

Development and calibration of tumor models

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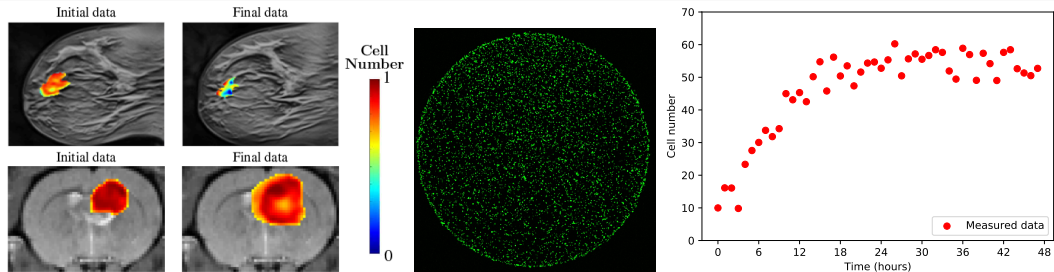


MINISTÉRIO DA
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E INOVAÇÕES

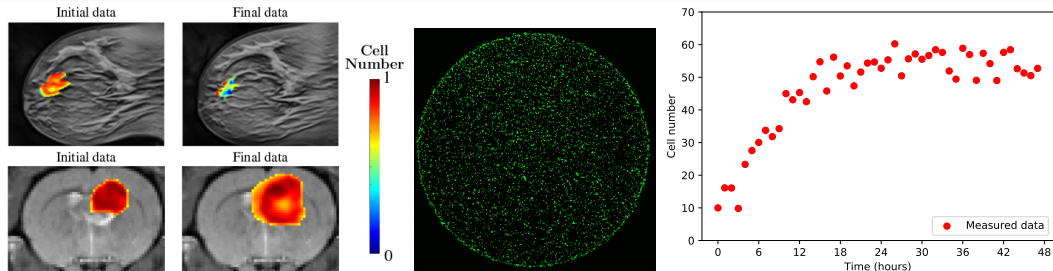


Model Calibration

Motivation



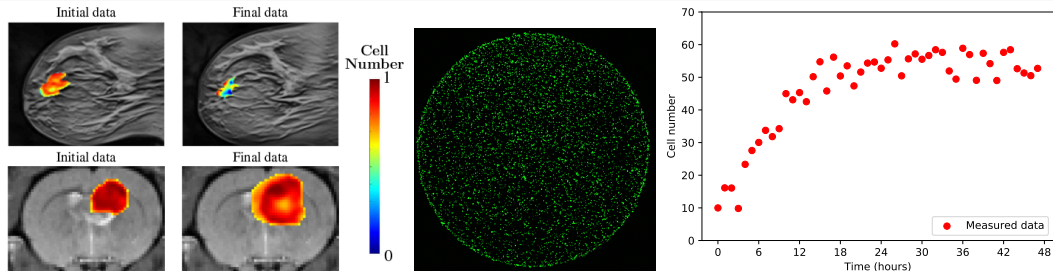
Motivation



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

- N : number of tumor cells;
- r : tumor growth rate;
- K : environment carrying capacity.

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Model Calibration

It is done to **adjust** the selected model parameters, such as growth and death rates, to obtain the best fit between the **model** predicted responses and the available **data**.

Frequentist and maximum likelihood approaches

- the probability of an event is the frequency with which the event is expected to be observed over infinite samples;
- the model parameters remain constant during the repeatable process;
- maximum likelihood approach: find the parameter that enables the model to deliver the best characterization of the true target distribution.

¹Oden et al., Encyclopedia of Computational Mechanics Second Edition (2017)

Model calibration: frequentist and Bayesian statistics¹

Frequentist and maximum likelihood approaches

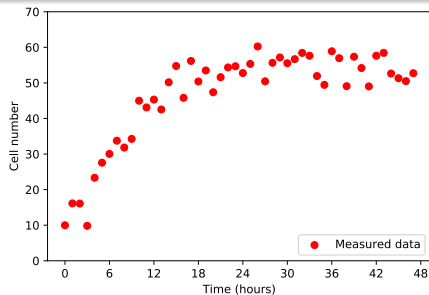
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Bayesian approach

- transfers information from prior knowledge and observation data to the estimated parameter;
- the estimated parameter is regarded as a random variable, and the true parameter is merely a realization of the random variable.

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Definitions



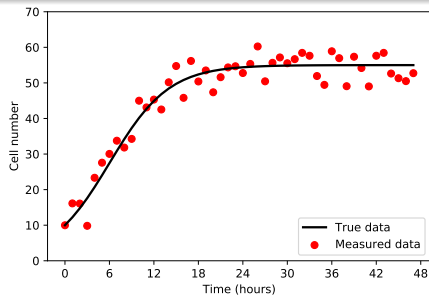
- D : measured data;

Mathematical model

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

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- $Y(\theta)$: model prediction;

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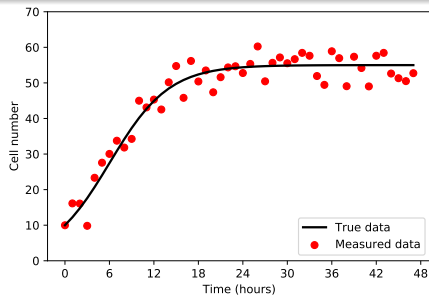


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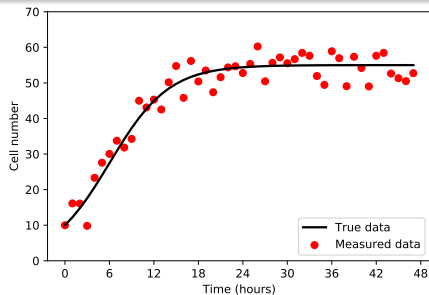
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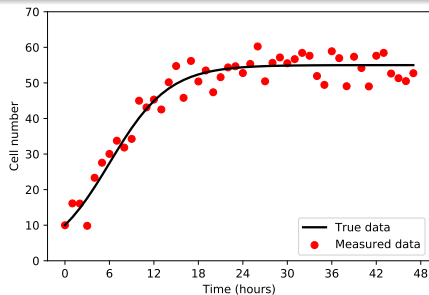
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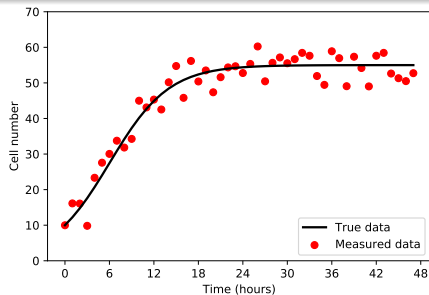
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Assuming:

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- 2 the model inadequacy is normally distributed ($\gamma \sim \mathcal{N}(0_{N \times 1}, \sigma_{model}^2 \mathbf{I}_{N \times N})$);
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$$\pi(\mathbf{D}|\theta) = \prod_{i=1}^{N_t} \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(D_i - Y_i(\theta))^2}{2\sigma^2}},$$

- N_t : the number of data points.

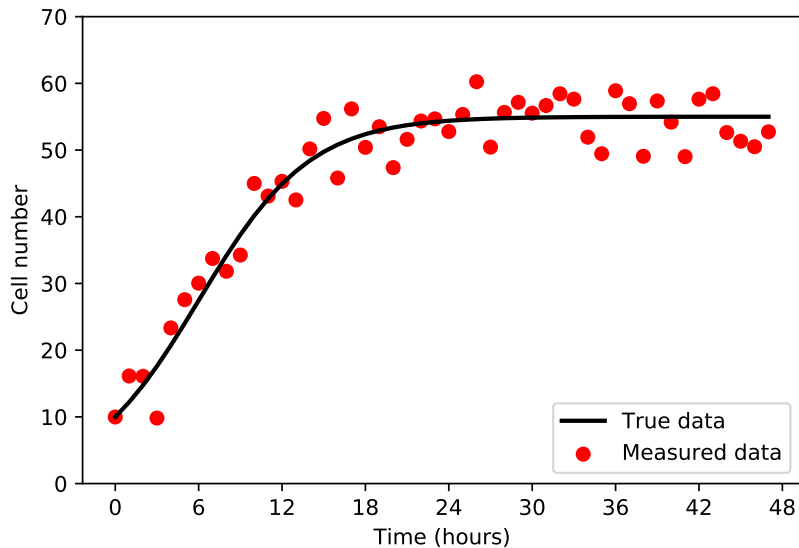
Maximum likelihood estimation

Find $\hat{\boldsymbol{\theta}} \in \Theta$, where Θ is the parameter space, that maximize the likelihood.

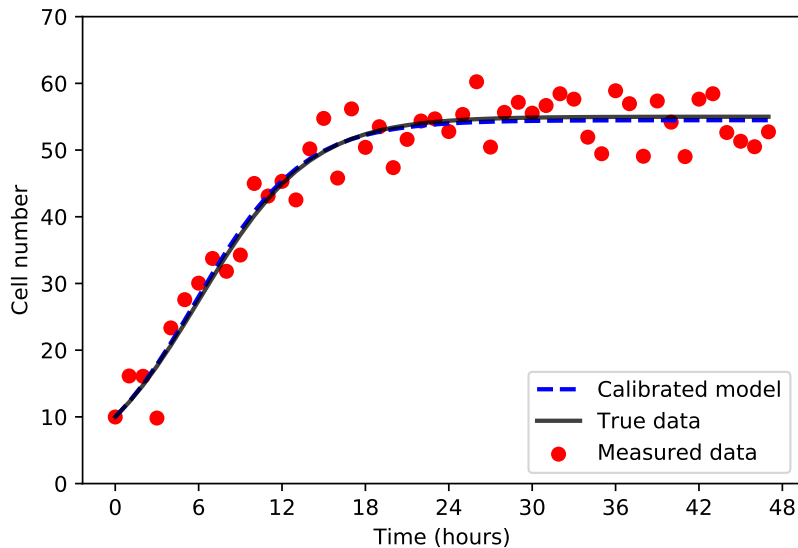
It is customary to work with the more manageable log-likelihood function.

$$\begin{aligned}\hat{\boldsymbol{\theta}} &= \operatorname{argmax}_{\boldsymbol{\theta} \in \Theta} [\log \pi(\mathbf{D}|\boldsymbol{\theta})]; \\ &= \operatorname{argmax}_{\boldsymbol{\theta} \in \Theta} \left[-\frac{N_t}{2} \log(2\pi) - \frac{N_t}{2} \log(\sigma^2) - \sum_{i=1}^{N_t} \frac{1}{2} \frac{(D_i - Y_i(\boldsymbol{\theta}))^2}{2\sigma^2} \right].\end{aligned}$$

Maximum likelihood estimation



Maximum likelihood estimation



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

$$r = 0.25$$

$$K = 59.14$$

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Converting to probability densities π , if A represents the parameter θ of a model, and B the observational data \mathbf{D} :

$$\underbrace{\pi(\theta|\mathbf{D})}_{\text{posterior}} = \frac{\overbrace{\pi(\mathbf{D}|\theta)}^{\text{likelihood}} \overbrace{\pi(\theta)}^{\text{prior}}}{\underbrace{\pi(\mathbf{D})}_{\text{evidence}}};$$

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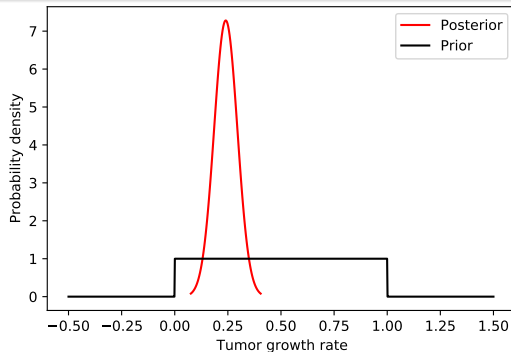
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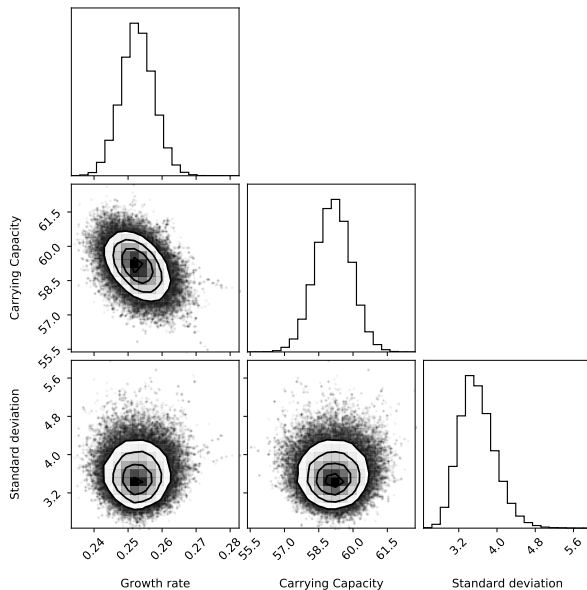


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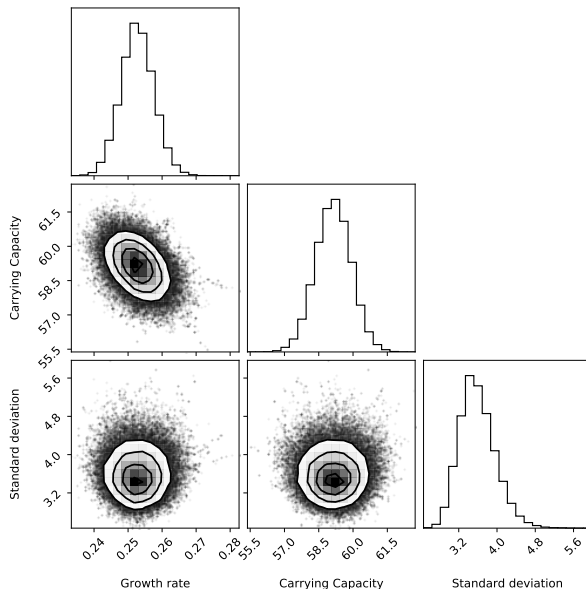
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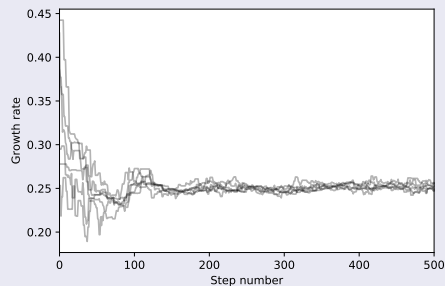


Bayesian approach



Markov Chain Monte Carlo:

Markov Chain Monte Carlo methods draw samples where the next sample is dependent on the existing sample, called a Markov Chain.



Bayesian approach

