Modelling Competition for Nutrients between Microbial Cultures Growing on Solid Agar Surfaces

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ABSTRACT

Motivation: The fitness of microbial strains can be estimated from the growth of cultures inoculated onto solid agar. In high-throughput procedures, an array of cultures is grown on the same agar plate and competition for nutrients between cultures is likely to affect growth. However, analysis assumes that cultures grow independently. We test a model of nutrient dependent growth and diffusion and try to correct for competition to provide more accurate and reliable fitness estimates.
Results: What should we say?
Availability and Implementation: CANS, a Python2 package developed for the analysis in this paper, is freely available from github pypi.
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1 INTRODUCTION

Dummy Lawless *et al.* (2010) citations (Heydari *et al.*, 2016) (Addinall *et al.*, 2008).

1.1 Subsection

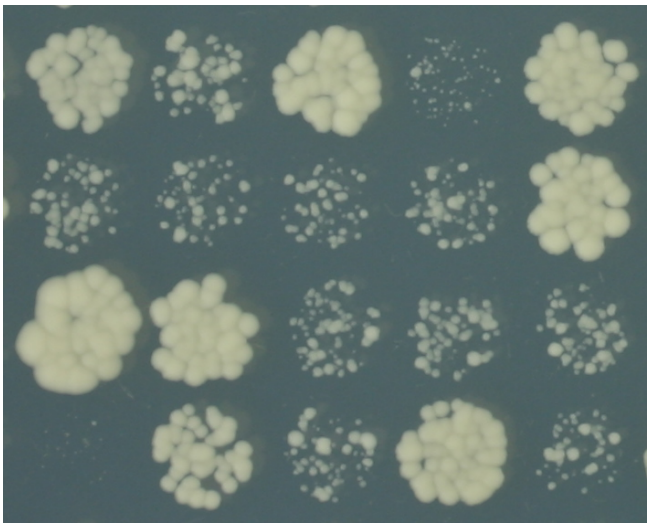

Figure 1: *A section of a plate from a QFA experiment (Addinall* et al.*, 2011).*

2 METHODS

2.1 Subsection

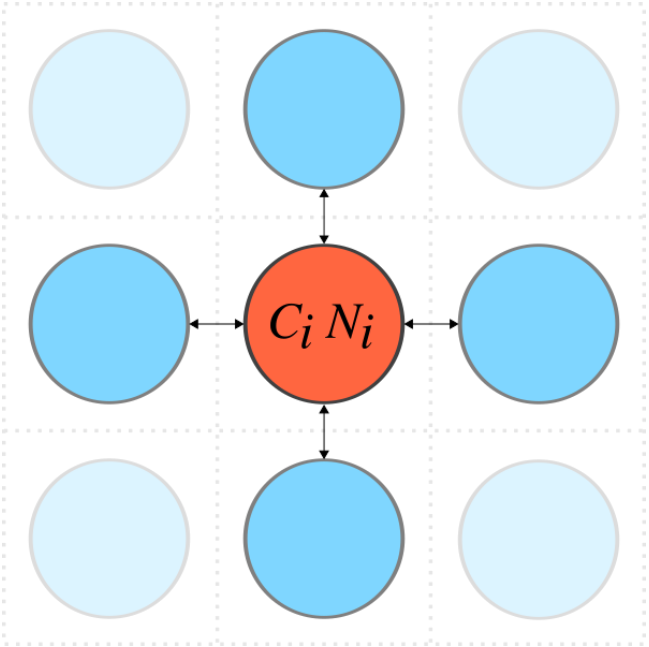

Figure 2: *Schematic of the modelling approach. Each circle represents a culture, indexed i, on solid agar and arrows represent diffusion of nutrients. C_i - amount of cells; N_i - amount of nutrients; darker blue circles- neighbourhood δ_i.*

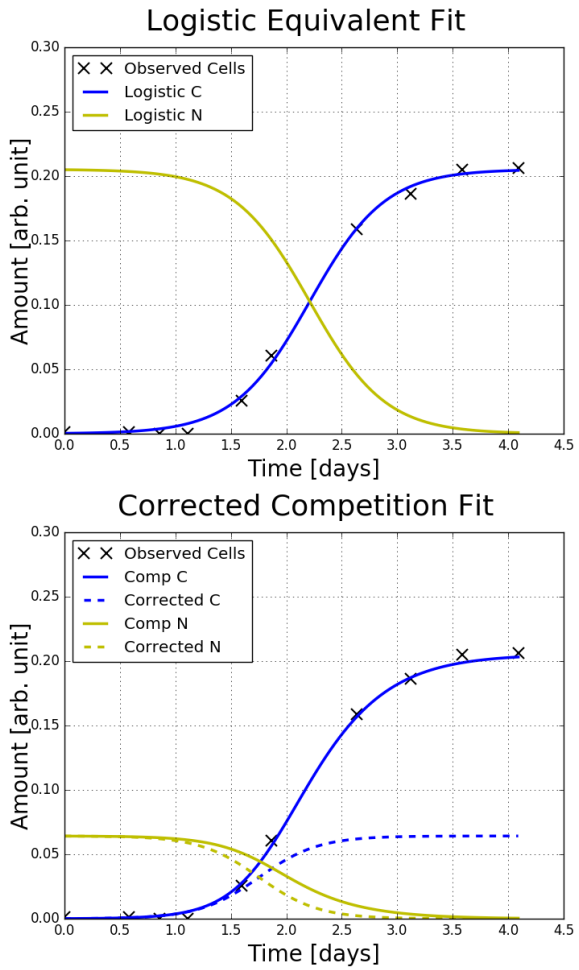

Figure 3: *PUT KN VALUES (and r and K) ON THE PLOT. (Could even put obj fun values). Fits to culture (R10, C3) of P15 (Addinall* et al.*, 2011) illustrating how the competition model can be seen as a correction to the logistic model. C - Cells; N - Nutrients. Top - Logistic Equivalent Fit; Bottom - Competition Fit (solid) and Corrected Logistic Equivalent Fit (dashed).*

3 RESULTS

(Palková *et al.*, 1997)

3.1 Subsection

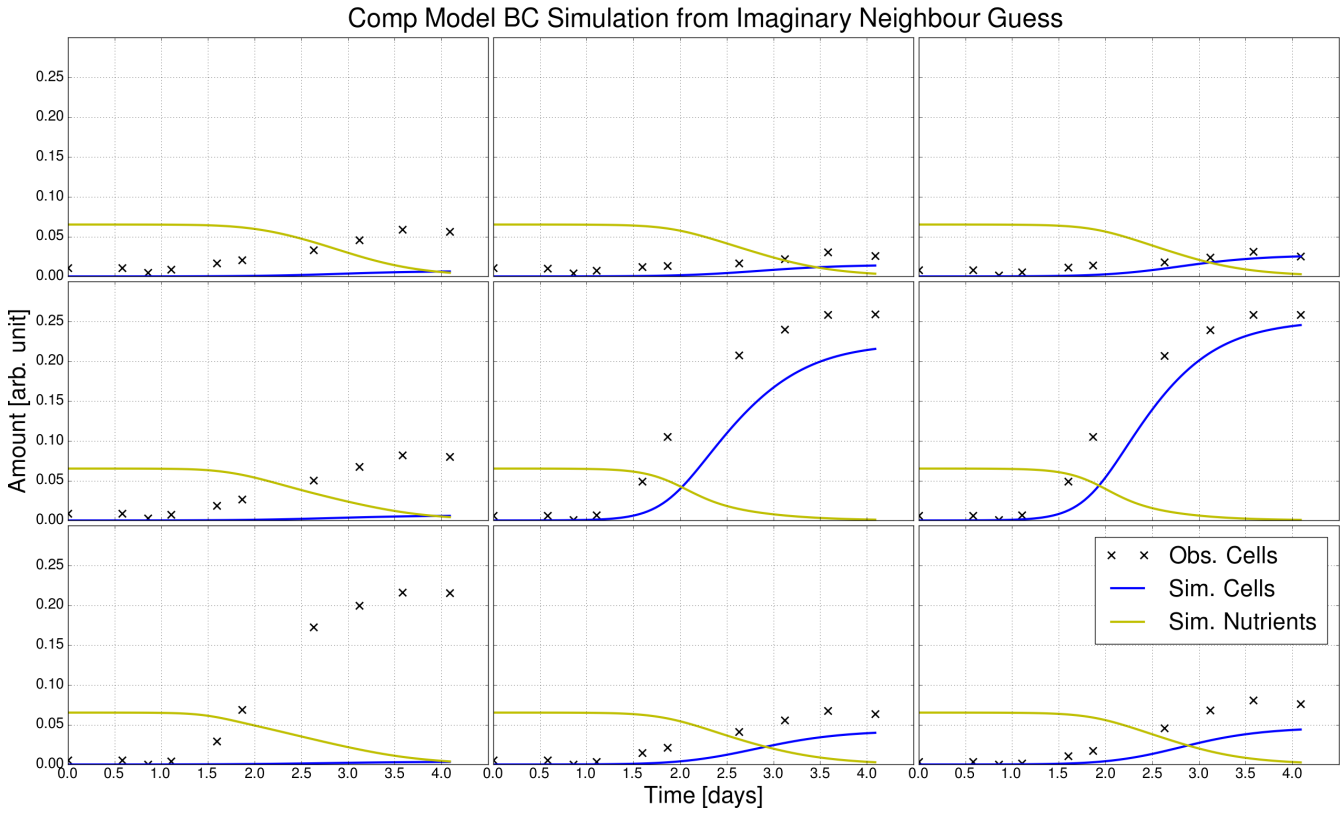

Figure 4: *Comp Model BC simulation using parameters from Imaginary Neighbour guessing of P15. NOT TO GO HERE This method of guessing requires a b-guess to be supplied to fix the faster growing neighbour. (I iterated through cell ratios. I iterated through a range of b guesses supplied at the plate level; running a different script with a C_0 guess, b_{guess}. It would probably have been better iterate through a list of b-guess values for each culture and choosing the estimated b value from the best fit of each culture. Guessing time is currently about four minutes which is fast compared to fitting which takes approximately three hours. However, this is unlikely to stop us from encountering local minima when we fit the Competition Model.*

Scripts were run with combinations of the following values. cellratios = np.logspace(-3, -5, num=5) fittype = ["imagneigh", "logeq"] zerokn = [True, False]

Each script looped through the following array of b values which were supplied to the initial guesser and used at the plate level.

for b-guess in [35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 95, 100, 150]:

Each b value is used to guess a complete set of parameters b parameters for every culture in the plate. Each of these parameter sets is then used as an initial guess to Competition Model fitting. For the 13 b-guesses we must run 13 Competition Model fits. It would be better and more efficient to loop through the b-guesses at the culture level. Each culture still undergoes imaginary neighbour guessing with each of the 13 b-guess values, but now, for each culture, we choose just the b estimate from the best of the 13 fits. This will produce one set of b guesses which should be superior to any of the guesses attained when iterating through b-guess at the plate level. Then we only need to fit the Competition Model to 1 guess rather than 13. This will reduce the number of scripts that need to be run in parallel, or the use of a finer grid over C_0, and should make convergence faster. However, if using a gradient method we are still likely to encounter local minima from these guesses. Instead, this improvement could be considered when developing a genetic algorithm (if initial guesses are required) or if fitting using a brute force method with a fine grid of fixed plate level parameters. We will see later that with true plate level parameters fixed we can recover good estimates for b using a gradient method. It may be possible to evolve candidates of plate level parameters, fix these, and minimize using the current gradient method.

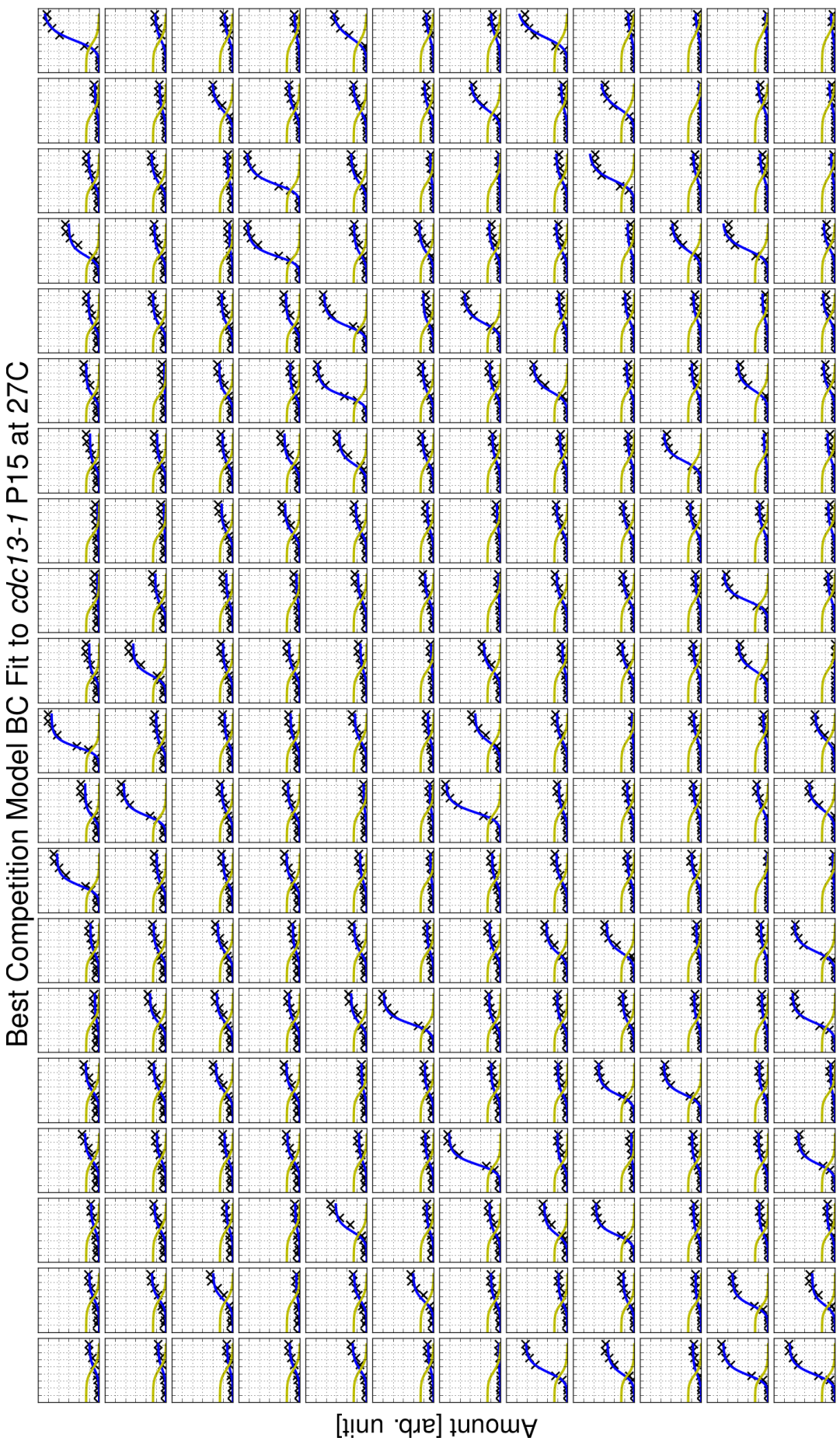

Figure 5: *(R5, C18) P15*

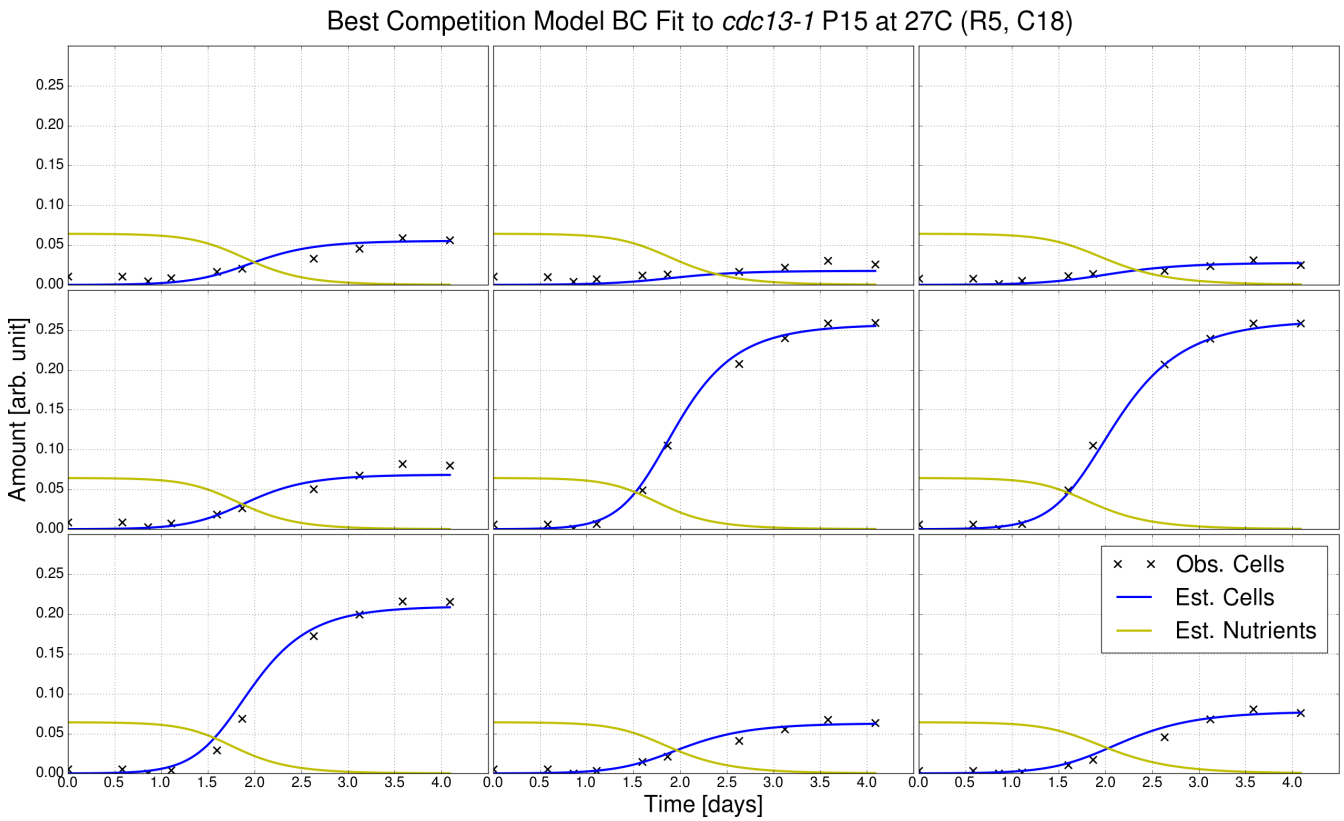

Figure 6: *(R5, C18) P15*

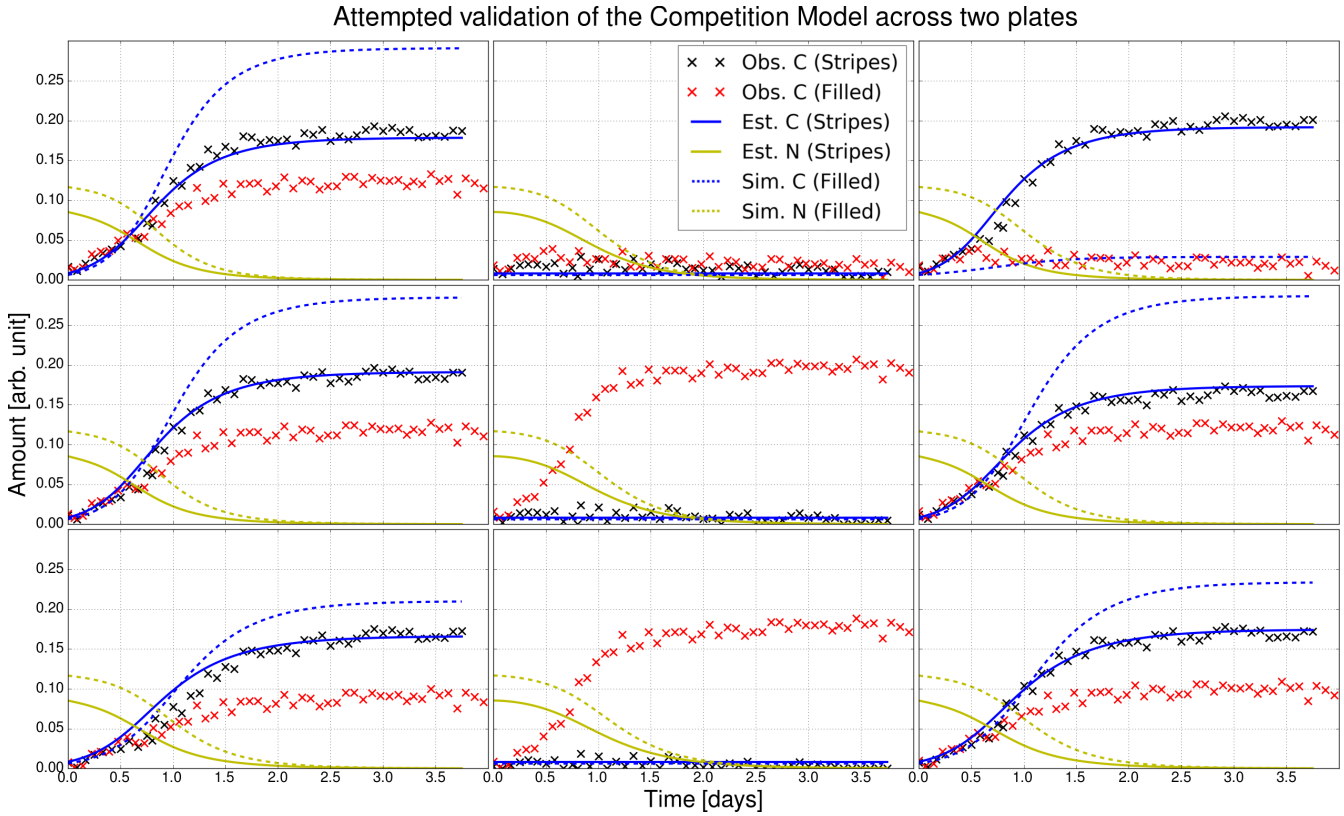

Figure 7: *(R9, C10) top-right possible pinning mistake. Bottom-left not close to any such mistake.*

4 DISCUSSION

4.1 Subsection

REFERENCES

Addinall, S.G. *et al.* (2008) A genomewide suppressor and enhancer analysis of cdc13-1 reveals varied cellular processes influencing telomere capping in saccharomyces cerevisiae. *Genetics*, **180**, 4, 2251–2266.

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Palková, Z. *et al.* (1997) Ammonia mediates communication between yeast colonies. *Nature*, **390**, 6659, 532–536.