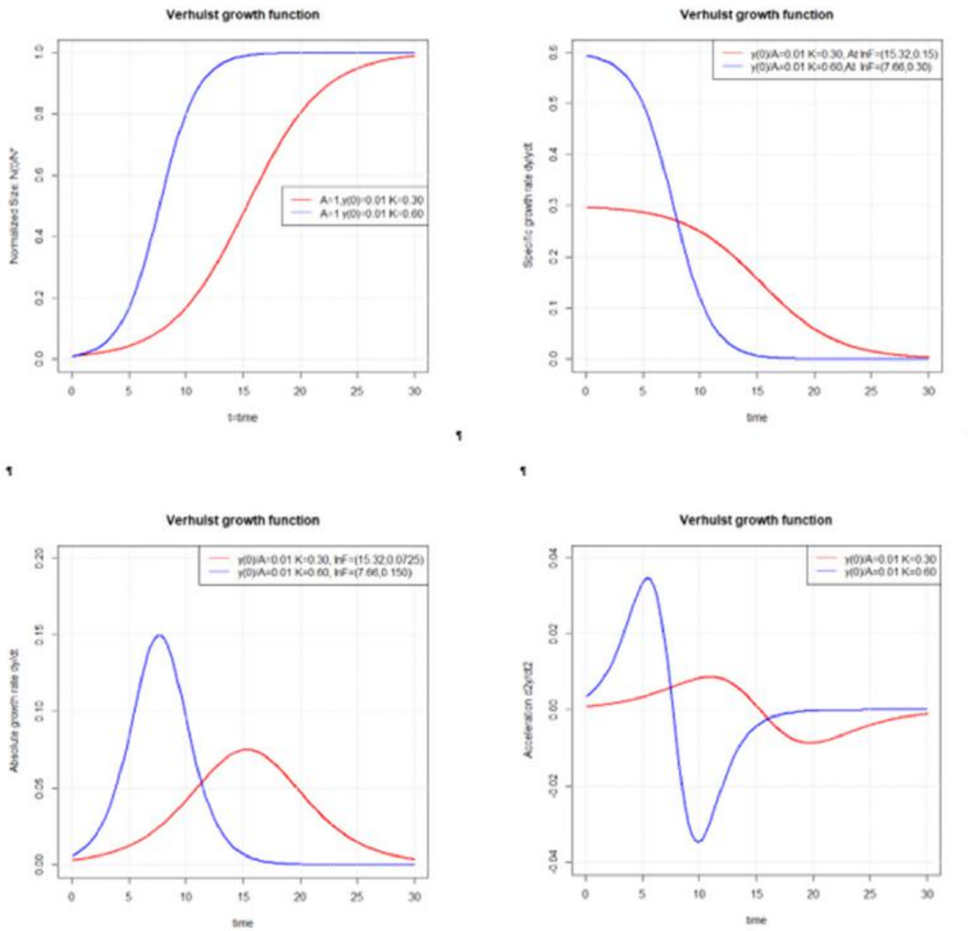
2-Verhust' logistic curve was largely ignored outside.

Was rediscovered by **Raymond Pearl** & **Lowell Reed** (Johns Hopkinks) in analyzing the Growth of the US population from the 1970 to 1910 census data (Pearl & Reed, 1920, PNAS, 6, 275-288) with an estimation of the carrying capacity of 197 M (exceeded around 1970).

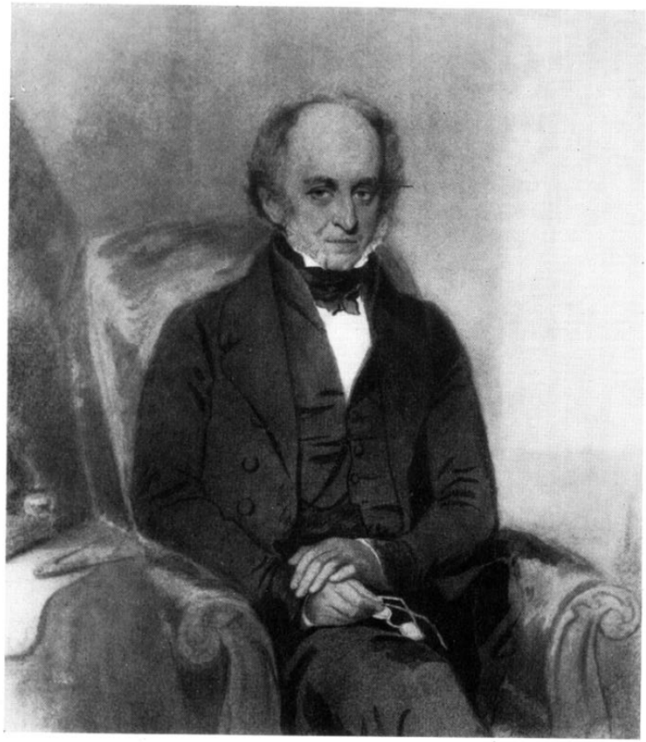
They also fitted Logistic-type skewed curves (PNAS, 1924) of growth of albino rats, regenerated Tadepole tails, Curcubita Pepo).

3-Logistic function at the basis of many variations and extensions (Allee, Predation, Delayed, Richards, etc…)

The Verhulst Logistic function: Figures



Benjamin GOMPERTZ (1779-1865)



BENJAMIN GOMPERTZ, 1779–1865

Gompertz Survival

The longevity distribution function has its counterpart the survival function and is defined as

$F(t) = \Pr(T \le t) = 1 - S(t)$, $T > 0$

the death time T being a rv with density $f(t) = F'(t) = -S'(t)$

The instantaneous mortality rate at time adjusted for time interval, survival rate at start, known as risk function or failure rate or mortality force is

$$h(t) = Lim \frac{\Pr(t \le T < t + dt \mid T > t)}{dt} = Lim \frac{S(t) - S(t+dt)}{S(t)dt}$$

$$h(t) = -\frac{S'(t)}{S(t)} = -d\left[\ln(S(t)\right] \Rightarrow S(t) = \exp\left[-\underbrace{\int_0^t h(u)du}_{H(t)}\right]$$

Gompertz observing a geometric increase of human mortality rate with age proposed:

$$\boxed{h(t) = a\exp(bt)}, \quad \boxed{S = \exp\left\{\frac{a}{b}\left[1 - \exp(bt)\right]\right\}}$$

Alternative for $h(t)$ increase : Gompertz-Makeham, Logistic, Weibull (see DL Wilson, 1994)

The Gompertz survival function: Example

D.L. Wilson / Mech. Ageing Dev. 74 (1994) 15–33 27

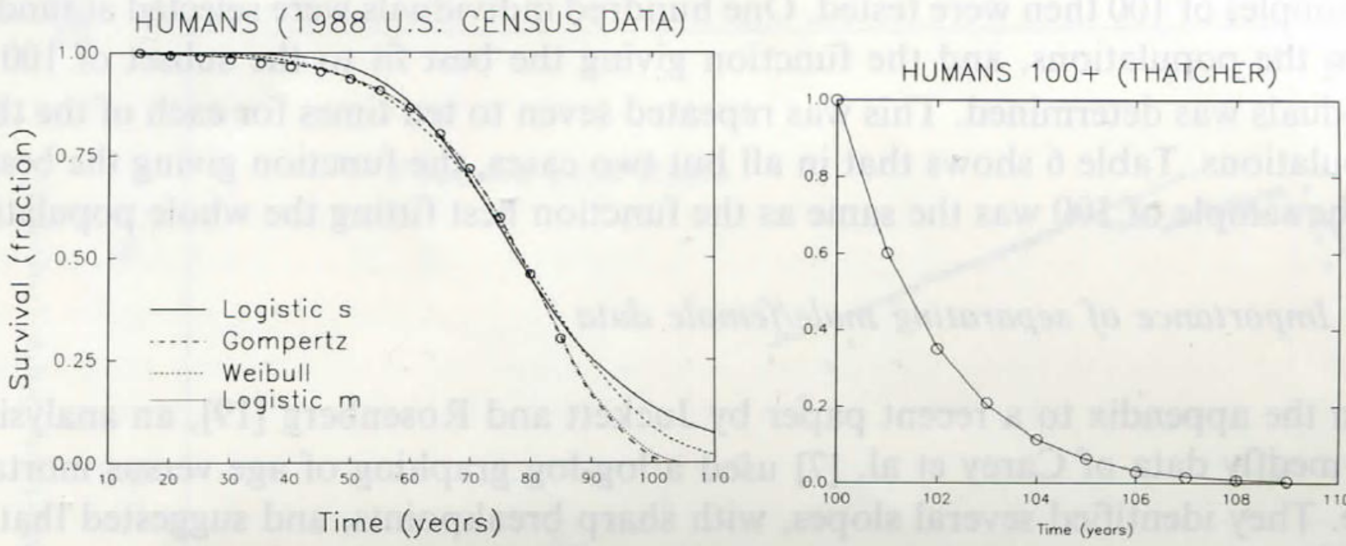


Fig. 6. Survival curves for humans. Data (from 1988 U.S. Census [13] and from Thatcher [14]) shown as open circles. Four survival functions are shown for the U.S. Census data, as indicated. The Gompertz curve and the logistic mortality curve are almost coincident. The best-fit curve from the Gompertz survival function is shown with the Thatcher data.

The Gompertz Growth Function

1) $\frac{dy}{ydt} = \mu$ (specific GR) 2) $\frac{d\mu}{\mu dt} = -K$ 3) $\mu = \mu_0 \exp(-Kt)$

4) $dy/y = \mu_0 \exp(-Kt)dt$ 5) $\ln(y) = -\frac{\mu_0}{K}\exp(-Kt) + Cst$

6) $\ln y/y_0 = \frac{\mu_0}{K}\left[1 - \exp(-Kt)\right]$ $\ln A/y_0 = \frac{\mu_0}{K} = B$ $\ln y/A = -B\exp(-Kt)$

8) Growth function: $\boxed{y = A\exp\left[-B\exp(-Kt)\right]}$ and $\boxed{\ln\left[\ln\left(\frac{A}{y}\right)\right] = \ln B - Kt}$

Here B stands for $B = \ln A/y_0$ and $\boxed{y = A\exp\left[\ln(y_0/A)\exp(-Kt)\right]}$ Rogers et al (1988)

From (4) $dy/y = KB\exp(-Kt)dt$ 9) Growth rate: $\boxed{dy/dt = Ky\ln(A/y)}$

Specific Growth Rate: 10) $\boxed{\mu = dy/ydt = K\ln(A/y)}$

Gompertz /Another parameterization

Parameterization in μ_0, K, y_0

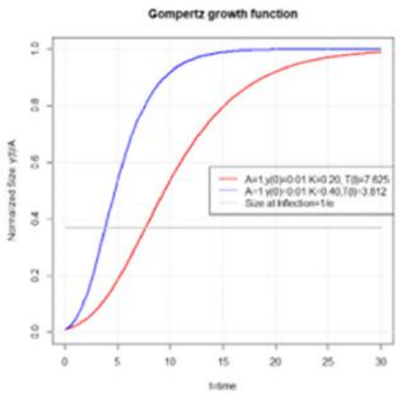
6) $\ln \frac{y}{y_0} = \frac{\mu_0}{K}\left[1 - \exp(-Kt)\right]$

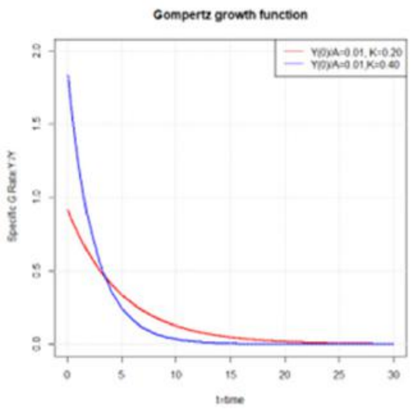
7) $\boxed{y = \boxed{y_0} \exp\left\{ \frac{\boxed{\mu_0}}{K} \left[1 - \exp(-\boxed{K} t) \right] \right\}}$ Gompertz-Laird (Laird, 1964-65-69)

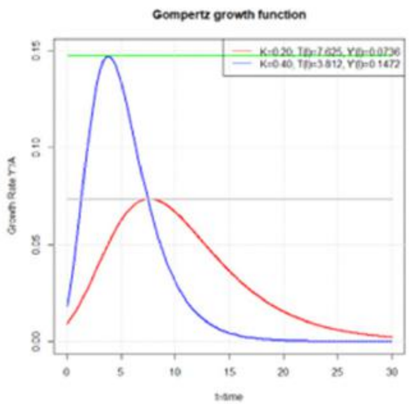
8) $\frac{dy}{dt} = \mu_0 y \left[1 - \frac{K}{\mu_0} \ln\left(\frac{y}{y_0} \right) \right]$ Thornley & France (2007)

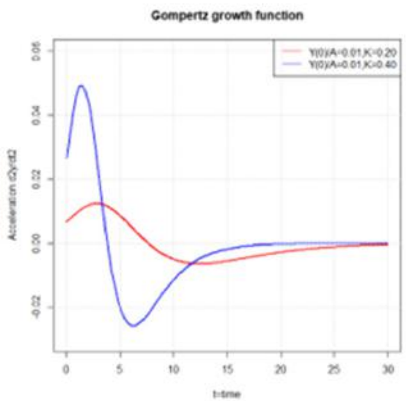
$\ln A / y_0 = \frac{\mu_0}{K} \Rightarrow \boxed{A = y_0 \exp\left(\frac{\mu_0}{K} \right)}$ upper asymptote depends on both y_0 and μ_0

The Gompertz Growth Function: Curves









The Gompertz Growth Function/

Winsor (1932) The Gompertz as a Growth Curve, PNAS,18,(1),1-8

Wright (1926) appears to have first suggested the use of the Gompertz curve for biological growth. He says:

"In organisms, on the other hand, the damping off of growth depends more on internal changes in the cells themselves, the process which Minot called cytomorphosis. The average growth power as measured by the percentage rate of increase tends to fall at a more or less uniform percentage rate, leading to asymmetrical types of S-shaped curves of which the form $\log \log \frac{k}{y} = a(b - x)$ is a simple example, instead of the logistic curve $\log \left(\frac{k}{y} - 1\right) = a(b - x)$."

Gompertz: applications

- Primary focus on studying mortality patterns & survival analysis
  - Humans & Laboratory species
- Epidemics eg Covid-19
- Models of bacterial growth: Zwietering et al, 1990
- Growth of animals and plants: Wright (1926) & Winsor (1932)
  - Cattle (Jersey cows): Davidson (1924)
  - Wild birds & Poultry: Mignon-Grasteau et al (1999, 2000)
  - Fish: Zweifel & Lasker (1976), Ricker (1979)
  - Leaves : Causton & Venus (1981)
  - Forestry : INRAE, ENGREF, IPSIM, CIRAD
- Models of tumor growth and metastatic spreading
  - Laird (164, 1965, 1969), Norton (1988), Gerlee (2013), Benzekry et al (2014)
- Diffusion models in Economics eg Marketing

A unified approach: Richard’s growth function

- Inadequation for real growth curves « to conform satisfactorily with any of the three (functions) »
- Tendency to add extra time polynomial terms and other reparameterization tricks to some of them (eg Logistic)
  - Variable coefficients: A(t), K(t)
  - Vertical Shifts
- Parsimonious extension (an extra parameter) from both theoretical and possible mechanistic considerations to facilitate comparison

Francis John RICHARDS (1901-1965)

Francis John RICHARDS (1901-1965)

- Excellent student at Birmingham University
  - Graduated in Botany & Chemistry
  - Athletic & literary activities (long jump, rugby, stage)
- Plant physiology at Rothamsted experimental station
  - Crop nutrition requirements : NPK on barley
  - Factorial design experiments applying RA Fisher's stat methods
  - Mathematical modelling: growth function
  - Director of the Plant & Nutrition & Physiology in 1954
- Hobbies
  - Archeology, photography,
  - Number theory (Fibonacci), astronomy, entomology (lepidoptera)

The Richards GF/ Re-arranging the ODE

1) Mitscherlich $dy/dt = K(A-y)$

- $\frac{d\tilde{y}}{dt} = K(1-\tilde{y})$ with $\tilde{y} = y/A$
- $\frac{d(1-\tilde{y})}{\boxed{1-\tilde{y}}} = -Kdt$

2) Gompertz $dy/dt = Ky\ln(A/y)$

- $\frac{d\tilde{y}}{dt} = -Ky\ln(\tilde{y})$
- $\frac{d(-\ln\tilde{y})}{\boxed{-\ln(\tilde{y})}} = -Kdt$

3) Verhulst $dy/dt = K\frac{y}{A}(A-y)$

- $\frac{d\tilde{y}}{dt} = K\tilde{y}(1-\tilde{y})$
- $-\frac{d\tilde{y}}{\tilde{y}(1-\tilde{y})} = \frac{d(\tilde{y}^{-1}-1)}{\boxed{\tilde{y}^{-1}-1}} = -Kdt$

The Richards unified GF/ Box-Cox Transformation

The 3 functions of $1-\tilde{y},\ -\ln(\tilde{y}),\ \tilde{y}^{-1}-1$ are Box-Cox transforms, (a-part from sign)

$$\boxed{z(\tilde{y},\alpha)=\begin{cases}\dfrac{1-\tilde{y}^{\alpha}}{\alpha} & \alpha\neq 0\\ -\ln\tilde{y} & \alpha=0\end{cases}}$$

- ⋆ Negative BC positive function, monotonically decreasing with $\tilde{y}$
- ⋆ Continuity at $\alpha\to 0$
- ⋆ Statistical properties: variance , distribution

Simple idea: apply $z(\tilde{y},\alpha)$ not only for discrete (1,→0, -1) but for continuous α to define the ODE of the new (autonomous) GF: $\boxed{\dfrac{dz}{dt}=-Kz}$

$-\boxed{K}$ can be viewed as the slope of $\ln\left[z(\tilde{y},\alpha)\right]$ plot against time (t): $\ln\left[z(\tilde{y},\alpha)\right]=\ln\left[z(\tilde{y}_0,\alpha)\right]-\boxed{K}t$

Inverse function: $t-\underbrace{t_0}_{0}=K^{-1}\ln\left[z_0/z\right]=K^{-1}\ln\left[(1-\tilde{y}_0^{\alpha})/\left(1-\tilde{y}^{\alpha}\right)\right],\ \alpha\neq 0$

$0<\alpha<1$: Chapman -Richards; 1959 Richards' extension to $\alpha<0$

Richards/ G-Function & G-Rate

From $z' = -Kz$ with $z = \left(1 - \tilde{y}^{\alpha}\right)/\alpha$

1) Growth function (GF)

$$z'/z = -K \Rightarrow d\left(\ln z\right) = -Kt + C$$

For $t = 0,\ C = \ln z_0$ with $z_0 = \dfrac{1 - \tilde{y}_0^{\alpha}}{\alpha} > 0$

$$z(t) = z_0 \exp(-Kt) \Rightarrow y = A\left[1 - \alpha z_0 \exp(-Kt)\right]^{1/\alpha}$$

$z(t) \propto z_0$ at t fixed

$y_0 - form:$ $$y(t) = A\{1 - [\underbrace{1 - \left(y_0 / A\right)^{\alpha}}_{B}]\exp(-Kt)\}^{1/\alpha}$$

K =minus the specific growth rate of $z(t)$.

2) Growth rate (ODE defining GF)

$$\frac{1}{\alpha}.-\alpha.\frac{\tilde{y}^{\alpha}}{\tilde{y}}.\tilde{y}' = -\tilde{y}^{\alpha}\frac{\tilde{y}'}{\tilde{y}} = -Kz \Rightarrow \frac{\tilde{y}'}{\tilde{y}} = K\tilde{y}^{\alpha}z = Kz_{-\alpha}$$

ODE: $$y' = \frac{K}{\alpha}y\left[(A/y)^{\alpha} - 1\right]$$

The Richards GF/ Inflection coordinates

The 2nd derivative (Acceleration) obtained via

$$y' = yKz_{-\alpha} \Rightarrow y'' = K\left(y'z_{-\alpha} + yz'_{-\alpha}\right)$$

$$\boxed{y'' = \frac{K}{\alpha} y'\left[(1-\alpha)(A/y)^{\alpha} - 1\right]}$$

$y'' = 0$ with a change of sign below and above gives

$\boxed{y_I = A(1-\alpha)^{1/\alpha}}$ for $\alpha < 1$ Now: $\frac{y'}{y} = \frac{K}{\alpha}\left[(A/y)^{\alpha} - 1\right]$

Then $\boxed{y'(t_I)/y(t_I) = K/(1-\alpha)}$ and $\boxed{y'(t_I) = AK(1-\alpha)^{\frac{1}{\alpha}-1}}$

$$\left[y(t_I)/A\right]^{\alpha} = 1 - \alpha \underbrace{z_0 \exp(-Kt_I)}_{1} \Rightarrow t_I = K^{-1} \ln z_0$$

The Richards unified GF/ The 3 Forms

From $y = A\left[1-\alpha z_0 \exp(-Kt)\right]^{1/\alpha}$

All the usual forms can be easily derived:

1) The y_0 form

$$y(t) = \boxed{A}\left[1-\left[1-\left(\boxed{y_0}/A\right)^{\alpha}\right]\exp(-\boxed{K}t)\right]^{1/\boxed{\alpha}}$$

2) The t_I-form ($\alpha < 1$) whatever sign(α) $z_0 > 0$, $\ln(z_0) = Kt_I$

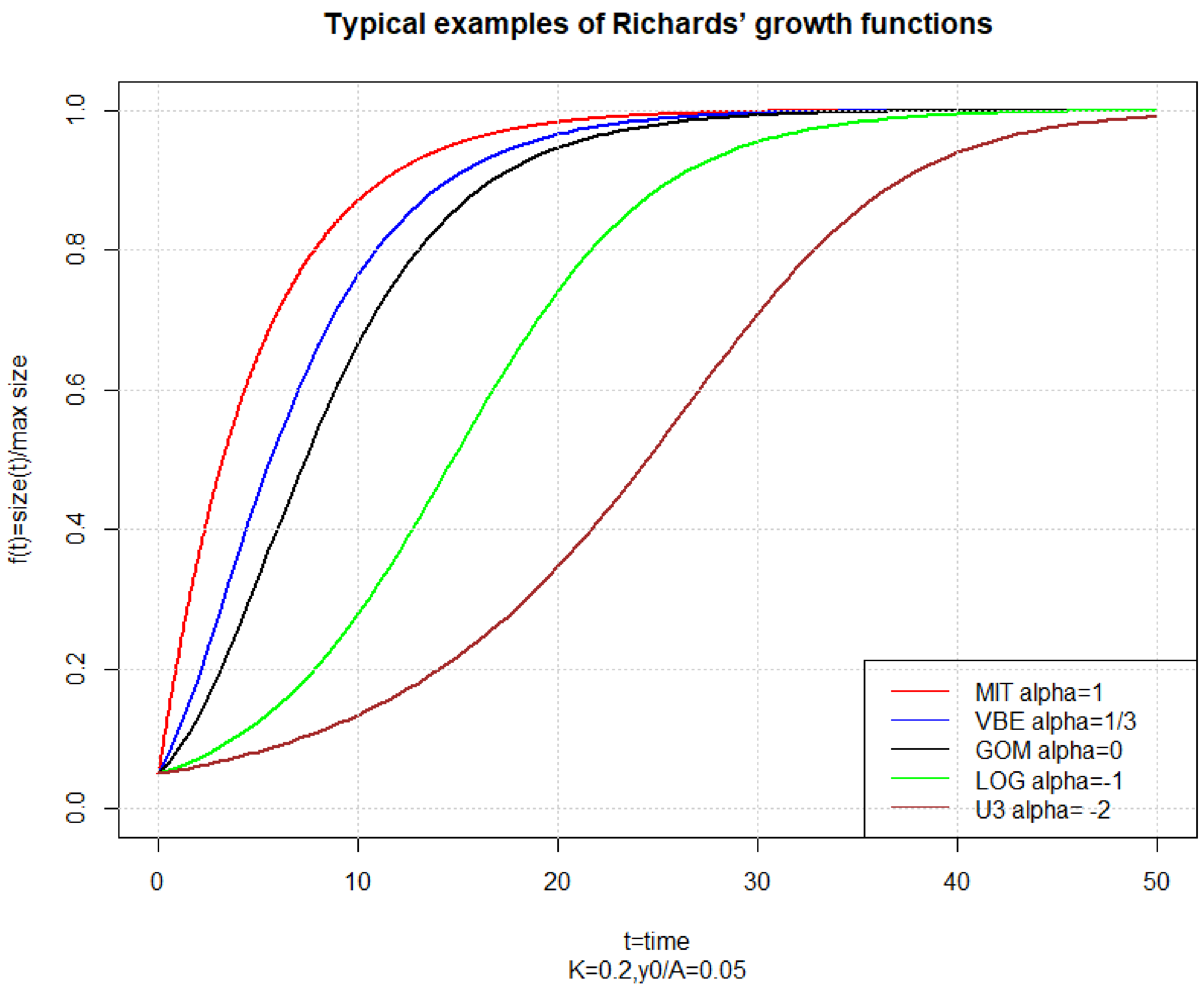
$$y(t) = \boxed{A}\left[1-\boxed{\alpha}\exp\left[-\boxed{K}(t-\boxed{t_I})\right]\right]^{1/\alpha}$$

3) The Unified (t_I; K_U) form (Tjorve & Tjorve,2017)

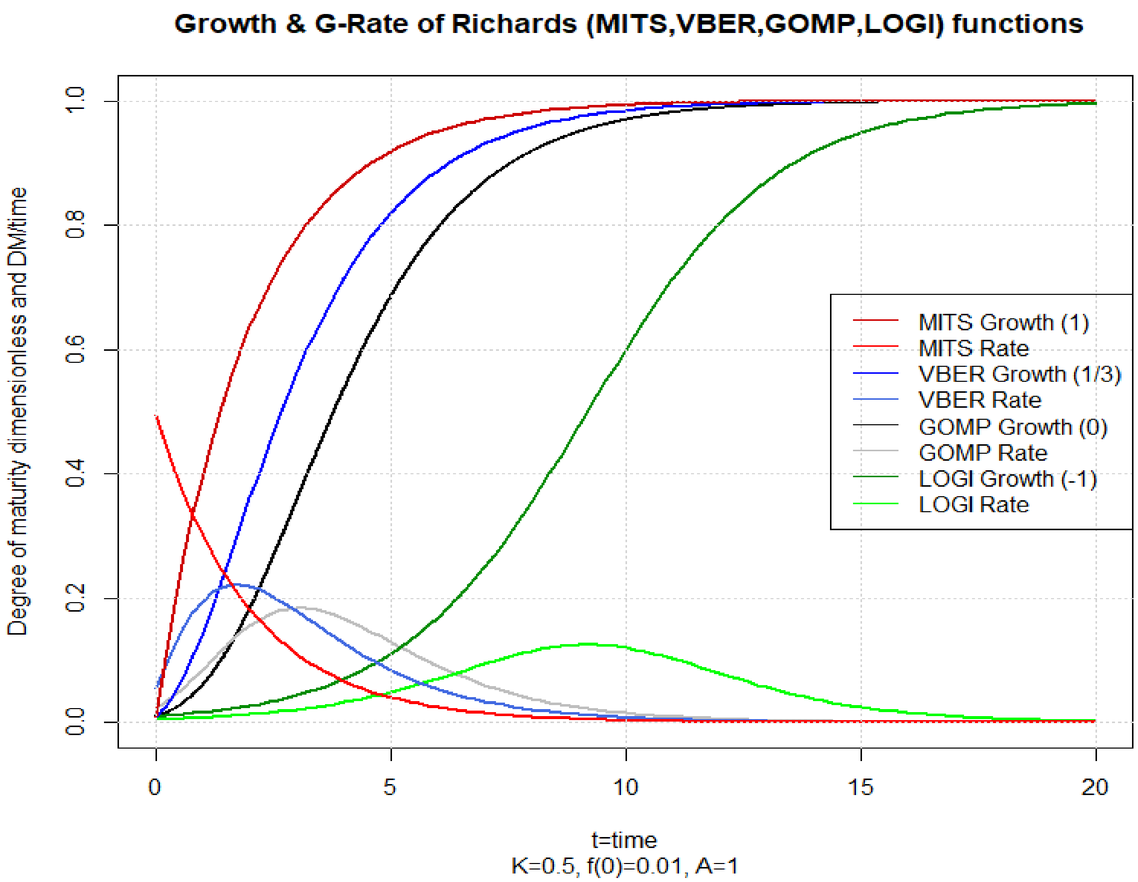
$y'(t_I)/A = K\left(1-\alpha\right)^{\frac{1}{\alpha}-1} = K_U$ replace K by $K_U\left(1-\alpha\right)^{1-\frac{1}{\alpha}}$

$$y(t) = \boxed{A}\left[1-\boxed{\alpha}\exp\left[-\left(1-\alpha\right)^{1-\frac{1}{\alpha}}\boxed{K_U}(t-\boxed{t_I})\right]\right]^{1/\alpha}$$

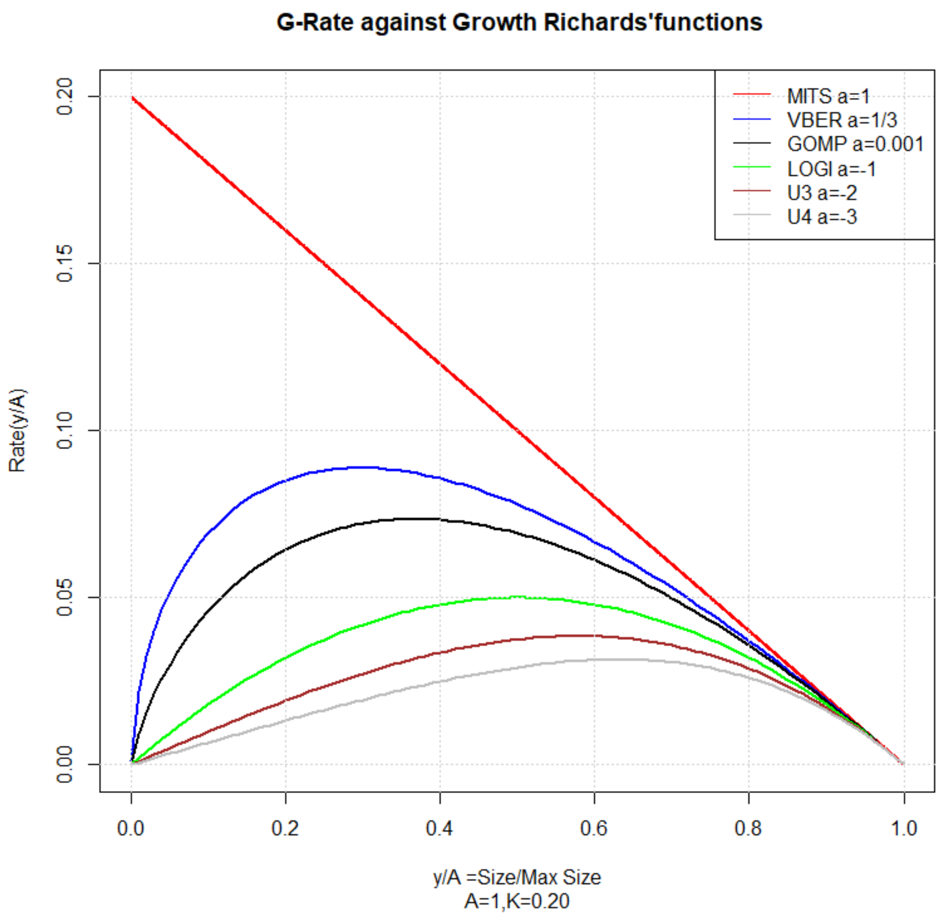
4 parameters of practical interest allowing comparison between fonctions


Typical examples of Richards' growth functions
f(t)=size(t)/max size
0.0
0.2
0.4
0.6
0.8
1.0
0
10
20
30
40
50
t=time
K=0.2,y0/A=0.05
MIT alpha=1
VBE alpha=1/3
GOM alpha=0
LOG alpha=-1
U3 alpha= -2

Richards: Growth and Growth Rate



G-Rate against Growth



Growth rate: definitions

Let's $y_t = f(t)$ be a Richards' sigmoid growth function defined on $(-\infty,+\infty)$ or $(\tau_0,+\infty)$ with $f(t) \underset{t\to+\infty}{\to} A$ (maximum size) and $f(t) \underset{t\to-\infty}{\to} 0$ or $f(\tau_0)=0$, and $f(t=0)=y_0$.

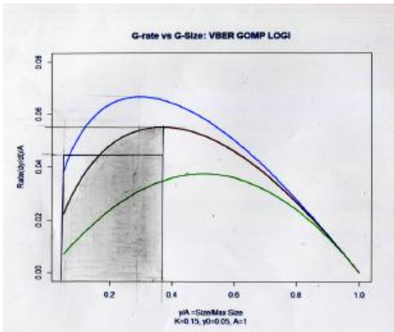
Two ways to compute an averaged growth rate:

1)The usual definition with change in size averaged over time:

$$\boxed{\overline{V}_{t;1-2} = (t_2 - t_1)^{-1} \int_{t_1}^{t_2} f^{'}_{(\tau)} d\tau = (y_2 - y_1)/(t_2 - t_1)}.$$

2)Remember ODE being autonomous: $f'(t) = h(f(t),\theta)$, one can plot h against f on the interval (y_1, y_2), resulting in

$$\boxed{\overline{V}_{y;1-2} = (y_2 - y_1)^{-1} \int_{y_1}^{y_2} h(f)df}$$

What matters in the dynamics is its 

state variables.

Growth rate: definitions

Since $df = \frac{df}{dt}dt$, and $\frac{df}{dt} = h(f)$ then $h(f)df = \frac{df}{dt}.\frac{df}{dt}dt$

$$\bar{v}_{y;1-2} = (y_2 - y_1)^{-1}\int_{y_1}^{y_2} h(f)df = \left(\int_{t_1}^{t_2}\left(\frac{df}{d\tau}\right)^2 d\tau\right) / \left(\int_{t_1}^{t_2}\left(\frac{df}{d\tau}\right)d\tau\right)$$

a weighted mean of $f'(t) = h(f(t))$ giving higher weight $w(t) = f'(t)$ to higher growth rates (ie around the inflection point) rather than to the ends of time growth.

La Vallée (1965) defined

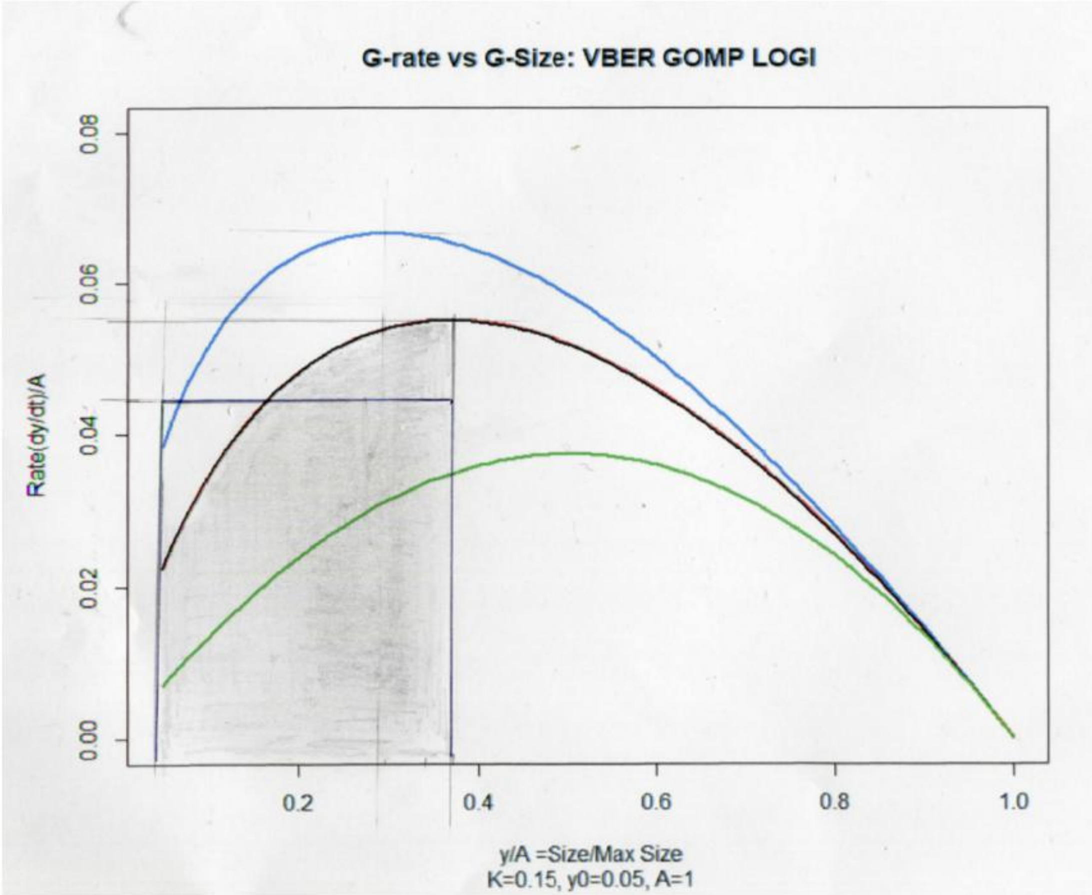
$d(t_1,t_2) = \int_{t_1}^{t_2}\left(\frac{df}{d\tau}\right)^2 d\tau$ as the intrinsic time duration on (t_1,t_2)

$d(0,t) = \int_0^t\left(\frac{df}{d\tau}\right)^2 d\tau$ as the intrinsic time

Growth rates: computation

- $y' = \frac{K}{\alpha} y\left[(A/y)^{\alpha} - 1\right] \Rightarrow \tilde{y}' = \frac{K}{\alpha}\tilde{y}\left(\tilde{y}^{-\alpha} - 1\right)$ for $\tilde{y} = y/A$
- $F_{\tilde{y};0-\tilde{y}} = \int_0^{\tilde{y}} f' df = K\alpha^{-1}\int_0^{\tilde{y}} f\left(f^{-\alpha} - 1\right)df$
- $F_{\tilde{y};0-\tilde{y}} = K\frac{2\left(\tilde{y}_t^{2-\alpha} - \tilde{y}_t^2\right) + \alpha\tilde{y}_t^2}{2\alpha(2-\alpha)}$
- $\boxed{F_{0-1} = \bar{v}_{0,1} = \frac{K}{2(2-\alpha)}}$
- $F_{\tilde{y}_1;\tilde{y}_2} = F_{0;\tilde{y}_2} - F_{0;\tilde{y}_1}$ $\boxed{\bar{v}_{\tilde{y}_1;\tilde{y}_2} = \left(F_{0;\tilde{y}_2} - F_{0;\tilde{y}_1}\right)/\left(\tilde{y}_2 - \tilde{y}_1\right)}$
- $\bar{v}_{t_1;t_2} = \left(\tilde{y}_2 - \tilde{y}_1\right)/\left(t_2 - t_1\right)$ with $t_2 - t_1 = K^{-1}\ln\left[z_1/z_2\right] = K^{-1}\ln\left[(1-\tilde{y}_1^{\alpha})/\left(1-\tilde{y}_2^{\alpha}\right)\right]$

G-Rate against Growth



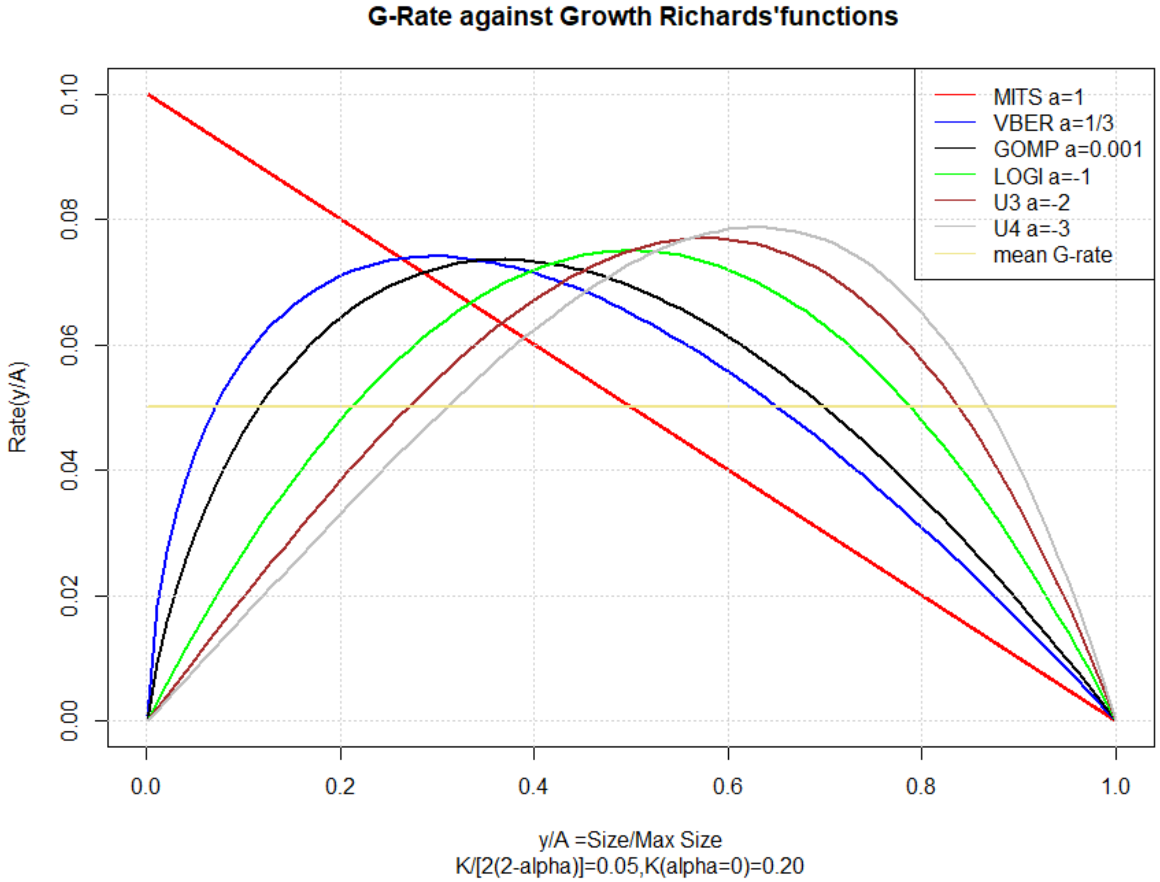
Growth rates: example

Table 1: the two average growth rates : a numerical example

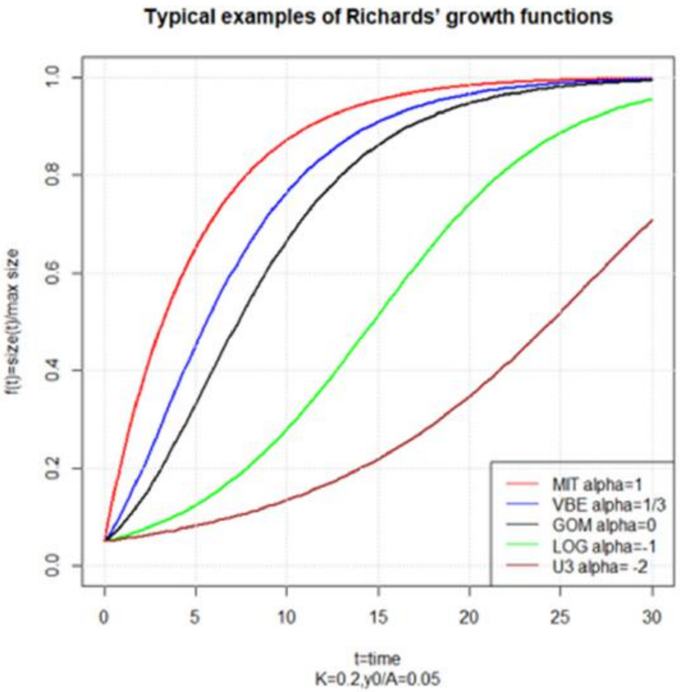
	Von Bertalanffy	Gompertz	Verhulst
y0	0.05	0.05	0.05
y1	0.2963	0.3678	0.5000
y1-y0	0.2963	0.3678	0.5000
t0	0	0	0
t1	4.2609	7.3139	19.6296
t1-t0	4.2609	7.3139	19.6296
V(t0; t1)	0.0578	0.0435	0.2292
V(y0;y1)	0.0590 *+2.08%*	0.0458 *+5.45%*	0.2737 *19.40%*

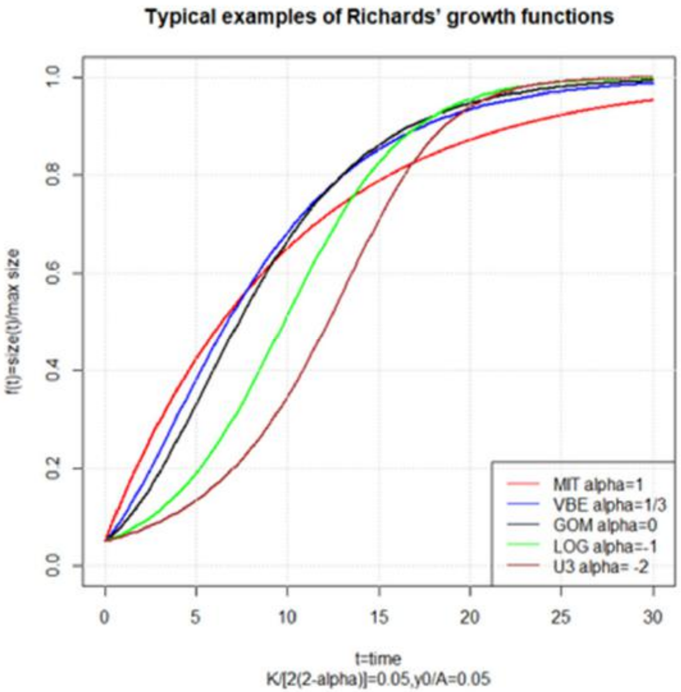
y0 starting value at t0=0; y1 size at inflection time t1 for K=0.15, A=1,y0=0.05
Relative increase of V(y1;y2) vs V(t1;t2)

Mitscherlich, Verhulst, Gompertz : a short overview



The Richards GF/Representation





The Richards GF/features

α		-2		-1		0		1/3		1
m=1- α		3		2		1		2/3		0
Name		U3		Logistic		Gompertz		Bertalanffy		Mistcherlich
Sigmoid	SIG	SIG	SIG	SIG	SIG	SIG	SIG	SIG	SIG	
X-start	LAS	LAS	LAS	LAS	LAS	LAS	XSP	XSP	XSP	XSP
Size at Inflection/A		0.578		0.500		1/e=0.368		0.296		

LAS: Lower Asymptote   XSP:X axis Starting Point Y(XST)=0   Size at inflection/A Size max: $(1-\alpha)^{\frac{1}{\alpha}} = m^{\frac{1}{1-m}}$

The von Bertalanffy-Pütter ODE

Growth-rate emerges from the energetic balance between

“Anabolism” (“Aufbau” biosynthesis) and

“Catabolism” (“Zerfall” degradation)

each of them being a function of body mass (Putter, 1920)

$$\frac{dW}{dt} = aW^m - bW^n$$

For Von Bertalanffy : $m = 2/3$ surface (L^2 dim) for O_2 consumption (surface law) and $n = 1$ (body law)

disputed by Kleiber ,1932; West Brown Enquist, 1997; Escala, 2022) with $m = 3/4$, relating basal metabolic rate to body mass; see Lecuit’s (2020) course at College de France

Underline theory of allometry $y = bx^a$ based on scale invariance and similarity (Galileo 1638; Kleiber 1920; Huxley, 1932; Teissier 1934; Brody, 1945) in relation to the MLT system.

The von Bertalanffy-Pütter ODE

$$\frac{dW}{dt} = \eta W^m - \kappa W \Rightarrow \frac{W'}{W} = \kappa\left[\frac{\eta}{\kappa}\frac{1}{W^{1-m}} - 1\right]$$

Letting $\kappa(1-m) = K$ and $\frac{\eta}{\kappa} = A^{1-m} \Rightarrow \eta, \kappa$ same sign

- $\boxed{\frac{dW}{dt} = \frac{K}{1-m} W\left[\left(\frac{A}{W}\right)^{1-m} - 1\right]}$ same as with $a = 1-m$
- OK for $0 < \alpha < 1$ $(0<m<1) \Rightarrow W' > 0$
- $\alpha < 0$ $(m > 1) \Rightarrow (A/W)^{\alpha} - 1 = (W/A)^{-\alpha} - 1 < 0$

$\Rightarrow K > 0 \Rightarrow \kappa < 0$ and $\eta<0$ incompatible with VBER interpretation

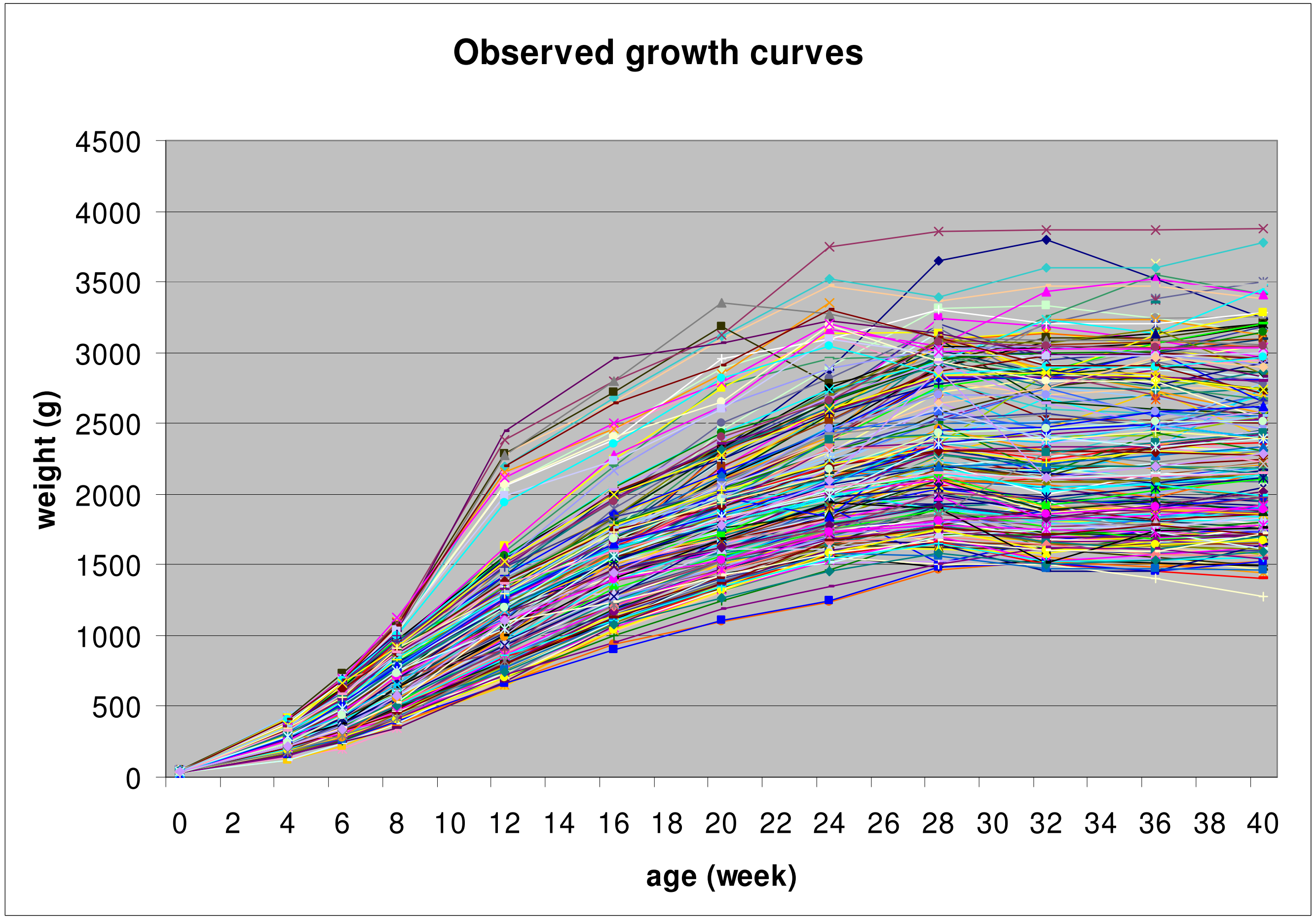
Noted by Richards (page 292) "Yet if used empirically, m being assessed from growth data themselves instead of dubious relevant metabolic studies, VB's function will find its chief application with values over 1"

Application: growth of chicken

- Divergent selection experiment on chicken growth carried out at INRAE by Ricard (1975) on weight at 2 ages: 8,36 weeks
- 5 lines:
  - -+ LH (X11) +- HL (X22)
  - ++ HH (X33) --LL (X44)
  - Control C (X88)
- Data=3058 weight records on 265 females of the last generation at 0,4,6,8,12,…,40 wks of age (12 points)
  - 122 missing data (4 « outliers »)

Ricard et al (1975) Mignon-Grasteau et al. (2000) Jaffrézic et al (2006)

Chicken data: Observed G curves



Observed Growth curves by strain: Ricard et al,1975

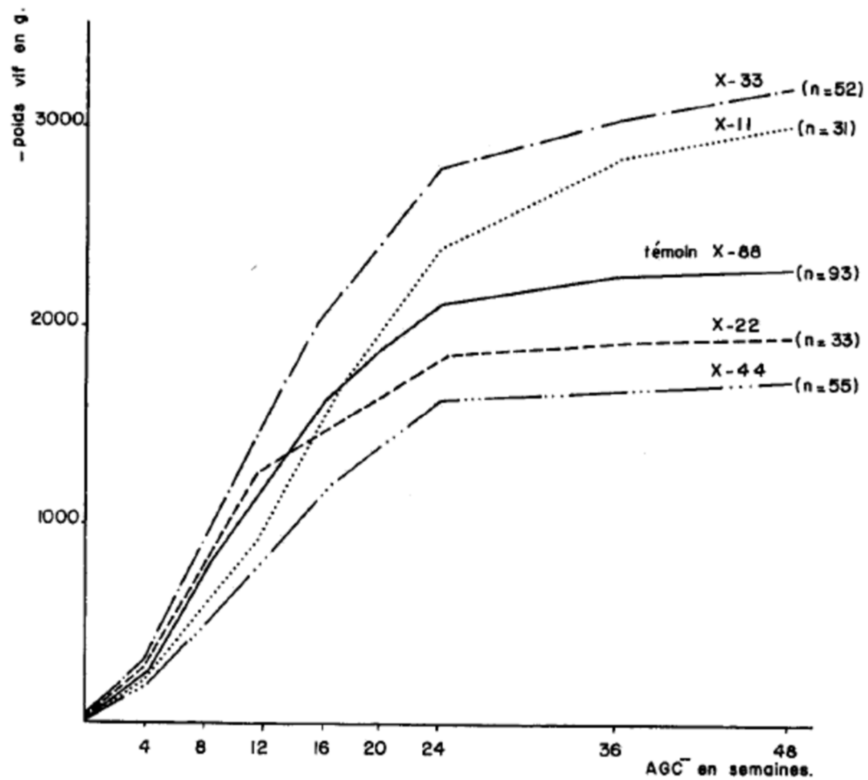
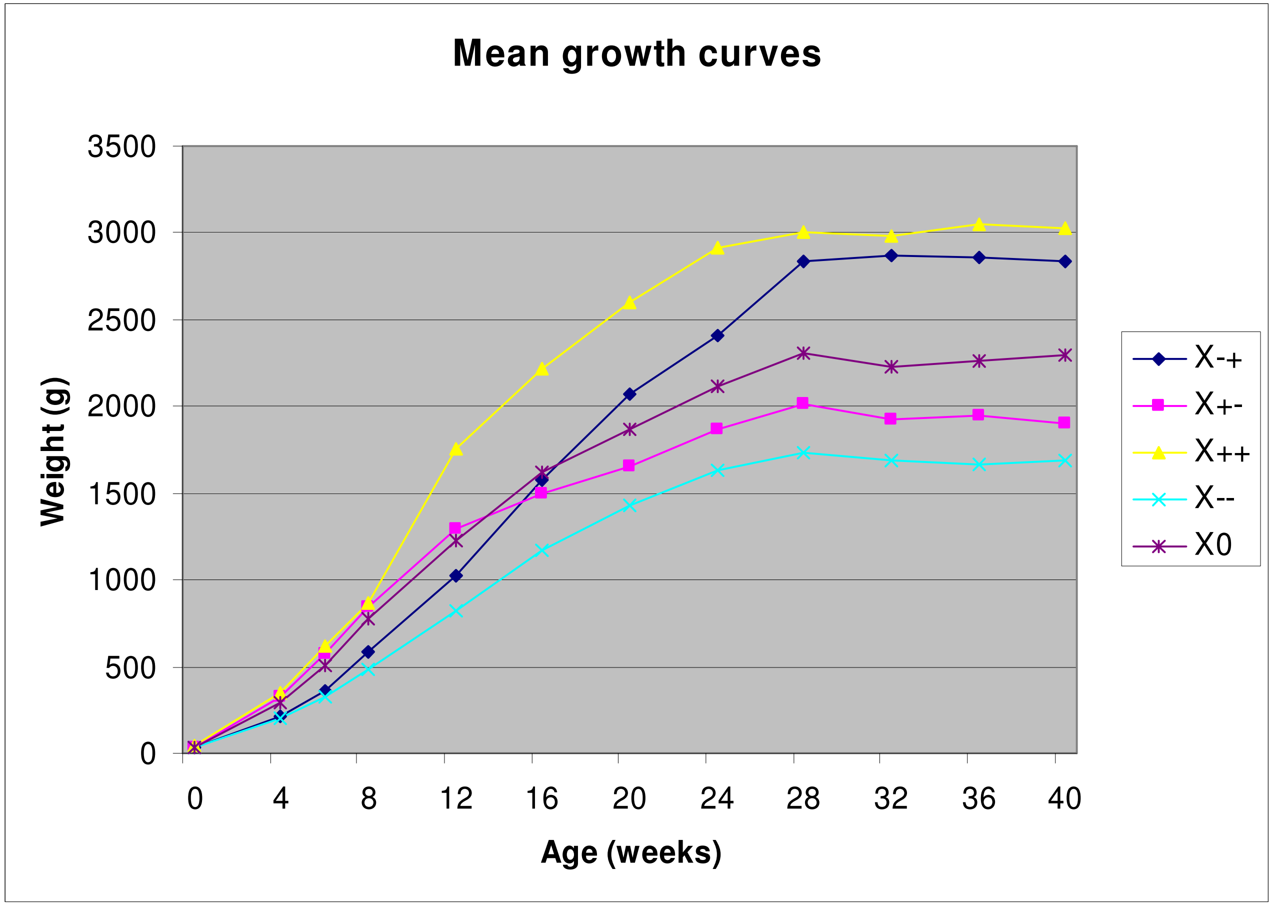


FIG. 4. — *Courbes de croissances obtenues pour un lot de poules nées en 1973*

Chicken data: Observed G curves by strain



Model: 1st stage

$$Y_{hi,t} \mid \sim \mathcal{N}\left[f(\phi_{hi}), \sigma^2_{hi,t} \right]$$

$$f_t(\phi_{hi}, m) = A_{hi}\left\{1-(1-m)\exp\left[-K_{hi}\left(t-T_{hi}\right)\right]\right\}^{\frac{1}{1-m}}$$

$$\sigma^2_{hi,t} = g(\boldsymbol{\gamma}, z_{hi}) \text{ eg } \sigma^2_{hi,t} = \exp(a_h + b_h t + c_h t^2)$$

Model/2nd stage

$$\phi_{hi} = \left(A_{hi}, T_{hi}, K_{hi}\right)'$$

$$\phi_{hi} \mid \boldsymbol{\beta}_h, \Sigma \sim \mathcal{N}\left(\boldsymbol{\beta}_h, \boldsymbol{\Sigma}\right)$$

$$\boldsymbol{\beta}_h = (\alpha_h, \tau_h, \kappa_h)'$$

$$\boldsymbol{\Sigma} = \left\{\sigma_{ij}\right\} \text{ pd symmetric}$$

$$m \sim m_{\inf} + \left(m_{\sup} - m_{\inf}\right) beta(c,c)$$

Model: Hyperparameters

3rd stage: hyperparameters: σ^2, $\boldsymbol{\beta}, \mathbf{G}_0$,

$\boxed{\sigma^{-2} \sim \mathcal{G}\left(½\nu, ½\nu\sigma_*^2\right)} \Rightarrow \mathrm{E}\left(\sigma^{-2}\right) = \sigma_*^{-2} \quad \mathrm{Var}\left(\sigma^{-2}\right) = 2\sigma_*^{-4} / \nu$

If $\mathcal{G}(\varepsilon, \varepsilon)$ with $\varepsilon \rightarrow 0, \left[\sigma^2\right] \propto \sigma^{-2}$ Jeffeys' non informative prior

Prefer $\boxed{\sigma \sim U\left(0, \sigma_{\text{sup}}\right)}$ Gelman (2006)

$\boxed{\boldsymbol{\beta} \sim \mathcal{N}\left(\boldsymbol{\beta}_0, \mathbf{H}\right)}$; Often $\mathbf{H}^{-1} \rightarrow \mathbf{0}$ (Non informative)

$\boxed{\Sigma^{-1} \sim \mathcal{W}\left[\left(\rho\Sigma_0\right)^{-1}, \rho\right]} \Rightarrow \mathrm{E}\left(\Sigma^{-1}\right) = \Sigma_0^{-1}$ WinB: $\Sigma^{-1} \sim \text{dwish}\left[\left(\rho\Sigma_0\right), \rho\right]$

Parameter estimation

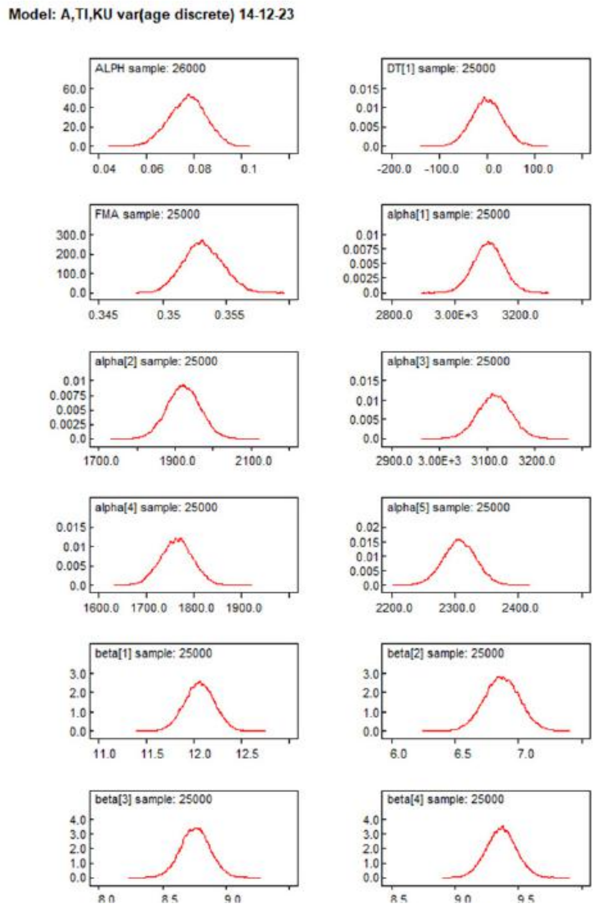
Parameter	Strain	Homoskedastic	Heteroskedastic*
Alpha	ALL	-0.186 [-0.248;-0.132]**	0.098 [0.080;0.114]**
A (g)	LH	3020 ± 44	3260 ± 62
	HL	1958 ± 42	1938 ± 43
	HH	3099 ± 35	3090 ± 36
	LL	1741 ± 33	1833 ± 40
	C	2330 ± 26	2323 ± 26
TI (wks)	LH	13.12 ± 0.20	12.58 ± 0.19
	HL	7.91 ± 0.19	6.84 ± 0.14
	HH	9.65 ± 0.16	8.63 ± 0.18
	LL	10.32 ± 0.17	9.69 ± 0.18
	C	9.63 ± 0.14	8.42 ± 0.10
KU (%)	LH	4.83 ± 0.15	4.01 ± 0.10
	HL	6.08 ± 0.18	6.81 ± 0.11
	HH	6.16 ± 0.14	5.76 ± 0.09
	LL	5.70 ± 0.14	4.85 ± 0.09
	C	5.46 ± 0.10	5.63 ± 0.06
DIC	ALL	36604 (pD=596)	34291 (pD=693)#

* $\sigma^2_{e(ht)} = \exp\left(a_h + b_h t + c_h t^2\right)$ ** (2.5; 97.5 p.100) credible limits

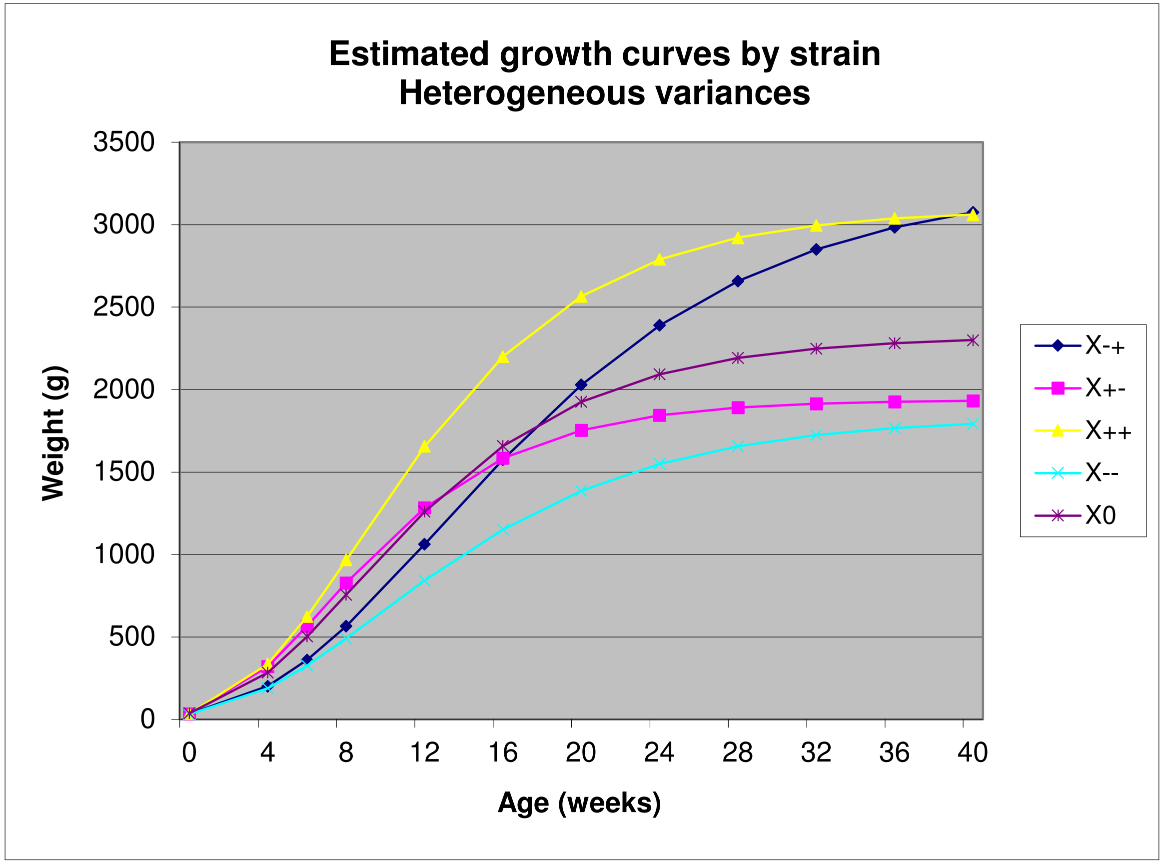
$DIC = D\left(\bar{\theta}\right) + 2p_D;\ p_D = \bar{D} - D\left(\bar{\theta}\right)$ # DIC Gompertz: 34475

Table: Parameter estimation of Richards' GF applied to chicken data: A, TI, KU model under homoscedastic and heteroskedastic models

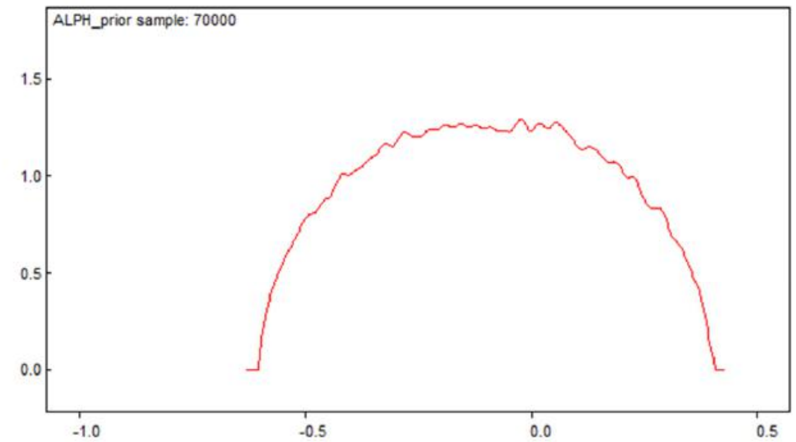
Posterior distributions: an example



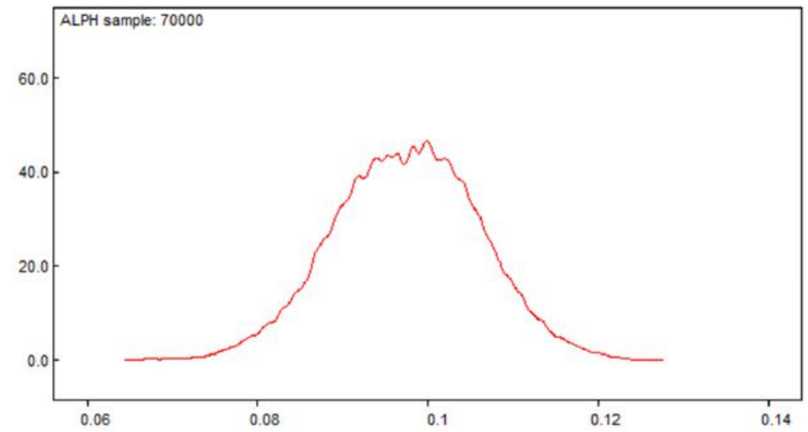
Fitted growth curves by strain



Prior & Posterior of the shape parameter (α)



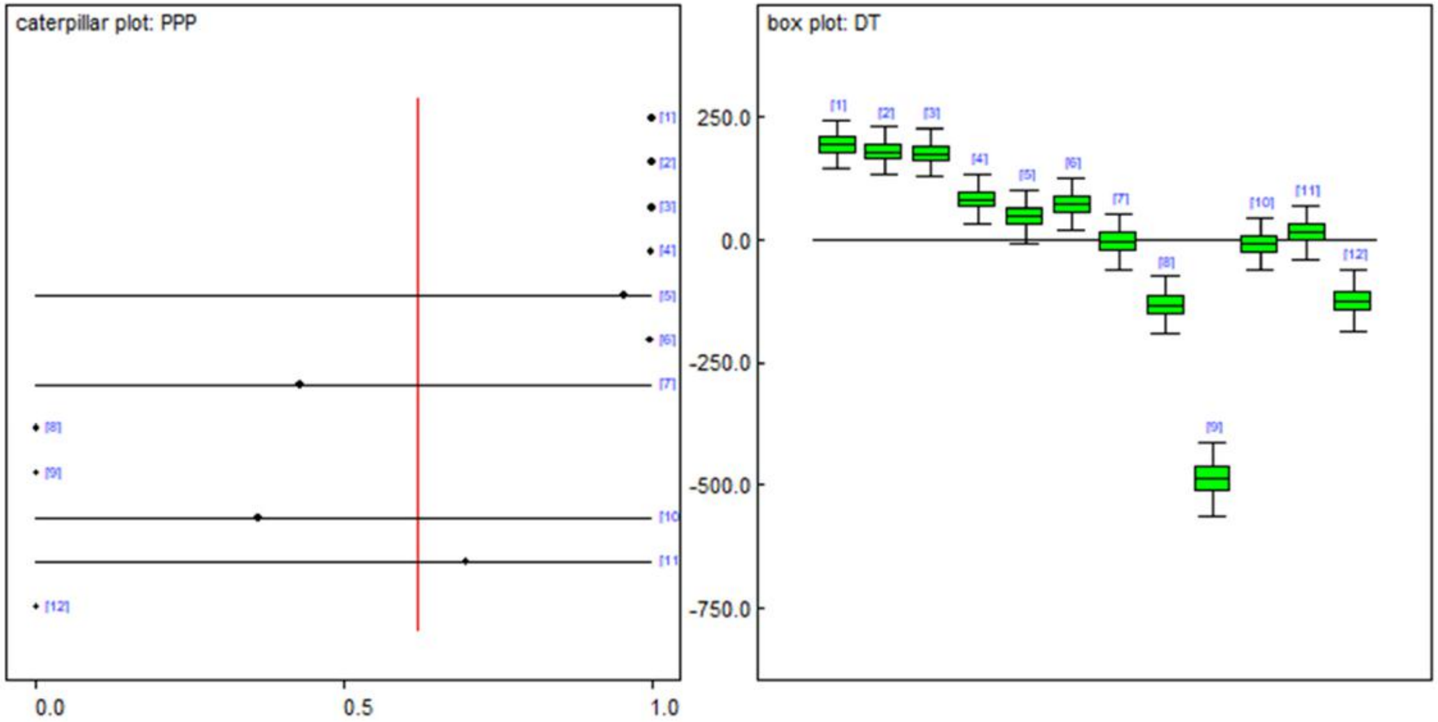
node	mean	sd	MC error	2.5%	median	97.5%	start	sample
ALPH_prior	**-0.09908**	0.2498	9.569E-4	**-0.5389**	**-0.09834**	**0.3388**	5001	70000



node	mean	sd	MC error	2.5%	median	97.5%	start	sample
ALPH	**0.09755**	0.008427	3.417E-4	**0.08089**	**0.09769**	**0.1138**	5001	70000

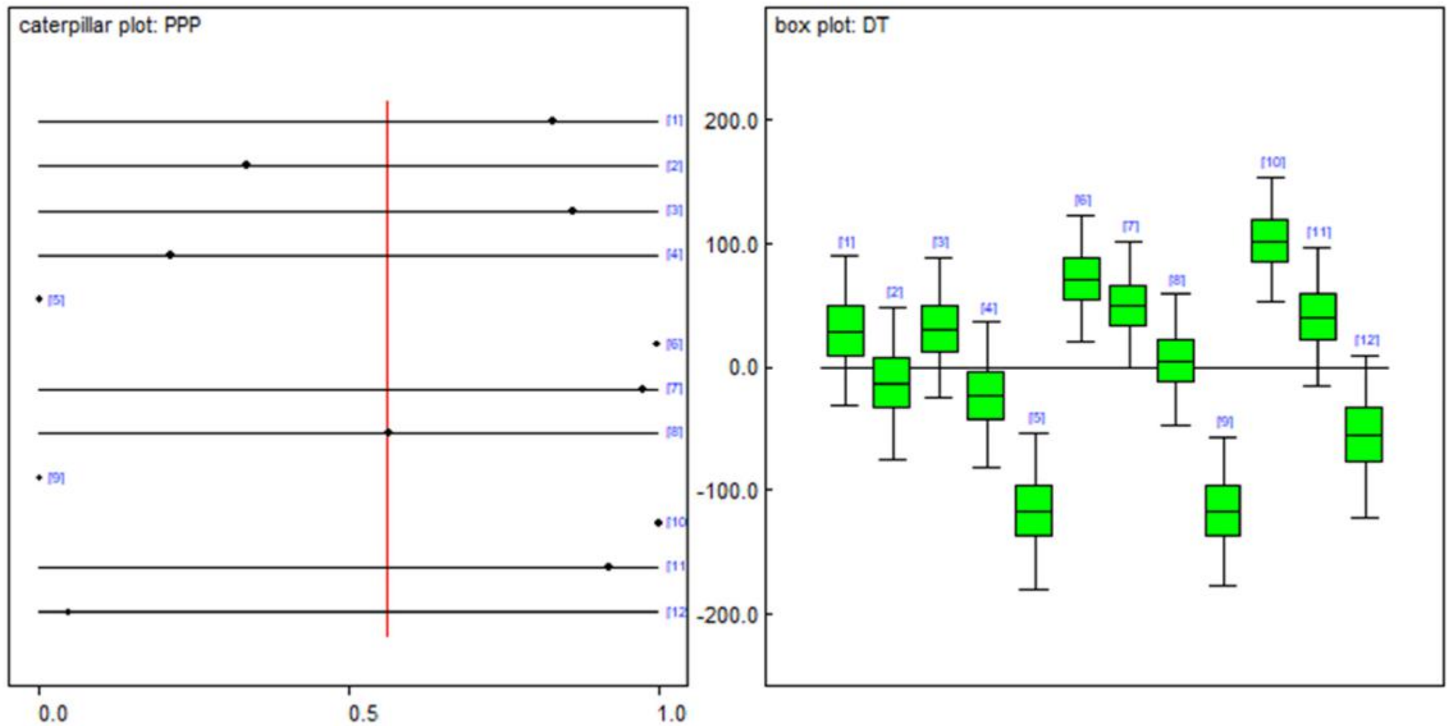
Model: A,TI,KU, alpha, Heterogeneous Residual variance

PPP values: model A, TI, KU, alpha, Homo Residual Var



PPP values based on a chi2square discrepancy statistics T(y) with PPP=Prob(T(yrep)>T(yobs)); DT=T(yrep)-T(Yobs)
overall PPP =0.504. Model A, TI, KU, alpha, homegeneous variance

PPP values: model A, TI, KU, alpha, Hetero Residual Var



Overall PPP=0.498 Model: A,TI,KU,alpha Heterogeneous Residual Variance

Model comparison: residual variance

Table : Comparison of models for residual variance

	Model[a]	Shape α	#Par[b]	DIC[c]	ΔDIC[c]
0	Homoskedastic (Fixed M)	-0.153	1	40705	+4101
1	Homoskedastic (Mixed M)	-0.189	1	36604	0
2	Age quadratic : logvar	0.065	3	35037	-1567
3	Age discrete	0.078	12	34717	-1887
4	Age (2) by Strain : log var	0.098	15	34291	-2313
5	Age (D)+Strain : log var	0.096	16	34300	-2304
6	C+Power of growth mean	0.085	3	34590	-2014

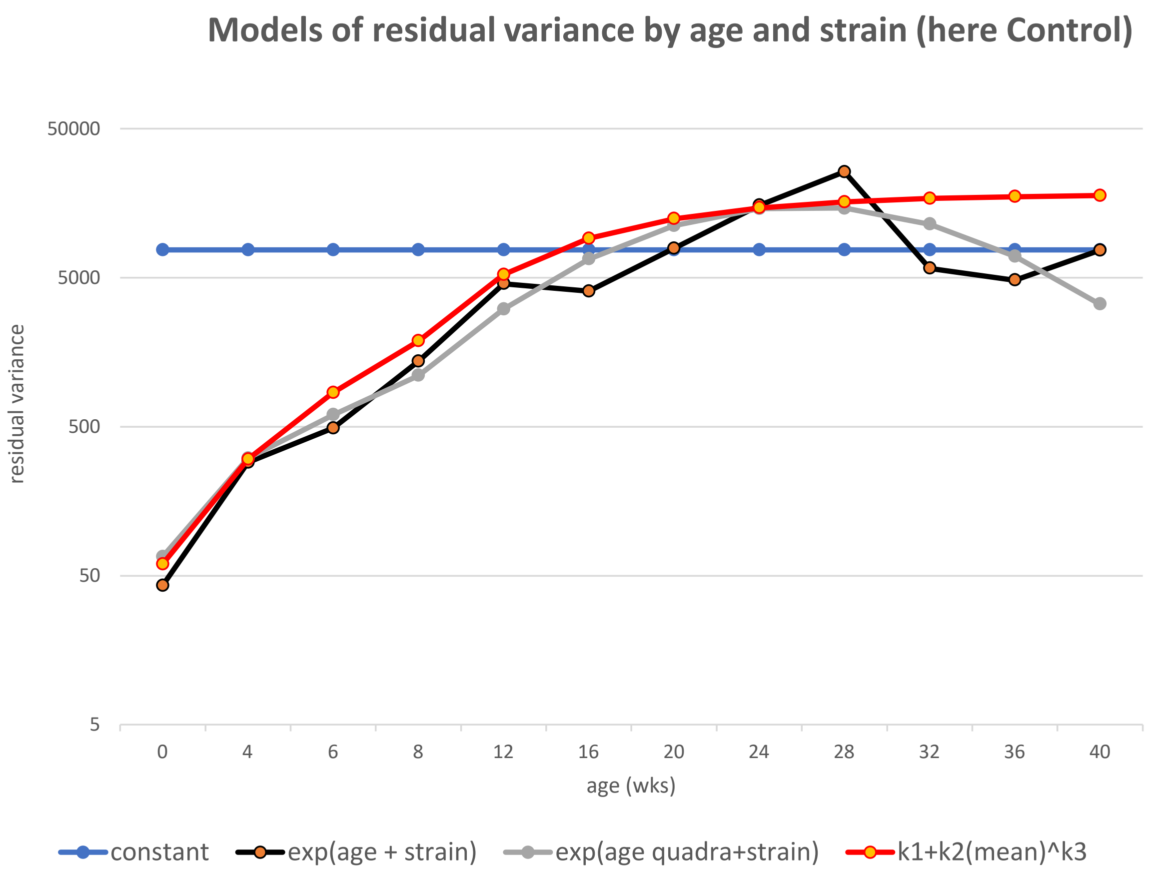
a: **0**: NLFM $\sigma_e^2 = Cst$; **1**: NLMM+ $\sigma_e^2 = Cst$; **2**: $\sigma_{e(t)}^2 = \exp\left(a + bt + ct^2\right)$;

3: $\sigma_{e_j}^2, j = 1,.,12$; **4** : $\sigma_{e(ht)}^2 = \exp\left(a_h + b_h t + c_h t^2\right)$; **5**: $\sigma_{e(hj)}^2 = \exp\left(souche(h) + age(j)\right)$

6: $\sigma_{e(hj)}^2 = \lambda_1 + \lambda_2 \left(eta[h,j]\right)^{\lambda_3}$ where $eta[h,j] = \alpha_h \left[1 - (1-m)\exp(-\kappa_h \left(t_j - \tau_{I,h}\right)\right]^{1/(1-m)}$.

b: No of parameters for the residual variance model

Models for residual variance



Another parameterization

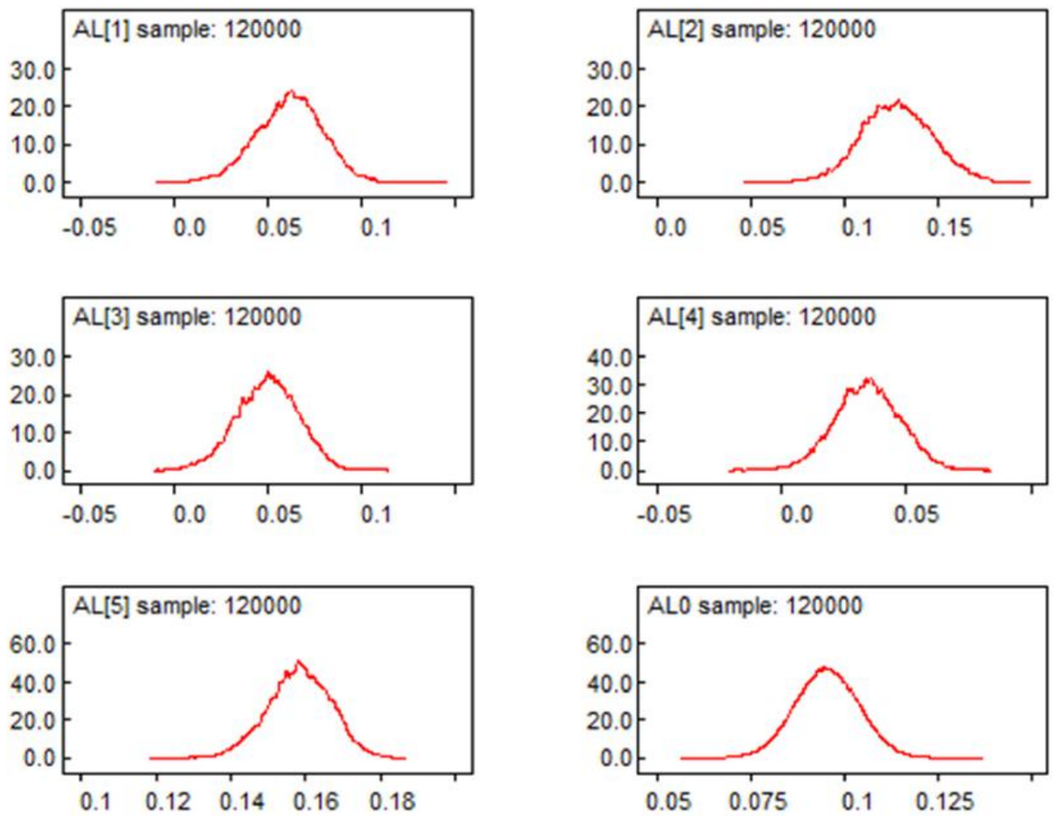
Table Estimation under the Y0 initial condition parameterization

Parameter	Strain	Mean	(2.5%;97.5%) CI
Alpha	LH	0.061	0.024; 0.095
	HL	**0.128**	0.091; 0.166
	HH	0.050	0.016; 0.080
	LL	0.034	0.010; 0.059
	C	0.158	0.141; 0.174
	ALL	0.0955	0.079; 0.112
A (g)	LH	3183	3053; 3316
	HL	1939	1857; 1939
	HH	3072	3003; 3141
	LL	1744	1677; 1811
	C	2337	2287; 2387
Y0(g)*	LH	38.3	35.7; 40.9
	HL	34.7	31.7; 37.8
	HH	40.9	39.2; 42.6
	LL	33.8	32.8; 34.8
	C	36.5	35.4; 37.6
TI (wks)	LH	12.64	12.37; 12.94
	HL	6.74	6.61; 6.74
	HH	8.74	8.65; 8.74
	LL	9.55	9.44; 9.55
	C	8.24	8.18; 8.24
DIC	ALL	33907 (pD=515)	

A(LH)-A(HL)=-0.067 [-0.120 ; -0.016]   A(HL)-A(C)=-.030 [-0.071; 0.011]

*”Fixed Effect” no individual effet

Shape parameter distribution by strain



Discussion-Conclusion

- Extensions
  - Further unification: Weibull, Hosfeld, Schumacher, Levakovic (Garcia, 2005)
  - Exploiting similarity with CDF : eg Blumberg with a beta as growth rate
  - Multivariate statistical analysis
  - SDE mixed models:
  - Garcia (1980); Donnet & Samson (2007), Donnet et al (2010), Campillo et (2013)

$$df^*(t,\phi) = F[f^*(t,\phi), t, \phi]dt + \gamma dB(t)$$

- Domain of applications
  - Cancerology: tumor growth via Gompertz
  - Ecology: West, Brown & Enquist,1997 (3/4 scaling law); Lecuit
  - Epidemiology: COVID-19

Discussion-Conclusion

- Although highly criticized (Cusset, 1991) Richards growth functions provides a unified approach of some important autonomous sigmoid functions (Mitscherlich, von Bertalanffy, Gompertz, Verhulst, et..)
- A prerequisite for applications and research work in this domain
- Can be implemented via Bayesian inference techniques with some benefits (handling missing data and making predictions)
- Need for a careful set up of the functional and residual parts
- Care also required in parameterization: coherence, interpretation and feasability

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