The model is a three-dimensional ODE system with variables corresponding to living cells, denoted by , dead cells denoted by , and nutrients denoted by .

The equations of the model are

We consider three cases for the growth rate :

Non-dimensionalize by taking , , , the scaled model is

where and . The growth rate functions are now

where .

Model:

Scaled model:

Optical density:

Initial Conditions: (parameter), ,

Parameters to fit:

~~Case (1): – 6 parameters~~

~~Case (2): – 9 parameters~~

~~Case (3): – 10 parameters~~

Anaerobic Growth

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Model 1 | | Model 2 | | Model 3 | |
|  | SSE | AIC | SSE | AIC | SSE | AIC |
| E. faecalis | 0.2627 | -895.5 | 0.0062 | -1426.1 | 0.0060 | -1430.8 |
| C. albicans | 0.0322 | -1197.8 | 0.0331 | -1187.1 | 0.0111 | -1342.8 |
| P. aeruginosa | 0.0496 | -1135.7 | 0.0505 | -1126.1 | 0.0143 | -1305.5 |
| S. odorifera | 0.1055 | -1026.9 | 0.0527 | -1120.1 | 0.0388 | -1161.7 |

Aerobic Growth

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Model 1 | | Model 2 | | Model 3 | |
|  | SSE | AIC | SSE | AIC | SSE | AIC |
| E. faecalis |  |  |  |  |  |  |
| C. albicans |  |  |  |  |  |  |
| P. aeruginosa |  |  |  |  |  |  |
| S. odorifera |  |  |  |  |  |  |

E. faecalis anaerobic

|  |  |  |
| --- | --- | --- |
|  |  |  |

Figure 1: Best fitting parameters for E. Faecalis anaerobic growth

C. albicans anaerobic

|  |  |  |
| --- | --- | --- |
|  |  |  |

Figure 2: Best fitting parameters for C. albicans anaerobic growth

P. aeruginosa anaerobic

|  |  |  |
| --- | --- | --- |
|  |  |  |

Figure 3: Best fitting parameters for P. aeruginosa anaerobic growth

S. odorifera anaerobic

|  |  |  |
| --- | --- | --- |
|  |  |  |

Figure 4: Best fitting parameters for S. odorifera anaerobic growth

E. faecalis anaerobic

|  |  |  |
| --- | --- | --- |
|  |  |  |

Figure 5: Best fitting parameters for E. Faecalis aerobic growth

C. albicans anaerobic

|  |  |  |
| --- | --- | --- |
|  |  |  |

Figure 6: Best fitting parameters for C. albicans aerobic growth

P. aeruginosa anaerobic

|  |  |  |
| --- | --- | --- |
|  |  |  |

Figure 7: Best fitting parameters for P. aeruginosa aerobic growth

S. odorifera anaerobic

|  |  |  |
| --- | --- | --- |
|  |  |  |

Figure 8: Best fitting parameters for S. odorifera aerobic growth

E. faecalis doubling time = ~48 minutes (Vebø, Solheim et al. 2010) =>

Bacteria: E. Faecalis – facultative anaerobe, bacteria

C. albicans – a yeast, pathogenic in immunocompromised people, fermentative since it’s a yeast

P. aeruginosa – facultative anaerobe, prefers aerobic conditions though, but can grow anaerobically

S. odorifera – facultative anaerobe, opportunistic pathogen in immunocompromised people

**Notes:** dead cells can be used as nutrients after they lyse, ~~ask about the cx^2 term~~

Logistic growth - x/k or (x+y)/k?

Greg can run expierments again to get more info about death rates, living dead ratio

Fit data to see if they know the proportion of OD to density, if they don’t then fit from data

OD is assumed to be proportional to number of cells, but this is only true in limited circumstances, actual measurements are not fully understood with regards to cell count (Stevenson, McVey et al. 2016)

~~Ask Greg: Is OD linear, ie is 0.3-0.4 the same increase in density as 0.4-0.5~~

Capsules are 200-300 uL

To save matlab figure as a vector image:

exportgraphics(gcf,'vectorfig.pdf','ContentType','vector')

AIC paper, (Akaike 1973)

J = SSE, M = number of data points, Np = number of parameters. Jones does this in (Mutua, Perelson et al. 2019)

Talk to Greg 3/18: maybe persistor cells (latent?), optical density saturates around OD = 1

Identifiability: Sensitivity Matrix, Zika paper

Results

First: Explanation of data

Second: Model selection, AIC

Third: Estimation of parameters

Fourth: Sensitivity

Fifth: Maybe about aerobic vs anaerobic

Akaike, H., Ed. (1973). Information theory and an extension of the maximum likelihood principle. Budapest, Hungary, Akadémiai Kiadó.

Mutua, J. M., A. S. Perelson, A. Kumar and N. K. Vaidya (2019). "Modeling the Effects of Morphine-Altered Virus Specific Antibody Responses on HIV/SIV Dynamics." Scientific Reports **9**(1): 5423.

Stevenson, K., A. F. McVey, I. B. N. Clark, P. S. Swain and T. Pilizota (2016). "General calibration of microbial growth in microplate readers." Scientific Reports **6**(1): 38828.

Vebø, H. C., M. Solheim, L. Snipen, I. F. Nes and D. A. Brede (2010). "Comparative Genomic Analysis of Pathogenic and Probiotic Enterococcus faecalis Isolates, and Their Transcriptional Responses to Growth in Human Urine." PLOS ONE **5**(8): e12489.