

Supplementary Figures

Supplementary figure 1: plot of all tumor volumes for double and single (control) tumor groups

Supplementary figure 2: single tumor model fit. Exponential model

Supplementary figure 3: single tumor model fit. Gompertz model

Supplementary figure 4: single tumor model fit. Power law model

Supplementary figure 5: single tumor growth models: delay analysis

Supplementary figure 6: double-tumors growth models fits. Competition model

Supplementary figure 7: double-tumors growth models fits. Angiogenesis inhibition (SIA)

Supplementary figure 8: double-tumors growth models fits. Proliferation inhibition. Log-kill effect

Supplementary figure 9: double-tumors growth models fits. Proliferation inhibition. $(P_i + Q_i)$ as source of IFs

Supplementary figure 10: residuals analysis of the other models

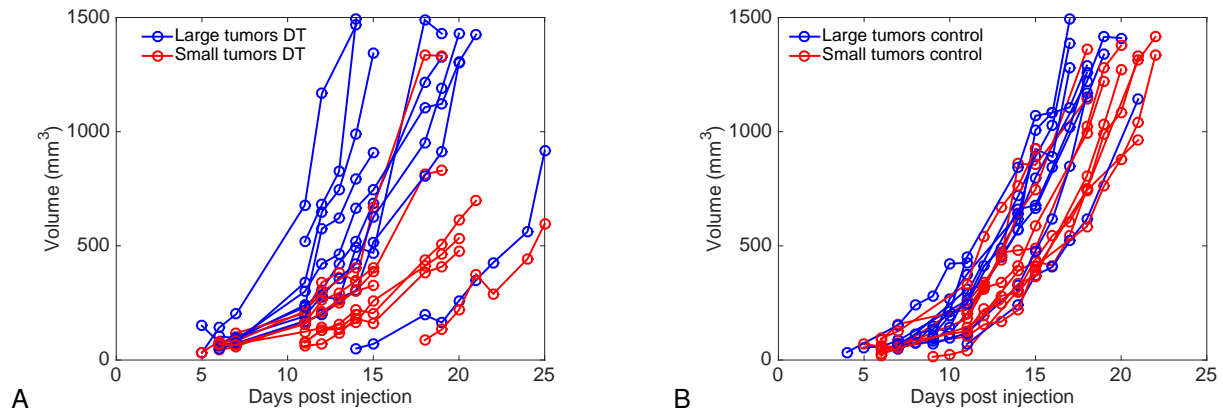
Supplementary figure 11: additional fits of 10 remaining animals of the control group under the “proliferation inhibition” model

Supplementary table 1: models equations

Supplementary table 2: goodness-of-fit metrics of these three single tumor growth models.

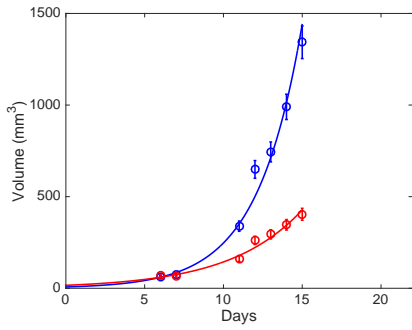
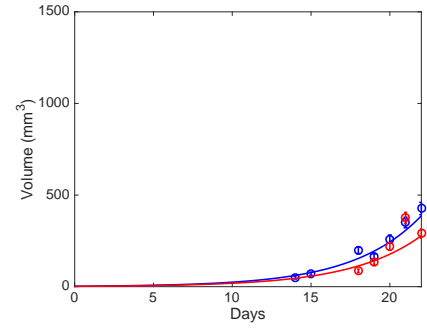
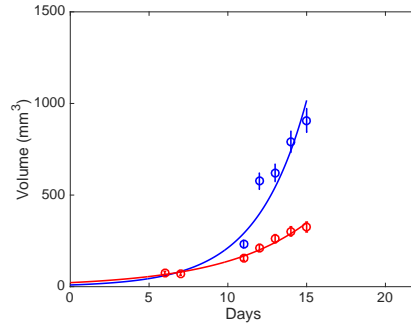
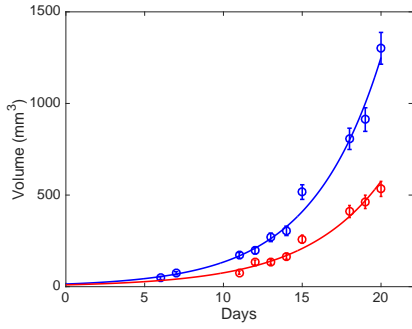
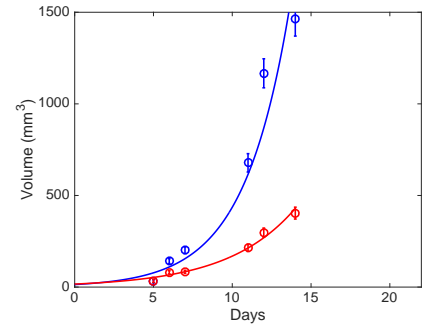
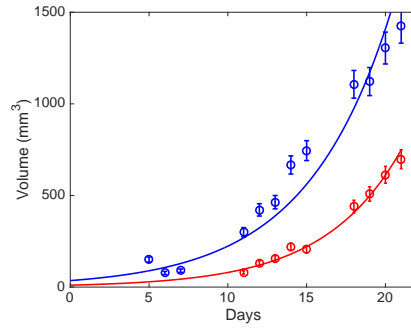
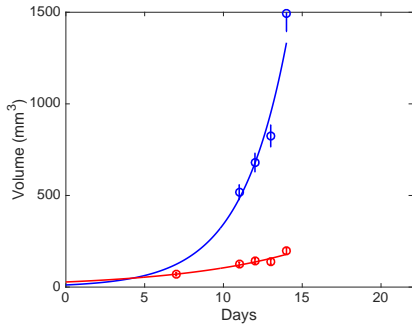
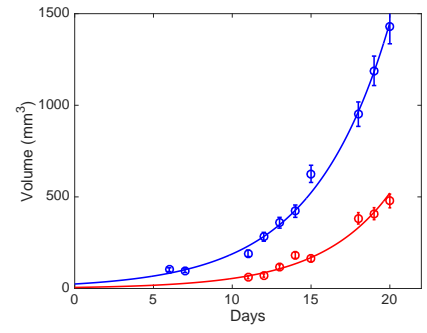
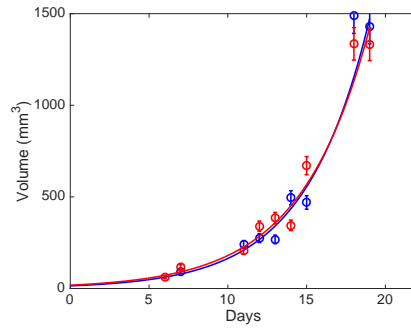
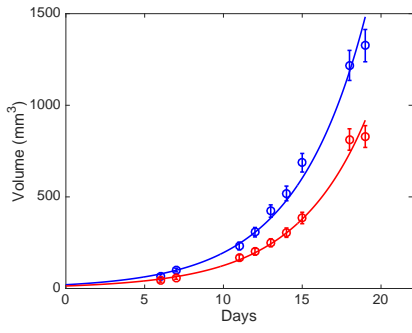
Supplementary table 3: parameter values and identifiability of the Gompertz, power law and “proliferation inhibition” model for the single tumor growth fits

Supplementary figure 1: plot of all tumor volumes for double and single (control) tumor groups

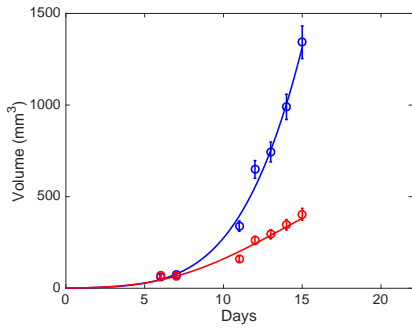
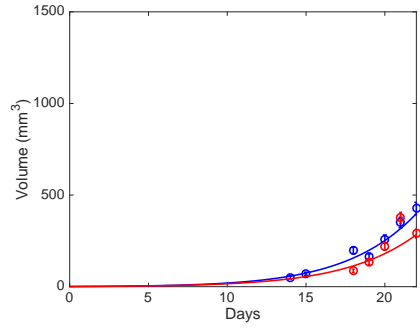
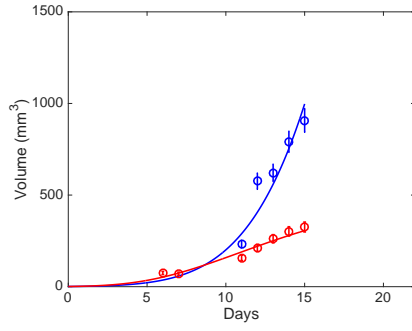
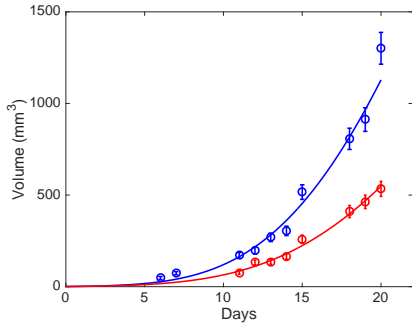
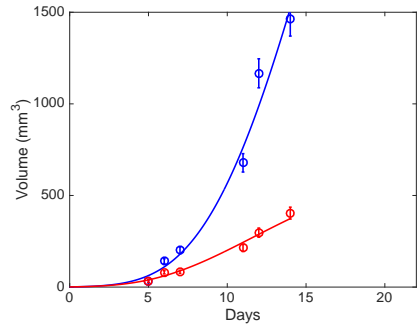
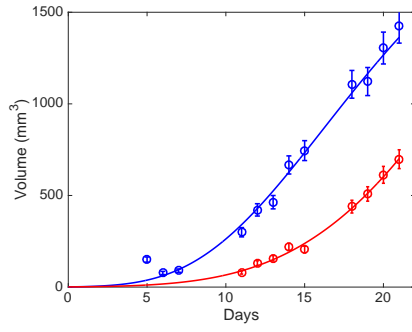
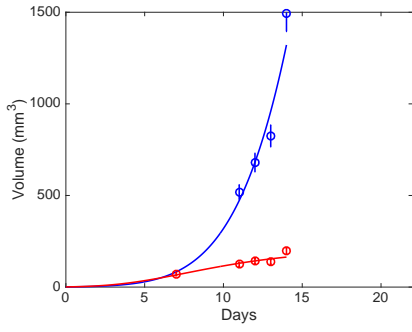
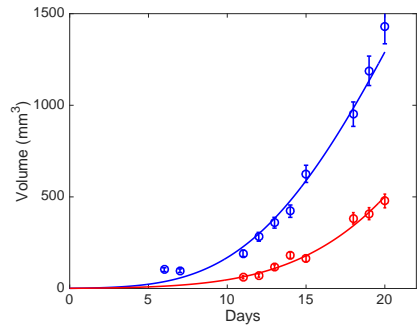
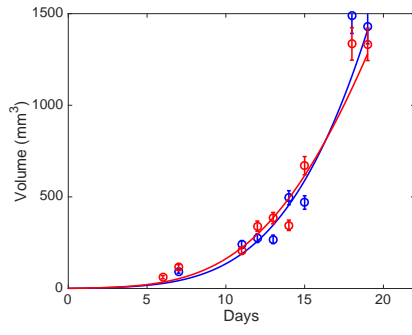
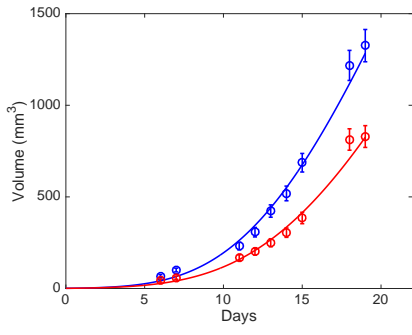


Growth curves were plotted and distinguished between large and small tumors for the double (A) and single (control) (B) groups. In the second case, artificial pairings were considered between tumors of the control group to determine large and small tumors that would have occurred by randomness only (i.e. under independent growth conditions). DT = double tumors group

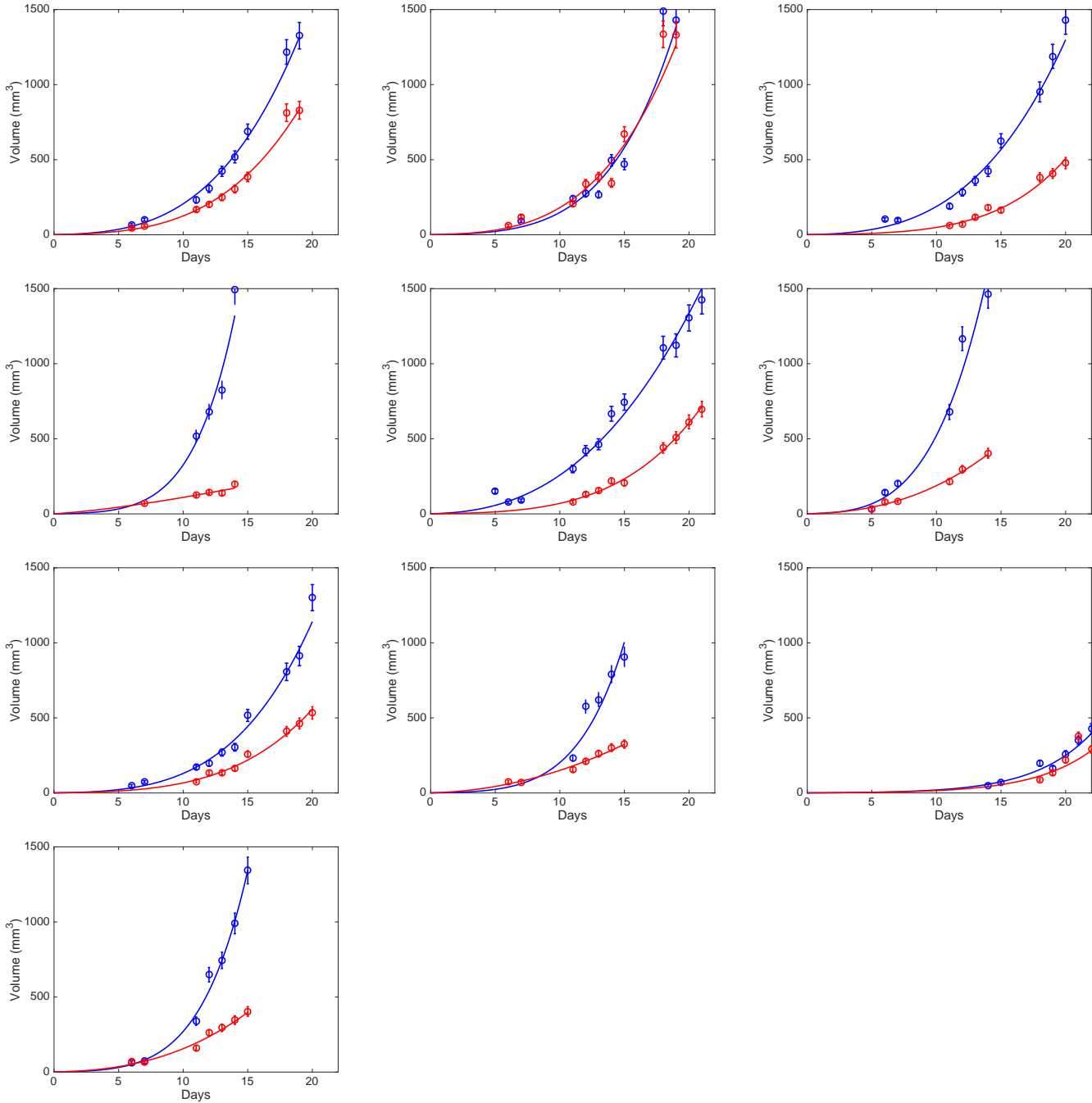
Supplementary figure 2: single tumor model fit. Exponential model



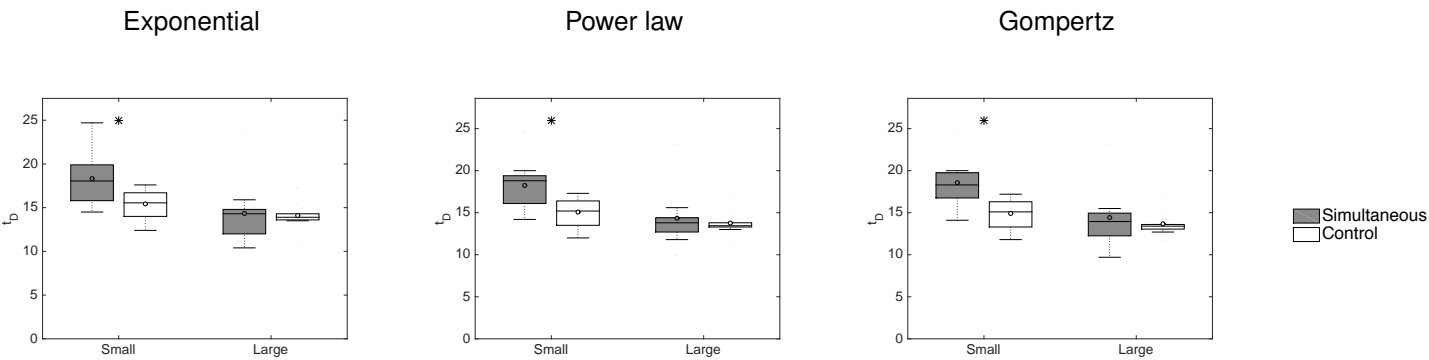
Supplementary figure 3: single tumor model fit. Gompertz model



Supplementary figure 4: single tumor model fit. Power law model



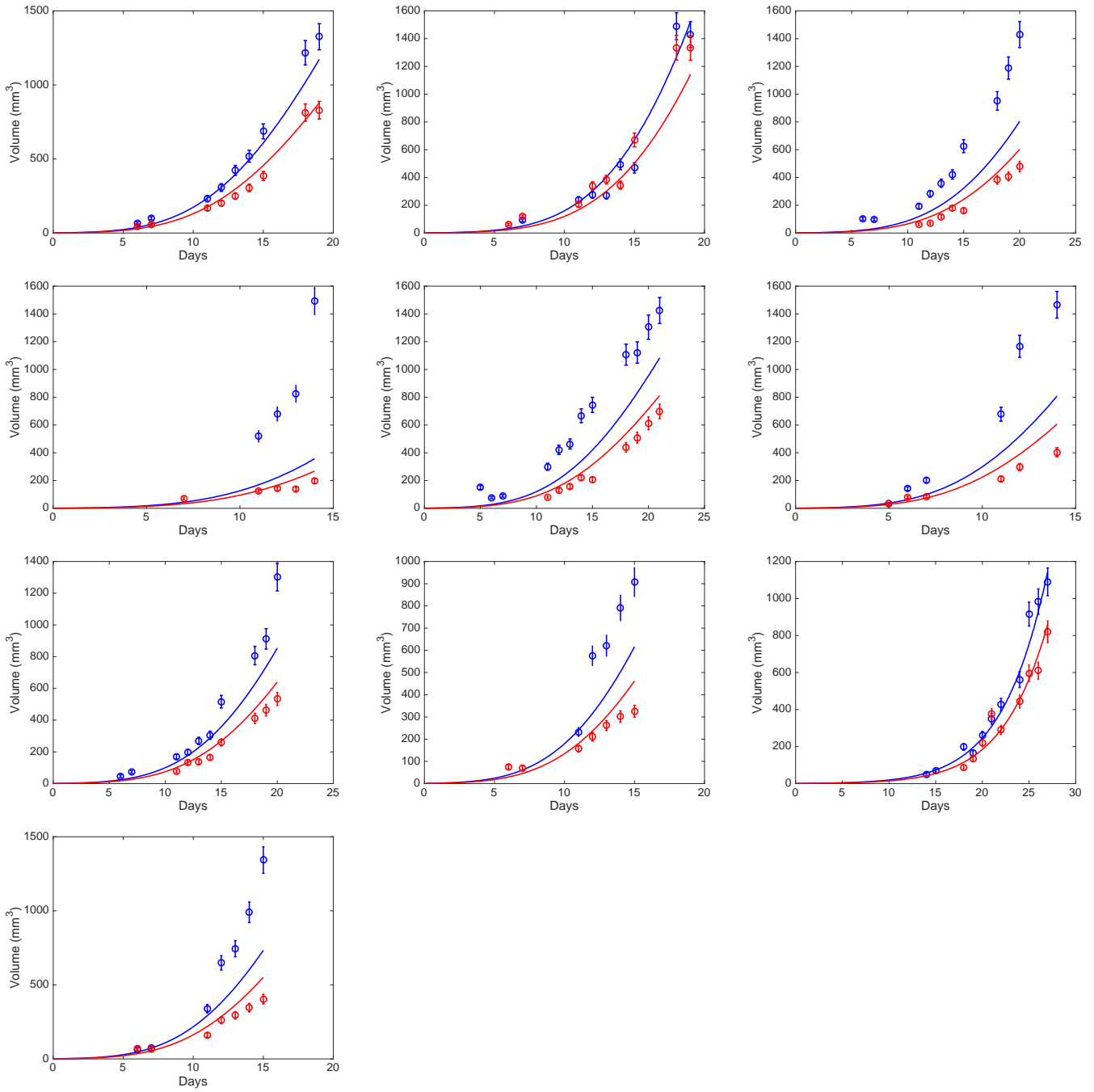
Supplementary figure 5: single tumor growth models: delay analysis



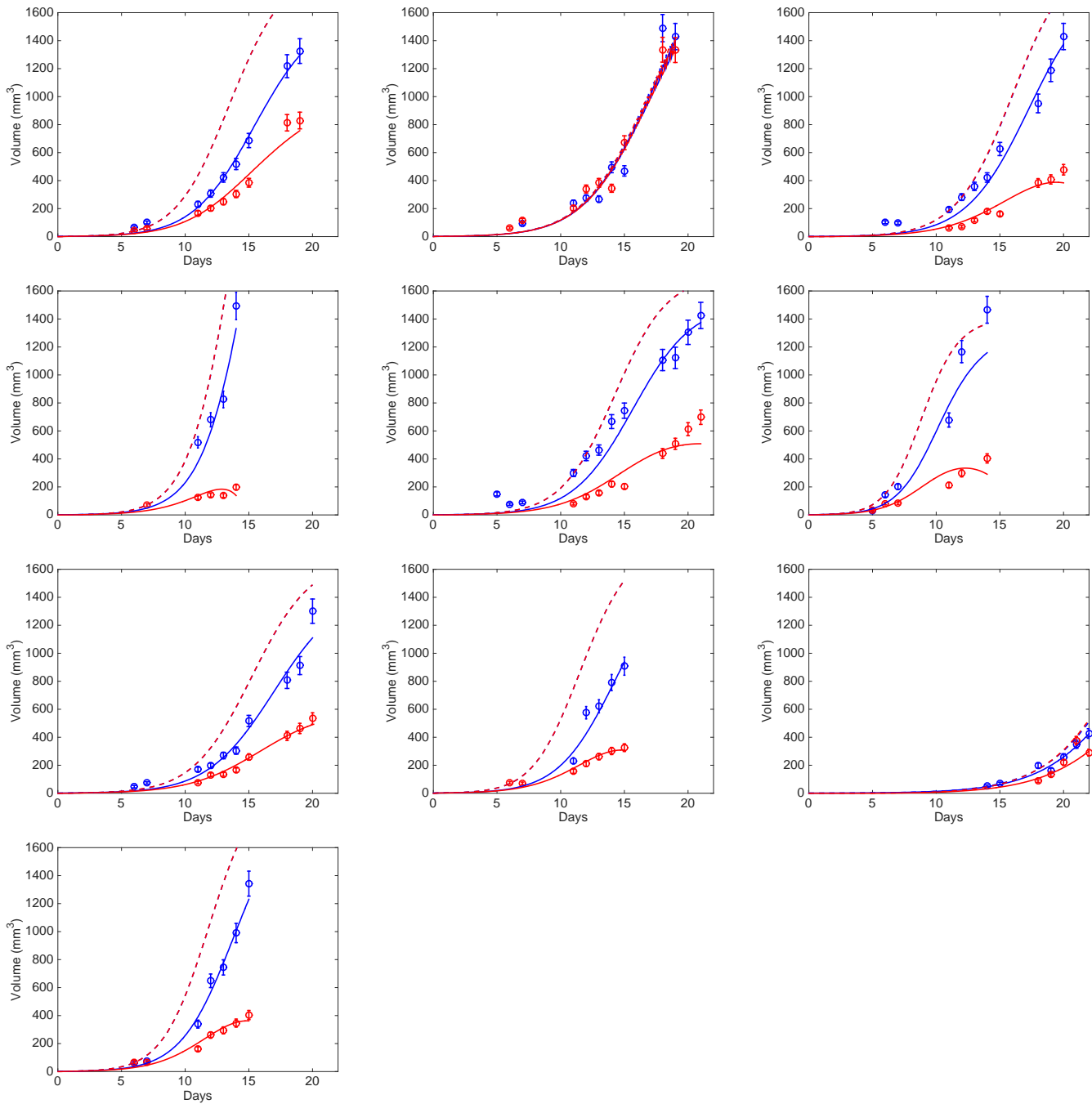
Time t_D to reach a threshold volume $V_D = 500 \text{ mm}^3$ for growth extrapolated from the fitted models.

* = $p < 0.05$, Student's t-test with unequal variance.

Supplementary figure 6: double-tumors growth models fits. Competition model

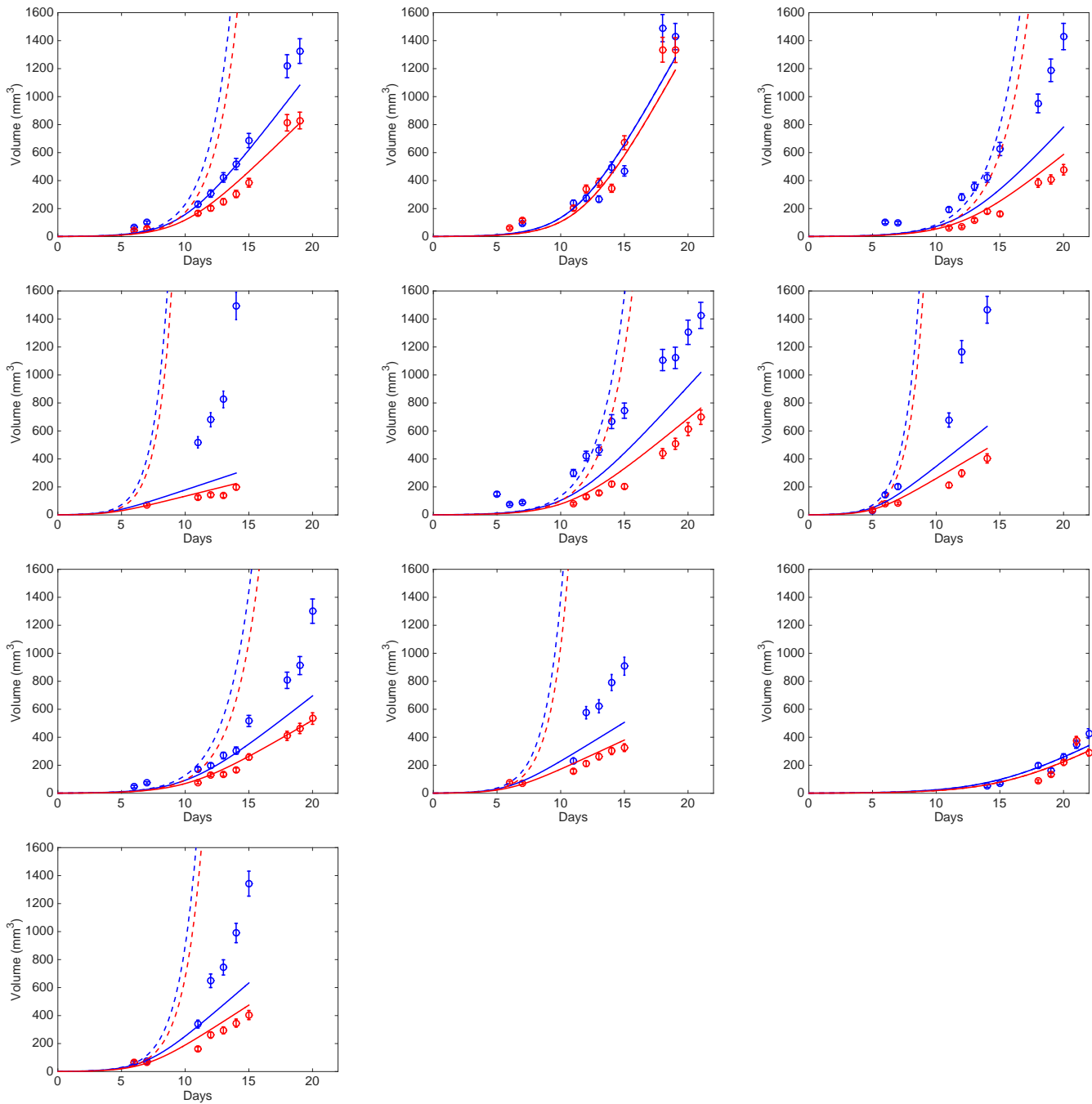


Supplementary figure 7: double-tumors growth models fits. Angiogenesis inhibition (SIA)



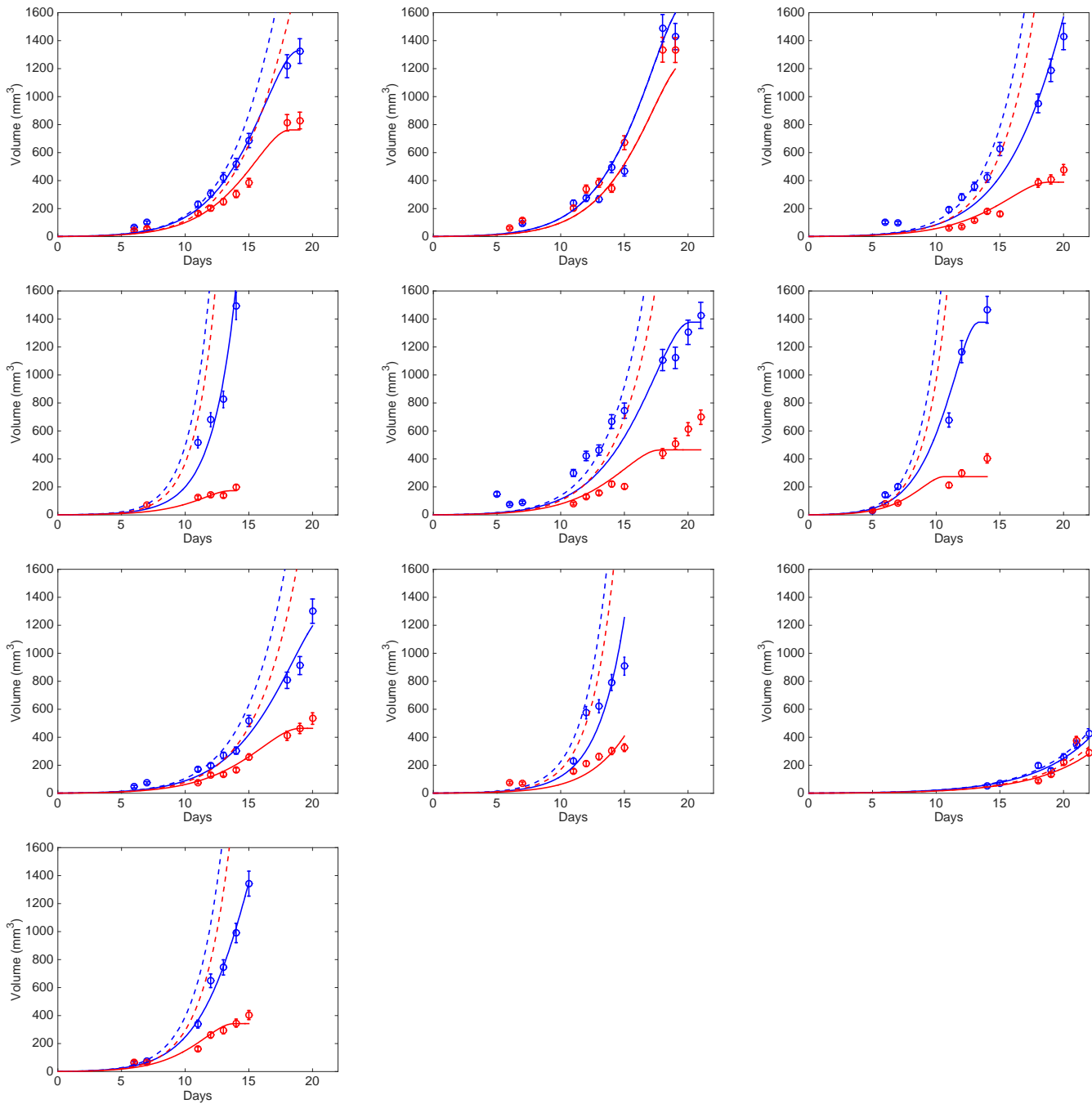
Dashed lines are simulations with no interactions between the two tumors, i.e. with the parameters inferred from the fits except for parameter e set to zero. Growth differences are only due to the difference in initial condition.

Supplementary figure 8: double-tumors growth models fits. Proliferation inhibition. Log-kill effect



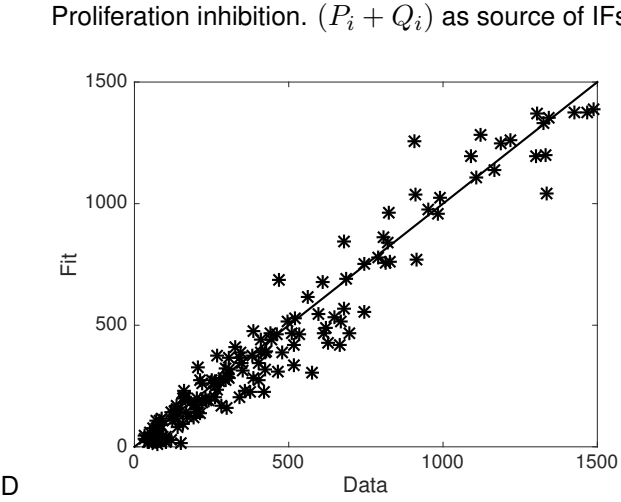
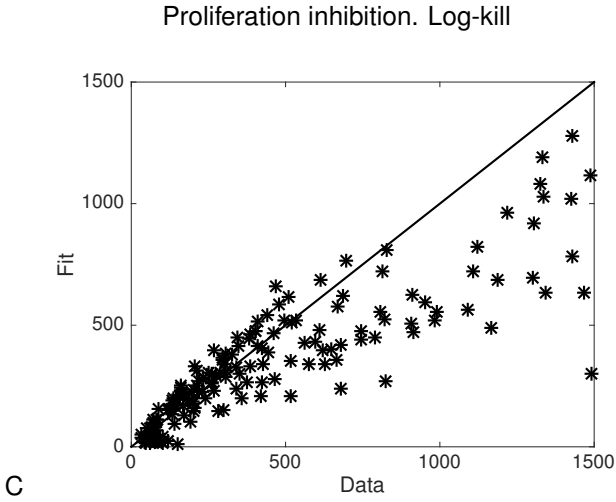
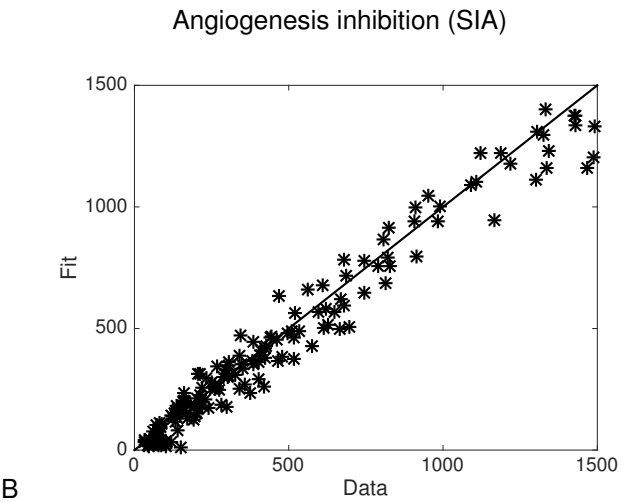
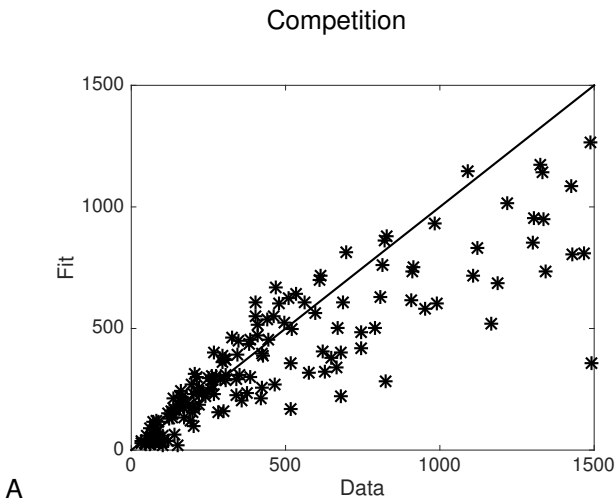
Dashed lines are simulations with no interactions between the two tumors. Growth differences are only due to the difference in initial condition.

Supplementary figure 9: double-tumors growth models fits. Proliferation inhibition. ($P_i + Q_i$) as source of IFs

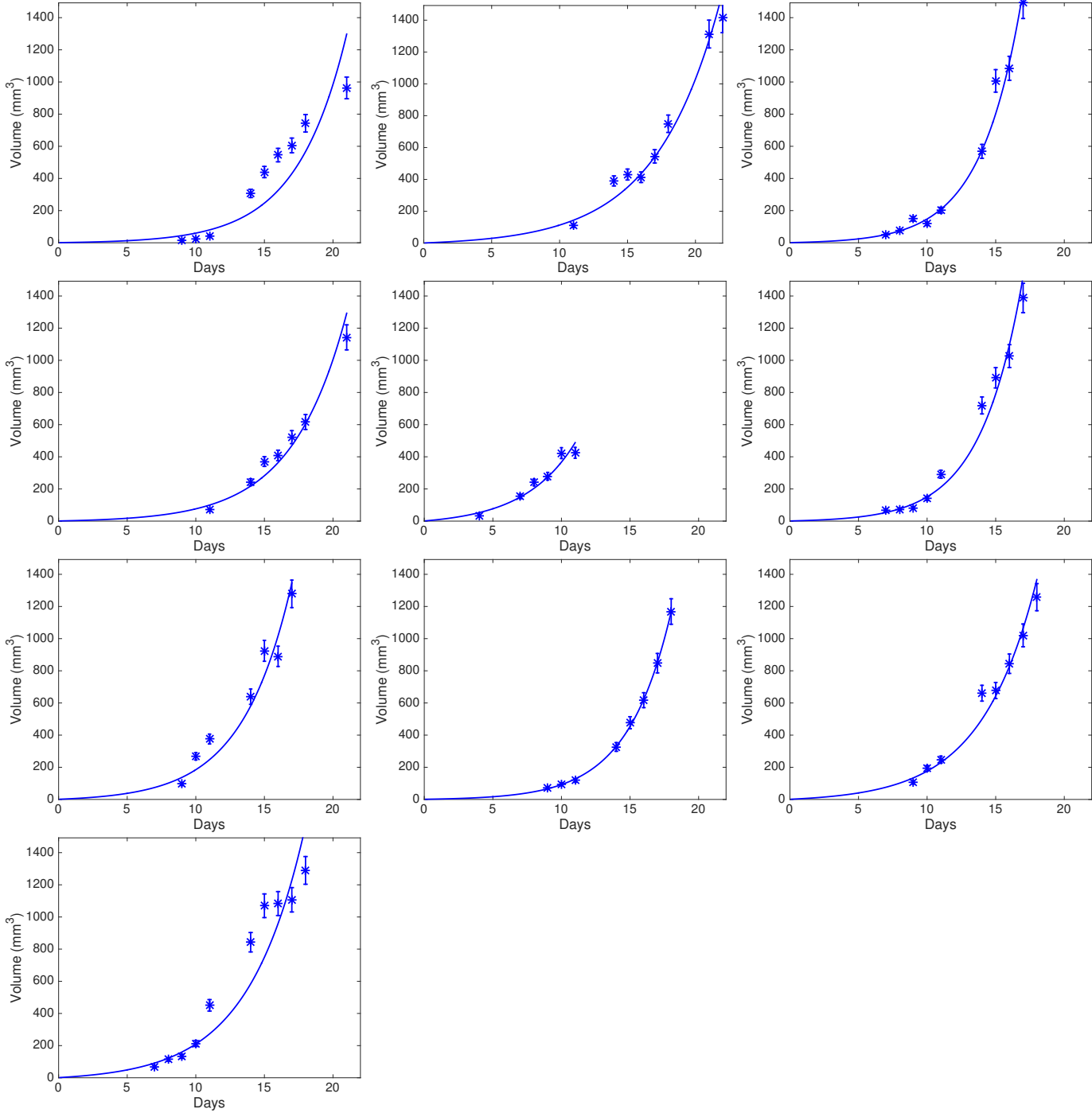


Dashed lines are simulations with no interactions between the two tumors. Growth differences are only due to the difference in initial condition.

Supplementary figure 10: residuals analysis of the other models



Supplementary figure 11: additional fits of 10 remaining animals of the control group under the “proliferation inhibition” model



Supplementary table 1: models equations

Model name	Equations
Competition	$\begin{cases} \frac{dV_1}{dt} = aV_1 \ln\left(\frac{K}{V_1+V_2}\right) & V_1(t=0) = V_{0,1} \\ \frac{dV_2}{dt} = aV_2 \ln\left(\frac{K}{V_1+V_2}\right) & V_2(t=0) = V_{0,2} \end{cases}$
Angiogenesis inhibition	$\begin{cases} \frac{dV_1}{dt} = aV_1 \ln\left(\frac{K_1}{V_1}\right) & V_1(t=0) = V_{0,1} \\ \frac{dK_1}{dt} = bK_1 - dV_1^{2/3}K_1 - eV_2\mathbb{1}_{K_1>K_0} & K_1(t=0) = K_0 \\ \frac{dV_2}{dt} = aV_2 \ln\left(\frac{K_2}{V_2}\right) & V_2(t=0) = V_{0,2} \\ \frac{dK_2}{dt} = bK_2 - dV_2^{2/3}K_2 - eV_1\mathbb{1}_{K_2>K_0} & K_2(t=0) = K_0 \end{cases}$
Proliferation inhibition	$\begin{cases} \frac{dP_1}{dt} = \alpha P_1 - (\beta P_1 + \gamma(P_1 + P_2))\mathbb{1}_{P_1>0} & P_1(t=0) = V_{0,1} \\ \frac{dQ_1}{dt} = (\beta P_1 + \gamma(P_1 + P_2))\mathbb{1}_{P_1>0} & Q_1(t=0) = 0 \\ V_1 = P_1 + Q_1 \\ \frac{dP_2}{dt} = \alpha P_2 - (\beta P_2 + \gamma(P_1 + P_2))\mathbb{1}_{P_2>0} & P_2(t=0) = V_{0,2} \\ \frac{dQ_2}{dt} = (\beta P_2 + \gamma(P_1 + P_2))\mathbb{1}_{P_2>0} & Q_2(t=0) = 0 \\ V_2 = P_2 + Q_2 \end{cases}$
Proliferation inhibition (log-kill)	$\begin{cases} \frac{dP_1}{dt} = \alpha P_1 - (\beta P_1 + \gamma(P_1 + P_2))P_1 & P_1(t=0) = V_{0,1} \\ \frac{dQ_1}{dt} = (\beta P_1 + \gamma(P_1 + P_2)) & Q_1(t=0) = 0 \\ V_1 = P_1 + Q_1 \\ \frac{dP_2}{dt} = \alpha P_2 - (\beta P_2 + \gamma(P_1 + P_2))P_2 & P_2(t=0) = V_{0,2} \\ \frac{dQ_2}{dt} = (\beta P_2 + \gamma(P_1 + P_2)) & Q_2(t=0) = 0 \\ V_2 = P_2 + Q_2 \end{cases}$

Model name	Equations
Proliferation inhibition ($P+Q$)	$\left\{ \begin{array}{l} \frac{dP_1}{dt} = \alpha P_1 - (\beta V_1 + \gamma (V_1 + V_2)) \mathbb{1}_{P_1 > 0} \quad P_1(t=0) = V_{0,1} \\ \frac{dQ_1}{dt} = (\beta V_1 + \gamma (V_1 + V_2)) \mathbb{1}_{P_1 > 0} \quad Q_1(t=0) = 0 \\ V_1 = P_1 + Q_1 \\ \frac{dP_2}{dt} = \alpha P_2 - (\beta V_2 + \gamma (V_1 + V_2)) \mathbb{1}_{P_2 > 0} \quad P_2(t=0) = V_{0,2} \\ \frac{dQ_2}{dt} = (\beta V_2 + \gamma (V_1 + V_2)) \mathbb{1}_{P_2 > 0} \quad Q_2(t=0) = 0 \\ V_2 = P_2 + Q_2 \end{array} \right.$

Supplementary table 2: goodness-of-fit metrics of these three single tumor growth models.

Model	SSE	AIC	RMSE	R2	p
Power law	0.117(0.0158 - 0.713)[1]	-12.3(-34.5 - 2.95)[1]	0.4(0.145 - 0.957)[2]	0.983(0.784 - 0.998)[2]	
Gompertz	0.121(0.019 - 0.67)[2]	-11.6(-32.4 - 2.39)[2]	0.394(0.159 - 0.928)[1]	0.984(0.815 - 0.997)[1]	
Proliferation inhibition	0.159(0.00741 - 0.883)[3]	-10.1(-33.2 - 4.88)[3]	0.45(0.0994 - 1.07)[3]	0.966(0.7 - 0.999)[3]	

SSE = Sum of Square Errors, AIC = Akaike Information Criterion, BIC = Bayesian Information Criterion, R2 = coefficient of determination. # = number of parameters.

Supplementary table 3: parameter values and identifiability of the Gompertz, power law and “proliferation inhibition” model for the single tumor growth fits

Model	Par.	Unit	Median value (CV)	NSE (%) (CV)
Power law	α	$\text{mm}^{3(1-\gamma)} \cdot \text{day}^{-1}$	0.921 (41.9)	10.6 (55)
	γ	-	0.788 (9.35)	3.42 (62.4)
Gompertz	α_0	day^{-1}	1.84 (35.7)	9.28 (65.3)
	β	day^{-1}	0.0792 (43)	12 (74.4)
Proliferation inhibition	α	day^{-1}	3.71 (54.4)	21.4 (61.7)
	$\beta + \gamma$	day^{-1}	3.45 (59)	24.5 (74.5)

Par. = parameter. CV = coefficient of variation. NSE = normalized standard error.