Reproducing the non-mixed growth curve from the well-mixed data.

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1 Summary

I have been trying to reproduce the experimental growth curve in a non-mixed single well using Bartek's well-mixed data. I have tried to do this using 2 approaches: (1) using the full stochastic simulation where I model nutrient molecules explicitly and calculate local nutrient densities to determine the growth rate and (2) using a system of 2 coupled PDEs modeling bacteria and nutrient fields in 2D, solved using mathematica. Note an assumption used in each: we assume a linear relation between bacterial and substrate density. That is, in determining the growth rate due to the local substrate concentration I have used Barteks growth function $g(n)$ but have replaced n with $(1 - s)$.

The 2 approaches do not match.

Neither reproduces the experimental growth curve.

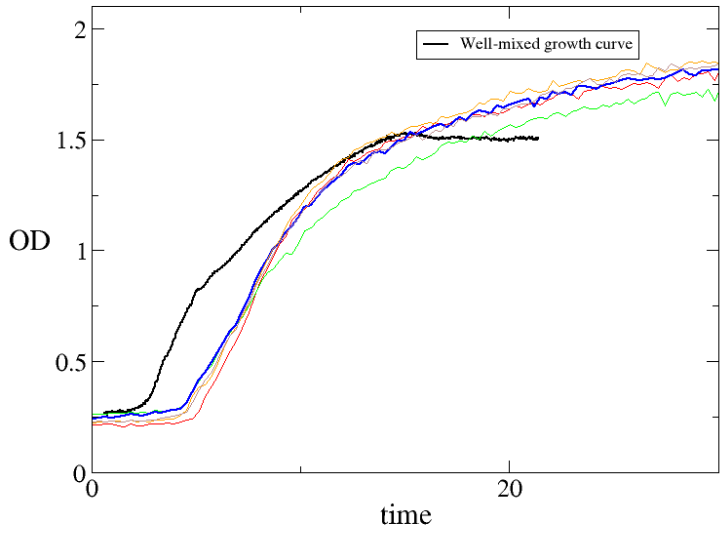

Figure 1: Bartek's "raw" experimental growth curves. Black curve is a well-mixed experiment, all others are from non-mixed wells. Normally I will scale the y-axis to range from 0 to 1.

2 Stochastic simulation

2.1 Well-mixed: Simulation and experiment

Aside: one thing I have noticed is that the stochastic simulation and experimental growth curves do not actually match without me doing an appropriate scaling of time. Figure 2 shows this. This was due to the wrong choice of "max_growth_rate" which was 2.0 before. Changing this to 1.0 for $K = 10^5$ gave perfect fit with no rescaling. Also, the initial number of bacteria will affect if we need to shift the curve along the x-axis. I could use these fittings to determine the experimental initial innoculation size. In all of the plots that follow, to facilitate comparison I will have rescaled the y-axis (OD) to run from 0 to 1, and I may have rescaled the x-axis (time) by an arbitrary amount.

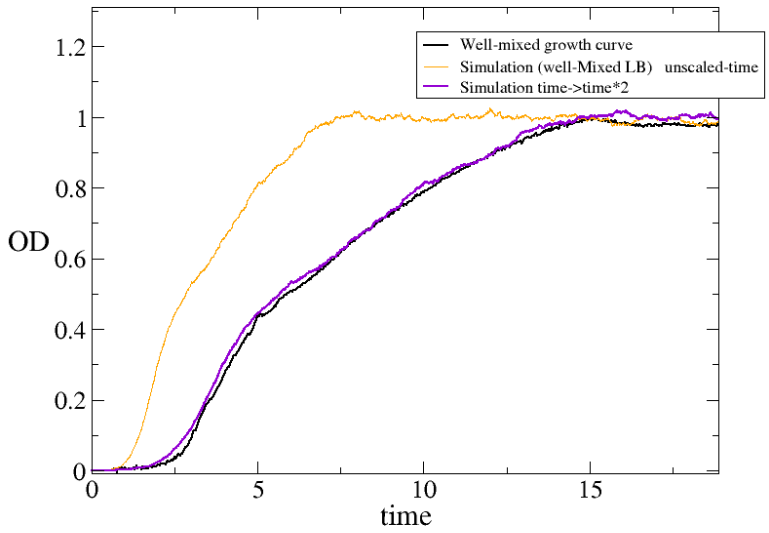

Figure 2: Comparing single-well growth curves from simulation and experiment. Black: scaled experimental growth curve; orange: full stochastic simulation; purple: orange curve with time re-scaled by a factor of 2. Good match between simulation and experiment in the well-mixed case.

2.2 Non-mixed

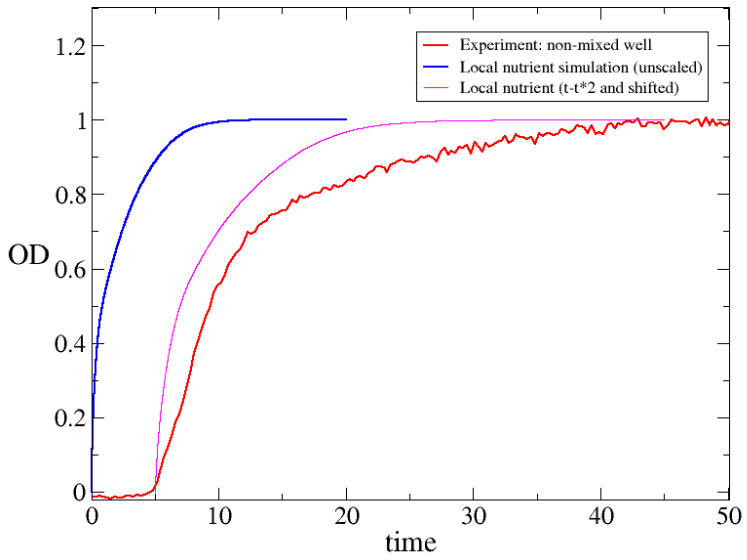

Figure 3: The local nutrient stochastic simulations (blue) do not match the non-mixed experimental growth curves (red). Pink curve is the blue curve with time scaled by factor of 2 and shifted along x-axis. I have simulated this system for different diffusion constants of bacteria and nutrients and different initial conditions (bacteria evenly distributed, located at top of well, or located in centre of well) and each has produced a very similar growth curve – none have an exponential growth period. I do not know why this is the case.

3 Coupled PDEs in mathematica

$$\frac{\partial N(x,y,t)}{\partial t} = D_B \nabla^2 N + N g[1 - S(x,y,t)], \tag{1}$$

$$\frac{\partial S(x,y,t)}{\partial t} = D_S \nabla^2 S - N g[1 - S(x,y,t)], \tag{2}$$

where $g[S]$ is the well-mixed growth function from Bartek's experiments. To simulate the well-mixed system below I convert these to ODEs by removing the diffusion term.

3.1 Well-mixed

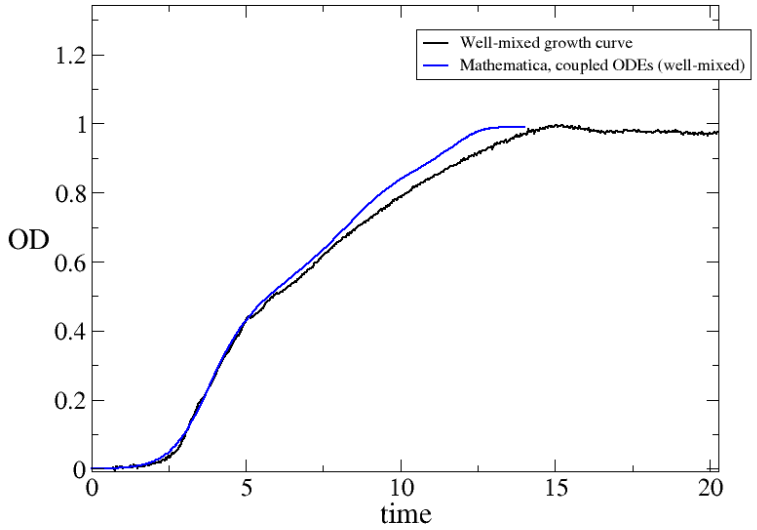

Figure 4: Well-mixed single-well growth curves. Experimental curve (black) vs coupled ODEs (i.e. well-mixed) (blue).

3.2 Non-mixed

I have tried various initial conditions, well-dimensions and diffusion constants but the outcome is always very different to that found from my stochastic local-nutrient simulations.

3.3 Bacteria density-dependence

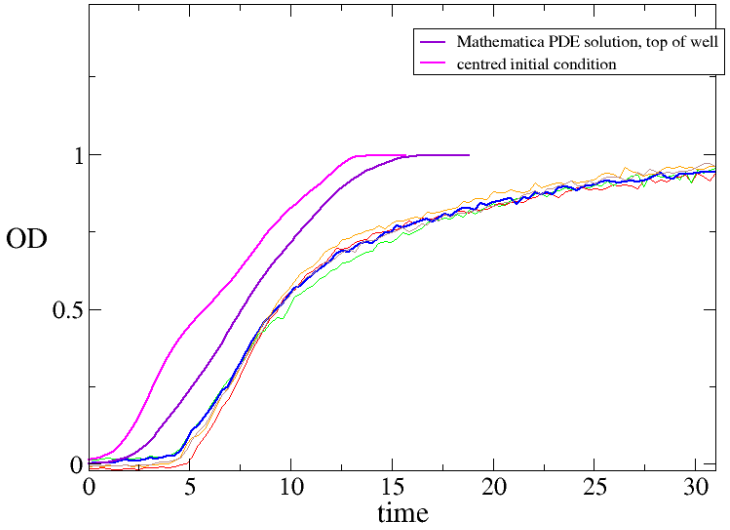

Figure 5: Non-mixed single-well growth curves. Coupled PDEs (violet and pink), experimental curves (all others). The initial condition used in the violet system was: $N(x, y, 0) = 1E^{-9}(xy)^2(L_x - x)^2(L_y - y^2)^2$ so that bacteria are initially located near the top of the well, and the nutrient was evenly distributed throughout the (2D) well. Parameters: $D_B = D_S = 0.2$, $L_x = 3.25$, $L_y = 11$. We see that the kinked shape of the well-mixed curve is lost but the match is poor – especially at higher bacterial densities. The pink curve had bacteria initially centred: $N(x, y, 0) = 0.000005(xy)^2(L_x - x)^2(L_y - y)^2 + 0.001$ with $D_B = D_S = 0.5$ and the shape of this growth curve resembles that of the well-mixed case. Thus we can alter the shape of the growth curve by altering the initial conditions.

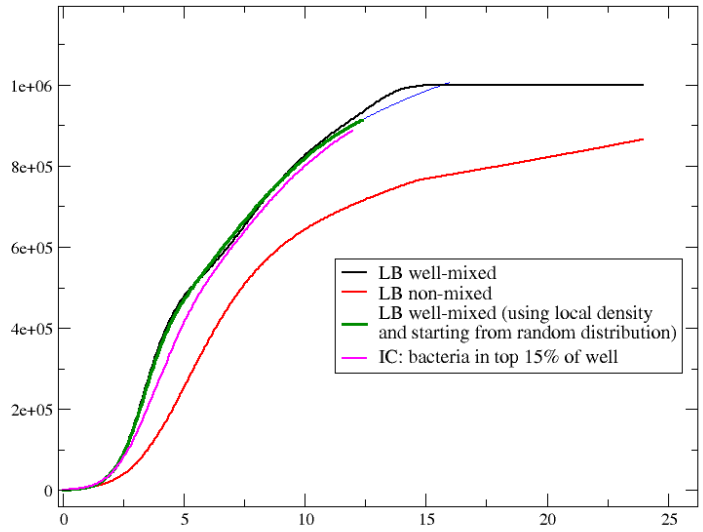

Figure 6: Rosalind's idea. This plot shows what I did initially: nutrient it not explicitly measured but instead of calculating the bacterial density in the entire well I find the local density and use this to determine the growth rate. There are 2 plots using this local bacteria density (green starts from an initially even distribution of bacteria throughtout well, while in the pink curve I place all initial bacteria in the top 15% of the well). I think what this shows is that for the given diffusion parameter ($D = 1.5$) the system essentially behaves as if it was well-mixed. This makes me think that the solution of the PDEs using a local nutrient density from mathematica is likely correct, since it more closely resembles the well-mixed solution, while my stochastic simulation with local nutrient density is very wrong for some reason.