Mathematical Models for Biomedicinal and Environmental Sciences

Luigi Preziosi

POLITECNICO DI TORINO

Index

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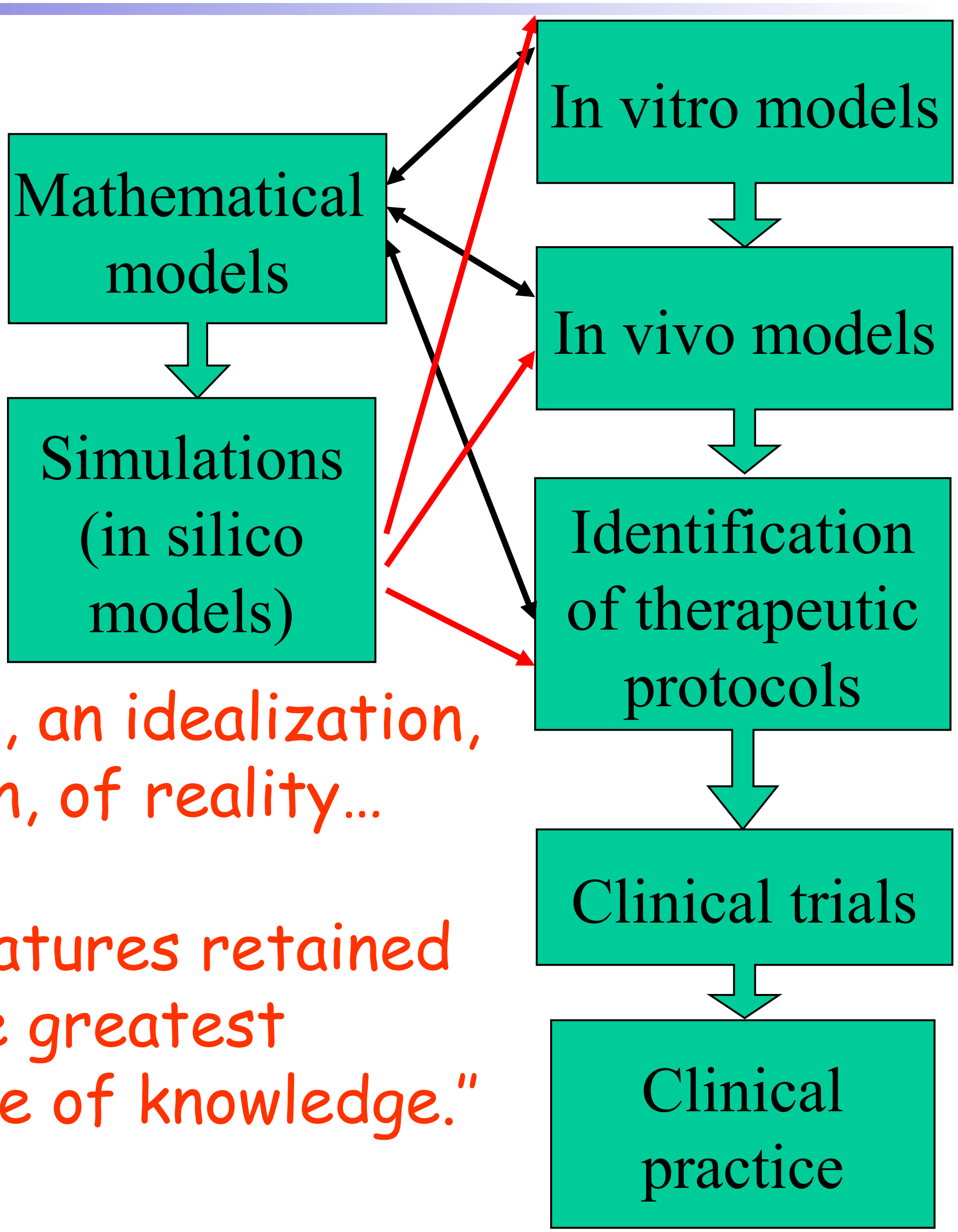
Modelling cycle in medicine

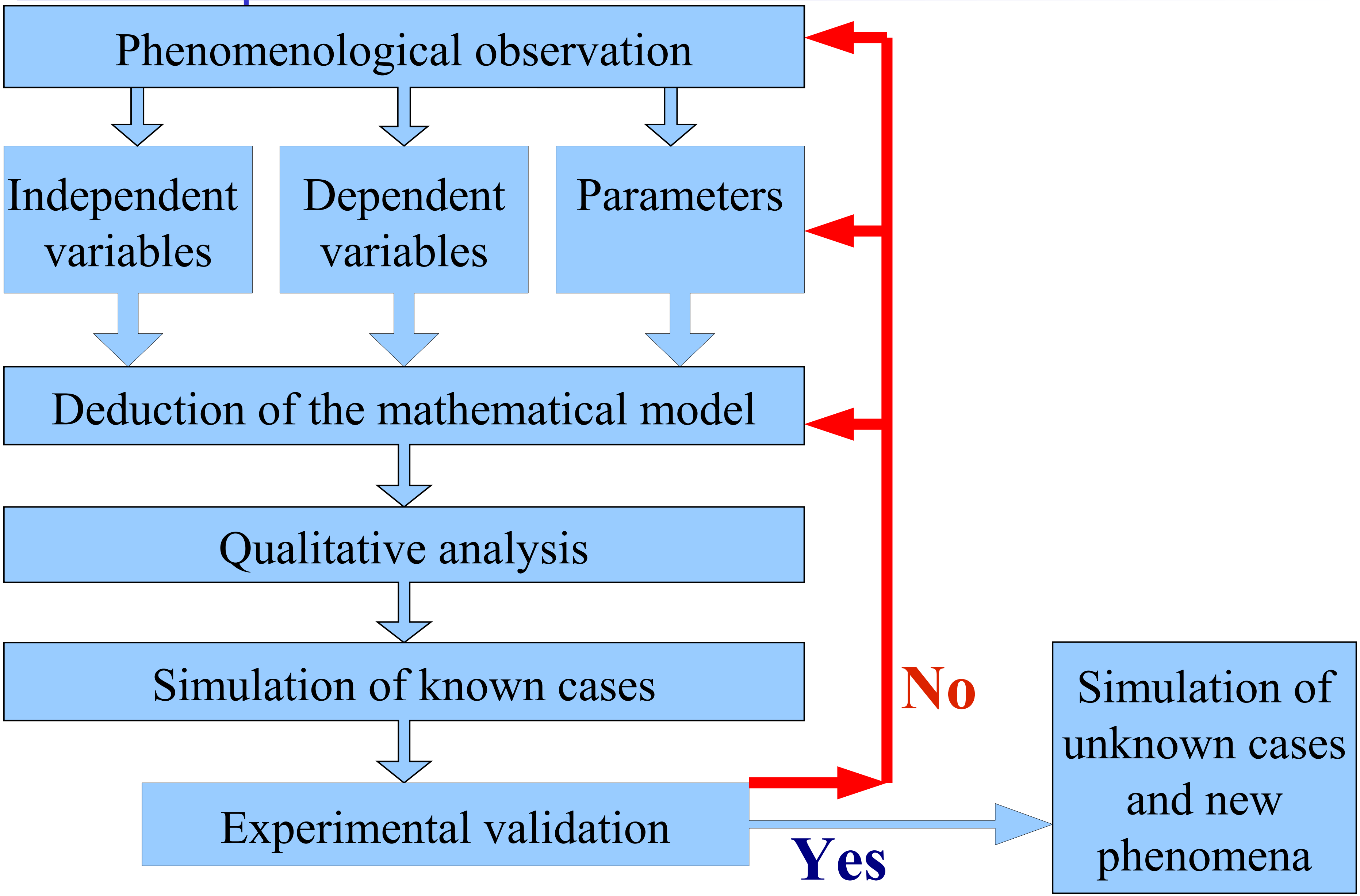


Alan Turing

"All models are a simplification, an idealization, and consequently a falsification, of reality…

…It is to be hoped that the features retained for discussion are those of the greatest importance in the present state of knowledge."

Modelling cycle for medicine



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Choice of variables

Population in a country	→ $N(t)$ o $\rho(t)$
Spatial localization of the population	→ $\rho(\mathbf{x}, t)$
Age-structured population	→ $N(t, a)$
Sexual population	→ $M(t), F(t), B(t), A(t)$
Age-structured sexual population	→ $M(t, a), F(t, a)$

Choice of effects and parameters

Population in a country → N(t) o $\rho(t)$

Natural birth and death rates → Dependence ?

Diffusion of a disease → Another equation for the diffusion of the disease ?

Immigration

Mating → Introducing sex and/or age ?

Spatial localization of the population → $\rho(\mathbf{x}, t)$

Moving → Dependence ?

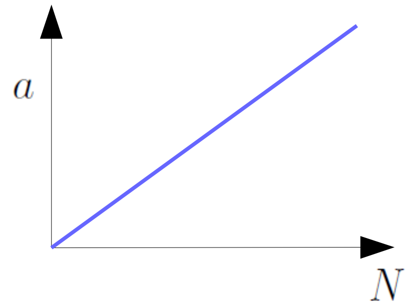
Exponential growth law (1798)

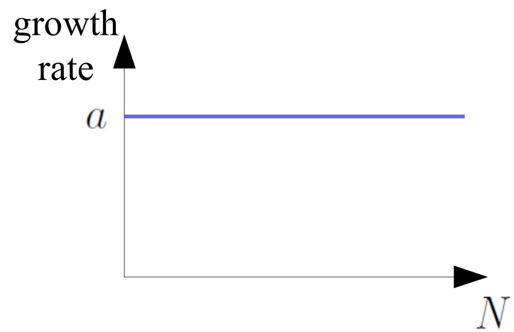
$$\frac{dN}{dt} = \overbrace{\gamma N}^{\text{growth}} - \overbrace{\delta N}^{\text{death}} = \overbrace{aN}^{\text{net growth}}$$

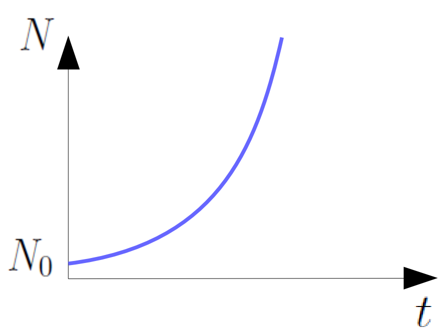
$$\frac{N'}{N} = a$$

growth rate

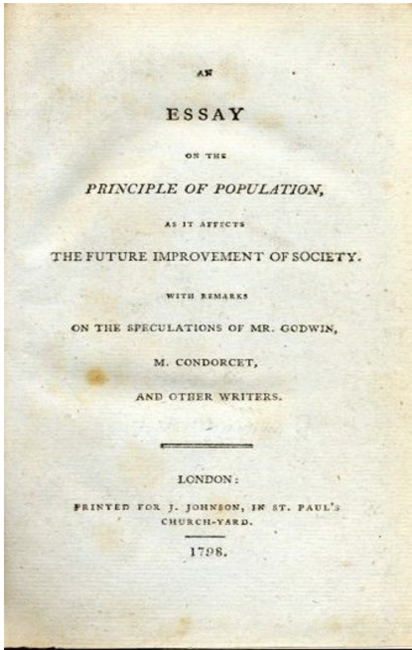
$$N(t) = N_0 e^{at}$$







Malthus



AN

ESSAY

ON THE

PRINCIPLE OF POPULATION,

AS IT AFFECTS

THE FUTURE IMPROVEMENT OF SOCIETY.

WITH REMARKS

ON THE SPECULATIONS OF MR. GODWIN,

M. CONDORCET,

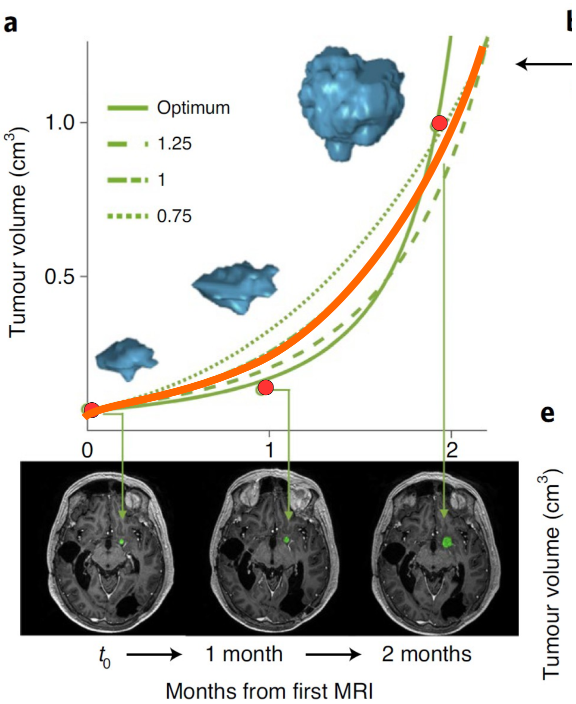
AND OTHER WRITERS.

LONDON:

PRINTED FOR J. JOHNSON, IN ST. PAUL'S CHURCH-YARD.

1798.

Explosive growth



$$\frac{dN}{dt} = aN^{\beta}$$

$$N(t) = \frac{N_0}{\left[1 - (\beta - 1)N_0^{\beta-1}at\right]^{1/(\beta-1)}}$$

Explosive growth

$$\frac{dV}{dt} = \alpha V^{\beta}$$

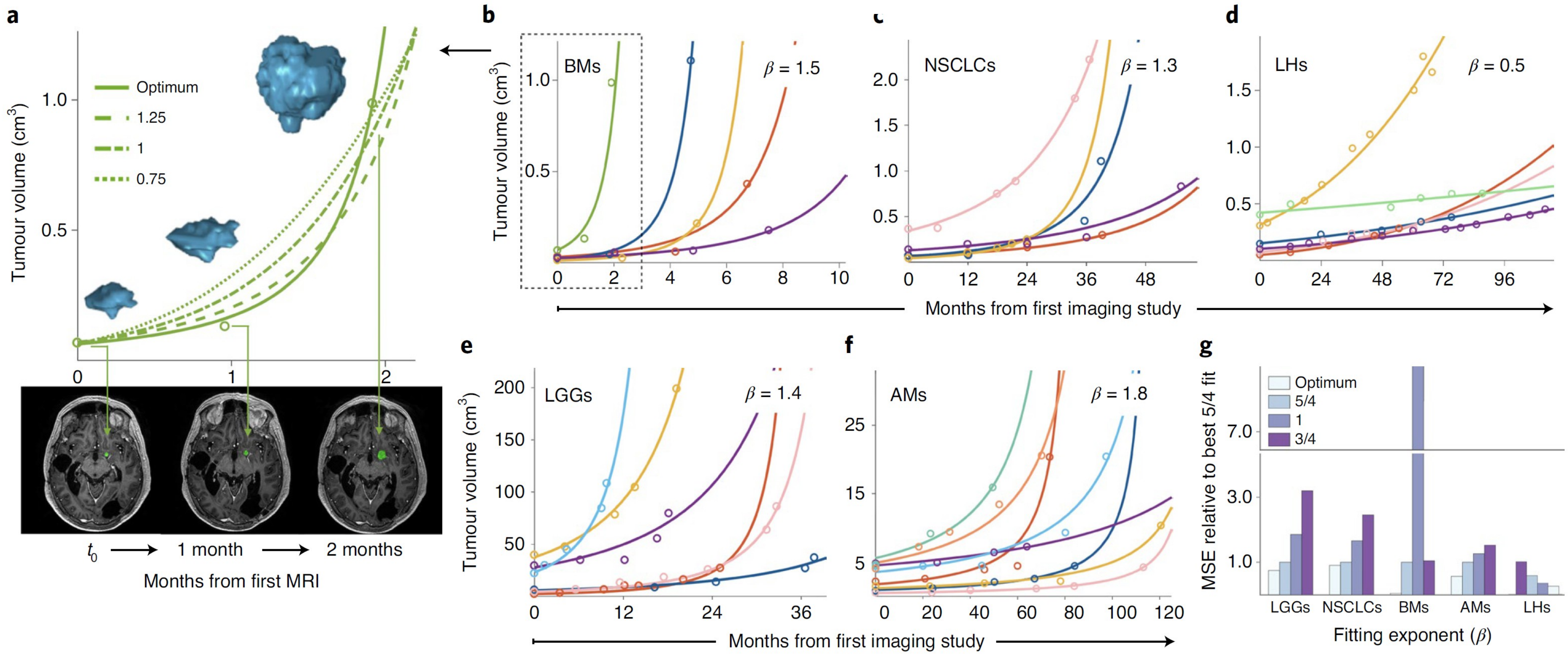


Fig. 2 | Explosive longitudinal volumetric dynamics of untreated malignant human tumours. a–g, Longitudinal volumetric data for patients with untreated brain metastases (BMs, **a**,**b**), low-grade gliomas (LGGs, **e**), NSCLCs (**c**), atypical meningiomas (AMs, **f**) and lung hamartomas (LHs, **d**). Solid curves show the fits with the optimal exponents (β values provided in each part) that give the smallest MSEs. The longitudinal three-dimensional (3D) reconstruction of a BM and representative axial slices highlighting tumour location at three time points are displayed in **a**, together with the fitting curves obtained for different exponents. MSE values for the five datasets and exponents 3/4, 1 and 5/4 (taken as a reference), in comparison with the optimal exponent, are shown in **g**. In **b**–**e**, the colours correspond to different patients.

Explosive growth

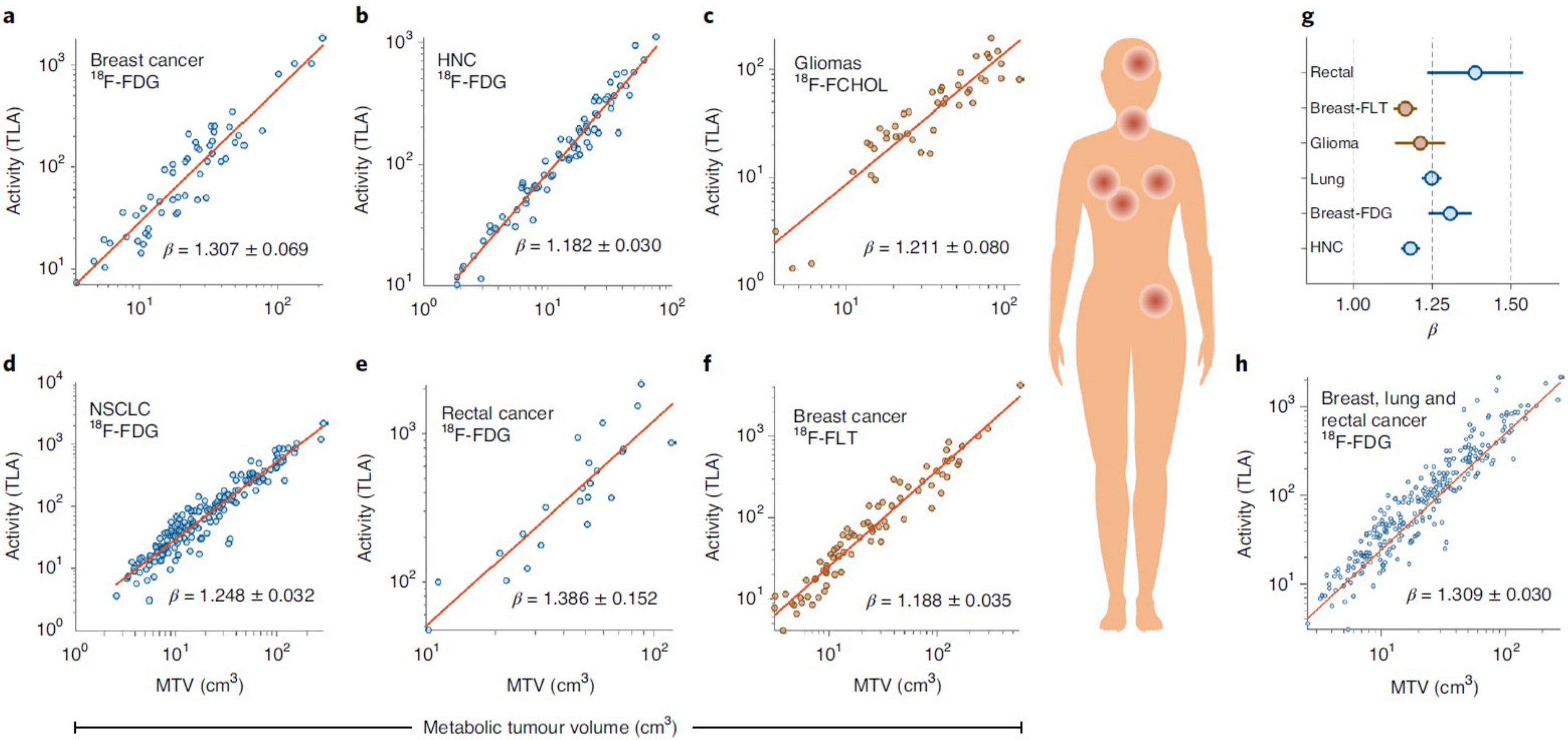
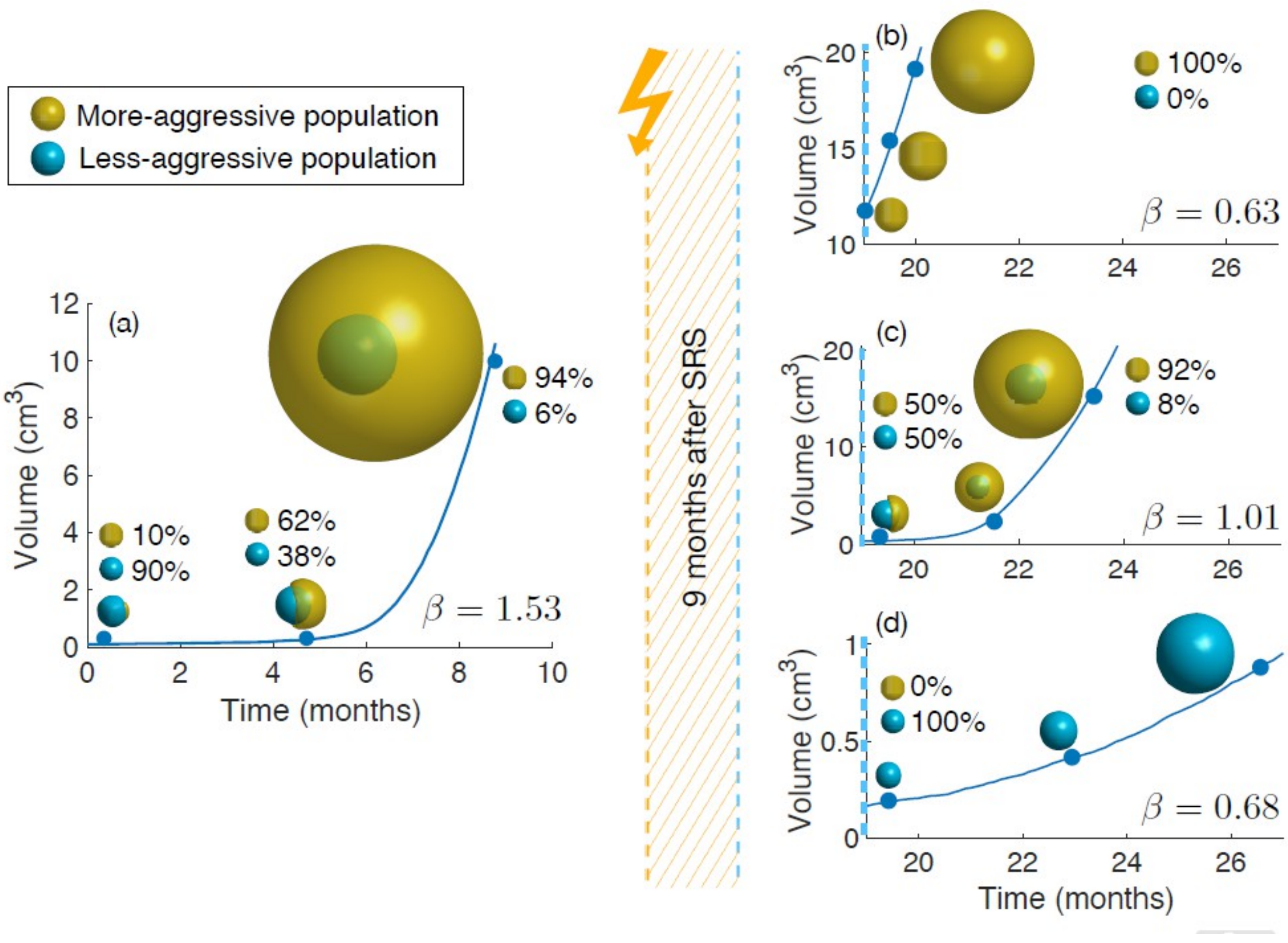
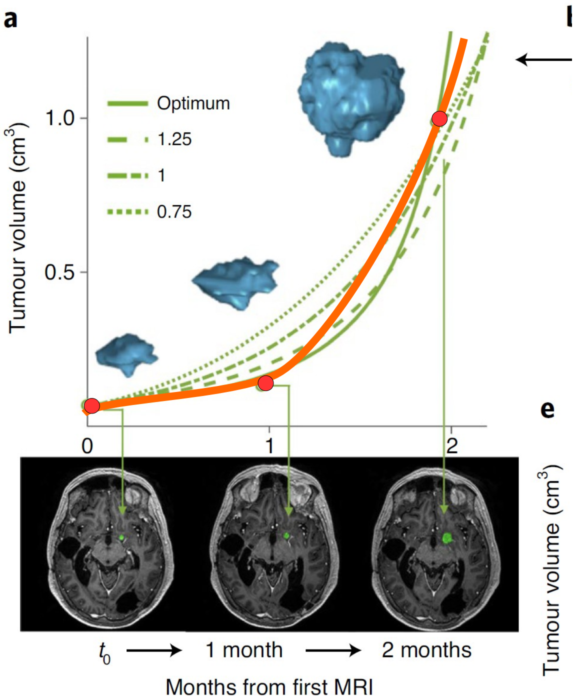


Fig. 1 | A superlinear scaling law governs glucose uptake and proliferation in human cancers. a–h, Log–log plots of TLA versus MTV for different types of cancer. ^{18}F-FDG uptake versus MTV from diagnostic PET for LABC, HNC, NSCLC and RC display superlinear ($\beta > 1$) allometric scaling laws (**a**,**b**,**d**,**e**). Diagnostic PET with proliferation radiotracers, either ^{18}F-FLT for breast cancer (**f**) or ^{18}F-FCHOL for glioma (**c**), shows the same dependence, indicating that glucose is used mostly as a resource for biosynthesis. The fitted exponents cluster around $\beta = 5/4$ (**g**). Records of patients imaged at the same institution with an identical protocol (breast-FDG, lung and rectal cancers) show that a common scaling law governs the dynamics (**h**). Error bars in (**g**) correspond to the standard error (s.d.) in the fitted parameter β obtained using fitlm.

Why faster than exponential?



Two populations



$$\begin{cases} \dfrac{dN}{dt} = aN - bN \\ \dfrac{dM}{dt} = bN + cM \end{cases}$$

$$N_{tot}(t) = N(t) + M(t) = \frac{N_0}{b+c-a}\left[e^{ct} + (c-a)e^{(a-b)t}\right]$$

$$\frac{dN}{dt} = a(t)N$$

If $a(t) = at$ $\quad N = N_0 e^{at^2/2}$

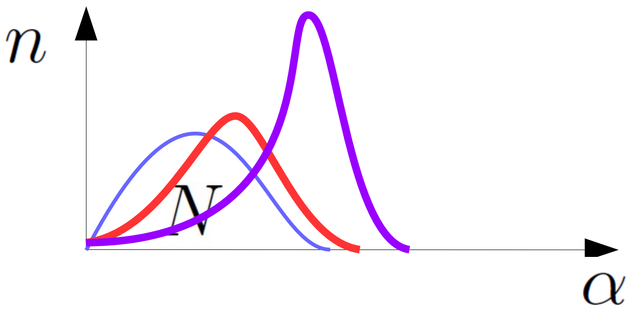
Internal phenotype

$$\begin{cases} \dfrac{dN}{dt} = a(u)N \\ \\ \dfrac{du}{dt} = b(t,u) \end{cases}$$

aggressivity

$$n = n(t, \alpha)$$

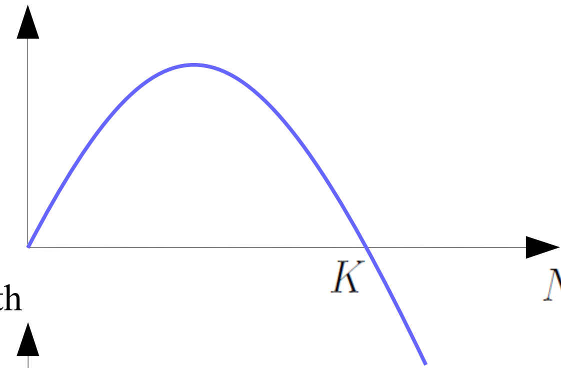
$$N(t) = \int_0^{+\infty} n(t,\alpha)\, d\alpha$$



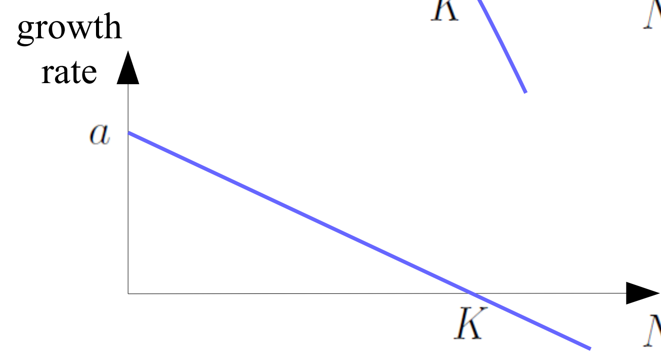
$$\frac{\partial n}{\partial t} = \epsilon \frac{\partial^2 n}{\partial \alpha^2} + \gamma(\alpha, N)n - \delta(\alpha, N)n$$

Logistic growth law (1838)

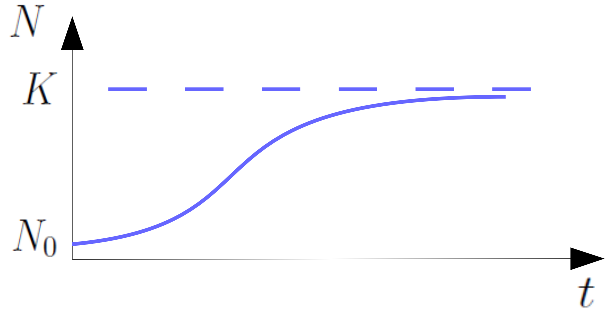
$$\frac{dN}{dt} = a\left(1 - \frac{N}{K}\right)N$$



$$\frac{N'}{N} = a\left(1 - \frac{N}{K}\right)$$



$$N(t) = \frac{K N_0}{N_0 + (K - N_0)e^{-at}}$$



Verhulst

Si la population croissait en progression géométrique, nous aurions l'équation $\frac{dp}{dt} = mp$. Mais comme la vitesse d'accroissement de la population est retardée par l'augmentation même du nombre des habitans, nous devrons retrancher de mp une fonction inconnue de p; de manière que la formule à intégrer deviendra

$$\frac{dp}{dt} = mp - \varphi(p).$$

L'hypothèse la plus simple que l'on puisse faire sur la forme de la fonction φ, est de supposer $\varphi(p) = np^2$. On trouve alors pour intégrale de l'équation ci-dessus

$$t = \frac{1}{m}\left[\log. p - \log.(m - np)\right] + \text{constante},$$

et il suffira de trois observations pour déterminer les deux coefficiens constans m et n et la constante arbitraire.

En résolvant la dernière équation par rapport à p, il vient

$$p = \frac{mp' e^{mt}}{np' e^{mt} + m - np'} \quad \ldots\ldots \quad (1)$$

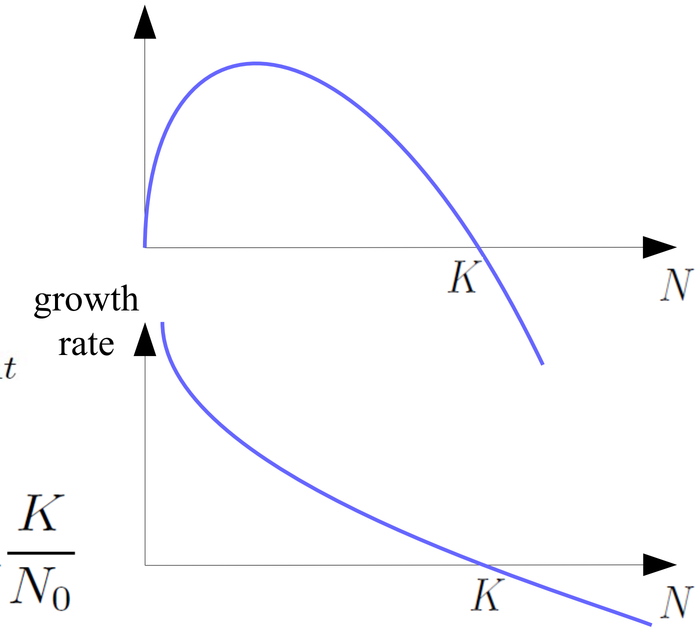
en désignant par p' la population qui répond à $t = o$, et par e la base des logarithmes népériens. Si l'on fait $t = \infty$, on voit que la valeur de p correspondante est $P = \frac{m}{n}$. Telle est donc *la limite supérieure de la population.*

Gompertz growth law (1825)

$$\frac{dN}{dt} = A \ln\left(\frac{K}{N}\right) N$$

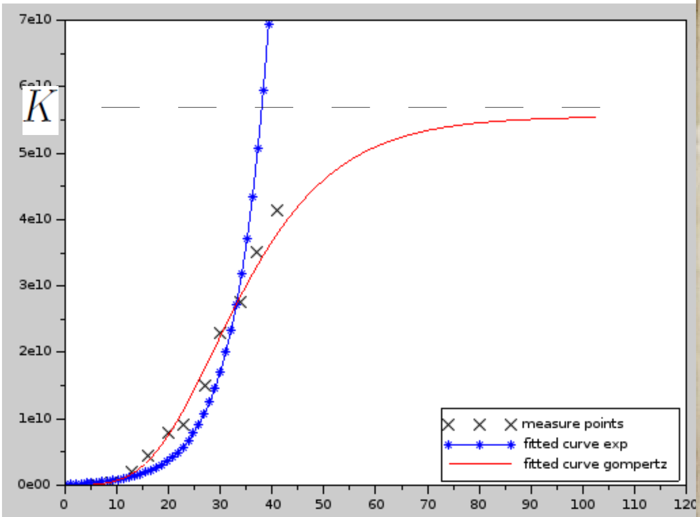
$$\frac{N'}{N} = A \ln\left(\frac{K}{N}\right) = \mu e^{-At}$$

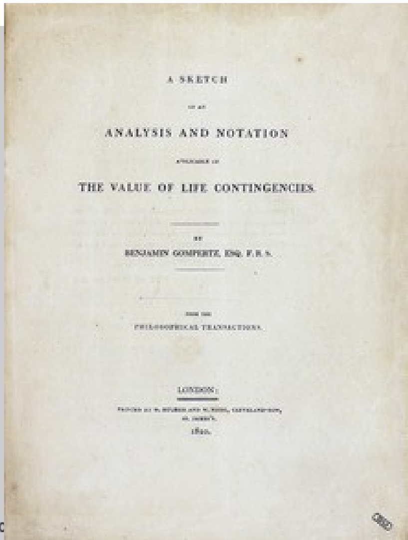
$$\mu = A \ln \frac{K}{N_0}$$



Gompertz

$$N(t) = N_0 \exp\left[\frac{\mu}{A}\left(1 - e^{-At}\right)\right]$$




A SKETCH

ANALYSIS AND NOTATION

THE VALUE OF LIFE CONTINGENCIES.

BENJAMIN GOMPERTZ, ESQ. F.R.S.

PHILOSOPHICAL TRANSACTIONS.

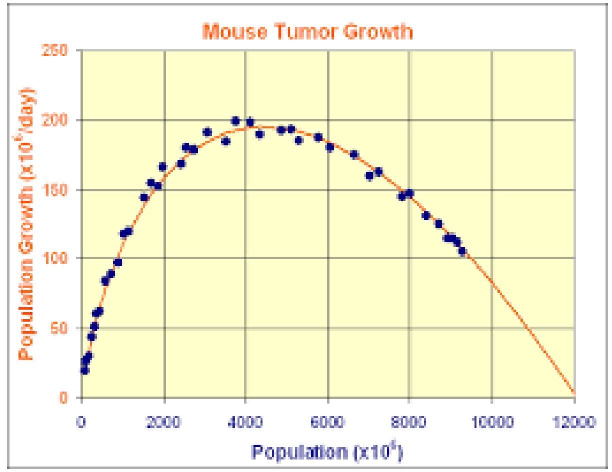
LONDON:

Gompertz growth law (1825)

$$\frac{dN}{dt} = A \ln\left(\frac{K}{N}\right) N$$

$$\frac{N'}{N} = A \ln\left(\frac{K}{N}\right) = \mu e^{-At}$$

$$\mu = A \ln \frac{K}{N_0}$$



Gompertz

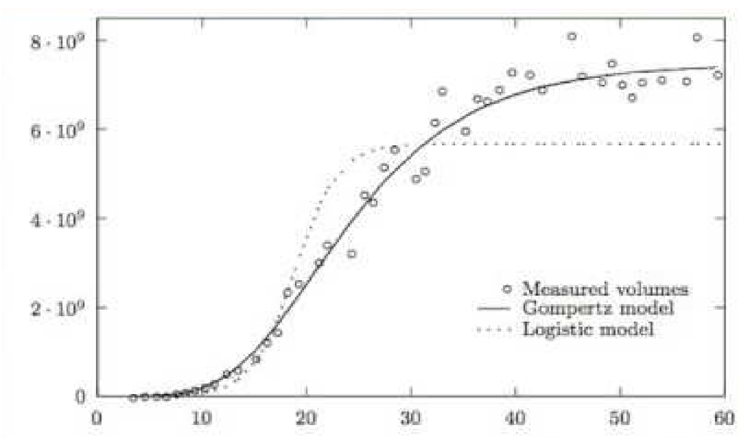
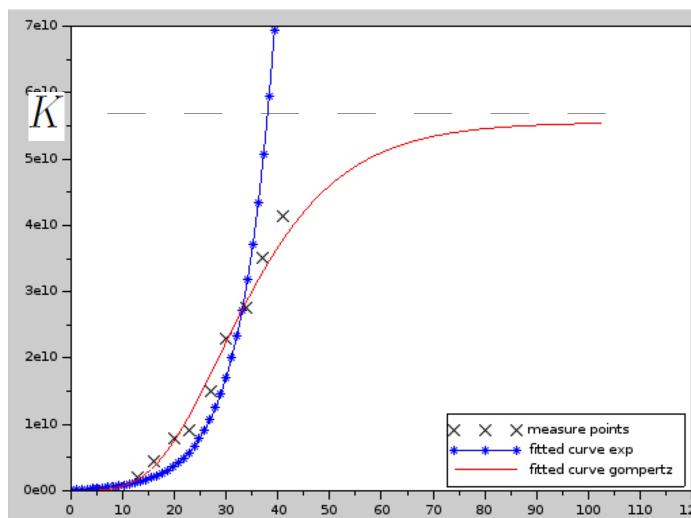
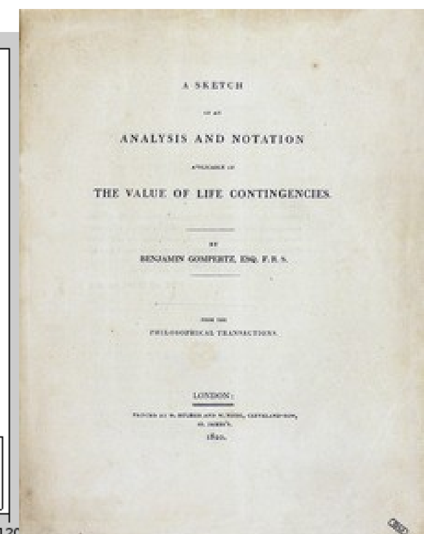


Figure 4. *Best-fit curves by Gompertz and logistic models (volumes in μm^3 vs. time in days)*





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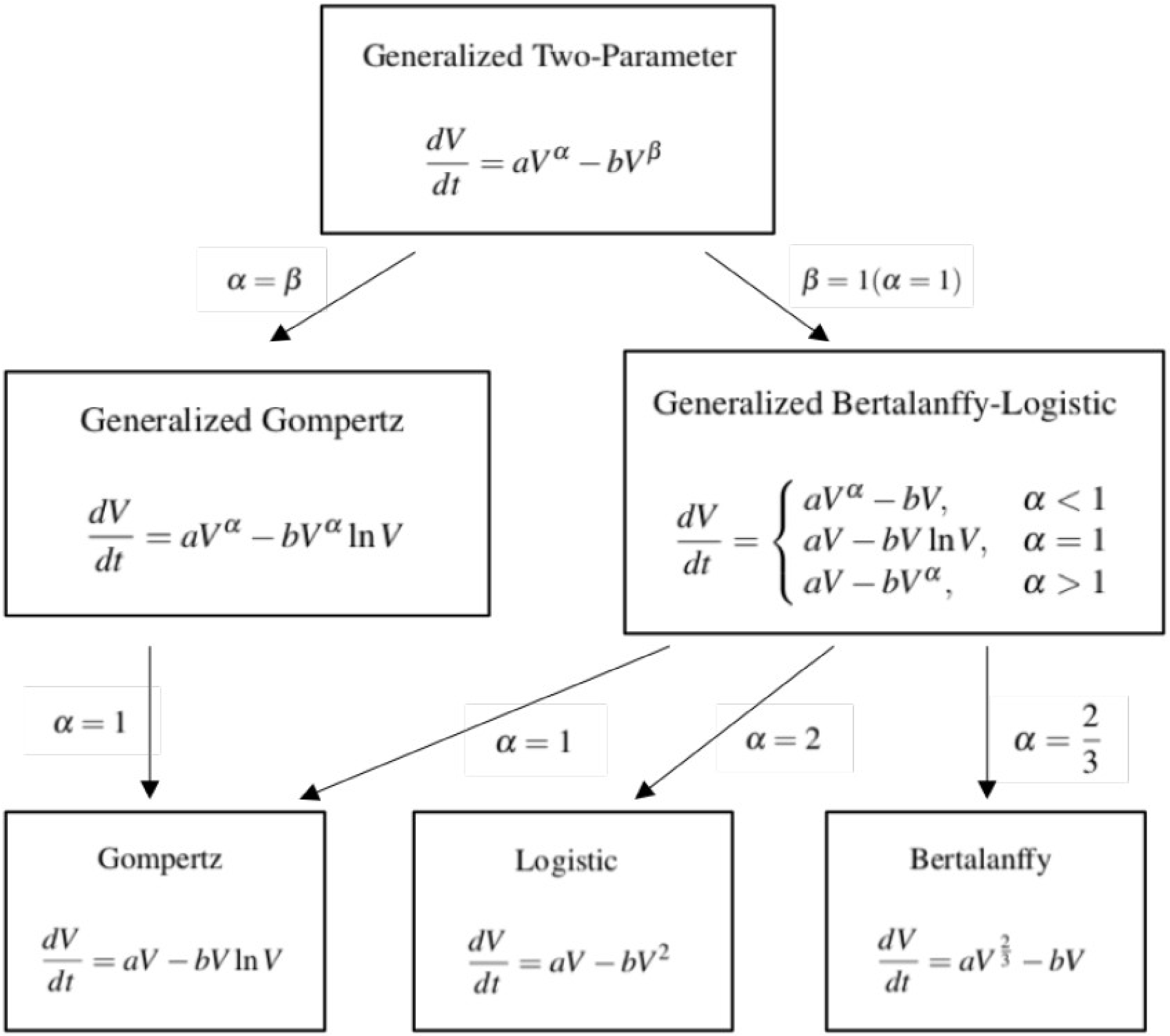
Other growth laws

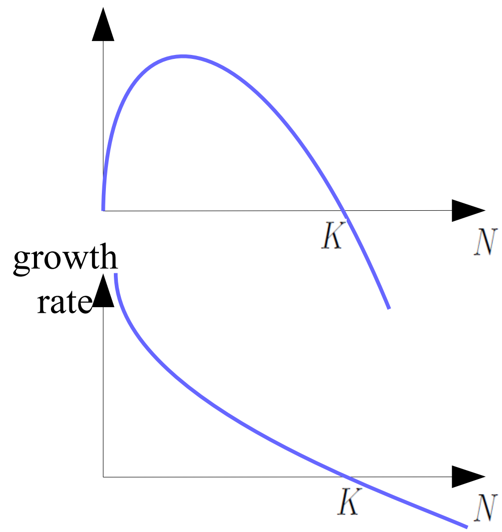


Other growth laws

von Bertalanffy (1949)

$$\frac{dN}{dt} = a\left[\left(\frac{K}{N}\right)^{1/3} - 1\right] N$$

$$\frac{N'}{N} = a\left[\left(\frac{K}{N}\right)^{1/3} - 1\right]$$



West (1997)

$$\frac{dN}{dt} = a\left[\left(\frac{K}{N}\right)^{1/4} - 1\right] N$$

$$\frac{N'}{N} = a\left[\left(\frac{K}{N}\right)^{1/4} - 1\right]$$