Development and calibration of tumor models

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PÁTRIA AMADA BRASIL
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TMG

INSTITUTE FOR COMPUTATIONAL ENGINEERING & SCIENCES
ODEN

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TEXAS ADVANCED COMPUTING CENTER

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The University of Texas at Austin

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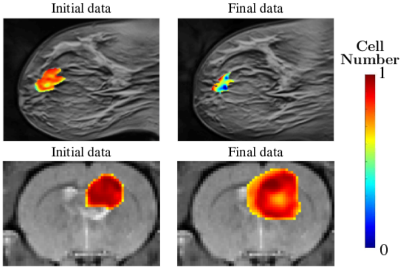
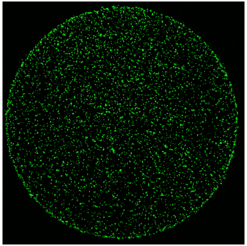
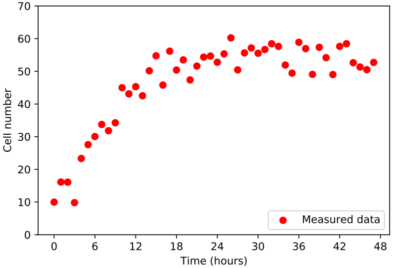
Model Calibration

Motivation



Initial data
Final data
Initial data
Final data
Cell Number
1
0





Cell number
Time (hours)
Measured data
0
10
20
30
40
50
60
70
0
6
12
18
24
30
36
42
48

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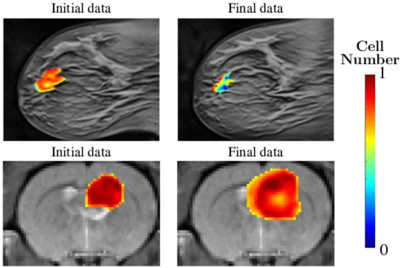

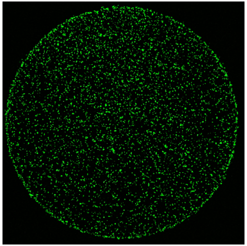

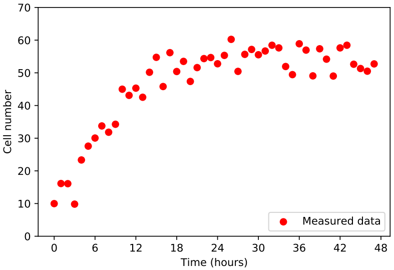

$$\frac{dN}{dt} = gN\left(1 - \frac{N}{K}\right),$$

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

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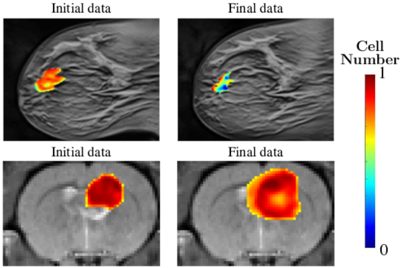

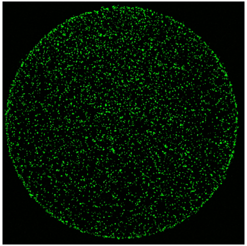

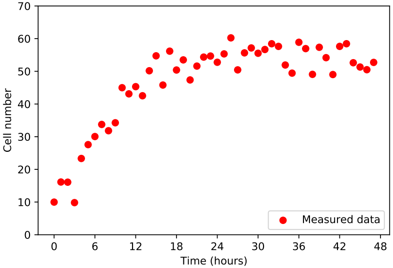

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Model Calibration

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.

Model calibration: frequentist and Bayesian statistics[1]

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.

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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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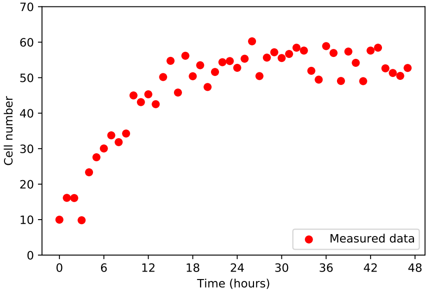
Definitions



- $\boldsymbol{D}$: measured data;

Mathematical model

$$\boldsymbol{Y}(\boldsymbol{\theta}) = \frac{dN}{dt} = gN\left(1 - \frac{N}{K}\right),$$

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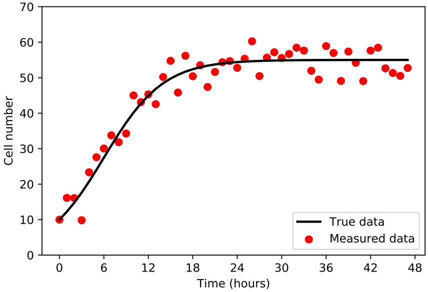

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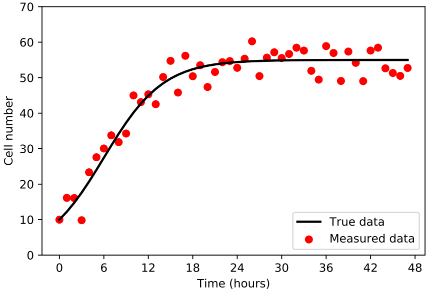

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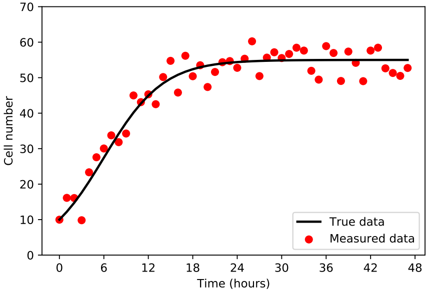

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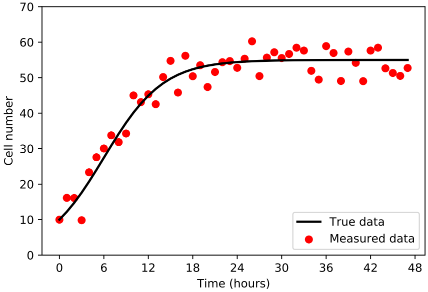

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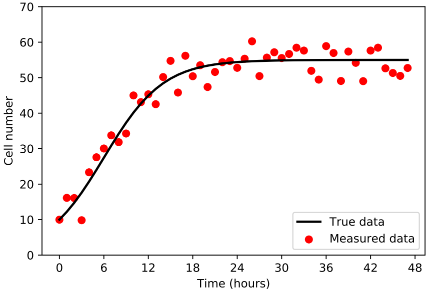

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Likelihood

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$$\pi(\boldsymbol{D}|\boldsymbol{\theta}) = \prod_{i=1}^{N_t} \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(D_i - Y_i(\boldsymbol{\theta}))^2}{2\sigma^2}},$$

- N_t: the number of data points.

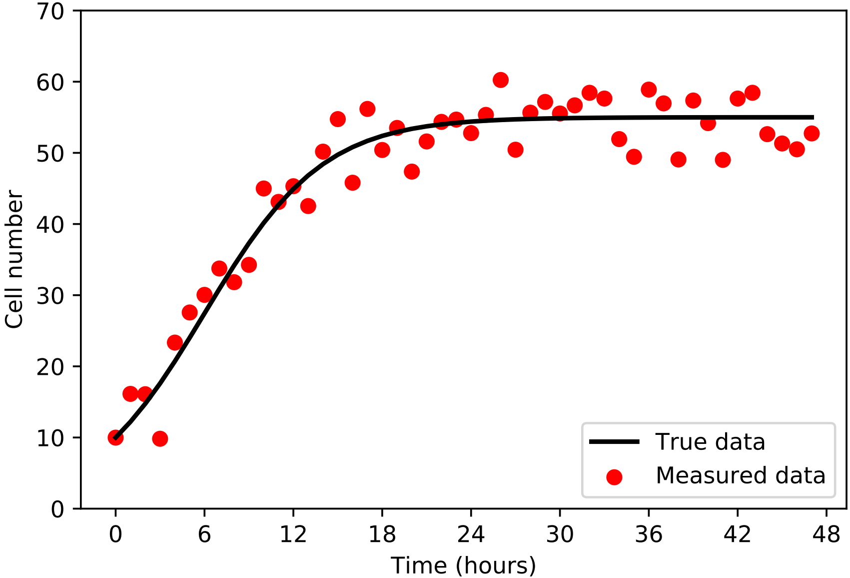
Maximum likelihood estimation

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.

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

Maximum likelihood estimation



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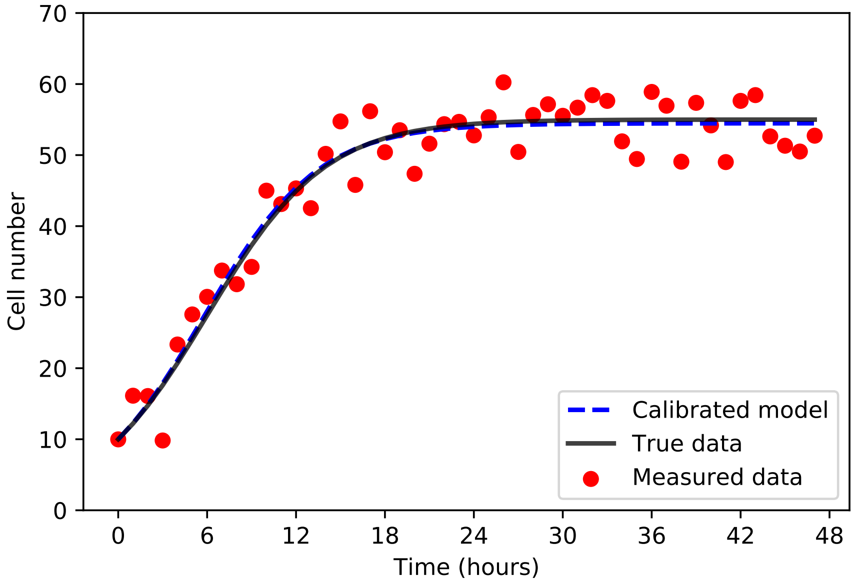

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Converting to probability densities π, if A represents the parameter $\boldsymbol{\theta}$ of a model, and B the observational data $\boldsymbol{D}$:

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\underbrace{\pi(\boldsymbol{\theta}|\boldsymbol{D})}_{\text{posterior}} = \frac{\overbrace{\pi(\boldsymbol{D}|\boldsymbol{\theta})}^{\text{likelihood}}\,\overbrace{\pi(\boldsymbol{\theta})}^{\text{prior}}}{\underbrace{\pi(\boldsymbol{D})}_{\text{evidence}}}; \qquad \pi(\boldsymbol{D}) \int_{\Theta} \pi(\boldsymbol{D}|\boldsymbol{\theta})\pi(\boldsymbol{\theta})\,\mathrm{d}\theta
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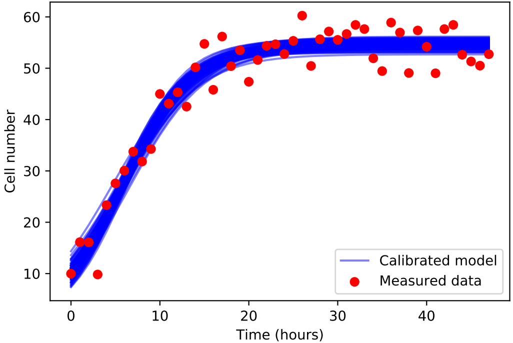

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