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Modeling Sporulation Decisions in *Bacillus subtilis* as Optimal Evolutionary Decision-Making

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***Abstract*— The decision by the bacterium *Bacillus subtilis* to produce spores has been an area of intense study in the molecular cell biology field. Though mechanisms describing *how* the decision is made are becoming better understood, the reasons *why* the decision is made are still nebulous. Spore formation is known to be a survival mechanism, but the circumstances under which it is preferred over other mechanisms have not been carefully examined. In an attempt to address this issue quantitatively, we introduce simple models and a control framework to compare two bacterial survival strategies: sporulation and a simple reduction in metabolic activity. Our findings provide evidence that the decision to sporulate may be the outcome of an underlying optimal control problem to contend with expected future environmental challenges.**

I. Introduction

Bacillus subtilis is a soil-dwelling bacterium that is able to form resilient, dormant, and morphologically distinct cell types, called spores. Spores are capable of reanimation in the future [1], [2]. This process, called sporulation, is primarily triggered by nutrient deprivation and protects against possible environmental stressors such as heat, radiation, and harmful chemicals [3], [4], [5], [6]. Sporulation is an evolutionary trait to deal with unfavorable environmental conditions, possibly enabling the maximization of the "fitness" of the species. This "fitness" metric can be defined in several different ways, but for a quickly-reproducing population, it often refers to number of progeny [7], [8].

Once triggered, sporulation is an irreversible process [9], [10]. Therefore, if nutrient deprivation triggers sporulation, subsequent introduction of additional nutrients will be disregarded. The decision to sporulate should consequently not be taken lightly by the cell. Indeed, the species must accommodate the possibility that higher fitness may be realized by delaying the commitment to sporulate. To deal with this important decision, each *B. subtilis* cell possesses a relatively complex signal integration network called the phosphorelay [1], [11]. This activates a "master regulator" protein by donating or removing phosphate from proteins within the relay [1], [12], [13], [14]. Phosphate is added to the phosphorelay by nutrient deprivation [12], [15], [16] and removed by putative sensing of low population density [17], [18], [19]. For a single cell, once the number of activated "master regulator" molecules passes a certain threshold, sporulation is initiated [20], [21].

Once a *B. subtilis* cell commits to sporulation, a specialized cell division takes place [22]. Instead of forming two identical daughter cells, sporulating cells form distinct daughter cells that act together to create a single spore. One daughter cell, the "mothercell," engulfs the other "prespore" daughter cell shortly after division in a process similar to phagocytosis [22]. The prespore continues to develop with the help of the mothercell until it is fully mature, at which point the mothercell releases the spore by lysing (bursting). Mothercell lysis provides an additional source of nutrients for other growing cells, though the event takes place several hours after the initial commitment to sporulation [23]. Thus, the sporulation process not only reduces the number of growing cells that are consuming nutrients, but it also provides an additional source of food when the mothercell lyses. This may give rise to "population heterogeneity," which is a heterogeneous timing (across the population) of the decision to commit to sporulation [23], [24]. This phenomenon is observed in florescence microscopy images of an isogenic colony of *B. subtilis* cells growing in a nutrient-poor environment. Whatever its underlying cause, population heterogeneity suggests that the sporulation decision may be viewed as a population-level control problem to maximize the fitness of the colony.

Sporulation is one of several survival strategies used in response to nutrient limitation, collectively classified as "dormancy" [25]. In contrast to sporulation, which results in the formation of a morphologically distinct structure, other survival strategies observed in laboratory settings are realized by a sharp reduction in metabolic activity without the formation of a distinct dormant cell [25], [26], [27]. Examples of these morphologically indistinct cells include viable but non-culturable cells and persisters [25], and, like sporulation, they exhibit population heterogeneity [27]. Common across the microbial world [28], metabolic reduction (or "dormancy" in the sequel) provides many of the benefits of sporulation without the complexity and energetic costs of spore formation [25]. This leads to the question of the possible benefits of sporulation over dormancy. By casting each survival strategy as an optimal control problem, we can quantitatively investigate a particular situation where sporulation is preferred over dormancy. This paper will provide a framework for the analysis of sporulation and dormancy, starting with simple models in Section II, a formulation of a control problem behind the survival strategies in Section III, and results comparing sporulation to dormancy in Section IV. We close in Section V by summarizing our findings and detailing future work.

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II. Model

A. Sporulation model

Since population heterogeneity occurs at the colony level, population-level dynamics need to be modeled. The decision to sporulate is made once per cell cycle [29]. Assume that a group of $m_V(t)$ cells makes a decision to commit $p(t)$ cells to spores at time t. The remaining $1-p(t)$ cells not committed to sporulation will divide to produce $2(1-p(t))m_V(t)$ growing cells. A fraction of this group $q(t)$ will die during the course of their cell cycles, and at the end of the cell cycle the decision to sporulate is repeated [24], [30]. Since spores are resilient to environmental stressors, they are assumed to not die. We also assume the nutrient level is not high enough to exit the spore state, so sporulation is an irreversible process. Denoting one generation as the time between cell cycles and assuming the cell cycles for all cells are synchronous, a simple (deterministic) model describing the colony dynamics is given by Equations 1–3.

$$m_V(t+1) = 2(1-p(t))(1-q(t))m_V(t) \tag{1}$$

$$m_S(t+1) = m_S(t) + p(t)m_V(t) \tag{2}$$

$$q(t+1) = \begin{cases} 0 & \text{if } z(t) < 0 \\ z(t) & \text{if } 0 \le z(t) \le 1 \\ 1 & \text{if } z(t) > 1 \end{cases} \tag{3}$$

where $z(t) = q(t) + KM(t+1)$.

In these equations, the variables used are

$M(t) = m_V(t) - \delta p(t-\Delta)m_V(t-\Delta) - N(t)$

$m_V(t) =$ number of growing cells

$m_S(t) =$ number of cells committed to sporulation

$p(t) =$ decision variable for the fraction of cells that commit to sporulation

$q(t) =$ fraction of growing cells that perish during a cell cycle

$N(t) =$ nutrient added over one generation (normalized)

$\delta =$ parameter that describes the amount of nutrient released from mothercell lysis

$\Delta =$ time between commitment to sporulation and mothercell lysis

$K =$ parameter to describe the nutrient consumption by a growing cell

Since cells are assumed to strictly consume nutrients, $\delta < 1$.

A useful picture for the dynamics of $q(t)$ is offered in Figure 1. Notice that it is possible for $M(t) < 0$ if more nutrients are released from mothercell lysis and/or exogenously added to the environment than consumed by growing cells. In this case, the fraction of surviving growing cells increases. On the other hand, if $M(t) > 0$, then the nutrient level decreases and the fraction of dying cells increases. The motivation for choosing to model the death fraction dynamically is to capture the fact that without nutrient infusion, the nutrient level will always be decreasing with time.

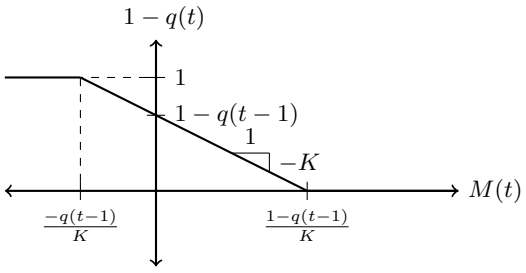

Fig. 1. Dynamics of $q(t)$.

B. Dormancy model

A simple, population-level model for dormancy is very similar to the sporulation model. However, the following differences need to be accommodated: non-negligible exit from dormant state even with low nutrient levels [31], and no mothercell lysis events. The energetic cost of forming a spore [11] is assumed to be negligibly higher than forming a dormant cell. We also assume that a dormant cell has no metabolic activity, so no growth or death are possible in the dormant state. A simple dormancy model can thus be written as

$$m_V(t+1) = 2(1-\alpha_1(t))(1-q(t))m_V(t) + \alpha_2(t)m_P(t) \tag{4}$$

$$m_P(t+1) = (1-\alpha_2(t))m_P(t) + \alpha_1(t)m_V(t) \tag{5}$$

$$q(t+1) = \begin{cases} 0 & \text{if } z_P(t) < 0 \\ z_P(t) & \text{if } 0 \le z_P(t) \le 1 \\ 1 & \text{if } z_P(t) > 1 \end{cases} \tag{6}$$

where $m_P(t)$ is the number of dormant cells, $\alpha_1(t)$ and $\alpha_2(t)$ are decision variables for the fraction of cells that commit to and exit dormancy, respectively, $z_P(t) = q(t) + KM_P(t+1)$, and $M_P(t) = m_V(t) - N(t)$.

III. Control Framework

The "choices" of $p(t)$, $\alpha_1(t)$, and $\alpha_2(t)$ are presumably the result of natural selection. This implies that values of these decision variables that lead to higher fitness for a bacterium will be passed on to future generations, while less successful decisions will terminate with the cells that were programmed with the inferior survival strategies. In addition, the decision variables may be optimal according to a fitness measurement, the choice of which is discussed below.

The notion of fitness as an evolutionary objective is central to the theory of evolutionary biology. Fitness has been interpreted as the ability to produce offspring [32]; future reproductive success [33]; viability and fertility [34]; or survival, mating success, and fecundity [35]. A common theme underlying these definitions is the ability to pass genetic information to successive generation(s). For example, an organism is more likely to pass genetic information to the next generation if it has a high probability of surviving to

adulthood, finding a mate, and producing several offspring. If any of the three probabilities are small, then the fitness of an organism will also be relatively small. Though fitness may be applied to traits, individual organisms, populations, or species [33], [36], the general idea of passing genetic information to the next generation applies universally. Natural selection favors high relative fitness, and it is appealing to visualize evolution as an optimization problem where fitness for a particular environment is maximized.

Though the idea of fitness is clear, measuring fitness is generally challenging. This makes the idea of "maximizing fitness" ambiguous because the ability to pass genetic information to the next generation in a given environment can be quantified in many different ways. The probability of surviving to adulthood [33], expected number of offspring [34], probability of survival relative to the highest survival probability in the environment [35], dominant Lyapunov exponent [26], [37], and expected growth rate of the population (for both continuous and discrete models) [35], [38], [39] have all been used to measure fitness. A generational time scale is almost always used for these fitness measurements [40], so the fitness of a trait, organism, population, or species is defined for a specific generation. This is consistent with defining fitness as the ability to pass genetic information to successive generation(s) in a given environment. For example, the fitness of an adult organism may be the expected number of offspring it produces that are able to survive to adulthood, or it may involve the ratio of viable offspring number to fertile parent number. The fitness may also be defined as the expected number of grand-offspring it produces that are able to survive to adulthood, or some multiplicative factor of viable grand-offspring to fertile parent number.

A natural choice for measuring fitness for *B. subtilis* is the number of viable progeny at some number of generations in the future [7], [8]. This fitness metric is consistent with the model proposed in Section II because of the generational time scale, and viable progeny can be interpreted as the number of genome copies; that is, $m_V(T) + m_S(T)$ or $m_V(T) + m_P(T)$ for some T generations in the future.

The survival strategies can therefore be assumed to be solutions to the optimal control problem

$$\begin{aligned} \mathbf{u}^* = \arg\max_{\mathbf{u}} \quad & J(T) \\ \text{s.t.} \quad & \text{system dynamics} \\ & 0 \le u(t) \le 1,\ t = 0, 1, \ldots, T-1 \end{aligned} \tag{7}$$

where $J(T) = m_V(T) + m_S(T)$ or $m_V(T) + m_P(T)$, and $\mathbf{u} := \{p(0), \ldots, p(T-1)\}$ or $\{(\alpha_1(0), \alpha_2(0)), \ldots, (\alpha_1(T-1), \alpha_2(T-1))\}$ is the decision policy, depending on the survival strategy being examined.

Clearly, the solution to Problem 7 depends on the expected environmental conditions in the future. To gain insight into the possible reasons why sporulation may be preferable to dormancy, we must restrict our attention to a situation where these are the dominant mechanisms for species survival. Specifically, we will examine the case when constant environmental conditions turn catastrophic at the $T-1$ generation ($T \gg 1$) with the simplification that decision policies are constant. We assume that $N(t) = N$ is large enough to support a nonzero growing cell population to the $T-1$ generation to avoid the possibility of the trivial sporulation policy $p \equiv 1$. By "catastrophic," we mean that environmental factors conspire to force $q(t) = 1\ \forall t \ge T-1$. We assume constant decision policies because N is constant and T is assumed to be very large (much larger than the settling time of the system dynamics), which will produce a constant optimal policy over most of the optimization horizon. These optimal control problems, henceforth denoted "long term catastrophe" problems, have the objective functions

$$J(T) = \begin{cases} m_S(T) & \text{for sporulation} \\ m_P(T) & \text{for dormancy} \end{cases}$$

since $m_V(T) = 0$ due to the catastrophe. The assumed environmental conditions and constant policy constraint are similar to those used in another bacterial survival study [41].

After the solutions for the long term catastrophe problems are computed for each survival strategy, the two optimal strategies can be compared. Theoretically, the strategy with the higher fitness would be preferred since it maximizes the population's fitness. This does not imply, however, that the lower-fitness strategy disappears due to competitive advantages that it may offer. In other words, the strategy that maximizes the fitness of a population does not necessarily correspond to an evolutionary stable strategy [38], [42]. Nonetheless, we will judge the performance of a survival strategy based on its fitness measurement $J(T)$.

IV. Results

Without loss of generality, assume $m_P(0) = m_S(0) = 0$.

A. Dormancy strategy for long term catastrophe problem

Since T is assumed to be much larger than the settling time of the system dynamics, the solution to Problem 7 for the dormancy strategy is very straightforward because we may ignore the transient response of the model. The objective function for constant decision variables is

$$J(T) = m_P(T) = \sum_{i=0}^{T-1} \alpha_1 (1-\alpha_2)^i m_V(T-1-i),$$

from which it is immediately clear that the optimal resuscitation term is $\alpha_2^* = 0$ since, although the dormancy model is generally not stable, $m_V(t)$ and $q(t)$ will always remain bounded (though not necessarily constant). If K is chosen small enough such that $q(t) < 1\ \forall t$, then $m_V(t) > 0\ \forall t$. For $m_V(t)$ and $q(t)$ periodic,

$$\sum_{i=0}^{T-1} q(i+1) - q(i) = \sum_{i=0}^{T-1} K M_P(i) \approx 0$$

since T is much larger than the system dynamics timescale. The objective function may be closely approximated by

$$J(T) \approx \alpha_1 N T. \tag{8}$$

Obviously, the argument that maximizes this cost function (α_1^*) is the maximum allowable α_1. From Equation 4,

$$\frac{1}{T}\sum_{i=0}^{T-1}\frac{m_V(i+1)}{m_V(i)} = \frac{1}{T}\sum_{i=0}^{T-1} 2\left(1-\alpha_1\right)\left(1-q(i)\right) \approx 1$$

where the approximation is good when T is much larger than the system dynamics timescale and $m_V(t)$ is periodic and has an average value much larger than the amplitude of its oscillations. Since the dormancy model is a population model, $m_V(t)$ should always be large, so the approximation is valid.

The average value of $q(t)$ is $\overline{q} = 1 - \frac{1}{2(1-\alpha_1)}$. From the constraint $0 \leq \overline{q} < 1$, the maximum value of α_1 is $\alpha_1^* = \frac{1}{2}$.

Note that by ignoring the transient response, we have assumed that the states $m_V(0)$ and $q(0)$ were already at the optimal configuration. Dropping this assumption will give approximately the same result (if T is large), though α_1^* will be very slightly less than $\frac{1}{2}$ if the optimal states are not reachable from the initial conditions with $\alpha_1 = \frac{1}{2}$ and $\alpha_2 = 0$. Nonetheless, we will assume $(\alpha_1^*, \alpha_2^*) = \left(\frac{1}{2}, 0\right)$ is the optimal dormancy strategy for the long term catastrophe environment.

B. Sporulation strategy for long term catastrophe problem

The optimal constant decision variable p for the sporulation strategy is found analogously. The cost function is

$$J(T) = m_S(T) = \sum_{i=0}^{T-1} p m_V(i),$$

where periodicity in $q(t)$ and large T give the following result, obtained from $\sum_{i=0}^{T-1} M(i) \approx 0$:

$$\sum_{i=0}^{T-1} m_V(i) \approx \frac{NT}{1-\delta p}$$

The cost function can therefore be closely approximated by

$$J(T) \approx \frac{p}{1-\delta p} NT \tag{9}$$

subject to the constraint $p \leq \frac{1}{2}$, which is derived in a similar manner as the constraint on α_1 for the dormancy model. Since it is assumed that cells do not create nutrients (i.e. $\delta < 1$), the maximizing p is readily found to be $p^* = \frac{1}{2}$.

The same caveat about reachability of the optimal states for the dormancy model applies to the sporulation model. Also, for both models, the approximations are exact if the numerical values for the parameters are chosen such that $m_V(t)$ and $q(t)$ approach constant values.

From Equations 8 and 9, it is clear that the sporulation survival strategy has a higher fitness than the dormancy survival strategy due to the mothercell lysis term. We may extend this result to special cases of time-varying decision policies (with $\alpha_2^* \equiv 0$) by further examining the effects of mothercell lysis, presented in Propositions 4.1 and 4.2. Note that, when $\alpha_2^* \equiv 0$, the dormancy model is equivalent to the sporulation model with $\delta = 0$.

Proposition 4.1: Let δ = amount of nutrient release by mothercell lysis. Suppose the decision policy $\mathbf{p} = \{p(0), p(1), p(2), \ldots\}$ and initial conditions are independent of δ. Suppose

$$K \leq \frac{1}{2\max_t m_V^\delta(t)} \tag{10}$$

and

$$\delta \geq \frac{m_V^\delta(t) - m_V(t)}{m_V^\delta(t) m_V^\delta(t+1-\Delta) p(t+1-\Delta) K}, \ \forall t \tag{11}$$

where $m_V^\delta(t)$ is the number of growing cells when $\delta > 0$. Then, for all initial conditions,

$$1 - q^\delta(t) \geq 1 - q(t), \ \forall t$$

where $q^\delta(t)$ corresponds to the case with mothercell lysis nutrient release, and $q(t)$ corresponds to the case without mothercell lysis nutrient release.

Equivalently, suppose the policy $\mathbf{p}$ and the initial conditions are independent of δ, the death fraction does not increase too rapidly, and δ is greater than some number. Then, the fraction of cells surviving to the next generation with mothercell lysis nutrient release for any $\delta > 0$ is always greater than or equal to the fraction of cells surviving to the next generation without mothercell lysis nutrient release.

Remarks: The condition (10) on K ensures that $q^\delta(t) - q^\delta(t+1) \leq \frac{1}{2}, \forall t$. It is possible that condition (11) may not be satisfied with the constraint $\delta < 1$.

Proof: Denote a variable $y^\delta(t)$ as being associated with the case of mothercell lysis nutrient release ($\delta > 0$) and $y(t)$ (without the superscript) as being associated with the case of no mothercell lysis nutrient release ($\delta = 0$). The result will be shown by induction.

(*Base step*). Since the initial conditions are identical ($q^\delta(0) = q(0)$ and $m_V^\delta(0) = m_V(0)$), and since the decision policies are the same, then $m_V^\delta(1) = m_V(1)$. Letting $M^\delta(1) = m_V^\delta(1) - \delta p(1-\Delta) m_V^\delta(1-\Delta) - N(1)$ and $M(1) = m_V(1) - N(1) = m_V^\delta(1) - N(1)$, the definitions for $q^\delta(1)$ and $q(1)$ clearly show that $1 - q^\delta(1) \geq 1 - q(1)$.

(*Inductive step*). Suppose $1 - q^\delta(\tau) \geq 1 - q(\tau)\ \forall \tau \leq t$. This implies that $m_V^\delta(\tau) \geq m_V(\tau)\ \forall \tau \leq t$ since the initial conditions are assumed to be identical and the control $\mathbf{p}$ is identical.

Showing that $1 - q^\delta(t+1) \geq 1 - q(t+1)$ is equivalent to showing that

$$\begin{aligned} & q^\delta(t) + K M^\delta(t+1) \leq q(t) + K M(t+1) \\ \Leftrightarrow\ & m_V^\delta(t+1) - m_V(t+1) \leq \\ & \qquad \delta p(t+1-\Delta) m_V^\delta(t+1-\Delta) + \frac{q(t) - q^\delta(t)}{K}. \end{aligned} \tag{12}$$

From the system dynamics,

$$\begin{aligned} m_V^\delta(t+1) - m_V(t+1) = \\ & 2(1-p(t))\left[(1-q^\delta(t))m_V^\delta(t) - (1-q(t))m_V(t)\right] \\ & \leq 2m_V^\delta(t)\left[1 - \frac{m_V(t)}{m_V^\delta(t)} - q^\delta(t) + q(t)\frac{m_V(t)}{m_V^\delta(t)}\right] \\ & \leq 2m_V^\delta(t)\left[1 - \frac{m_V(t)}{m_V^\delta(t)} - q^\delta(t) + q(t)\right] \end{aligned}$$

where the first inequality results from $1 - p(t) \leq 1$ and the second inequality results from $m_V^\delta(t) \geq m_V(t)$. From conditions (10) and (11), respectively,

$$\begin{aligned} m_V^\delta(t+1) - m_V(t+1) &\leq \frac{m_V^\delta(t) - m_V(t)}{m_V^\delta(t)K} + \frac{q(t) - q^\delta(t)}{K} \\ &\leq \delta p(t+1-\Delta)m_V^\delta(t+1-\Delta) + \frac{q(t) - q^\delta(t)}{K} \end{aligned}$$

$\forall t$, which satisfies Equation 12. Therefore, $1 - q^\delta(t+1) \geq 1 - q(t+1)$. ∎

Though Proposition 4.1 may seem obvious, the subtlety lies in the fact that a decreased fraction of cells dying puts a larger load on the nutrient supply, which will correspondingly increase the parameter $q(t)$.

Proposition 4.2: Suppose conditions (10) and (11) hold, and the initial conditions are independent of δ. Then, for all $T > 0$,

$$\max_{\mathbf{p}} m_S^\delta(T) \geq \max_{\mathbf{p}} m_S(T),$$

where $\mathbf{p} = \{p(0), p(1), \ldots, p(T-1)\}$.

Equivalently, suppose the initial conditions are independent of δ, $q(t)$ does not increase too rapidly, and δ is greater than some number. Then, the spore component of the fitness metric with mothercell lysis is at least as large as the spore component of the metric without mothercell lysis.

Proof: For any $T > 0$, the objective functions can be written as

$$\begin{aligned} m_S(T) &= \sum_{t=0}^{T-1} p(t)2^t m_V(0) \prod_{i=0}^{t-1}(1-p(i))(1-q(i)) \\ m_S^\delta(T) &= \sum_{t=0}^{T-1} p^\delta(t)2^t m_V(0) \prod_{i=0}^{t-1}(1-p^\delta(i))(1-q^\delta(i)). \end{aligned}$$

Denote the optimal policy and states with $*$. By definition,

$$\begin{aligned} \sum_{t=0}^{T-1} p^{\delta*}(t)2^t m_V(0) \prod_{i=0}^{t-1}(1-p^{\delta*}(i))(1-q^{\delta*}(i)) \geq \\ \sum_{t=0}^{T-1} p(t)2^t m_V(0) \prod_{i=0}^{t-1}(1-p(i))(1-q^\delta(i)) \end{aligned}$$

for any other policy with elements $p(t)$, including the optimal policy corresponding to the model with no mothercell nutrient release (with elements $p^*(t)$). Then,

$$\begin{aligned} \sum_{t=0}^{T-1} p^{\delta*}(t)2^t m_V(0) \prod_{i=0}^{t-1}(1-p^{\delta*}(i))(1-q^{\delta*}(i)) \geq \\ \sum_{t=0}^{T-1} p^*(t)2^t m_V(0) \prod_{i=0}^{t-1}(1-p^*(i))(1-q^\delta(i)) \end{aligned}$$

but since $1 - q^*(i) \leq 1 - q^\delta(i)\ \forall i \leq T-1$ (both under the same policy with elements $p^*(t)$), then

$$\begin{aligned} \sum_{t=0}^{T-1} p^*(t)2^t m_V(0) \prod_{i=0}^{t-1}(1-p^*(i))(1-q^\delta(i)) \geq \\ \sum_{t=0}^{T-1} p^*(t)2^t m_V(0) \prod_{i=0}^{t-1}(1-p^*(i))(1-q^*(i)). \end{aligned}$$

So, end to end, we are left with the inequality

$$\begin{aligned} \sum_{t=0}^{T-1} p^{\delta*}(t)2^t m_V(0) \prod_{i=0}^{t-1}(1-p^{\delta*}(i))(1-q^{\delta*}(i)) \geq \\ \sum_{t=0}^{T-1} p^*(t)2^t m_V(0) \prod_{i=0}^{t-1}(1-p^*(i))(1-q^*(i)), \end{aligned}$$

or

$$\max_{\mathbf{p}} m_S^\delta(T) \geq \max_{\mathbf{p}} m_S(T)$$

for all $T > 0$. ∎

C. Sporulation versus dormancy

By simple examination of Equations 8 and 9, the sporulation survival strategy has a higher fitness than the dormancy survival strategy in the long term catastrophe environment described in Section III. With conditions on K and δ, Propositions 4.1 and 4.2 extend the selection of sporulation over dormancy for time-varying decision policies in environments where $\alpha_2^* \equiv 0$ (no exit from dormant state) because the dormancy model becomes equivalent to the sporulation model with $\delta = 0$.

The choice of $\alpha_2^* \equiv 0$ is corresponds to extremely harsh environmental conditions, where it is better to "wait out the storm" and remain dormant instead of risk increased death in the growing state; indeed, since the cells knew of the catastrophe $T-1$ generations into the future in our particular example, it was better to devote resources to survival structures. The quantitative preference of sporulation over dormancy in extremely harsh environments is also consistent with the morphological differences between spores and metabolically-inactive cells. Whereas inactive cells survive by simply not interacting with their environment (thereby saving energy and resisting antibiotics, for example), spores are designed to protect the cell from harsh environmental conditions and have been recognized as the "hardiest known form of life on Earth" [6]. The results of this modeling exercise should therefore be expected.

V. Conclusions and Future Work

In this paper, two simple, phenomenological models for sporulation and dormancy were proposed. A control framework was presented that assumed the survival strategies, which were the results of natural selection, have evolved to maximize the fitness of a group of cells. The models and control framework were applied to a long term catastrophe environmental profile and sporulation was shown to have a higher fitness than dormancy in this particular scenario.

As long as no cells exit dormancy and some conditions hold, this result can be extended to decision policies that are allowed to vary in time. Our results are consistent with the common acknowledgment that spores are able to resist demanding environmental conditions, and if our models and evolutionary optimality assumptions are valid, provide a possible quantitative reason why sporulation has evolved.

We are working on corroborating these findings with actual experimental data. We have access to fluorescence microscopy images of sporulating colonies of *B. subtilis*, which will allow the validity of the sporulation model to be assessed. We are also working on other model formulations to more carefully examine the sporulation decision process in the context of evolutionary optimality.

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