

# Optimization Methods for Individual-based Model Parameter Estimation in Predictive Microbiology



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## INTRODUCTION

In the framework of microbiology, Individual-based Models (IbMs) are discrete models in which the main entities are microbes. Two examples of IbM simulations that have provided various and interesting results in microbiology are BacSim [4] and INDISIM [3]. Their use in simulations as ‘virtual experiments’ to predict the evolution of populations under specific conditions requires accurate setting of the parameters involved. Several methods for parameter estimation have been developed within the framework of continuous modelling. However, they are not usable with IbMs because they are generally based on gradient methods. The classic method for estimating the parameters of an IbM is the grid search, which involves great time expenditure. Thus, it is necessary to develop specific methods for estimating IbM parameters, which was the objective of this study. We adapted and tested two optimization methods for Individual-based Model parameter estimation: the Nelder-Mead Threshold Accepting (NMTA) [2,5] and the NEWUOA software for unconstrained optimization without derivatives [6].

## INDISIM, an IbM simulation

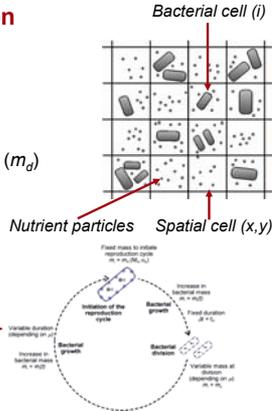
### Modelling the bacteria:

#### Characteristics:

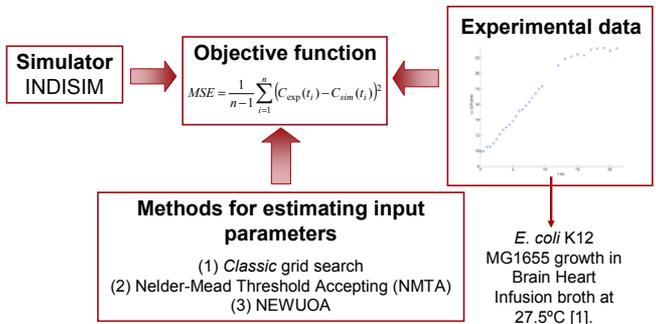
- Position
- Mass
- Mass to initiate cell division ( $m_d$ )
- Reproduction cycle status

#### Rules:

- Motion
- Nutrient uptake ( $u_{max}$ )
- Metabolism
- Reproduction cycle
- Viability

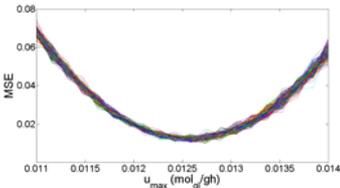


## ESTIMATING INDISIM PARAMETERS

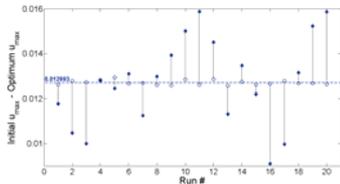


## RESULTS

### One-parameter estimation: $u_{max}$



The MSE for a grid search of  $u_{max}$ , for 149 runs executed with non-overlapping random number sequences.

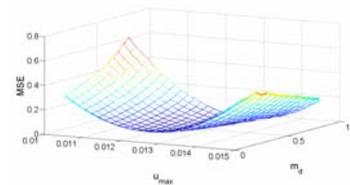


20 independent rounds of NEWUOA method for estimating the  $u_{max}$ : full rhombuses are the randomly chosen initial points, and open circles are the best estimate for each run.

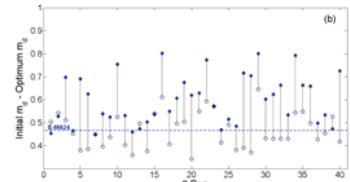
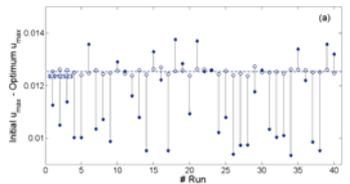
- ✓ No convergence problems were detected neither with NMTA and NEWUOA.
- ✓ The one-parameter NMTA optimization processes lasted 15 times longer than the one-parameter NEWUOA runs.
- ✓ The two-parameter NEWUOA optimization processes lasted just 1.2 times longer than the one-parameter NEWUOA runs.
- ✓ The three-parameter NEWUOA optimization processes (not shown) lasted between 1.2 and 2.4 times longer than the one-parameter NEWUOA runs.

		Grid search	NMTA	NEWUOA
One-parameter	$u_{max}$ $mol \cdot g^{-1} \cdot h^{-1}$	0.0126	0.0124	0.0127
	$u_{max}$ $mol \cdot g^{-1} \cdot h^{-1}$	0.0124	np	0.0125
Two-parameter	$m_d$ $pg$	0.40	np	0.47

### Two-parameter estimation: $u_{max}$ , $m_d$



Grid search for mass at division ( $m_d$ ) and maximum uptake rate ( $u_{max}$ ).



NEWUOA results for optimizing (a) maximum uptake rate ( $u_{max}$ ) and (b) mass at division ( $m_d$ ). Full circles are the initial points, and open circles are the best estimates for each run.

## CONCLUSIONS

NEWUOA proves to be a useful tool for IbM parameterization, although it requires a minimum knowledge of the parameters to be estimated in order to set the trust region radius. It was the fastest method, and the results had sufficient precision.

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