Development and calibration of tumor models

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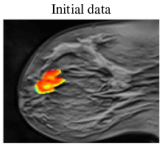
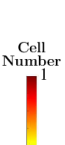
Model Calibration

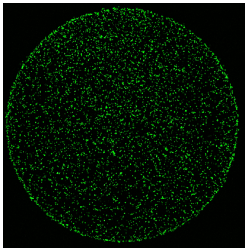
- Calibration Theory:
  - Maximum Likelihood Estimation
  - Bayesian Approach
- EMCEE Python Library[1]

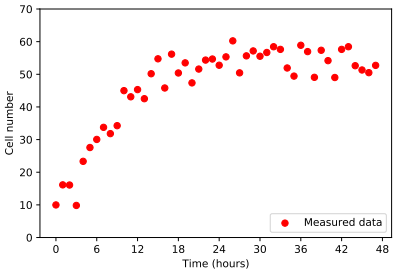
[1] Foreman-Mackey, Daniel, et al. "emcee v3: A Python ensemble sampling toolkit for affine-invariant MCMC." arXiv preprint arXiv:1911.07688 (2019).

Motivation

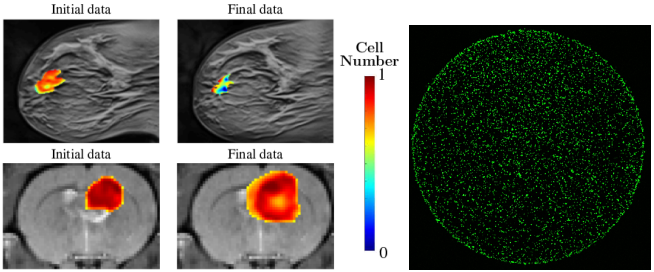

Initial data
Final data
Initial data
Final data

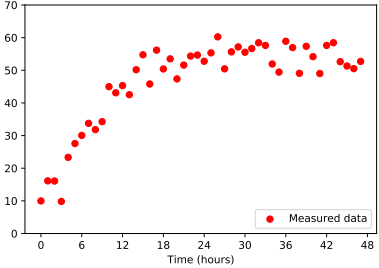

Cell
Number
1
0




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

Motivation





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

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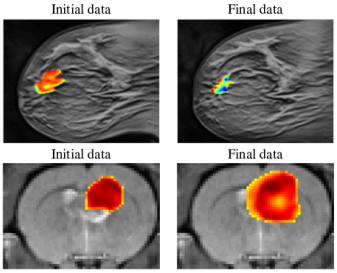

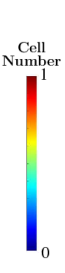

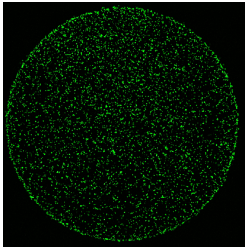

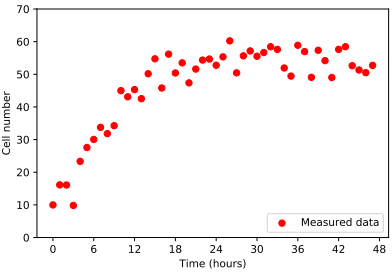

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Model Calibration

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[2]

Frequentist and maximum likelihood approaches

- there is an unknown but fixed parameter that represents the event;
- 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

- it maps prior beliefs about the parameters to new posterior beliefs in the light of observing the data;
- 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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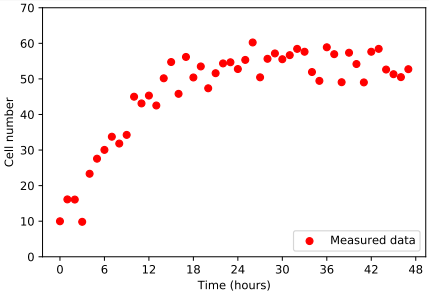
Definitions



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

Mathematical model

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

- $\boldsymbol{\theta}$: vector of model parameters, $\boldsymbol{\theta} = (r, K)$;
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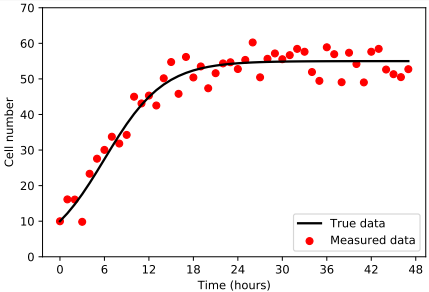

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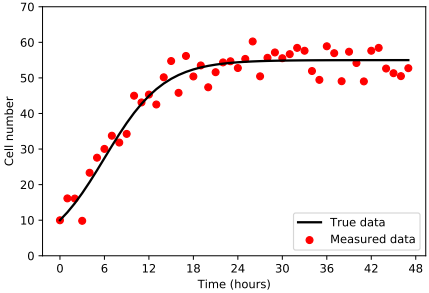

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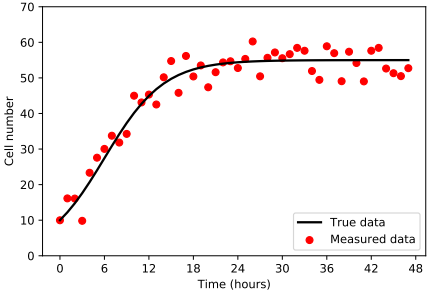

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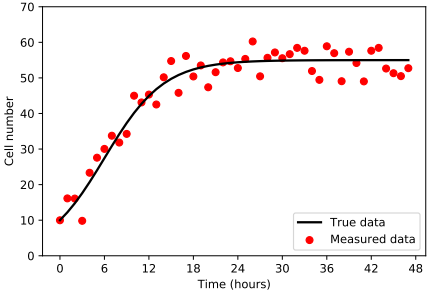

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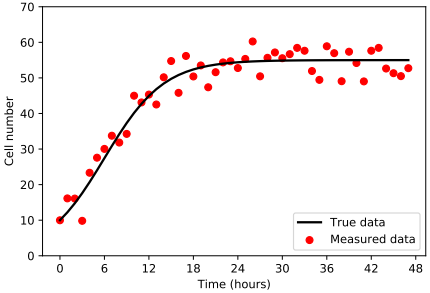

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Likelihood

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Assuming:

1. the experimental noise is normally distributed ($\boldsymbol{\epsilon} \sim \mathcal{N}(0_{N\times 1}, \sigma^2_{data}\boldsymbol{I}_{N\times N})$);
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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.

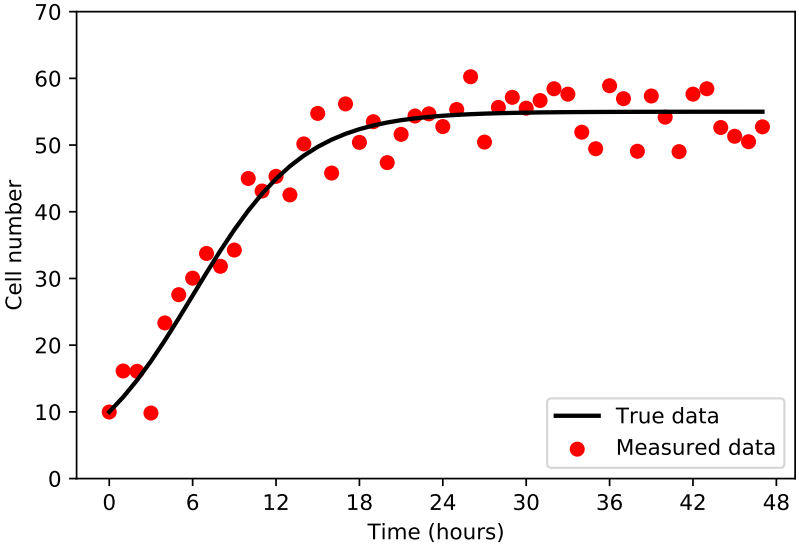
Maximum likelihood estimation

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.

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

Maximum likelihood estimation



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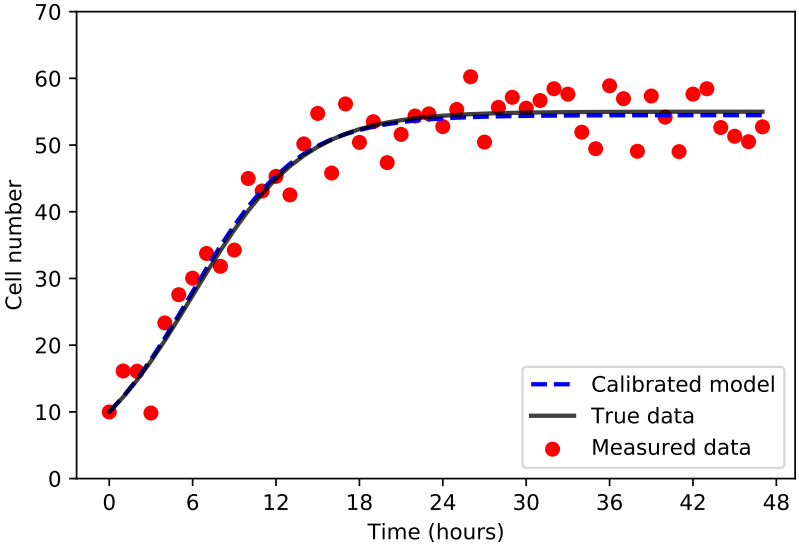

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right),$$

$r = 0.25$

$K = 59.14$

Bayesian approach

Given events A and B:

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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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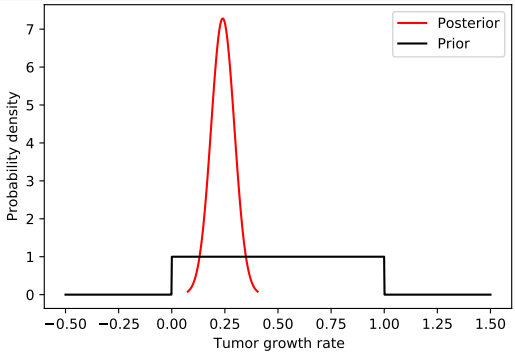

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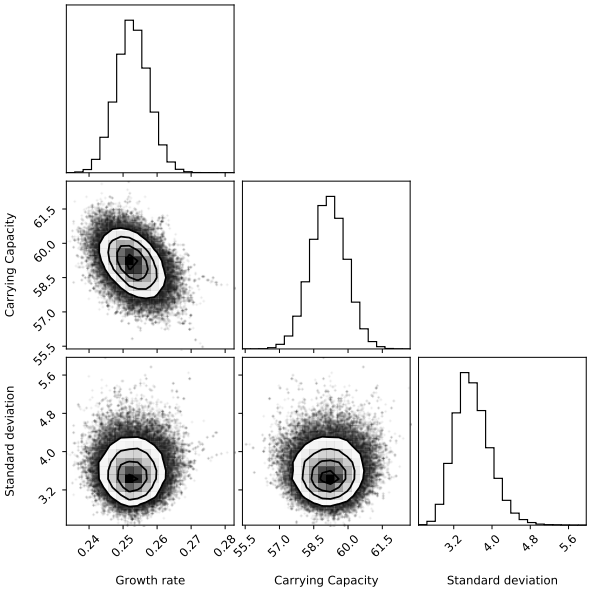

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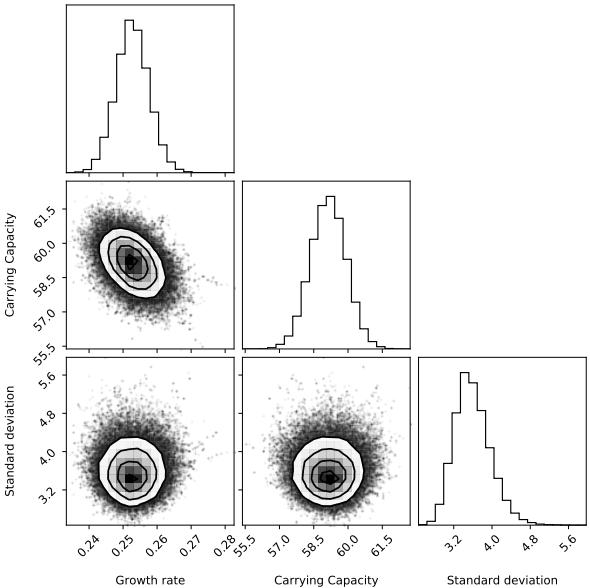
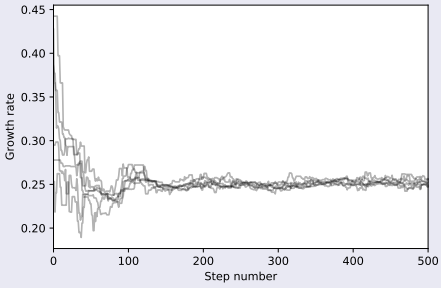


Markov Chain Monte Carlo:

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



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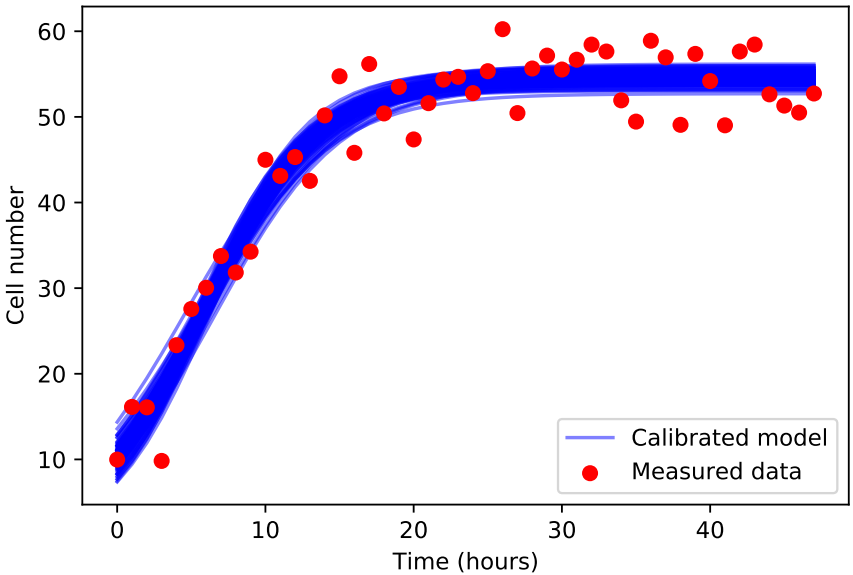

Jupyter Notebook - Binder and Discord

https://github.com/ernesto-lima/veraoIncc2021