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Monopoly Pricing of an Antibiotic Subject to Bacterial Resistance

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Abstract:
We develop a dynamic bio-economic model of bacterial resistance and disease transmission in which we characterize the pricing policy of a monopolist who is protected by a patent. After expiration, the monopolist behaves competitively in a generic industry having open access to the common pool of antibiotic efficacy and infection. The monopolist manages endogenously the levels of antibiotic efficacy as well as the infected population, which represent quality and market size respectively and achieves, at least temporarily, higher such levels than a hypothetically myopic monopolist who does not take into account the dynamic externalities. The pricing policy and the biological system are characterized by the *turnpike* property. Before the patent vanishes, the monopolist behaves more and more myopically, leading to a continuous decrease in the price of the antibiotic. Once the generic industry takes over, a discontinuous fall in price occurs. Whether a prolongation of the patent is socially desirable depends on the relative levels of antibiotic efficacy and infection.

Keywords: Antibiotic efficacy, public health, monopoly pricing, renewable resource, optimal control, turnpike, patent length

JEL Classification: I18, L12, Q21

1 Introduction

Pharmaceutical firms that produce an antibiotic are usually given temporary monopoly power through a patent, granted in order to recover the incurred investment in R&D and by this to encourage future innovation of new drugs. The granting of this monopoly power ignores the fact that this also gives the firm some control over the levels of the drug's treatment efficacy on the one hand, as well as of the infected population on the other. This control stems from the fact that the antibiotics sold to the community help cure the infected, and thus decreases the level of infection, at least in the short run. However, a too intensive use of antibiotics within the community may lead to an increase in the bacterial resistance of the drug – the mirror image of its treatment efficacy – via the natural selection of drug-resistant bacteria over time.[1] The purpose of this paper is to study this aspect of the pricing policy of a monopolist whose market is protected by a patent and who is aware of the existing externalities. Whether the monopolistic pricing policy is socially desirable as compared to the subsequent generic industry is also considered.

Bacterial resistance to antibiotics has recently attracted the interest of economists. Most have put the emphasis on the determination of the socially optimal use of the antibiotic over time, ignoring the analysis of the market outcome. These include Laxminarayan and Brown (2001), Rudholm (2002), Wilen and Msangi (2003), Rowthorn and Brown (2003) and Gersovitz and Hammer (2004). Very few have considered explicitly how the market will allocate the antibiotic use over time. Fischer and Laxminarayan (2005) is an exception, as are Herrmann and Gaudet (2009) and Mechoulan (2007). Fischer and Laxminarayan (2005) treat the problem as that of the sequential exploitation by a monopolist of exhaustible resources pools (the stock of efficacy of the antibiotics) when a setup cost must be incurred to access the next pool of resource (the next antibiotic). They show that whether the monopolist exploits the efficacy of the existing antibiotic faster or slower, and hence introduces the new drugs sooner or later than is socially optimal, depends on whether there are many or few

[1] See Levy (1992) for a useful overview of the subject of antibiotic resistance.

new drugs left to be developed. Herrmann and Gaudet (2009) model a generic industry as composed of antibiotic producers that have open access to the common resource pool of antibiotic efficacy and compare the market outcome in this case to the social optimum. It is shown that, depending on the bio-economic parameters of the model, in particular the cost of production and the increase in the recovery rate that results from treatment, the steady-state level of antibiotic efficacy that results from the generic industry may be lower or higher than is socially optimal. Mechoulan (2007) shows in a highly stylized model of disease transmission that while a social planner prefers eradication of infection (if possible), a monopolist achieves a steady state with a positive level of infection. Adding intertemporal resistance built-up to the model, the author concludes that re-activating patent rights may be socially desirable if the increase in resistance is sufficiently high.[2,3]

It is shown in this paper that a monopolist who benefits from a patent on the sale of an antibiotic, and who takes into account the effect of his sales on the efficacy of his antibiotic (the quality of his product) and on the evolution of the infected population (his market size), will tend to price so as to spend a period of time in the neighborhood of the steady-state price of an infinitely-lived monopolist. The length of the period of time in question will depend on the patent life. Thus, if the patent life is long enough, the price path will at first decrease towards the steady-state price of the infinitely-lived monopolist, remain in the neighborhood of this price (or possibly exactly on it) for an interval of time, and leave it as the end of the patent approaches. In that final phase, the monopolist acts more and more as a myopic monopolist, that is one who neglects the impact of his decision on the evolution of the antibiotic efficacy and the stock of infected population. As a result, price decreases

[2]In a much earlier contribution, Tisdell (1982) has argued that a monopoly may result in a socially optimal use of the drug, given the externality that results from antibiotic use. More recently Horowitz and Moehring (2004) have argued, using a diagrammatic analysis, that antibiotic resistance will tend to increase when the patent on an antibiotic expires which is also one of our findings in this paper for a particular class of bio-economics parameters.

[3]In connection to the vaccine market, Kessing and Nuscheler (2006) build a static model to analyze the monopoly pricing of a vaccine when demand for it is negatively affected by the expected rate of immunization. The monopolist exploits this externality, leaving poorer individuals untreated in order to increase the willingness-to-pay for the vaccine by richer individuals.

until it reaches the price charged by a myopic monopolist, just as the patent expires. The industry is then taken over by generic producers, with open access to the stock of efficacy of the antibiotic, and the price jumps down to average cost. Whether the turnpike property just described is exact or not and what length of time is spent near or at the infinitely-lived monopoly price depends on the bio-economic parameters and on the length of the patent life. The welfare implications of changing the duration of the patent depend on the state of the system and the time at which the announcement becomes effective. We find that prolonging the patent is only socially desirable when the level of infection is relatively low compared to the level of antibiotic efficacy. In fact, relatively higher levels of infection are contained more efficiently under a generic industry, as it charges a lower price implying more individuals to buy the antibiotic.

This paper is structured as follows. In Section 2, the epidemiological and economic models are presented. The monopolistic programme is characterized in Section 3. Two benchmark cases, which are the myopic monopolist and the infinitely lived monopolist are also considered for comparison in that section. The welfare implications of prolonging the patent are described in Section 4. We conclude in Section 5.

2 Model

The model has an epidemiological and an economic component. The epidemiological component (the so-called SIS-model) is borrowed from the epidemiological literature (see for instance Bonhoeffer *et al.*, 1997). It has already been used before in the economics literature by, among others, Laxminarayan and Brown (2001), Wilen and Msangi (2003) and Herrmann and Gaudet (2009). The economic component involves the interaction of the monopolist (on the supply side) with a derived demand for the antibiotic first presented in Herrmann and Gaudet (2009). We present the epidemiological model and the demand side of the economic component in what follows.

2.1 The epidemiological model

We assume that there is only one antibiotic treatment available to fight a particular infection. The infected population (I) is made up of those suffering from a drug-susceptible version of the infection (I_w) and those suffering from the drug-resistant version (I_r), both versions being naturally present in the system. The problem of antibiotic resistance arises as the bacterial strain causing the drug-resistant version of the infection becomes predominant in the system, since the drug-susceptible bacterial strain clears at higher rate under antibiotic treatment. This effect is generally referred to as *natural selection*, on which we will concentrate here.[4] In such a context, an appropriate measure of antibiotic treatment efficacy (w) is the ratio of the population being infected with the drug-suspectable version to the overall infected population, *i.e.* $w = I_w/(I_w + I_r) = I_w/I$.

We assume the overall population to be constant and equal to N. The healthy population is then given by $S = N - I$. Let β be the rate of transmission of the infection between the healthy and the infected population. The SIS-model assumes that the rate of addition at time t to the infected population, either drug-resistant or drug-susceptible, is given by $\beta S(t)I_r(t)$ and $\beta S(t)I_w(t)$ respectively. The infected individuals may recover naturally, that is without taking the antibiotic. We denote the natural recovery rates from the drug-resistant and the drug-susceptible infection by r_r and r_w respectively. If all the infected individuals are treated with the antibiotic, the rate of recovery of those infected with the drug-resistant strain remains unchanged, while the rate of recovery of those infected with the drug-susceptible strain increases to $r_w + r_f$. If a fraction $f \in [0, 1]$ of the infected population is being treated with the antibiotic, the rate of recovery of those infected with the drug-susceptible strain will be $r_w + fr_f$. Hence the total infected population decreases at the rate $r_r I_r(t) + (r_w + fr_w)I_w(t)$.

The population dynamics can be summarized by the following system of differential

[4] Antibiotic resistance may not only be caused by natural selection, but also by the mutation of drug-susceptible strains when being continually in contact with the antibiotic, or by the transfer of plasmids, *i.e.* genetic material transferred from resistant towards susceptible strains and containing information on how to be resistant. See for instance Levy (1992).

equations:

$$\begin{aligned} \dot{I}_w &= (\beta S - r_w - f r_f) I_w \\ \dot{I}_r &= (\beta S - r_r) I_r \\ \dot{S} &= -\dot{I} = -\dot{I}_w - \dot{I}_r. \end{aligned} \tag{1}$$

Note that the evolution of the healthy population ($\dot{S}$) is the complement of the evolution of the infected population ($\dot{I}$), since we have assumed the overall population to be constant. Using this fact and the definition of antibiotic efficacy, we can rewrite system (1) as:

$$\dot{w} = w(1-w)[\Delta r - r_f f] \tag{2}$$

$$\dot{I} = I(\beta(N-I) - r_r + w[\Delta r - r_f f]) \tag{3}$$

where $\Delta r = r_r - r_w$ measures what is called in the epidemiological literature the fitness cost of resistance. The fitness cost can be understood as an opportunity cost of the resistant bacterial strains: they remain unaffected by antibiotic treatment, but this ability comes at the cost that they clear at a higher rate than drug-susceptible strains in the absence of antibiotic treatment.

We can now point out two important effects in the biological system that are apparent in equation (2): a positive fitness cost Δr implies renewability of the resource of antibiotic efficacy (fitness cost effect), while the additional recovery rate r_f helps clear drug-susceptible infections, leading potentially to the dominance of the drug-resistant version of the infection (natural selection effect). If a fraction $f = \Delta r / r_f$ of the infected population is treated with the antibiotic, those two effects cancel out. For all other admissible values of f, either one effect dominates, leading to an increase or decrease in the level of antibiotic efficacy. Assuming that both the fitness cost effect and the natural selection effect are apparent in the system, we must have $\Delta r / r_f < 1$.

There exist three steady-state configurations to the epidemiological dynamics described by (2) and (3). Let w^{SS} and I^{SS} denote the steady-state values of w and I respectively. For

any $f \neq \Delta r/r_f$, we have $\dot{w} = 0$ for $w = 0$ or $w = 1$ and there are two distinct steady states, given by:

$$(I^{SS}, w^{SS}) = \left(\frac{\beta N - r_r}{\beta}, 0\right) \quad \text{and} \tag{4}$$

$$(I^{SS}, w^{SS}) = \left(\frac{\beta N - r_w - r_f f}{\beta}, 1\right) \tag{5}$$

For $f = \Delta r/r_f$, we have $\dot{w} = 0$ for any value of w and hence all

$$(I^{SS}, w^{SS}) = \left(\frac{\beta N - r_r}{\beta}, w \in [0, 1]\right) \tag{6}$$

constitute steady states. We will assume throughout the paper that the biological parameters imply that the infection cannot be eradicated, nor dominate the whole system, so that the steady states of infection must be interior, $0 < I^{SS} < N$.[5]

If the treatment rate f were to remain *constant* over time, then, in order to reach the steady state at which $w^{SS} = 1$, the fraction, say f_1, of the infected population being treated must satisfy $f_1 < \Delta r/r_f$. The steady state $w^{SS} = 0$ will be reached if a fraction, say f_2, gets treatment over time with $f_2 > \Delta r/r_f$. For the corresponding steady-state levels of the infected population, this implies

$$\frac{\beta N - r_r}{\beta} < \frac{\beta N - r_w - r_f f_1}{\beta}$$

Thus the steady state at which antibiotic efficacy reaches its upper bound ($w^{SS} = 1$), corresponds to a relatively higher level of the infected population than the steady state at which antibiotic efficacy is lowest ($w^{SS} = 0$). For an interior steady state of w, which is reached if a fraction, say f_3, of the infected population gets treatment, with $f_3 = \frac{\Delta r}{r_f}$, the steady-state level of infection is equal to $(\beta N - r_r)/\beta$.

[5]Thus, we must have $\beta N - r_r > 0$ for steady states (4) and (6) to be interior. The positiveness of steady state (5) is implied by the fact that it can only be reached with $f < \Delta r/r_f < 1$ for an initial value of antibiotic efficacy $w_0 < 1$. It order to assure a positive level when $w_0 = 1$, we assume $\beta N - r_f - r_w > 0$. We also want to make sure that the system doesn't become dominated by infection when out of steady state. Assuring that less individuals fall ill than are healthy if recovery rates were zero ($\beta SI < S$), it can be shown that a sufficient condition for this is $\beta < 1/N$. For the particular case of a perfectly efficient drug ($w = 1$), assuring infection to remain present when there are no healthy individuals left in the system ($S = 0$) is implied by the sufficient condition $\dot{I}_w = -[r_w + r_f]I_w < I_w$, or $r_w + r_f < 1$.

A representative evolution of the state variables starting from an interior state (I_0, w_0) and corresponding to the cases f_1 and f_2 just described is illustrated in Figure 1. Figure 1 represents a phase diagram and shows the $\dot{I}$-isocline and the corresponding forces driving the system when away from the isocline (as indicated by the arrows) under the two different regimes corresponding to the treatment rates f_1 or f_2.[6] In the case of $f_1 < \Delta r/r_f$ the continuous lines apply, and the system tends to the steady state at which $w^{SS} = 1$, since the fitness cost effect dominates. In the case of $f_2 > \Delta r/r_f$ the dashed lines apply, and the system tends to the steady state at which $w^{SS} = 0$, since the natural selection effect of resistant bacterial strains dominates. For $f = \frac{\Delta r}{r_f}$, both effects cancel out so that the level of antibiotic efficacy remains constant and the system converges to a steady state as defined in (6) (not shown in the Figure).

The crucial point is that the dynamic system is non-stationary with respect to the treatment rate f. If f changes over time, the $\dot{I}$-isoclines will also change. Values of f closer to the critical value $\Delta r/r_f$ imply steeper $\dot{I}$-isoclines. If the sequence of f converges monotonously to $\Delta r/r_f$ from above or from below, the isoclines will pivot around the point $((\beta N - r_r)/\beta, 0)$ and the dynamic system will converge to an interior steady state (see for instance Herrmann and Gaudet (2009) for the case of the generic industry).

2.2 The demand

The market demand for the antibiotic is derived under three main assumptions. First, we assume that individuals are vertically differentiated with respect to their valuation θ of being in good health, the distribution function of which is $F(\theta)$ over the population N. Second, we assume that consumers do not behave strategically, thus abstracting from consumers stockpiling (or waiting to buy) antibiotics when an increase (or decrease) in price is expected. Third, we assume that infected individuals do not know whether they suffer from the drug-

[6] Analytically, the $\dot{I}$-isocline is derived by setting $\dot{I} = 0$, which gives $I = 0$ or $w = \tilde{w}(I) = \frac{\beta(I-N)+r_r}{\Delta r - r_f f}$. For $f < \Delta r/r_f$, the isocline has a positive slope, while it is negative for $f > \Delta r/r_f$. If f equals the critical fraction $\Delta r/r_f$, the $\dot{I}$-isocline is a vertical line passing through I^{SS} as defined in (6).

resistant or the drug-susceptible versions of the disease. However, we assume that they know the current treatment efficacy of the antibiotic, $w(t)$, and the natural recovery rates from either infection. If the spread of infection and the valuation of being in good health are independent events, the probability of recovering from infection without antibiotic treatment is $\pi(w) = wr_w + (1-w)r_r$. With antibiotic treatment, recovery from infection will occur with a higher probability of $[\pi(w) + wr_f]$.[7]

The gross utility derived from health considerations by the individual of type θ will therefore be given by:

$$u(\theta) = \begin{cases} \theta & \text{if in good health} \\ \pi(w)\theta & \text{if infected and not taking the antibiotic} \\ [\pi(w) + r_f w]\theta & \text{if infected and taking the antibiotic.} \end{cases}$$

Only infected individuals whose valuation of being in good health is sufficiently high will buy the antibiotic. Denote by $\tilde{\theta}$ the type who is indifferent between buying the antibiotic or not when infected. The value of $\tilde{\theta}$ is determined by: $\pi(w)\tilde{\theta} = [\pi(w) + r_f w]\tilde{\theta} - p$, which means that

$$\tilde{\theta} = \frac{p}{r_f w}. \tag{7}$$

Thus infected individuals with $\theta \geq \tilde{\theta}$ will buy the antibiotic and those with $\theta < \tilde{\theta}$ will not. The fraction of the infected population willing to buy the antibiotic is $[1 - F(\tilde{\theta})]$, and, since individual demand is unitary, total demand is given by: $Q = I\left[1 - F\left(\frac{p}{r_f w}\right)\right]$. Therefore the inverse demand function is: $P\left(\frac{Q}{I}, w\right) = r_f w F^{-1}\left(1 - \frac{Q}{I}\right)$. For simplicity, let us assume that θ is distributed uniformly over the population, with supports $[0, 1]$. The inverse demand function then becomes: $P\left(\frac{Q}{I}, w\right) = r_f w\left(1 - \frac{Q}{I}\right)$. Notice that the intercept of the inverse demand is $r_f w$ and its slope is $r_f w/I$. The variable w can be viewed as an (endogenous) index of the quality of the drug, which can vary between zero and one, while I is the market size for the antibiotic. For $w = 0$, demand is identically zero. For a given value of the infected population, I, the inverse demand curve pivots upwards through the point $(Q, p) = (I, 0)$ as

[7] Using the aforementioned assumptions on the biological parameters allows to show that the last two expressions are indeed positive and smaller than unity.

the quality of the antibiotic increases from zero to one and demand is at its highest when $w = 1$.

The ratio Q/I represents the fraction of the infected population treated and is thus equal to the parameter f in the dynamic constraints (2) and (3). The inverse demand function can therefore be rewritten as a function of the fraction of the infected population being treated and the efficacy of the antibiotic to give:

$$P(f, w) = r_f w(1 - f). \tag{8}$$

3 The monopolistic pricing behavior

We assume that a patent exists, assigning exclusive rights to a monopolistic firm to sell the antibiotic for an exogenously given period of time $T \in (0, \infty]$, after which the antibiotic is sold by a generic industry.[8] A non-myopic monopolist is characterized by the fact that he takes into account the impact of his current decisions on future levels of antibiotic efficacy and infection, and thus on the evolution of the quality of his product and its market size over time. Hence, the quality and market size of the antibiotic are determined endogenously in the system.[9] The instantaneous profit function of the monopolist is given by $\Pi(t) = [r_f w(t)(1 - f(t)) - c]f(t)I(t)$, where c is the constant unit cost of the antibiotic. For ease of reference to the epidemiological model, we will treat the fraction of the infected population to which the antibiotic is sold, $f(t)$, as the control variable, and infer the market clearing price $p(t)$ from the inverse demand function. The objective function of the monopolist is given by:

$$\max_{\{0 \leq f(t) \leq 1\}} \int_0^T e^{-\rho t} \Pi(t) dt + V^g(T) \tag{9}$$

[8] We thus abstract from the R&D process before the patent is granted. Kingston (2000) presents historical notes on the R&D of the first antibiotics, and addresses aspects related to the patenting process of antibiotics.

[9] The management of antibiotic efficacy (and infection) by the monopolist may reveal impossible if bacteria can easily become cross-resistant to several antibiotics. In such a case, even if a monopolist were to sell fewer amounts of the antibiotic over time, the level of antibiotic efficacy may decline due to an intensive use of other antibiotics on behalf of other producers, which are linked to the same resource pool of antibiotic efficacy. In the limit, open-access to that pool may arise, leaving the monopolist without any influence on the quality of his patented product.

subject to the equations (2) and (3). The bequest function $V^g(T)$ accounts for the profits of the former monopolist once he has become one of the competitive producers of the generic industry after the expiration of the patent. Assuming that all generic producers have access to the same technology as the monopolist does, the equilibrium in that generic industry will be such that price equals the average production cost and economic profits are zero. Hence $V^g(T) = 0$. Such a generic industry and the resulting evolution of antibiotic efficacy and infection are addressed in Herrmann and Gaudet (2009).[10]

This optimization program contrasts with that of a myopic monopolist, who takes the quality and market size at each instant of time as given and who does not take into account the long-run effects of his current decisions. As a consequence, a myopic monopolist maximizes (9) neglecting the dynamic constraints (2) and (3). We will treat this subsequently as one of two benchmarks.

With respect to the non-myopic monopolist, the current-value Hamiltonian associated to problem (9) is given by:

$$\begin{aligned} H(f, w, I, \mu, \lambda) &= [r_f w(1-f) - c]fI \\ &\quad + \mu w(1-w)[\Delta r - r_f f] + \lambda I(\beta(N-I) - r_r + w[\Delta r - r_f f]) \end{aligned} \tag{10}$$

and its derivative with respect to the control variable f is:

$$\frac{\partial H}{\partial f} = [r_f w(1-2f) - c]I - r_f w[\mu(1-w) + \lambda I], \tag{11}$$

where μ and λ are the shadow values associated to the level of antibiotic efficacy and the stock of infected population respectively.

The following conditions, as well as (2) and (3), are necessary for inter-temporal profit

[10]The entry decision of a generic firm may depend on the market size and revenues of the incumbent firm before the patent expires, and also of the type of the pharmaceutical product sold, as shown empirically by Scott Morton (2000), leaving some antibiotic markets potentially without any generic competition.

maximization:

$$\frac{\partial H}{\partial f} \leq 0, \quad \frac{\partial H}{\partial f} f = 0, \quad f \geq 0 \quad \text{or} \quad \frac{\partial H}{\partial f} \geq 0, \quad \frac{\partial H}{\partial f}(1-f) = 0, \quad f \leq 1 \tag{12}$$

$$\dot{\mu} - \rho\mu = (\Delta r - r_f f)[\mu(2w-1) - \lambda I] - r_f I(1-f)f \tag{13}$$

$$\dot{\lambda} - \rho\lambda = \lambda[2\beta I - \beta N + r_r - w(\Delta r - r_f f)] - r_f w(1-f)f + cf \tag{14}$$

$$\lim_{t\to T} e^{-rt} w(T) \geq 0, \quad \lim_{t\to T} e^{-rt}\mu(T) \geq 0, \quad \lim_{t\to T} e^{-rt}\mu(T)w(T) = 0 \tag{15}$$

$$\lim_{t\to T} e^{-rt} I(T) \geq 0, \quad \lim_{t\to T} e^{-rt}\lambda(T) \geq 0, \quad \lim_{t\to T} e^{-rt}\lambda(T)I(T) = 0 \tag{16}$$

Condition (12) is the first-order condition for the maximization of the Hamiltonian with respect to $f(t)$ at each instant t. It can never be optimal for the monopolist to sell the antibiotic to the overall infected population ($f = 1$). This makes current profits negative without generating compensating future profits. Indeed setting $f = 1$ inevitably decreases the level of antibiotic efficacy and infection, or at least decelerates the increase in the level of infection, and thus negatively affects the future quality and market size of the antibiotic. We will therefore necessarily have $\partial H/\partial f \leqq 0$. However, it may be optimal to have $f = 0$, thus postponing production and allowing antibiotic efficacy and infection to rise as fast as possible.

Conditions (13) and (14) are the arbitrage equations that determine the evolution of $\mu(t)$ and $\lambda(t)$ over time. Conditions (15) and (16) are the transversality conditions. In the case of a finite patent life, they state that whenever there is a strictly positive stock of antibiotic efficacy or of the infected population left at the end of the patent lifetime ($w(T) > 0,\ I(T) > 0$), then that stock must be of no value to the non-myopic monopolist. The same reasoning applies in the limit as t tends to infinity in the case of an infinitely long lasting patent.

In the case of an interior solution, $(0 < f^m < 1)$, equation (12) can be written as:

$$r_f w(1 - 2f^m) = c + \frac{r_f w}{I}\left[\mu(1-w) + \lambda I\right]. \tag{17}$$

Condition (17) states that the marginal revenue (the left-hand side of equation (17)) must be equal to the full marginal cost of treatment (the right-hand-side). Both shadow values

will be positive. This reflects the fact that the stock of the infected population can be viewed as an "asset" by the monopolist, since it represents market size when the antibiotic is economically viable.[11]

An interior solution f^m is represented graphically in Figure 2, where the solid and dotted lines represent the downward-sloping demand and marginal revenue function respectively. This figure shows a momentary view of the monopolist's choice given the dynamic system is in state (w, I) at time t. As in the standard static monopoly model, the monopolist will always serve a fraction such that demand is elastic, ruling out admissible values of f in the interval $(1/2, 1]$. The reason for this is the same as the reason why $f = 1$ cannot be an optimal policy for the monopolist. Incurring a loss at a current instant of time would have to be compensated by higher profits somewhere in the future. But this is not the case, since such a policy would lead to lower levels of quality and market size and thus cannot lead to higher profits. This implies that whenever $\Delta r/r_f \in [1/2, 1]$, the fitness cost effect dominates, *i.e.* the level of antibiotic efficacy will be increasing over time, as the optimal fraction f served by the monopolist will always be lower than $1/2$ (for $c > 0$). For $\Delta r/r_f \in [0, 1/2)$, the fraction served by the monopolist may be lower, equal or higher than the critical value of $\Delta r/r_f$, implying an increasing, constant or decreasing movement of antibiotic efficacy over time.

Before turning to the monopolist that benefits from a limited patent lifetime, we will address two useful benchmark cases. The first one has already been mentioned and refers to the myopic monopolist, while the second one is that of an infinitely-lived, non-myopic monopolist, the analysis of which will allow us to determine the steady states of the system.

[11] Herrmann and Gaudet (2009) characterize the socially optimal use of an antibiotic. In that case, the level of infection represents a bad to society, such that a negative shadow value is attributed to it, while antibiotic efficacy still is a valuable asset. At the social optimum then, the price of the antibiotic – not its marginal revenue – is equalized to the full marginal cost of antibiotic use, which may be lower than the marginal production cost due to the negative shadow cost of infection.

3.1 The myopic monopolist

In this section we consider the pricing policy, and its impact on the dynamics of antibiotic efficacy and infection, when the antibiotic is sold by a myopic monopolist. The myopic monopolist maximizes the flow of discounted profits without taking into account the impact of his current decision, $f(t)$, on future levels of antibiotic efficacy, and on the future stock of the infected population. He thus attributes a zero shadow value to the quality and market size of the antibiotic, which implies $\mu(t) = 0$ and $\lambda(t) = 0$. This optimization problem could be interpreted as a "static" one within a continuously changing environment. Accounting for the implied zero shadow values in equation (12), the first order condition for an interior solution can be written as:

$$r_f w(1-2f)I \quad = \quad cI, \tag{18}$$

i.e. marginal revenue equals marginal production cost, which is the producer's "short-run" cost of antibiotic use. Denote by $f^{\infty}(t)$ the fraction of the infected population buying the antibiotic when sold by a myopic monopolist, and by $p^{\infty}(t)$ the corresponding price. From condition (18) we obtain:

$$f^{\infty}(t) = \begin{cases} \frac{1}{2}\left(1 - \frac{c}{r_f w(t)}\right) & \text{, if } r_f w > c \\ 0 & \text{, otherwise.} \end{cases} \tag{19}$$

With the inverse demand function stated in (8), we get:

$$p^{\infty}(t) = \begin{cases} \frac{1}{2}\left(r_f w + c\right) & \text{, if } r_f w > c \\ r_f w & \text{, otherwise.} \end{cases} \tag{20}$$

If the antibiotic is economically viable, the myopic monopolist sells it to a positive fraction of the infected population and charges the corresponding market clearing price. If the antibiotic is not economically viable, he charges the choke price $r_f w$, and does not sell at all. Both, the fraction of the infected population buying the antibiotic, $f^{\infty}(t)$, as well as the price charged by the myopic monopolist, $p^{\infty}(t)$, are increasing in the level of antibiotic efficacy, the quality aspect of the antibiotic, while $f^{\infty}(t)$ is decreasing and $p^{\infty}(t)$ is increasing in the unitary production cost c. Notice that they are both independent of the level of infection.

3.1.1 The steady states under myopic monopolistic pricing

Consider first the epidemiological steady state given by (4), at which the level of antibiotic efficacy is exhausted completely ($w^{SS} = 0$) and demand vanishes. Any positive production of the antibiotic would lead to losses for the myopic monopolist, so that the monopolist would find it optimal not to produce at all by setting $f^{SS} = 0$. The steady state would therefore be characterized by:

$$\left(f^{SS}, I^{SS}, w^{SS}\right) = \left(0, \frac{\beta N - r_r}{\beta}, 0\right) \tag{21}$$

With a positive production cost $c > 0$, this steady state can be ruled out. This is because the myopic monopolist, by setting $f^{\infty}(t) = 0$ whenever the antibiotic is not economically viable, allows the level of antibiotic efficacy to recover ($\dot{w} > 0$), and therefore it cannot reach its lower limit at which $w^{SS} = 0$.

In the epidemiological steady state given by (5), the quality of the drug is maximal. From (19), we find $f^{\infty} = (1 - c/r_f)/2$. Therefore, the steady state will be characterized by:

$$\left(f^{SS}, I^{SS}, w^{SS}\right) = \left(\frac{1}{2}\left(1 - \frac{c}{r_f}\right), \frac{\beta N - r_w - \frac{1}{2}(r_f - c)}{\beta}, 1\right). \tag{22}$$

Finally, steady states as defined in (6) occur when $f^{\infty} = \Delta r / r_f$, which is only optimal for the myopic monopolist whenever the level of antibiotic efficacy $w(t)$ satisfies:

$$\frac{\Delta r}{r_f} = \frac{1}{2}\left(1 - \frac{c}{r_f w(t)}\right). \tag{23}$$

Hence the unique steady state of this type is given by:

$$\left(f^{SS}, I^{SS}, w^{SS}\right) = \left(\frac{\Delta r}{r_f}, \frac{\beta N - r_r}{\beta}, \frac{c}{r_f - 2\Delta r}\right), \tag{24}$$

for the case where parameters satisfy $r_f > 2\Delta r$, *i.e.* the natural selection effect dominates the fitness cost effect.

Notice that the steady-state configurations (22) and (24) are mutually exclusive. Which one is relevant depends on the bio-economic parameters of the model. To be more precise, if $c = r_f - 2\Delta r$, they are indistinguishable at $w^{SS} = 1$. Whenever $c < r_f - 2\Delta r$, then (24)

must be the relevant steady-state configuration, because this is incompatible with (19) when evaluated at $w^{SS} = 1$. Whenever the parameters satisfy $c/(r_f - 2\Delta r) > 1$, or $r_f < 2\Delta r$ then (22) must be the relevant steady-state configuration, because it must then be the case that $w^{SS} = 1$ and $f^{SS} = (1 - c/r_f)/2 < \Delta r/r_f$. The economic intuition of which steady state applies is clear. The steady state of type (22) applies independently of the production cost c, if the fitness cost effect dominates the natural selection effect ($r_f < 2\Delta r$), assuring a strong renewability of the drug efficacy. As the myopic monopolist behaves like a static one, selling on the elastic part of the demand curve, such that $f^{\infty} < 1/2 < \Delta r/r_f$, antibiotic efficacy necessarily increases and converges to $w^{SS} = 1$. However, if the natural selection effect dominates the fitness cost effect, then both steady state are possible depending on the relative magnitude of the production cost.

3.1.2 The transition to steady state under myopic monopolistic pricing

The stock of infected population $I(0) = I_0 \in (0, N]$ and the stock of antibiotic efficacy $w(0) = w_0 \in (0, 1)$ are given exogenously in the system at time $t = 0$. One could conjecture on the one hand, that a newly developed drug is characterized by an efficacy level that is relatively close to unity and lies above or below its steady state. On the other hand, the level of infection may initially lie on its steady-state value, or in the case of an infection "event", it may lie above it. In what follows, we will show that the system will tend asymptotically from an initial state (I_0, w_0) to the relevant steady-state configuration. Let I and II denote states for which $w > w^{SS}$ and III and IV denote states for which $w < w^{SS}$, with states I and III lying to the left of the $\dot{I} = 0$ isocline, while states II and IV lie to its right in (I, w)-space. This is shown in Figure 3 for the steady-state configuration (24), where the $\dot{I} = 0$ isocline is represented for $f^{\infty} = \Delta r/r_f$, at which the natural selection and fitness cost effects are in balance.[12] The evolution of the levels of antibiotic efficacy $w(t)$ and infection $I(t)$ depends on the fraction of the infected population $f^{\infty}(t)$ to which the myopic monopolist sells the

[12]The $\dot{I} = 0$ isocline is non-stationnary. Recall footnote 6. The ensuing analysis also applies to the steady-state configuration with $w^{SS} = 1$ where the initial state (I_0, w_0) is either of type III or IV.

antibiotic over time, or equivalently, on the price charged $p^{\infty}(t)$.

We first concentrate on the characterization of $f^{\infty}(t)$, $p^{\infty}(t)$ and $w(t)$, before addressing the evolution of the level of infection and the transition to steady state in general. Differentiating equations (19) and (20) with respect to time for any steady-state configuration gives:

$$\dot{f}^{\infty} = \frac{c}{4r_f}(2\Delta r - r_f)\frac{1-w}{w^2}\left[w - \frac{c}{r_f - 2\Delta r}\right] \tag{25}$$

$$\dot{p}^{\infty} = \frac{r_f^2 w^2}{c}\dot{f}^{\infty} \tag{26}$$

Suppose for now the antibiotic to be economically viable. If the steady-state configuration is of type (22), we have $w(t) \leqq w^{SS} = 1$ with $t \in [0, \infty)$ so that:

$$f^{\infty}(t) = \frac{1}{2}\left(1 - \frac{c}{r_f w(t)}\right) < \frac{1}{2}\left(1 - \frac{c}{r_f}\right) < \frac{\Delta r}{r_f},$$

implying by equation (2) the level of antibiotic efficacy $w(t)$ to be increasing over time for initial states of types III and IV. This steady-state configuration occurs only when $c/(r_f - 2\Delta r) > 1$ or $r_f - 2\Delta r < 0$ and thus implies, by equations (25) and (26), that the fraction served as well as the price charged by the myopic monopolist must be increasing over time. This is because the increase in quality shifts the demand and marginal revenue curves upwards (for any given level of infection). As the level of antibiotic efficiency approaches its upper bound, the increase in the treatment rate and in the price slow down as $\dot{f}$ and $\dot{p}$ tend to zero.

If the steady-state configuration is of type (24), we have for any $t \in [0, \infty)$:

$$f^{\infty}(t) = \frac{1}{2}\left(1 - \frac{c}{r_f w(t)}\right) \gtreqless \frac{\Delta r}{r_f} \quad \Leftrightarrow \quad w(t) \gtreqless \frac{c}{r_f - 2\Delta r} = w^{SS},$$

where w^{SS} is the steady-state level of antibiotic efficacy in that configuration. Hence, the fraction $f^{\infty}(t)$ is larger, smaller or equal to the critical fraction $\Delta r/r_f$ depending on whether the current level of antibiotic efficacy $w(t)$ is larger, smaller or equal to the long-run steady-state level w^{SS}. It follows that $w(t)$ is decreasing over time when the initial state is of type

I or II, and increasing when it is of type III or IV. If $w_0 = w^{SS}$, then the level of antibiotic efficacy remains constant over time ($\dot{w} = 0$). Convergence of $w(t)$ to steady state will occur monotonously (from above or from below). As $w(t)$ approaches the long-run steady state w^{SS}, $\dot{f}$ and $\dot{p}$ tend to zero, and the fraction served must tend to the critical value of $\Delta r/r_f$. When the steady-state value for antibiotic efficacy is reached, $w^{SS} = c/(r_f - 2\Delta r)$, we must simultaneously have $f^{\infty} = \Delta r/r_f$ from equation (23) and $\dot{f^{\infty}} = 0$ from equation (25).

We have seen so far that the evolution of the variables w, f^{∞} and p^{∞} can be characterized independently from the level of infection, or the market size of the antibiotic, I, the evolution of which we now consider. Equation (3), which determines the evolution of the level of infection, can be rewritten, after substituting for f^{∞} and rearranging, as:

$$\frac{\dot{I}}{I} = \beta(I^{SS} - I) + \frac{1}{2}(r_f - 2\Delta r)\left[w^{SS} - w\right] \tag{27}$$

where I^{SS} and w^{SS} are defined as in the relevant steady-state configuration (22) or (24). Equation (27) states that the relative increase in the level of infection is a function of the relative distance of the state variables from their long-run steady-state levels. Suppose $(r_f - 2\Delta r) > 0$ such that no steady-state configuration can be excluded from the outset. Then, unambiguously, $\dot{I} < 0$ as long as $I > I^{SS}$ and $w > w^{SS}$, and $\dot{I} > 0$ as long as $I < I^{SS}$ and $w < w^{SS}$. Now suppose the particular case where $I_0 = I^{SS}$ and $w > w^{SS}$. Thus, the initial state is of type II, and by equation (27), $\dot{I}(0) < 0$, *i.e.* the level of infection falls below its steady-state level, such that $I^{SS} - I > 0$ initially while we still have $w > w^{SS}$. The level of infection will decrease, making the difference $I^{SS} - I$ increase, while $w^{SS} - w(< 0)$ increases as shown earlier. The first term on the right-hand side of equation (27) eventually cancels the second one. When this happens, we have $\dot{I} = 0$, *i.e.* the system crosses the $\dot{I}$-isocline and switches from type II to type I. After this, we have $\dot{I} > 0$, and $I^{SS} - I$ decreases while $w^{SS} - w(< 0)$ increases. This continues until the steady state is reached. The overshooting of the level of infection which may occur when departing from an initial state of type II is reversed when departing from a state of type III.[13]

[13] If $c/(r_f - 2\Delta r) > 1$ holds, the level of antibiotic efficacy tends to its upper bound. The steady state is

To summarize, assume that the marginal cost of producing the antibiotic is relatively low, and that the efficacy level of a newly patented antibiotic is relatively high (initial state of type I or II). Based on the preceding analysis, a myopic monopolist will price the antibiotic such that some of the antibiotic efficacy is "extracted" over time, with the system converging to a "sustainable" steady state, at which the fitness cost effect and the natural selection effect are in balance. This happens because consumer demand adjusts to the decreasing level of antibiotic efficacy, a fact which the monopolist takes into account, ignoring however the evolution of infection. An overshooting in the level of infection may occur depending on the location of its initial state when a relatively high (mild) use is made of the antibiotic, the efficacy of which is relatively high (low).

3.2 The infinitely-lived monopolist

The case of an infinitely-lived monopolist ($T = \infty$) represents another benchmark for the analysis of how a non-myopic monopolist subject to a patent manages antibiotic efficacy and infection over time. As it turns out, the infinitely-lived monopolist tends to achieve higher levels of antibiotic efficacy over time and in steady state than the myopic monopolist. The non-myopic control also benefits the spread of infection, asit prevents the level of infection from falling as sharply below its steady-state value as in the myopic outcome. This is because the non-myopic infinitely-lived monopolist prices the antibiotic at a level where the marginal revenue equals the *full marginal cost* of selling the antibiotic.

3.2.1 The steady states

Setting $\dot{w} = \dot{I} = \dot{\mu} = \dot{\lambda} = 0$ generates the set of steady states that may be reached when the antibiotic is sold by a non-myopic monopolist. The epidemiological steady state of type

then as defined in (22). Unambiguously, $\dot{I} < 0$ for states of type IV, while the overshooting pattern may occur for states of type III ($I > I^{SS}$ temporarily). The same steady state is reached if the condition $r_f - 2\Delta r < 0$ holds, and $\dot{I} < 0$ for states of type IV and the overshooting pattern with respect to the level of infection may then occur for initial states of type III. The discussion in the text shows that the system will reach the neighbourhood of the relevant steady state, and in connection with the local stability of that steady state (which can be shown by standard methods of linearizing the dynamic system around the relevant steady state), establishes its *global* stability under the myopic monopolistic programme.

(4), at which the antibiotic is completely inefficient ($w = 0$), and which we found could not be reached under the myopic monopolistic programme, cannot be reached either under the non-myopic programme. As before, the monopolist would incur losses by selling the antibiotic when its efficacy is below the economic viability level ($w < c/r_f$). He would prefer not to sell at all ($f = 0$), allowing the level of antibiotic efficacy to increase.

In the epidemiological steady state given by (5), antibiotic efficacy is at its upper bound ($w = 1$). Replacing $w = 1$ in (12) and in (14) with $\dot{\lambda} = 0$ yields two equations in f and λ, the unknowns of which can be solved for (see the Appendix). At this steady state we will therefore have:

$$(f^{SS}, I^{SS}, w^{SS}) = \left(\frac{a}{2} - \sqrt{\left(\frac{a}{2}\right)^2 - b}, \frac{\beta N - r_w - r_f f^{SS}}{\beta}, 1 \right) \tag{28}$$

where a and b are determined in the Appendix as:

$$\begin{aligned} a &= \frac{2}{3r_f}[\rho + \beta N - r_w + r_f - c] \\ b &= \frac{\left(1 - \frac{c}{r_f}\right)(\rho + \beta N - r_w)}{3r_f}. \end{aligned}$$

Finally, there is a unique steady state of the type characterized by (6). This steady state is shown in the Appendix to be given by:

$$(f^{SS}, I^{SS}, w^{SS}) = \left(\frac{\Delta r}{r_f}, \frac{\beta N - r_r}{\beta}, -\frac{B}{2A} + \sqrt{\frac{c}{A} + \left(\frac{B}{2A}\right)^2} \right) \tag{29}$$

where

$$\begin{aligned} A &= \Delta r(r_f - \Delta r)\frac{\beta N - r_r}{\rho(\rho + \beta N - r_r)} \\ B &= (r_f - 2\Delta r) - \Delta r \frac{r_f - \Delta r}{\rho} + \frac{\Delta r c}{\rho + \beta N - r_r}. \end{aligned}$$

Steady-state configurations (28) and (29) are mutually exclusive. In fact, when $w^{SS} = 1$ in (29) they are indistinguishable with respect to the level of antibiotic efficacy. This will occur when the bio-economic parameters satisfy

$$c = \tilde{c}(r_f) = \frac{-\Delta r\left[2(\beta N - r_r + \rho) - \Delta r\right]}{\beta N - r_r + \rho - \Delta r} + r_f, \tag{30}$$

which can be derived from setting $w^{SS} = 1$ and solving for the cost c. For $c \leq \tilde{c}(r_f)$, the monopolistic steady state will be defined as in (29), while for $c > \tilde{c}(r_f)$ the steady state will be defined as in (28). Equation (30) represents a positively sloped straight line in $(r_f, c)-$space, the intercept of which is negative when infection cannot be eradicated from the system.[14]

Figure 4 shows the line $\tilde{c}(r_f)$, as well as the economic viability condition $c = r_f$ in the $(r_f, c)-$space for admissible values of $r_f \in [2\Delta r, \beta N - r_w]$. *Ceteris paribus*, for any given value of the cost c, higher values of the additional recovery rate r_f (and thus lower values of the critical fraction $\Delta r/r_f$) imply an interior steady-state level of antibiotic efficacy (configuration (29)). This is because the optimal fraction of the infected population served by the monopolist, f, as defined in (12), is then higher than the critical fraction $\Delta r/r_f$, which leads to a decreasing level of antibiotic efficacy and makes the steady-state configuration given by (28) unattainable. Stated differently, a high value of the additional recovery rate r_f implies a relatively high selective pressure on the drug-sensitive version of the infection (I_w), rendering the achievement of the maximum value of antibiotic efficacy ($w^{SS} = 1$) impossible.

Comparing the interior steady-state configurations of the myopic and the non-myopic monopolist as defined in (24) and (29) shows that both the fraction of the infected population that buys the antibiotic, f^{SS}, and the level of the infected population, I^{SS}, are identical. The steady-state levels of antibiotic efficacy differ however in this steady-state configuration. It can be shown, assuming $c/(r_f - 2\Delta r) < 1$, that the non-myopic steady-state level w^{SS} is always higher than the one reached under the myopic programme: $w^{SS} > \frac{c}{r_f - 2\Delta r} \equiv w_\infty^{SS}$, indicating that the non-myopic, infinitely-lived monopolist considers antibiotic efficacy as a valuable asset. The locus of parameter configurations such that $w_\infty^{SS} = 1$ is given by $c = r_f - 2\Delta r$ and is also shown in Figure 4.

[14] Whenever the denominator on the right-hand side of equation (30) is positive, the ordinate is negative. This is indeed the case as $\beta N - r_r + \rho - \Delta r > \beta N - r_r - \Delta r = \beta N - 2\Delta r - r_w > \beta N - r_f - r_w > 0$, where the last inequality follows from the assumption made in footnote 5 and the next-to-last inequality follows from $r_f - 2\Delta r > 0$, which makes the evolution non-trivial as both, the fitness cost and natural selection effects exist.

3.2.2 The transition to steady state

Because of the complex nature of the dynamic system involved in the monopolistic optimal control problem, numerical simulations have been used to explore the transition to the steady state.[15] Those simulations show that depending on the bio-economic parameters of the model, the system may tend to the steady state as defined in (28), for which $w^{SS} = 1$, or to the "interior" steady state as defined in (29), for which $f^{SS} = \Delta r / r_f$. In what follows, we concentrate our analysis on the production cost c and the additional recovery rate r_f, and refer to the classification of steady states as presented in Figure 4. Recall, that this is a benchmark analysis. It will allow us subsequently to qualify the "turnpike" evolution of the system in the case of a finite patent life.

Suppose the parameter configuration of c and r_f is such that they fall below the line $\tilde{c}(r_f)$, and the steady state reached is interior for the monopolist as defined in (29). Starting from the four different types of initial states (I_0, w_0), indicated by I to IV, the trajectories of the state variables and of the evolution of the monopolistic treatment rate are shown in Figures 5 and 6 respectively. For comparison, we have also drawn the paths resulting under the myopic programme. In Figures 5 and 6 non-myopic paths are indicated by thicker lines. All state paths have in common that they converge towards their respective steady state, indicating that the dynamic system is stable under both regimes, with the non-myopic steady-state level of antibiotic efficacy being greater than the myopic one, *i.e.* $w^{SS} > w_\infty^{SS}$.

Consider the paths departing from initial states of types III and IV, which lie below the economic viability level c/r_f, such that no antibiotic is sold initially under any regime. Since the evolution of antibiotic efficacy $\dot{w}$ is independent of I, myopic and non-myopic state paths departing from an initial state of types III and IV coincide as long as $f = 0$. Before that

[15] We make use of a standard value function iteration algorithm, as proposed in Judd (1998, page 413) for a discrete time version of the model. The baseline parameters used throughout the rest of the paper assure that infection can neither be eradicated, nor dominate the system. We retain for our simulations, unless specified differently for comparative dynamics: $\beta = 0.6$, $N = 1$, $r_r = 0.17$, $r_w = 0.15$, $\Delta r = 0.02$, $r_f = 0.3$, $c = 0.1$ $\rho = 0.03$, although many other parameter configurations are conceivable. They do however not lead to qualitatively different results with respect to how the policy of the infinitely-lived, non-myopic monopolist compares to that of the myopic one.

phase ends, the paths of the state variables join in a unique path (see Figure 5). Once the antibiotic has become economically viable, the myopic monopolist immediately starts selling to a fraction f^{∞} as defined in (19), which again does not depend on the level of infection. The two myopic state and control paths therefore continue to coincide and converge to the steady state (24). The convergence occurs with a slight overshooting in the level of infection as described in section 3.1.2. Although the non-myopic monopolist reaches the economic viability level at the same time as the myopic one, he starts selling later as can be seen from Figure 6. This is because the non-myopic monopolist attributes positive shadow values to the levels of antibiotic efficacy and infection, implying a full marginal cost higher than c. During this phase we thus have $\partial H/\partial f < 0$, *i.e.* the monopolist waits for the quality to rise even more in order to compensate for the full marginal cost, and starts selling when $\partial H/\partial f = 0$. For the non-myopic monopolist, the positive overshooting pattern is more pronounced than for the myopic one, as he has an interest in facing a 'high' demand in the future.

Consider now the initial states of type I and II in Figure 5, characterized by a high level of antibiotic efficacy – which one may conjecture for a newly developed and patented drug – and a relatively low (type I) or high (type II) level of infection. When departing from an initial state of type I, the monopolist manages the initially low level of infection (the market size), in such a way as to have it increase faster than the myopic monopolist while keeping high values of antibiotic efficacy. Comparing the treatment rates in Figure 6 under both regimes, it becomes apparent that the non-myopic monopolist sells to a low fraction of the infected population initially, thus allowing the level of infection to increase relatively fast.[16] When departing from an initial state of type II, the non-myopic monopolist serves a decreasing fraction, and this at a lower level than the myopic monopolist initially. This allows him to soften the overshooting of infection below its steady-state level, thus assuring a relatively higher market size over time (see Figure 5). As can be seen from Figure 6, the non-myopic monopolist sells to a higher fraction of the infected population in the longer run

[16]The level of antibiotic efficacy also increases initially, something which cannot occur under the myopic regime.

than the myopic one. This is due to subsequently higher levels of antibiotic efficacy and is advantageous because the level of infection is also higher. It is interesting to note that the decisions of a non-myopic monopolist crucially depend on his discount rate. Notably, it can be shown numerically that a higher discount rate makes the non-myopic monopolist less patient. Figure 7 (upper left) shows the trajectory of the state variables for a non-myopic monopolist corresponding to the baseline discount rate, as well as to a higher one, when departing from initial states of type I and II. It turns out that the overshooting pattern is more pronounced for an initial state of type II and that the steady-state level of antibiotic efficacy is lower. Thus, a more impatient monopolist does "invest" less in future market size and quality with the benefit of higher, present profits. This is reflected by the state path lying closer to the one of the myopic monopolist. Figure 7 also shows the comparative dynamics with respect to the parameters c, β and r_w.

Figure 8 displays the evolution of prices and the level of antibiotic efficacy when the initial state is of type II. Prices are decreasing under both regimes and reflect the evolution of antibiotic efficacy. We have also drawn the hypothetical price $p^H(t)$, that a myopic monopolist would charge if he were to be at the same state (I, w) as the non-myopic one. The prices charged by the non-myopic monopolist are higher than those charged by the hypothetical myopic monopolist, thus restricting the fraction of the infected population to which the antibiotic is sold, and finally leading to a higher steady-state value of antibiotic efficacy.

If bio-economic parameters c and r_f belong to the region lying between the line $\tilde{c}(r_f)$ and the economic viability line ($c = r_f$), as depicted in Figure 4, initial states (I_0, w_0) can only be of type III or IV, as has been explained earlier for case of the myopic monopolist (recall footnote 13). Numerical simulations confirm that the system now tends to the steady state of type (28). The convergence to that steady state is similar to what has been described before with respect to the initial states of type III and IV. Leaving unchanged the biological parameters, notably r_f, this case occurs for example for a sufficiently higher value of the

production cost c, implying at the same time an economic viability level which is higher.

3.3 Finite patent life: $T < \infty$

Consider now the realistic case of a patent of finite duration ($T < \infty$). The antibiotic is then sold by a monopolist during the life of the patent and by a generic industry afterwards. Since the monopolist knows that he will make zero economic profits after the expiration of the patent, he will attach no importance to the levels of antibiotic efficacy and infection that are left for the generic industry. At time T, he should thus attribute zero value to the levels of antibiotic efficacy and infection, if positive, and behave like a myopic monopolist. This is indeed the case, as can be seen from the transversality conditions (15) and (16). As the monopolist cannot operate below the economic viability level, c/r_f, nor eradicate infection from the epidemiological system, we must have $w(T) > 0$ and $I(T) > 0$, which from equations (15) and (16) implies:

$$\mu(T) = \lambda(T) = 0. \tag{31}$$

Hence, at the instant the patent expires, the pricing policy of the non-myopic monopolist must be identical to the myopic one defined in (19) and (20) and evaluated at state $(I(T), w(T))$. The shadow values will evolve continuously over time as described by equations (13) and (14) and will reach $\mu(T) = \lambda(T) = 0$ at time T.[17] At T, we can calculate the rate of change in the shadow values making use of (31) and obtain:

$$\begin{aligned} \dot{\mu}(T) &= -r_f I(T)(1 - f(T))f(T) < 0, \\ \dot{\lambda}(T) &= -r_f w(T)(1 - f(T))f(T) < 0. \end{aligned}$$

Due to the continuity in the evolution of the shadow values, we can conclude that the shadow values are positive and decreasing at least during a time period before the patent's expiration. This implies a decreasing full marginal cost for given levels of antibiotic efficacy and of the

[17] Jumps in the shadow values could be caused by binding constraints on the state variables. This can however be excluded as $w^{SS} = 0$ and $w^{SS} = 1$ cannot be reached in finite time and infection cannot be eradicated nor dominate the whole system because of the parameter values assumed in section 2.1.

infected population, leading to an increase in the fraction of the infected population served towards the end of the patent life time in order to satisfy equation (12). The non-myopic monopolist thus behaves "more and more myopically" as the patent approaches its expiration date.

Numerical analysis shows for the parameter configuration which would lead to the interior steady state in the infinite horizon problem, as defined in (29), that the non-myopic monopolistic programme is characterized by a turnpike property with the steady state (I^{SS}, w^{SS}) serving as the turnpike. If T, the length of the patent life, is sufficiently large, then the turnpike is "exact": the system reaches the steady state and remains there for a finite period of time before leaving it at some point before the patent expires.

Figure 9 and Figure 10 show the trajectories of antibiotic efficacy and infection, as well as the fraction of the infected population that buys the antibiotic when it is sold by a non-myopic monopolist. We also plot the outcome under the myopic monopolistic regime for purpose of comparison. The approach to the steady state is identical to that of the infinite horizon problem, which has been described in the preceding section. At the interior steady state (I^{SS}, w^{SS}), we have $f^{SS} = \Delta r / r_f$. What is of interest in the case of a finite patent life is the monopolistic policy once the path leaves the turnpike. The monopolist then sells to an increasing fraction of the infected population, $f(t) > f^{SS}$, as can be seen in Figure 10. This leads to a decrease in the levels of antibiotic efficacy and infection (the state trajectory moves in the south-western direction in Figure 9), and thus to a decreasing price as shown in Figure 11. This occurs because the monopolist associates lower shadow values to the quality aspect of the drug (w) and to the market size (I), as he knows that he will make zero profits after the patent has expired and tends to behave more and more like a myopic monopolist. At time T, the non-myopic monopolist behaves exactly like a myopic monopolist and charges the myopic price as defined in (20). To see this, consider the prices charged by a hypothetical myopic monopolist $p^H(t)$ who faces the same state as the non-myopic one in Figure 11. It is at T that the pricing schemes $p(t)$ and $p^H(t)$ represented by the thin continuous and dotted

lines join.

For an insufficiently long patent life, the turnpike property of the monopolistic programme is not exact: the path approaches the steady state (I^{SS}, w^{SS}) and remains in its neighborhood for a finite period of time before leaving to satisfy the transversality conditions. This is shown in Figure 12, where we depict the trajectories of the fraction of the infected population buying the antibiotic as an example. The heavy lines indicate the treatment rates $f(t)$ for the non-myopic monopolist, which finally approach the steady-state level of $\Delta r/r_f$ from above when departing from initial states of type I and II, and which approach it from below, when departing from initial states of type III and IV. In all cases, the treatment rate $f(t)$ increases towards the end of the patent and trajectories of $f(t)$ eventually join and reach the same level, which is higher than the critical level $(\Delta r/r_f)$.[18]

When the patent expires, the generic industry takes over, and an upward jump in the level of $f(t)$, accompanied by a fall in price occur. As the full marginal cost faced by the monopolist is equal to c at time T, the corresponding monopolistic price $p^m(T)$ is necessarily higher than the price of the generic industry which is given by $p^g = c$.

Finally, consider the parameter configuration under which the infinitely-lived monopolist would reach the steady state of type (28). In this case, if the patent life is sufficiently long, the system is again characterized by an exact turnpike, with the level of antibiotic efficacy reaching its upper bound, $w = 1$. The level of w will remain unchanged, even after leaving the turnpike in order for the costate variables to satisfy the transversality conditions. The decrease in the full marginal cost, which occurs after leaving the turnpike, is due strictly

[18]The question arises of what is the critical patent life T for an exact turnpike to exist. And in such a case, when is the turnpike reached, and when is it left again. The critical value of T is determined implicitly by the necessary conditions (12) to (16) characterizing the profit-maximizing monopolistic programme. Suppose T to be sufficiently long such that a turnpike exists. Denote by t_1 and t_2 the points of time when the turnpike is reached, and when it is left again. In order to obtain those dates, one would have to solve the differential equations $\dot{w}$, $\dot{I}$, $\dot{\mu}$, $\dot{\lambda}$ satisfying condition (12) and the boundary conditions $w(0) = w_0$, $I(0) = I_0$, $w(t_1) = w(t_2) = w^{SS}$, $I(t_1) = I(t_2) = I^{SS}$, $\mu(t_1) = \mu(t_2) = \mu^{SS}$, $\lambda(t_1) = \lambda(t_2) = \lambda^{SS}$ and $\mu(T) = 0$ as well as $\lambda(T) = 0$. One would first solve for t_2, and then for t_1. The critical value for a turnpike to exist, $\tilde{T}$, is then defined by $\tilde{T} = t_1 + t_2$. All those conditions should suffice to determine a unique trajectory of the state, co-state and control variables. The analytical resolution of the dynamic system however represents an arduous task.

to the decrease in the shadow value of infection, λ. This can be seen from equation (17), which simplifies for $w = 1$ to: $r_f(1 - 2f^m(t)) = c + r_f\lambda(t)$. As in the previous case, a falling full marginal cost is accompanied by an increase in the treatment rate, leading to a decrease in the level of infection. What differs under this parameter configuration, which is characterized by a marginal production cost (c) that is high relative to the increase in the recovery rate (r_f), is that the generic industry now inherits a perfectly effective antibiotic drug. The problem of antibiotic resistance would be non-existing after the generic industry takes over – a rather unrealistic conjecture for the parameter values. Indeed, one should not interpret this result as arguing in favor of the monopolistic industry from a social optimum point of view. The upper bound of antibiotic efficacy may also be attained by a generic industry under similar parameter configurations (see Herrmann and Gaudet, 2008). It is the relatively high marginal production cost compared to the increase in the recovery rate that makes the monopolist conservationist on the one side, and the generic industry "disciplined" on the other. In the real world, one may conjecture that the R&D costs are most important and that the marginal production cost is relatively low in the pharmaceutical industry.

Finally, we want to emphasize that the monopolistic outcome is not socially optimal, notably because infection represents a bad to society and an asset to the monopolist. Inducing a socially optimal behavior of the monopolist via economic incentives, like taxes or subsidies, is possible and they could be easily calculated in theory. It remains however a difficult task in reality, as they depend on regulation and insurance regimes, the analysis of which lies outside the scope of the present paper.[19]

4 Prolonging the patent length and related welfare implications

A prolongation of the patent at its termination date will be welfare-improving if it brings the intertemporal use of the antibiotic closer to what would be socially optimal, as has been characterized in Herrmann and Gaudet (2009). This issue has already been raised by regula-

[19]For a descriptive discussion of the problems that may be involved in the context of the U.K. National Health Service system, see Coast *et al.* (1998).

tory and governmental authorities. In particular, a prolongation has been proposed (but not adopted by Congress) by the U.S. Office of Technology Assessment (1995) as an incentive for the pharmaceutical industry to take into account the negative externality of antibiotic resistance. In our model, prolonging the patent, and hence the non-myopic monopolistic pricing, results in a reduction of the fraction of the population that buys the antibiotic as compared to the generic industry. This benefits the evolution of antibiotic efficacy, but comes at the cost of an increase in infection levels, at least in the short run. Hence, one can conjecture that a prolongation of the patent may be desirable from a societal point of view if antibiotic efficacy levels are low, and if the spread of infection is not much of an issue.

In what follows, we make the important assumption that changes in the patent duration at T are not anticipated by the monopolist. This allows us to abstract from a potential strategic behavior by the producer of the drug, the analysis of which lies outside the scope of this paper. The instantaneous welfare W at time t is defined as the surplus accruing to the entire population, net of production costs. Making use of the indifferent consumer $\tilde{\theta}$ defined in (7) and the inverse demand function $P(f, w)$ defined in (8), we calculate:

$$\begin{aligned} W(f, w, I) &= N \int_0^1 u(\theta) d\theta - cfI \\ &= \frac{1}{2}(N - I) + \frac{1}{2}\pi(w)I + \frac{1}{2}r_f w I f^2 + [r_f w(1 - f) - c]fI \end{aligned} \tag{32}$$

While the first term of equation (32) represents the mean valuation of the healthy population, and the last term is the producer surplus, the second and third terms relate to the expected surplus of the infected population of either recovering naturally, or by taking the antibiotic. The intertemporal welfare is the sum of the welfare occuring under monopoly and under the generic industry, which inherits the final state $(I(T), w(T))$ from the monopolist at time T when the patent ends. Since the monopolist faces a deterministic profit-maximizing program, we know that the final state $(I(T), w(T))$ is determined unambiguously by the initial state

(I_0, w_0) and the length of the patent T. We can therefore write:

$$\begin{aligned} V(I_0, w_0, T) &= \underbrace{\int_0^T e^{-\rho t} W^m(f^m, .)dt}_{\equiv V^m(.,T)} + \underbrace{\int_T^\infty e^{-\rho t} W^g(f^g, .)dt}_{\equiv V^g(.,T)} \\ &= V^m(I_0, w_0, T) + e^{-\rho T} \underbrace{\int_0^\infty e^{-\rho t} W^g(f^g, .)dt}_{\equiv \tilde{V}^g(I(T), w(T))}, \end{aligned} \tag{33}$$

where W^m and W^g represent the instantaneous social welfare when the fraction f^m or f^g of the population buys the antibiotic and the state of the system evolves accordingly. Differentiating $V(I_0, w_0, T)$ with respect to T gives the marginal welfare change at time T of increasing the patent length:

$$\frac{dV}{dT} = e^{-\rho T} \left[W^m(f^m(T), .) - \rho \tilde{V}^g(I(T), w(T)) + \frac{\partial \tilde{V}^g}{\partial w(T)} \frac{\partial w(T)}{\partial T} + \frac{\partial \tilde{V}^g}{\partial I(T)} \frac{\partial I(T)}{\partial T} \right] \tag{34}$$

The sum of the terms in brackets is the net current value at time T of marginally increasing the patent duration. The first two terms capture the immediate "gain" in current social welfare under monopoly, W^m, corrected for the "cost" of postponing the intertemporal welfare procured by the generic industry, $\rho \tilde{V}^g$. The other two terms take into account the impact of the change in the final state $(I(T), w(T))$ on the discounted welfare procured by the generic industry.

Since the sign of this expression is ambiguous, numerical simulations are used to address the welfare change implied by a modification in the patent length. Numerical simulation results are presented for various percentage increases in the patent length from its initially given value. This requires a new dynamic program for the monopolist to be solved with the horizon set at $\tilde{T} = xT$ where x is the percentage of the prolongation and with the initial state being $(I(T), w(T))$. The bio-economic parameters used for the numerical simulations are those from the baseline scenario (see footnote 15) with $T = 200$ time periods. Figure 13 refers to the state-space at time T. The particular final state $(I(T), w(T))$ from the baseline scenario is also shown. The Figure shows the contour lines of a zero welfare change ($dV = 0$) for a small increase in the patent length, $dT = 1\%$, and for longer increases in T up to

20% of the initial patent length. To the left of a contour line, we have $dV/dT > 0$, while $dV/dT < 0$ to its right. The shape of the contour line corresponding to a given increase in T confirms our intuition: a small increase in the patent length is only desirable from a societal point of view if the level of antibiotic efficacy is low relative to the level of infection. A longer prolongation of the patent duration is only socially desirable for an even lower level of antibiotic efficacy compared to a given level of infection.

Figure 13 suggests that, given the state $(I(T), w(T))$, a 1% prolongation of the patent length would increase welfare, while a 2.5% or higher prolongation would not. This is because replacing the generic industry by a non-myopic monopolist for the extra duration $\tilde{T} = xT$ will result in a reduction of the fraction of the population that buys the antibiotic during that time interval, because of the higher price. It results a higher infection level, which is an asset for the monopolist, but a bad for society. This finding conveys an important nuance to Mechoulan (2007) who shows that re-granting monopoly power to a non-myopic monopolist may be welfare improving in the context of antibiotic resistance. When addressing the re-granting of monopoly power, Mechoulan (2007) remains silent on the spread of infection, the state and dynamics of which we have considered explicitly in our analysis. In our model, a prolongation in the patent length can be welfare improving when the level of infection is sufficiently low as compared to the level of antibiotic efficacy. Longer increases in the patent duration necessitate even lower values of antibiotic efficacy in order to increase welfare. Our analysis suggests that relatively higher levels of infection are contained more efficiently under a generic industry, as a lower price is charged implying that more individuals buy the antibiotic.

5 Conclusion

This paper has focused on the pricing of an antibiotic drug by a non-myopic producer whose monopoly power is protected by a patent, in the context where the efficacy of the antibiotic (its quality) and the overall level of infection (the market size) are endogenously determined

by antibiotic sales over time. We show that the bio-economic system is characterized by a turnpike property. This means that the price will move towards the steady-state price level that would be charged by an infinitely-lived monopolist and will remain in the neighborhood of that price for a period of time. The period of time in question will depend on the length of the patent life. Towards the end of the patent protection, the monopolist will begin acting more and more myopically, leading to a continuous decrease in price. When the patent expires, a discontinuous fall in price occurs as the generic industry takes over. We argue that, for reasonable bio-economic parameters of the model, the steady state which is targeted by the monopolist brings two effects into balance: the fitness cost effect (benefiting antibiotic efficacy) and the natural selection effect (favoring a dominance of the drug-resistant version of the bacterial population). Thus, antibiotic efficacy will generally find itself somewhere between its upper and lower bound over a period of time. In that case, it will, in the end, start decreasing, as will the level of infection, reflecting the fact that the monopolist attaches less and less value to the quality and the market size of the antibiotic as the patent nears expiration.

We also find insight with respect to the welfare implications of a prolongation of the patent. More particularly, it may be socially desirable to prolong the patent, if the level of infection is sufficiently low compared to the level of antibiotic efficacy. However, this result crucially depends on the proposed prolongation of the patent. A higher increase in the patent duration implies that the monopolist behaves non-myopically over a longer period of time and as such does not only benefit the evolution of antibiotic efficacy, but also favors the spread of infection, which represents a bad to society.

It should be pointed out that our results are obtained under some assumptions concerning the strategies available to the monopolist once the patent expires. For instance, the monopolist may have the possibility of practicing price discrimination for a while, by selling the brand name at a high price, and selling his own generic version before the patent has expired. This might lead to a Stackelberg-type market structure during the generic phase of

the industry. Another possibility that has not been taken into account is that the monopolist may attempt to "improve" the biological formula of the drug slightly, at a cost, in the hope of getting a new patent protection. Taking those additional possibilities into account would of course have an impact on the price path during the period of patent protection, but would not necessarily alter the underlying turnpike property described here. How exactly the price path would be affected is however a matter for further research.

Appendix

We first recall the full dynamic system, involving the state and co-state variables, which the monopoly solution must satisfy. It is given by:

$$\dot{w} = w(1-w)(\Delta r - r_f f) \tag{A–1}$$

$$\dot{I} = I(\beta(N-I) - r_r + w(\Delta r - r_f f)) \tag{A–2}$$

$$\dot{\mu} = \rho\mu + (\Delta r - r_f f)[\mu(2w-1) - \lambda I] - r_f I(1-f)f \tag{A–3}$$

$$\dot{\lambda} = \rho\lambda + \lambda[2\beta I - \beta N + r_r - w(\Delta r - r_f f)] - r_f w(1-f)f + cf \tag{A–4}$$

In addition, the first-order condition (12) for the maximization of the Hamiltonian must be satisfied at every point in time, including at a steady state. A steady-state solution is given by $\dot{w} = \dot{I} = \dot{\mu} = \dot{\lambda} = 0$.

A The steady state with $w^{SS} = 1$

Setting $w = 1$ in (A–1), we have $\dot{w} = 0$. Setting $\dot{I} = 0$, $\dot{\lambda} = 0$ and $w = 1$ in (A–2) and (A–4) gives:

$$I = \frac{\beta N - r_w - r_f f}{\beta} \tag{A–5}$$

$$\lambda = \frac{r_f(1-f)f - cf}{\rho + \beta I} \tag{A–6}$$

For convenience, we rewrite the first-order condition in (17) evaluated at $w^{SS} = 1$

$$r_f w(1-2f) = c + r_f w\lambda. \tag{A–7}$$

Replacing (A–6) into (A–7) gives an expression in the treatment rate f, which we solve for to obtain:

$$f_{1,2} = \frac{a}{2} \pm \sqrt{\left(\frac{a}{2}\right)^2 - b} \tag{A–8}$$

where

$$a = \frac{2}{3r_f}[\rho + \beta N - r_w + r_f - c] \tag{A–9}$$

$$b = \frac{\left(1 - \frac{c}{r_f}\right)(\rho + \beta N - r_w)}{3r_f} \tag{A–10}$$

Both values of $f_{1,2}$ are admissible solutions, and we cannot exclude any of them analytically. Our numerical simulations however suggest that the solution is unique and given by:

$$f^{SS} = \frac{a}{2} - \sqrt{\left(\frac{a}{2}\right)^2 - b} \tag{A–11}$$

B The intermediate steady state with $f^{SS} = \frac{\Delta r}{r_f}$

For an interior solution to the maximization of the Hamiltonian, f must satisfy equation (17), in addition to (A–1)-(A–4). Setting $f = f^{SS} = \Delta r/r_f$, we have $\dot{w} = 0$, from (A–1), and from (A–2):

$$I^{SS} = \frac{\beta N - r_r}{\beta}. \tag{A–12}$$

Setting $\dot{\mu} = 0$ in (A–3) and substituting for f^{SS^*} and I^{SS^*}, we get the steady-state solution for μ:

$$\mu^{SS} = \frac{\Delta r}{r_f} \frac{I^{SS}(r_f - \Delta r)}{\rho} \tag{A–13}$$

We still need to determine the steady-state levels of antibiotic efficacy, w^{SS}, and of the shadow price of infection, λ^{SS}. Setting $\dot{\lambda} = 0$ in (A–4) and substituting for f^{SS} and I^{SS} we get:

$$\lambda = \frac{\Delta r}{r_f} \frac{w(r_f - \Delta r) - c}{\rho + \beta N - r_r}. \tag{A–14}$$

Since $f^{SS} = \Delta r/r_f$ is the monopoly solution in this steady state, price $p = r_f w(1 - \Delta r/r_f)$ must be higher than the marginal production cost c, implying a positive value of λ. Substituting for f^{SS}, I^{SS}, μ^{SS} and λ from (A–14) into (17), we get a binomial in w, the solutions of which are:

$$w = -\frac{B}{2A} \pm \sqrt{\frac{c}{A} + \left(\frac{B}{2A}\right)^2} \tag{A–15}$$

where

$$\begin{aligned} A &= \Delta r(r_f - \Delta r) \frac{\beta N - r_r}{\rho(\rho + \beta N - r_r)} \\ B &= (r_f - 2\Delta r) - \Delta r \frac{r_f - \Delta r}{\rho} + \frac{\Delta r c}{\rho + \beta N - r_r}. \end{aligned}$$

The expression for A is positive, while the sign of B depends on the parameters of the model. In order to exclude solutions with $w < 0$ for all B, the admissible solution for w is

$$w^{SS} = -\frac{B}{2A} + \sqrt{\frac{c}{A} + \left(\frac{B}{2A}\right)^2}. \tag{A–16}$$

Depending on the set of parameters, we have $w^{SS} < 1$ or $w^{SS} = 1$. The condition $w^{SS} \leq 1$ can be written as:

$$c \leq \Delta r \frac{\Delta r - 2(\rho + \beta N - r_r)}{\rho + \beta N - r_r - \Delta r} + r_f. \tag{A–17}$$

In the case of a zero fitness cost $\Delta r = 0$, the condition (A–17) becomes $c \leq r_f$, which is always verified if the antibiotic is economically viable at the maximum value of antibiotic efficacy ($w = 1$).

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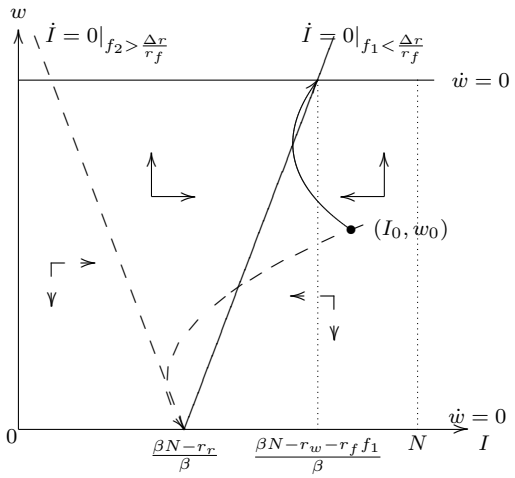

Figure 1: The phase diagram

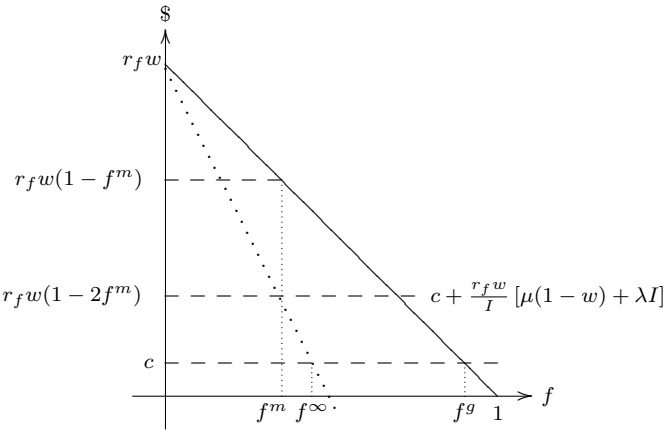

Figure 2: Monopolistic interior solution f^m at state (w, I) at time t

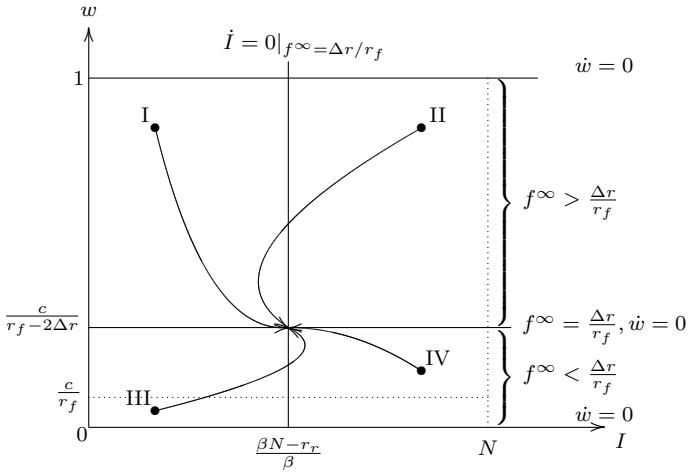

Figure 3: Convergence to steady state under the myopic monopolistic programme

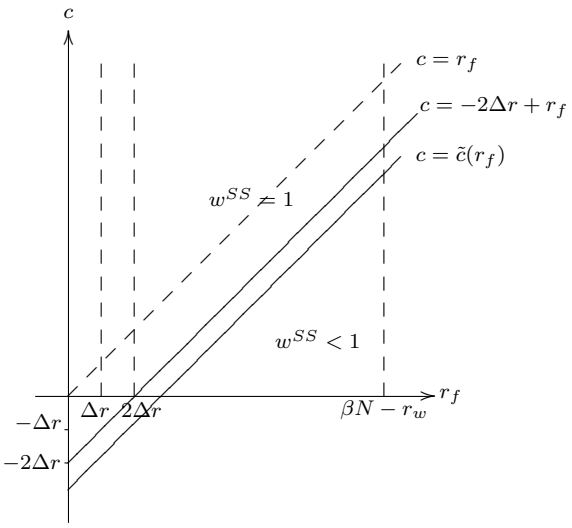

Figure 4: Steady-state configurations

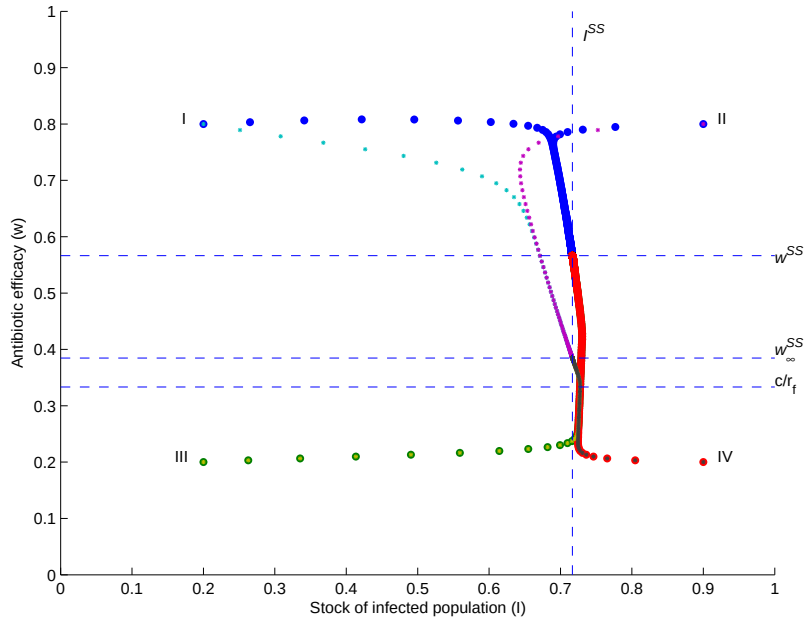

Figure 5: Convergence to interior steady state

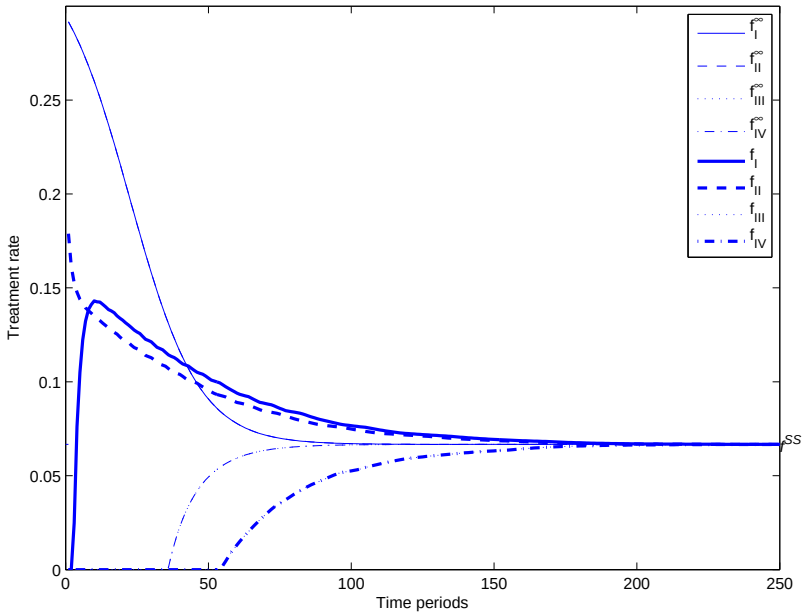

Figure 6: Treatment rates converging to $f^{SS} = \frac{\Delta r}{r_f}$

Note that trajectories f_I^{∞} and f_{II}^{∞}, as well as f_{III}^{∞} and f_{IV}^{∞} coincide with each other, as the myopic treatment rate is a function of the level of antibiotic efficacy only. This also applies to f_{III} and f_{IV}, as the non-myopic monopolist sets $f = 0$ at the beginning and the state trajectories join together and then are confounded.

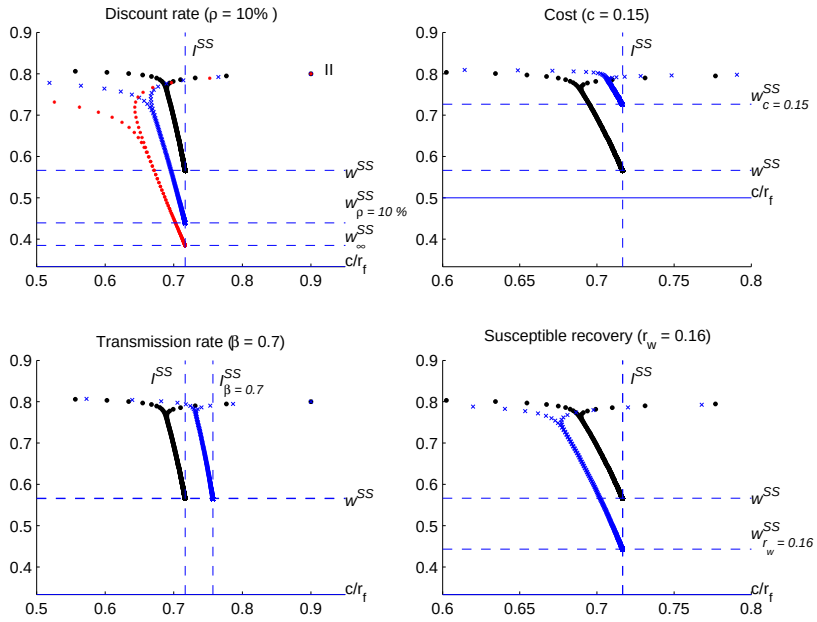

Figure 7: Comparative dynamics of chosen parameters

An increase in the discount rate makes the non-myopic monopolist more impatient, as explained in the text. A higher cost increases the steady-state value of w, while the overshooting of I is reduced via lower treatment rates. A higher transmission rate increases the steady state of I, and lowers slightly that of w (admittedly difficult to see). The qualitative impact of a decrease in r_r parallels that of increasing β, with the overshooting pattern being more pronounced (not shown). A higher recovery rate from the susceptible strain (or due to antibiotic treatment) increases the overshooting of I below its steady-state level, which is compensated by lowering w (not shown).

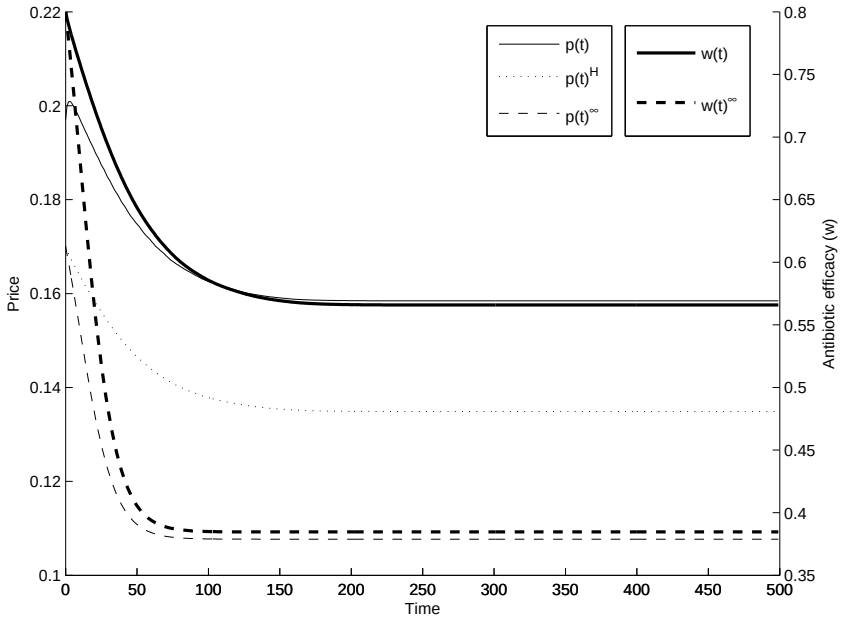

Figure 8: Price paths departing from initial state of type II

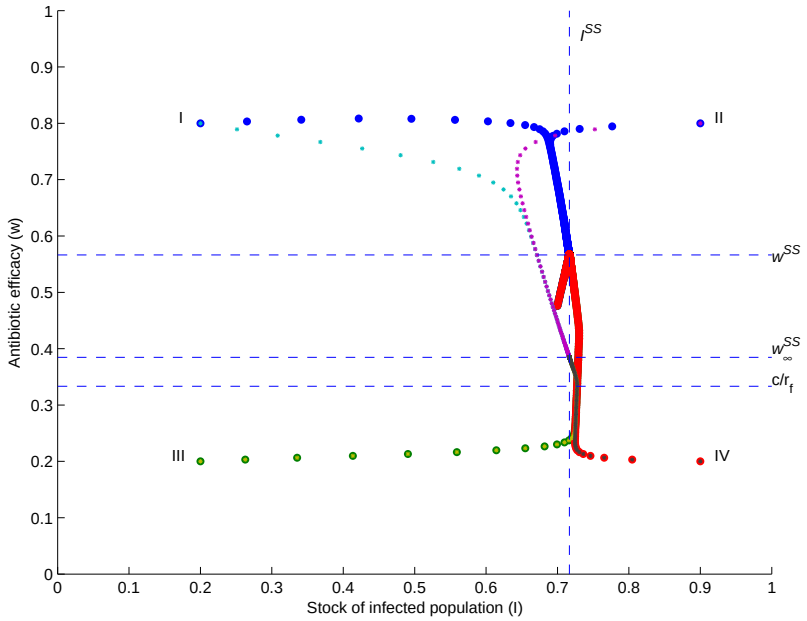

Figure 9: Evolution of state variables (I, w) and the turnpike

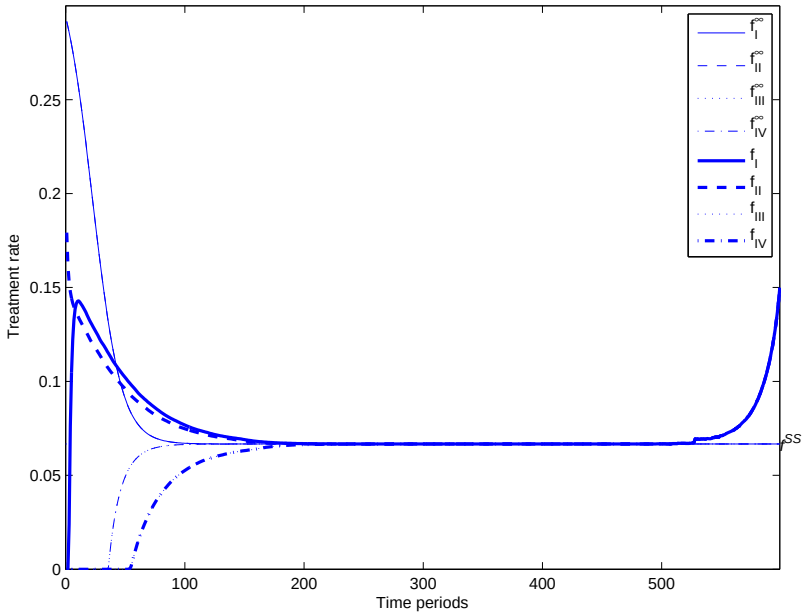

Figure 10: Evolution of treatment rate f and the turnpike

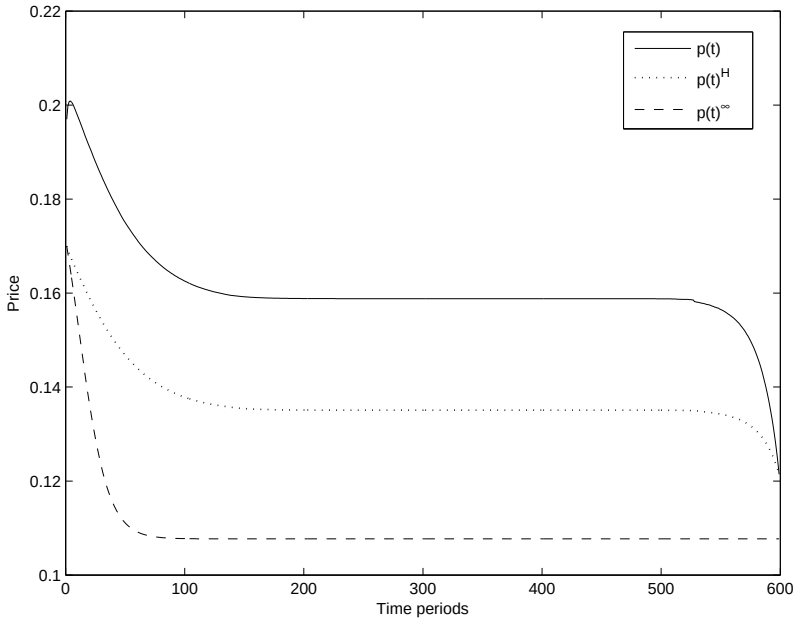

Figure 11: Price paths departing from initial state of type II and the turnpike

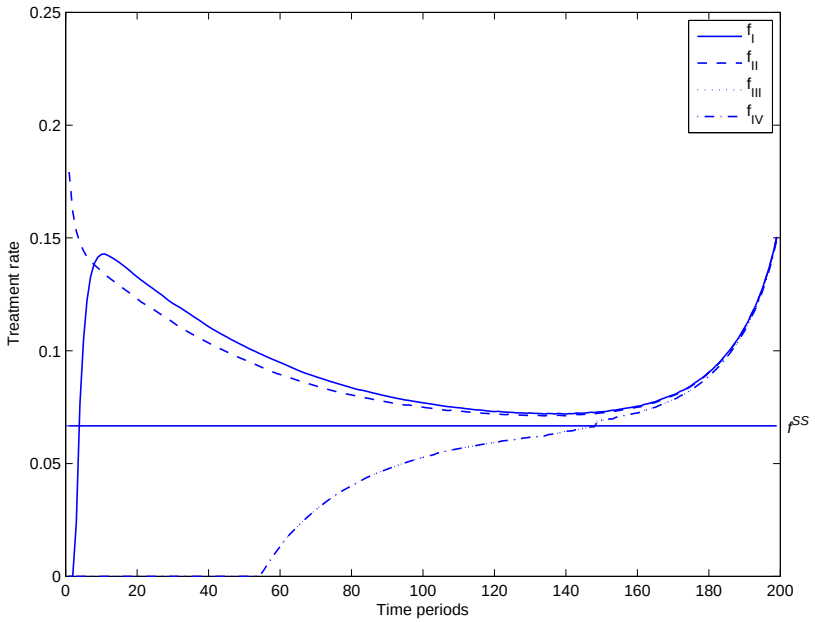

Figure 12: Evolution of treatment rate f with approximate turnpike

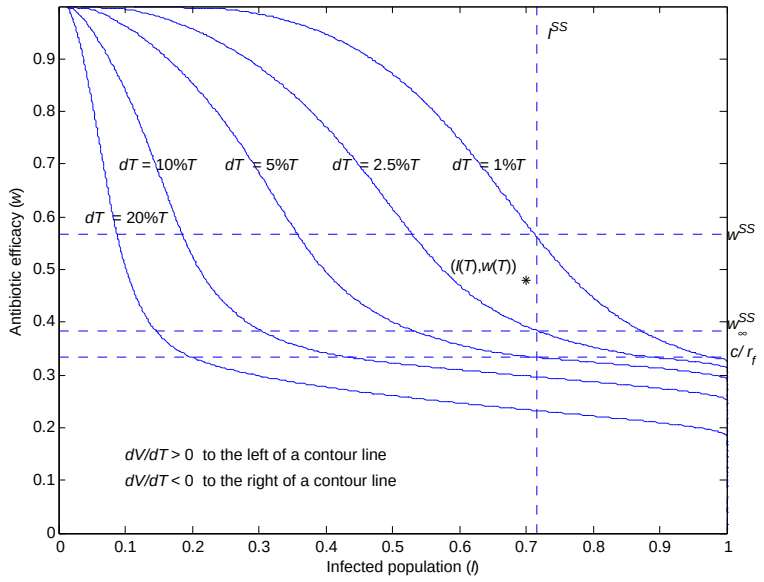

Figure 13: Welfare impacts of prolonging the patent length