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Stochastic analysis of a full system of two competing populations in a chemostat

D. Voulgarelis [a,c,*], A. Velayudhan [b], F. Smith [c]

[a] Centre for Mathematics, Physics and Engineering in the Life Sciences and Experimental Biology, University College London, UCL, Physics Building, Gower Pl, London WC1E 6BT, UK
[b] Department of Biochemical Engineering, University College London, Bernard Katz Building, Gordon Street, London WC1H 0AH, UK
[c] Department of Mathematics, University College London, Gower Street, London WC1E 6BT, UK

HIGHLIGHTS

- The model used here includes Monod kinetics and death rates for two competing species in a chemostat.
- The modelling combines asymptotic analysis, stochastic Langevin systems and Fokker-Planck results.
- The long-term behaviour in many circumstances is predicted to favour one particular species.
- The long-term predictions are different from previous classic predictions in the field.

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ABSTRACT

This paper formulates two 3D models using stochastic differential equations (SDEs) of two microbial populations in a chemostat competing over a single substrate. These models have two distinct noise sources. One is general noise whereas the other is dilution-rate-induced noise. Nonlinear Monod growth rates are assumed and the paper is mainly focused on the parameter values where coexistence is found in the deterministic model. Nondimensionalising the equations around the point of intersection of the two growth rates identifies the dimensionless substrate feed as a large parameter. This in turn is used to perform an asymptotic analysis leading to a reduced 2D system of equations describing the dynamics of the populations on and close to a line of steady states obtained previously from the deterministic stability analysis. That reduced system allows the formulation of a spatially 2D Fokker-Planck equation which, when solved numerically, admits results similar to those from the SDEs. Contrary to previous suggestions, one particular population becomes dominant at large times. Finally, we briefly explore the case where death rates are included.

1. Introduction

1.1. Motivation

For decades the growth of bacterial/cell populations has been a subject of great interest to modellers. The reason behind the popularity of these systems is of course the industrial and ecological importance of competing population growth processes as well as the richness and complexity of the dynamics arising from even simple systems of a few competing organisms. When exploring these systems, coexistence of the different populations is of great significance. One of the best known papers on analysis of coexistence of competing populations is the paper by Stephanopoulos et al. (1979) where they explored the dynamics of two microbial populations competing for a single substrate. Before that paper it was proven in Aris and Humphrey (1977) that if the substrate concentration is kept at the break-even point of the two populations and the dilution rate constant at that value then both populations can coexist. The result was also generalized and proven for multiple competing populations in Hsu (1978) with the use of Lyapunov

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* Corresponding author at: Department of Mathematics, University College London, Gower Street, London WC1E 6BT, UK.

E-mail address: dimitrios.voulgarelis.14@ucl.ac.uk (D. Voulgarelis).

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functions. However that situation presents a knife-edge event where the extinction of one or of the other population occurs if the dilution rate diverges from this exact value (El Hajji and Rapaport, 2009). The main result by Stephanopoulos et al. was that this extinction occurs due to the noise present in the control of the dilution rate in every chemostat. The interesting conclusion was that either population can become extinct depending on the value of the dilution rate and the initial conditions.

A chemostat is an automated bioreactor in which spent medium which contains metabolic products, microorganisms and left over nutrients is continuously removed while fresh medium is added at the same rate to keep the volume constant (Novick and Szilard, 1950). That rate is called the dilution rate and in the case where it is smaller than the growth rate of the micro-organism that micro-organism will grow. The chemostat provides a powerful means of systematically investigating how growth rate impacts processes of the cells such as gene expression and metabolism and the regulatory networks that control the rate of cell growth. Moreover, cells grown in chemostat for generations can be used to study their adaptive evolution in environmental conditions that limit cell growth (Ziv et al.). One of the most important characteristics of the chemostat for multiple microorganism populations competing over a single substrate is the Competitive Exclusion Principle (CEP). Per the CEP in the above scenario only one population will survive. More specifically the one that has the lowest break-even concentration will survive while the other will be led to extinction. The break-even concentration is the concentration of the nutrient such that the specific growth of a microorganism is equal to the dilution rate. A great number of papers have focused on proving the CEP for different growth function assumptions and removal rates. Most of the papers use deterministic equations to describe the evolution of populations in the chemostat while a few have recently addressed what happens when stochasticity is taken into account with either linear growth rates (Xu and Yuan, 2016) or with only a single population (Ji and Yuan, 2014; Xu and Yuan, 2015).

1.2. Aim

The aim of this paper is to explore the idea of coexistence by simulating the dynamics of the full equations for two microbial populations and one substrate for non-linear Monod growth functions with general noise as well as dilution rate induced noise as explored in Stephanopoulos et al. (1979). The rest of the paper begins with **materials and methods**, where we present the stochastic version of the full model, for both cases, in the form of a set of three stochastic differential equations (SDEs) of the Langevin type. Beforehand an asymptotic analysis, which is performed for the case where the substrate feed is large to aid our understanding of the system, shows an intricate structure within the dynamics and provides a simplified two-dimensional version from which we can derive and numerically solve the Fokker-Planck equation readily. Finally we examine the case were death rates are added to the model solely for the dilution rate noise case. The next section after that is **Results and discussion**. Here, the equations are numerically solved and simulated for the parameter values of the same two microbial populations used in Stephanopoulos et al. (1979). Following the results section, our work and findings are summarized in **Further discussion** and finally in the last section named **Conclusion** we raise possible issues as well as possible extensions to our work.

2. Materials and methods

For two populations in a chemostat competing over a single substrate the dimensionless equations are given by:

$$\frac{dx}{dt} = x(f(z) - \theta), \tag{1}$$

$$\frac{dy}{dt} = y(g(z) - \theta), \tag{2}$$

$$\frac{dz}{dt} = \theta(z_f - z) - xf(z) - yg(z). \tag{3}$$

Here $f(z), g(z)$ represent the dimensionless growth rates given by the following equations:

$$f(z) = \frac{a_1 z}{b_1 + z}, \tag{4}$$

$$g(z) = \frac{a_2 z}{b_2 + z}. \tag{5}$$

A list of the parameters and their definitions is given in Table 1.

The non-dimensionalisation was performed around the break-even concentration of the substrate assuming that there is such. In the case of the parameter values used in Stephanopoulos et al. (1979) which will also be used here, there is such a point. In the dimensionless system the two growth rates break even when $z = 1$ in which case $f(z), g(z)$ are also equal to one. In order to have coexistence of the two populations the value of the dimensionless dilution rate, θ, must be one. Then it can be shown using linear stability that there is a line of steady states given by $y = z_f - x - 1$ (Stephanopoulos et al., 1979).

Eqs. (1)–(3) were simplified in Stephanopoulos et al. (1979) and the system reduced to one dimension before introducing the noise term in the dilution rate. In our analysis, by contrast, the noise term is introduced in the full equations without further simplifications, first, and computational studies are made; afterwards a self-consistent asymptotic treatment is also applied to complement the numerical approach and provide further comparisons.

2.1. Stochastic Langevin equations

It was been shown in Imhof and Walcher (2005) that in a chemostat system of the form (1)–(3) stochastic effects can be added as follows:

$$dx = x(f(z) - \theta_0)dt + \sigma_1 x dW_1(t), \tag{6}$$

$$dy = y(g(z) - \theta_0)dt + \sigma_2 y dW_2(t), \tag{7}$$

$$dz = \left[\theta_0(z_f - z) - xf(z) - yg(z)\right]dt + \sigma_3 z dW_3(t). \tag{8}$$

Here W_i are independent Wiener processes (Brownian motions).

In the case of stochasticity being solely due to random fluctuation in the dilution rate the equations are different. Here, the dilution rate θ fluctuates around a mean value and so:

$$\theta = \theta_0 + \zeta(\tau), \tag{9}$$

Here, $\zeta(\tau)$ is a Gaussian random noise. Substituting that back into (1)–(3), a system of stochastic differential equations is found:

Table 1
Parameters and their values for *E. coli* and *Spirillum* sp. respectively.

Parameter (dimensionless)	Definition	Value	Reference
θ	Dilution rate	Varying	–
z_f	Substrate feed	15,000	–
a_i	Maximum growth rate	2.911, 1.636	Stephanopoulos et al. (1979)
b_i	half-saturation coefficient	1.911, 0.636	Stephanopoulos et al. (1979)
σ	Noise intensity	Varying	Our model
θ_0	Dilution rate mean	1	–