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Microbial dormancy and boom-and-bust population dynamics under starvation stress

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ABSTRACT

We propose a model for the growth of microbial populations in the presence of a rate-limiting nutrient which accounts for the switching of cells to a dormant phase at low densities in response to decreasing concentration of a putative biochemical signal. We then show that in conditions of nutrient starvation, self-sustained oscillations can occur, thus providing a natural explanation for such phenomena as plankton blooms. However, unlike results of previous studies, the microbial population minima do not become unrealistically small, being buffered during minima by an increased dormant phase population. We also show that this allows microbes to survive in extreme environments for very long periods, consistent with observation. The mechanism provides a natural vehicle for other such sporadic outbreaks, such as viral epidemics.

1. Introduction

In this paper we address a question which sometimes arises in population biology, particularly when populations oscillate. Such situations are commonly modelled by a set of differential equations, and it is not unusual for the resulting calculated populations to reach very low levels; so low, in fact, that in reality the population would go extinct (Campillo and Lobry, 2012). Examples of this are the study by Murray et al. (1986) on recurrent fox rabies outbreaks, which was criticized by Mollison (1991) for precisely this reason (the 'atto-fox' effect, cf. Cruickshank et al. (1999) and Renshaw (2005)). Models of the immune response commonly exhibit such features (Dibrov et al., 1977a, b; Fowler, 1981) (perhaps because extinction of antigens is desirable), as do population models with delay (Fowler, 1982; Fowler and Mackey, 2002), and more generally, those exhibiting 'boom-and-bust' dynamics, including plankton blooms (Huppert et al., 2005; Mahadevan et al., 2012), glycolytic oscillations (Goldbeter, 1996) and oceanic calcifiers (Omta et al., 2013).

A number of the above studies focus on models which represent the simple interaction between a population and its rate-limiting nutrient. These include the models of Omta et al. (2013), Huppert et al. (2005), and Goldbeter (1996), and the same basic model is used in a microbial context by Sanchez-Vila et al. (2013). It is in this latter context that our interest lies. To be specific, the model structure of interest is that shown in Fig. 1. It represents an input of nutrient C (for example, in a chemostat) which feeds a microbial population B, which undergoes growth as well as death. The resulting mathematical model takes the form

$$\dot{B} = kYCB - dB,$$

$$\dot{C} = I - kCB, \tag{1.1}$$

where for simplicity we ignore Monod kinetics (which in any case has a cosmetic effect, which we discuss in further detail later). In these equations, k is a rate constant, Y is a yield coefficient, d is death rate, and I represents the nutrient input rate.

Some comments on the choice of a constant nutrient supply I should be made. In a bacterial growth experiment in a petri dish, there is no supply, but an initial rich nutrient concentration is given. A more environmentally realistic experiment is the chemostat reactor, in which nutrient is supplied in the input liquid feed, as in (1.1), but is limited by the drainage from the reactor, even in the absence of bacterial consumption. The equivalent of a chemostat in a soil system is, for example, supply of oxygenated rainwater or other nutrient supply, e.g., wastewater, and its removal to an underlying saturated aquifer. Particularly in wastewater systems, it is typically the case that microbial consumption removes all the nutrient, and this underpins the neglect of a sink term of the form $-C/\tau$ in (1.1), where τ would be a residence time for the system. Our neglect of such a term, if relevant, is equivalent to an assumption that the residence time is much longer than the dynamical time scales of interest.

The dynamics of the model (1.1) are simply studied, see for example Omta et al. (2013). There is a steady state which is stable

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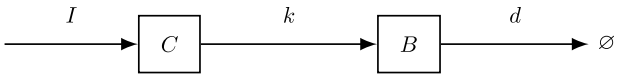

Fig. 1. Schematic of simple biomass/nutrient dynamics. B represents (microbial) biomass, while C represents nutrient, for example organic carbon CH_2O. I is the prescribed input rate of nutrient, k the rate constant in converting nutrient to biomass, and d is the microbial death rate.

but excitable, particularly when the supply of nutrient is small. It is in this context that transient oscillations occur, in which temporal spikes of biomass growth occur at regular intervals, separated by periods where the biomass becomes extremely small. The reason for this striking behaviour can be found by an asymptotic analysis of the model, as was demonstrated by Fowler (2013). In further work, Fowler et al. (2014) extended the model to a system of competing microbial populations, and showed that self-sustained oscillations occur in conditions of starvation, and these solutions were analysed by Fowler (2014). Again, the minima in the microbial populations are so low that in practice, actual extinction would occur. The use of the word 'starvation' in the present context does not necessarily connote a complete absence of nutrient, but refers to conditions in which a suitable comparative measure of the input is small. For (1.1), this takes the form

$$I \ll d/kY; \tag{1.2}$$

in the present context, 'starvation' is further described below.

And yet, as we know, bacteria can be found in the most inhospitable environments. According to Kirchman (2012, p. 9), while normal soils may contain 10^9 cells g^{-1}, even in deep environments kilometres below the Earth's surface, there may be of the order of 10^3 cells g^{-1} which are viable. This is in contrast to the implication of the simple model (1.1) and its more sophisticated variants, which seem to imply that in starvation conditions, microbial extinction would occur in practice. Simply, if C is too low, (1.1) implies that $B \to 0$. And yet, it is suggested that the 'normal' states for many environmental bacteria are similar to starvation conditions (Roszak and Colwell, 1987).

It is this conundrum that we wish to address, in the context of (1.1). In one sense, the answer is obvious. If bacteria remain viable in starvation conditions, then they must be in a dormant state (Stevenson, 1978; Kaprelyants et al., 1993), where the normal processes of respiration and growth (and death) are stalled. Dormancy is widely seen in the bacterial world (Lennon and Jones, 2011) in a variety of forms which allow populations to persist through environmental challenges, even over geological timescales (Hoehler and Jørgensen, 2013). Dormancy is increasingly viewed as an important evolutionary hedging strategy for survival (Shoemaker and Lennon, 2018; Locey et al., 2017), with recognized importance in medicine (Rittershaus et al., 2013; Harms et al., 2016; Lipworth et al., 2016), and soil systems and ecosystem modelling (Wang et al., 2014; He et al., 2015; Joergensen and Wichern, 2018). Various terms describe the different manifestations and types of dormancy in different fields: sporulation, latency, quiescence, persisters. The common trait is the ability to switch between an active form and a hardy, relatively inactive form which can survive and subsequently reactivate or reseed an active population. This necessitates the introduction of a second microbial population A, in which respiratory and growth processes are absent. Our basic hypothesis is that at low population levels, a switch occurs, whereby active microbes switch from their normal birth/death cycle to a state of hibernation, from which they can be aroused in the presence of excess nutrient. This description of the switching process is very similar to the description of the blood cell growth model pioneered by Mackey and co-workers (Mackey, 1978; Haurie et al., 1998).

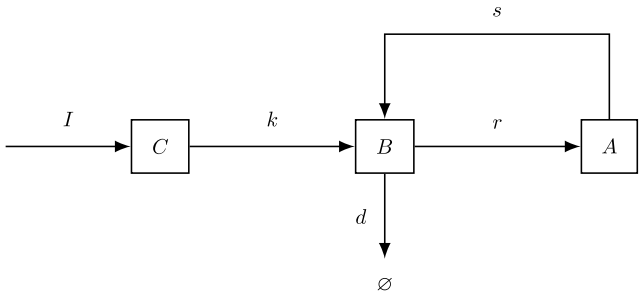

Fig. 2. Schematic of the dormancy model. B, C, I, k, d have the same meanings as in Fig. 1, A denotes microbes in the dormant state, and r and s denote state-dependent switching rates between active (B) and dormant (A) states.

There have been a number of other mathematical models which have been proposed to study the process of dormancy. Bär et al. (2002) modelled the response to intermittent water stress in drylands, comparing bacterial populations without a dormant state to those with the ability to enter and recover from a dormant state based on water availability alone. Malik and Smith (2006) modelled distinct active and dormant populations in a continuous flow planktonic culture, with nutrient-dependent dormancy entry and exit rate functions. They noted oscillatory transients in the approach to the survival steady state, but the model did not show sustained oscillatory solutions. Malik and Smith (2008) looked at the response of dormancy-capable populations to periodic and random switching between favourable and adverse conditions. Hadeler (2013) aimed to place a simple model of dormancy in a broader context of ecological models, analysing the effect of dormancy on periodic orbits in excitable systems. Ayati (2012) modelled bacterial dormancy strategies in batch culture with periodic partial reculturing into fresh media. He proposed a maturation model of dormancy under nutrient stress, in which reactivation of dormant cells occurs only when they have consumed a fixed amount of nutrient, which they are only able to do when nutrient concentration is above a threshold level. Ayati and Klapper (2012) applied a similar model to compare dormancy in chemostat suspended cultures with spatially-structured biofilm comprising active, dormant, and dead cells with nutrient supplied by diffusion from the free biofilm surface.

Mathematical modelling of dormancy is well-established (e.g., Wang and Levin, 2009; Stolpolsky et al., 2011, 2016). One possibility (Jones and Lennon, 2010) is to associate a switch from active to dormant states with the level of available nutrient. In our study, we will examine several possible forms for the functions governing awakening and hibernation, with a view to finding one which allows boom and bust dynamics, without exposing the population to extinction. The mathematical model which represents these ideas is presented in the following section.

2. Mathematical model

The modification of the schematic in Fig. 1 which describes our hypothesized microbial switching is shown in Fig. 2. The additional processes are a transformation (hibernation) of B to A by a cell-specific rate r, and the re-activation (awakening) of A at a cell-specific rate s. The switching between active and dormant states is described by modulating the rates s and r by awakening and hibernation functions p and q, respectively, each of them $\in (0, 1)$, and which can be thought of as cell-specific probabilities of switching mode. We will examine various different combinations of functional dependence. For example, the assumption of a nutrient-dependent switching (Jones and Lennon, 2010) would suggest p and q are respectively increasing and decreasing functions of C; if