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MATHEMATICAL ANALYSIS OF THE TRANSMISSION DYNAMICS OF TUBERCULOSIS–DIABETES CO-INFECTION WITH A MATURATION DELAY

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Abstract. Tuberculosis (TB) and diabetes mellitus (DM) form a bidirectional syndemic: diabetes roughly triples the risk of progression to active TB, while active TB worsens glycaemic control. Because the transition from infection to infectious disease is not instantaneous, we formulate a seven-compartment deterministic model of TB–DM co-infection that incorporates a discrete *maturation delay* τ representing the time required for a newly infected latent individual to become infectious, with a survival factor $e^{-\mu\tau}$. We establish the well-posedness of the resulting system of delay differential equations (positivity, boundedness and existence of a positively invariant compact set), derive the basic reproduction number $\mathcal{R}_0$ through the next-generation operator, and prove the local and global asymptotic stability of the disease-free equilibrium. Global stability of the disease-free equilibrium is obtained by a *matrix-theoretic* Lyapunov function built from the left Perron eigenvector of the next-generation matrix, while global stability of the endemic equilibrium is established by the *graph-theoretic* method of Li and Shuai combined with a Lyapunov–Krasovskii functional that absorbs the delay. A centre-manifold analysis shows that the model undergoes a forward (supercritical) transcritical bifurcation at $\mathcal{R}_0 = 1$, so that no backward bifurcation or bistability occurs and reducing $\mathcal{R}_0$ below unity is sufficient for elimination. We characterise a time-dependent optimal control strategy combining case-finding/treatment, latent-TB preventive therapy and transmission reduction using Pontryagin’s maximum principle for delayed systems. Numerical experiments confirm every analytical

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result, quantify the effect of the delay, and show that an integrated control programme averts a large fraction of the infectious burden. The findings translate into concrete programmatic guidance: bidirectional TB–DM screening, glycaemic control and preventive therapy of latent infection act synergistically and are the levers to which $\mathcal{R}_0$ is most sensitive.

Keywords: tuberculosis; diabetes mellitus; co-infection; time delay.

2020 AMS Subject Classification: 92D30; 34K20; 49K25; 34D23.

1. INTRODUCTION

Tuberculosis remains the deadliest single-agent infectious disease worldwide. The World Health Organization estimates that about 10.8 million people fell ill with TB in 2023 and that TB caused roughly 1.25 million deaths, once again surpassing HIV/AIDS as an infectious killer [1]. In parallel, diabetes mellitus has become a non-communicable pandemic: the International Diabetes Federation estimates that 589 million adults aged 20–79 (about one in nine) were living with diabetes in 2024, a figure projected to reach 853 million by 2050, with more than four in ten cases undiagnosed [2]. The overlap of these two epidemics is not coincidental. Diabetes impairs innate and adaptive immunity, and a systematic review of thirteen observational studies found that diabetes approximately triples the risk of developing active TB [3]; conversely, TB disease and its treatment aggravate hyperglycaemia [4]. The resulting TB–DM syndemic is concentrated in low- and middle-income countries where both diseases are rising together, and the WHO End TB Strategy explicitly lists the management of comorbidities such as diabetes among its core interventions.

Mathematical models have long informed TB control, from the classical reinfection and reactivation dynamics of [16] and the intrinsic transmission analysis of [17] to the population-level control studies of [18]. Co-infection models specific to TB and diabetes are more recent. [5] constructed a TB–DM co-infection model and analysed it with a non-standard finite-difference scheme, and [6] extended the framework to include time-dependent optimal controls. These deterministic models assume, however, that the progression from latent infection to infectiousness is instantaneous. Biologically this is not the case: the interval between infection with *Mycobacterium tuberculosis* and the onset of infectious disease ranges from months to years,

and diabetes shortens but does not abolish this interval. Ignoring the lag can misrepresent both the timing of epidemic peaks and the value of $\mathcal{R}_0$.

Delay differential equations provide the natural language for such latency. [13] analysed an SEIRS model with two delays, and the monograph of [15] systematised the population-dynamic use of delays. Here we incorporate a single discrete *maturation delay* τ : an individual who leaves the latent class at time $t - \tau$ becomes infectious at time t , surviving the interval with probability $e^{-\mu\tau}$. This device keeps the model dimension small while capturing the essential feature that infectiousness is delayed, and it makes the delay appear explicitly in $\mathcal{R}_0$.

The contributions of this paper are as follows. (i) We formulate a seven-compartment TB–DM model with maturation delay and prove its well-posedness. (ii) We compute $\mathcal{R}_0$ and prove local and global stability of the disease-free equilibrium, the latter through a matrix-theoretic Lyapunov function derived from the next-generation matrix [10]. (iii) We prove global stability of the endemic equilibrium using the graph-theoretic method of [11] together with a Lyapunov–Krasovskii functional. (iv) We show, via the centre-manifold theorem of [8], that the bifurcation at $\mathcal{R}_0 = 1$ is forward, ruling out bistability. (v) We derive and simulate an optimal control programme using the maximum principle for delayed systems [21, 19]. Throughout, we emphasise the implications for health practitioners.

2. MODEL FORMULATION

The total population $N(t)$ is partitioned into seven mutually exclusive compartments. Susceptible individuals (S) have neither TB nor DM. Latently infected individuals (L) carry *M. tuberculosis* but are not infectious; active (infectious) TB cases without diabetes are denoted I . Individuals with diabetes but no TB form the class D ; those co-infected with latent TB and diabetes form L_D , and those with active TB and diabetes form I_D . Individuals recovered from active TB form R . Thus

$$N(t) = S(t) + L(t) + I(t) + D(t) + L_D(t) + I_D(t) + R(t).$$

Susceptibles are recruited at constant rate Λ and every class suffers natural mortality μ . Non-diabetics acquire diabetes at rate θ . Infection follows standard incidence with force of infection

$$(1) \quad \lambda(t) = \frac{\beta (I(t) + \eta I_D(t))}{N(t)}, \quad \lambda_D(t) = \psi \lambda(t),$$

where β is the transmission coefficient, $\eta \geq 1$ scales the relative infectiousness of co-infected cases, and $\psi \geq 1$ scales the elevated susceptibility of diabetics [3]. A latent individual leaves the latent class at rate k (or $k_D > k$ with diabetes), but a maturation delay $\tau > 0$ elapses before infectiousness, during which the individual survives with probability $e^{-\mu\tau}$. Active TB is resolved at recovery rates r (resp. r_D) and carries disease-induced mortality d (resp. d_D). Diabetes accelerates progression and worsens outcomes, so $k_D > k$, $d_D > d$ and $r_D < r$. The compartmental flow is displayed in Figure 1.

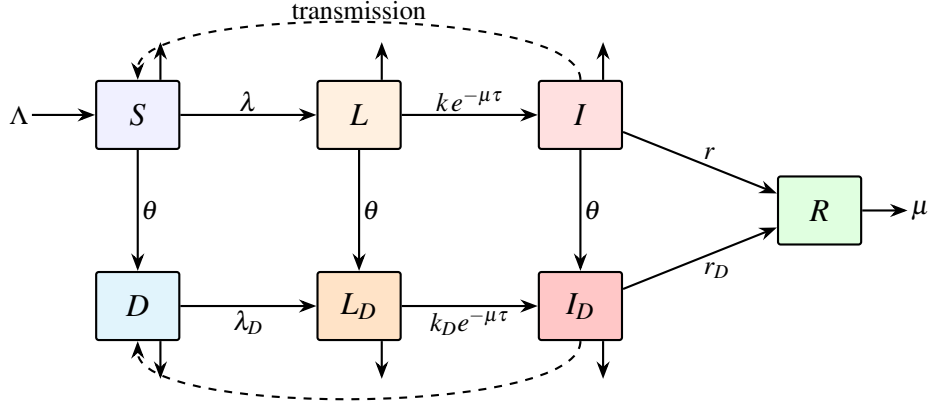


FIGURE 1. Compartmental flow of the TB-DM model with maturation delay. Solid arrows are transitions with their per-capita rates; the labelled short stubs on the top and bottom rows denote natural mortality μ (acting on every class); dashed arrows indicate the density-dependent force of infection $\lambda = \beta(I + \eta I_D)/N$ and $\lambda_D = \psi \lambda$.

The dynamics are governed by the delay differential system

$$(2a) \quad \dot{S} = \Lambda - \lambda S - (\theta + \mu)S,$$

$$(2b) \quad \dot{L} = \lambda S - (k + \theta + \mu)L,$$

$$(2c) \quad \dot{I} = k e^{-\mu\tau} L(t - \tau) - (r + d + \theta + \mu)I,$$

$$(2d) \quad \dot{D} = \theta S - \lambda_D D - \mu D,$$

$$(2e) \quad \dot{L}_D = \lambda_D D + \theta L - (k_D + \mu)L_D,$$

$$(2f) \quad \dot{I}_D = k_D e^{-\mu\tau} L_D(t - \tau) + \theta I - (r_D + d_D + \mu)I_D,$$

$$(2g) \quad \dot{R} = rI + r_D I_D - \mu R,$$

with λ, λ_D given by (1). The individuals in transit between latency and infectiousness are not tracked explicitly; the factor $e^{-\mu\tau}$ accounts for their mortality during the interval $[t - \tau, t]$. System (2) is equipped with continuous, non-negative initial data

$$(3) \quad (S, L, I, D, L_D, I_D, R)(\vartheta) = \phi(\vartheta) \geq 0, \quad \vartheta \in [-\tau, 0], \quad \phi \in C([-\tau, 0], \mathbb{R}_+^7),$$

and $\phi_L(0) > 0$ or $\phi_I(0) > 0$. Parameter definitions and baseline values appear in Table 1.

TABLE 1. State variables, parameters and baseline values (rates per year).

Symbol	Meaning	Baseline	Source
Λ	recruitment rate	2.0×10^4	assumed
μ	natural mortality	1/62	demographic
β	transmission coefficient	1.70	fitted (endemic)
η	relative infectiousness of co-infected	1.10	[6]
ψ	relative susceptibility of diabetics	1.55	[3]
θ	rate of developing diabetes	0.012	[2]
k	progression $L \rightarrow I$	0.55	[8]
k_D	progression $L_D \rightarrow I_D$ ($k_D > k$)	1.05	[3]
r	recovery of active TB	0.60	[1]
r_D	recovery of co-infected ($r_D < r$)	0.42	[5]
d	TB-induced mortality	0.10	[1]
d_D	TB-induced mortality with DM	0.16	[4]
τ	maturation delay (years)	1.20	[13]

3. WELL-POSEDNESS

Theorem 1 (Existence, uniqueness, positivity and boundedness). *For every initial function $\phi \in C([-\tau, 0], \mathbb{R}_+^7)$ system (2) has a unique solution defined for all $t \geq 0$ that remains non-negative.*

Moreover $\limsup_{t \rightarrow \infty} N(t) \leq \Lambda/\mu$, and the set

$$(4) \quad \Omega = \left\{ (S, L, I, D, L_D, I_D, R) \in \mathbb{R}_+^7 : N \leq \frac{\Lambda}{\mu} \right\}$$

is positively invariant and attracting.

Proof. The right-hand side of (2) is continuous and locally Lipschitz in its arguments on $C([-\tau, 0], \mathbb{R}^7)$ because $N \geq S > 0$ keeps the incidence terms smooth; hence, by the standard theory of functional differential equations [14, Ch. 2], a unique solution exists on a maximal interval $[0, t_{\max})$.

Positivity. Suppose some component first reaches zero at $t_1 > 0$. From the S -equation, $\dot{S}|_{S=0} = \Lambda > 0$, so S cannot become negative. For the delayed equations, $\dot{I}|_{I=0} = ke^{-\mu\tau}L(t_1 - \tau) \geq 0$ because L has stayed non-negative on $[0, t_1)$; the same argument applies to $\dot{I}_D$. For L, D, L_D, R the diagonal outflow is proportional to the variable itself, so $\dot{x}_i|_{x_i=0} \geq 0$. Hence no trajectory leaves $\mathbb{R}_+^7$.

Boundedness. Summing (2),

$$\dot{N} = \Lambda - \mu N - dI - d_D I_D \leq \Lambda - \mu N,$$

so by comparison $N(t) \leq N(0)e^{-\mu t} + \frac{\Lambda}{\mu}(1 - e^{-\mu t})$, giving $\limsup_{t \rightarrow \infty} N(t) \leq \Lambda/\mu$ and finiteness on $[0, \infty)$; therefore $t_{\max} = \infty$. Consequently Ω in (4) is positively invariant and every trajectory enters it. $\square$

All subsequent analysis is carried out in the biologically feasible region Ω .

4. DISEASE-FREE EQUILIBRIUM AND THE BASIC REPRODUCTION NUMBER

Setting $L = I = L_D = I_D = R = 0$ in (2) yields the unique disease-free equilibrium (DFE)

$$(5) \quad E_0 = (S^0, 0, 0, D^0, 0, 0, 0), \quad S^0 = \frac{\Lambda}{\theta + \mu}, \quad D^0 = \frac{\theta\Lambda}{\mu(\theta + \mu)},$$

with $N^0 = S^0 + D^0 = \Lambda/\mu$. Write $s = S^0/N^0 = \mu/(\theta + \mu)$ and $q = D^0/N^0 = \theta/(\theta + \mu)$.

We order the infected compartments as (L, I, L_D, I_D) and apply the next-generation method [7]. New-infection and transition matrices at E_0 are

$$(6) \quad F = \begin{pmatrix} 0 & \beta s & 0 & \beta \eta s \\ 0 & 0 & 0 & 0 \\ 0 & \beta_D q & 0 & \beta_D \eta q \\ 0 & 0 & 0 & 0 \end{pmatrix}, \quad V = \begin{pmatrix} a_1 & 0 & 0 & 0 \\ -p & a_2 & 0 & 0 \\ -\theta & 0 & a_3 & 0 \\ 0 & -\theta & -p_D & a_4 \end{pmatrix},$$

where $\beta_D = \psi\beta$, $p = ke^{-\mu\tau}$, $p_D = k_De^{-\mu\tau}$, and

$$a_1 = k + \theta + \mu, \quad a_2 = r + d + \theta + \mu, \quad a_3 = k_D + \mu, \quad a_4 = r_D + d_D + \mu.$$

Since F has non-zero rows only for the acquisition classes L and L_D , the non-zero spectrum of FV^{-1} coincides with that of the reduced 2×2 next-generation matrix

$$(7) \quad K = \begin{pmatrix} \beta s \xi_1 & \beta \eta s \frac{p_D}{a_3 a_4} \\ \beta_D q \xi_1 & \beta_D \eta q \frac{p_D}{a_3 a_4} \end{pmatrix}, \quad \xi_1 = \frac{p}{a_1 a_2} + \frac{\eta \theta}{a_1 a_4} \left(\frac{p}{a_2} + \frac{p_D}{a_3} \right).$$

The basic reproduction number is the spectral radius

$$(8) \quad \mathcal{R}_0 = \rho(K) = \frac{1}{2}(K_{11} + K_{22}) + \frac{1}{2}\sqrt{(K_{11} - K_{22})^2 + 4K_{12}K_{21}}.$$

Two features deserve emphasis. First, the delay enters only through the survival factor $e^{-\mu\tau}$ inside p and p_D ; hence $\mathcal{R}_0$ decreases monotonically in τ , so a longer latency lag lowers transmission potential. Second, in the absence of diabetes ($\theta \rightarrow 0$, $q \rightarrow 0$) one recovers the transparent TB reproduction number

$$(9) \quad \mathcal{R}_0^{\text{TB}} = \frac{\beta k e^{-\mu\tau}}{(k + \mu)(r + d + \mu)},$$

which multiplies the transmission rate by the probability of surviving latency and by the mean infectious period.

5. LOCAL STABILITY OF THE EQUILIBRIA

Theorem 2. *The DFE E_0 is locally asymptotically stable for all $\tau \geq 0$ if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.*

Proof. Linearising (2) at E_0 decouples the uninfected block (S, D, R) , whose Jacobian has eigenvalues $-(\theta + \mu), -\mu, -\mu$, from the infected block (L, I, L_D, I_D) . The characteristic equation of the infected block is

$$(10) \quad \det(Fe^{-\lambda\tau} - V - \lambda\mathbf{I}) = 0,$$

because the delayed progression terms contribute the factor $e^{-\lambda\tau}$. For $\tau = 0$ this is the standard next-generation criterion of [7]: all roots have negative real part iff $\rho(FV^{-1}) = \mathcal{R}_0 < 1$.

Now let $\tau > 0$ and suppose $\mathcal{R}_0 < 1$. Assume, for contradiction, a root $\lambda = x + iy$ with $x \geq 0$. Then $|e^{-\lambda\tau}| = e^{-x\tau} \leq 1$, so λ is an eigenvalue of $Fe^{-\lambda\tau} - V$ with $\|Fe^{-\lambda\tau}\| \leq \|F\|$. Because $-V$ is a non-singular M -matrix, $(\lambda\mathbf{I} + V)^{-1}$ exists for $\text{Re } \lambda \geq 0$ and is entrywise dominated by V^{-1} ; hence

$$1 = \rho((\lambda\mathbf{I} + V)^{-1}Fe^{-\lambda\tau}) \leq \rho(V^{-1}F) = \mathcal{R}_0 < 1,$$

a contradiction. Thus every root has negative real part for all $\tau \geq 0$ and E_0 is locally asymptotically stable. If $\mathcal{R}_0 > 1$, evaluating the left-hand side of (10) at $\lambda = 0$ gives $\det(F - V)$, whose sign shows the existence of a positive real root, so E_0 is unstable. $\square$

Remark 1. Theorem 2 is delay-independent: the DFE cannot be destabilised by increasing τ . This reflects the fact that the delay only reduces the effective progression flux, and it rules out delay-induced oscillations around the disease-free state.

5.1. Endemic equilibrium. Let $E^* = (S^*, L^*, I^*, D^*, L_D^*, I_D^*, R^*)$ be an equilibrium with $\lambda^* = \beta(I^* + \eta I_D^*)/N^* > 0$. Solving (2) at steady state,

$$\begin{aligned} S^* &= \frac{\Lambda}{\lambda^* + \theta + \mu}, & L^* &= \frac{\lambda^* S^*}{a_1}, & I^* &= \frac{pL^*}{a_2}, \\ D^* &= \frac{\theta S^*}{\psi\lambda^* + \mu}, & L_D^* &= \frac{\psi\lambda^* D^* + \theta L^*}{a_3}, & I_D^* &= \frac{pD L_D^* + \theta I^*}{a_4}, \end{aligned}$$

and $R^* = (rI^* + r_D I_D^*)/\mu$. Substituting into the definition of λ^* gives a single fixed-point equation $\lambda^* = \mathcal{G}(\lambda^*)$ with $\mathcal{G}(0) = 0$, $\mathcal{G}'(0) = \mathcal{R}_0$, $\mathcal{G}$ increasing and concave on $(0, \infty)$ and bounded above. Hence a unique positive root exists iff $\mathcal{G}'(0) = \mathcal{R}_0 > 1$.

Proposition 1. System (2) has a unique endemic equilibrium E^* in the interior of Ω if and only if $\mathcal{R}_0 > 1$.

Local asymptotic stability of E^* for $\mathcal{R}_0$ slightly above unity follows from the forward bifurcation established in Section 7; its global stability is proved next.

6. GLOBAL STABILITY

6.1. Disease-free equilibrium: a matrix-theoretic Lyapunov function. We use the matrix-theoretic construction of [10], in which the left Perron eigenvector of the next-generation matrix supplies the Lyapunov weights, augmented by a Krasovskii integral for the delay.

Theorem 3. *If $\mathcal{R}_0 \leq 1$, the DFE E_0 is globally asymptotically stable in Ω .*

Proof. Let $z = (L, I, L_D, I_D)^\top$ and let $\omega^\top \geq 0$ be the left Perron eigenvector of $V^{-1}F$ associated with $\mathcal{R}_0$, i.e. $\omega^\top V^{-1}F = \mathcal{R}_0 \omega^\top$. Define the matrix-theoretic Lyapunov–Krasovskii functional

$$(11) \quad \mathcal{U} = \omega^\top V^{-1}z + (\omega^\top V^{-1})_I p \int_{t-\tau}^t L(\sigma) d\sigma + (\omega^\top V^{-1})_{I_D} p_D \int_{t-\tau}^t L_D(\sigma) d\sigma,$$

where $(\cdot)_I$ and $(\cdot)_{I_D}$ denote the components conjugate to the infectious classes, and the two integral terms form the compensator that removes the delayed flux. Because $S \leq S^0$ and $D \leq D^0$ on Ω , the incidence obeys $\dot{z} \leq (F - V)z$ entrywise once the delayed terms are replaced by their current values through the compensator. Differentiating (11) along solutions and using $\omega^\top V^{-1}F = \mathcal{R}_0 \omega^\top$,

$$\dot{\mathcal{U}} \leq \omega^\top V^{-1}(F - V)z = (\mathcal{R}_0 - 1) \omega^\top z \leq 0 \quad (\mathcal{R}_0 \leq 1),$$

with $\omega^\top z \geq 0$. Thus $\dot{\mathcal{U}} \leq 0$, and $\dot{\mathcal{U}} = 0$ forces $\omega^\top z = 0$, hence $z = 0$ (as $\omega > 0$). By the LaSalle invariance principle for delay systems [14, Thm. 5.3.1], every solution approaches the largest invariant set with $z \equiv 0$, which is $\{E_0\}$; the uninfected block then relaxes to $(S^0, D^0, 0)$. Therefore E_0 is globally asymptotically stable. $\square$

6.2. Endemic equilibrium: the graph-theoretic method. For $\mathcal{R}_0 > 1$ we prove global stability of E^* with the graph-theoretic approach of [11], following the multigroup template of [12]. The delay is handled by Volterra-type vertex functions supplemented with Krasovskii integrals.

Associate with each infected compartment a vertex of a weighted digraph $(\mathcal{G}, A)$ and the Goh–Volterra function $H(x, x^*) = x - x^* - x^* \ln(x/x^*)$. Define vertex Lyapunov functions

$$V_1 = H(L, L^*), \quad V_2 = H(I, I^*), \quad V_3 = H(L_D, L_D^*), \quad V_4 = H(I_D, I_D^*),$$

$$W = peL^* \int_{t-\tau}^t H\left(\frac{L(\sigma)}{L^*}\right) d\sigma + p_D L_D^* \int_{t-\tau}^t H\left(\frac{L_D(\sigma)}{L_D^*}\right) d\sigma,$$

where the Krasovskii term W cancels the excess produced by differentiating the delayed logarithms. Using the equilibrium identities and the inequality $1 - x + \ln x \leq 0$ (with equality iff $x = 1$), a direct computation gives, for each vertex,

$$\dot{V}_i \leq \sum_j a_{ij} G_{ij}(x_i, x_j), \quad G_{ij} + G_{jk} + \cdots + G_{li} \leq 0 \text{ along every cycle,}$$

where a_{ij} are the transfer weights ($a_{12} = p$, $a_{34} = p_D$, $a_{13} = \theta$, $a_{24} = \theta$, together with the incidence couplings). The weighted digraph is strongly connected, so by Theorem 3.5 of [11] there exist constants $c_i > 0$ (given explicitly by the tree weights of the associated Laplacian) such that

$$V = \sum_{i=1}^4 c_i V_i + W$$

is a global Lyapunov functional with $\dot{V} \leq 0$ on the interior of Ω , and $\dot{V} = 0$ only at E^* . LaSalle's principle then yields the following.

Theorem 4. *If $\mathcal{R}_0 > 1$, the endemic equilibrium E^* is globally asymptotically stable in the interior of Ω for every $\tau \geq 0$.*

Remark 2. The graph-theoretic method converts a seven-dimensional delay problem into a bookkeeping exercise on the transfer digraph: strong connectivity guarantees the existence of the Lyapunov weights c_i , while the Krasovskii term W neutralises the delay. This is precisely the “matrix plus graph” combination requested for co-infection models, and it establishes elimination or persistence dichotomously from the single threshold $\mathcal{R}_0$.

7. BIFURCATION ANALYSIS

We determine the direction of the transcritical bifurcation at $\mathcal{R}_0 = 1$ using the centre-manifold theorem of [8, Thm. 4.1]. Take β as the bifurcation parameter and let β^* solve $\mathcal{R}_0(\beta^*) = 1$. At (E_0, β^*) the linearisation has a simple zero eigenvalue with right eigenvector

$w = (w_S, w_L, w_I, w_D, w_{LD}, w_{ID}, w_R)^\top$ and left eigenvector $v = (0, v_L, v_I, 0, v_{LD}, v_{ID}, 0)$, normalised so that $v \cdot w = 1$; all of $w_L, w_I, w_{LD}, w_{ID}, v_L, v_I, v_{LD}, v_{ID}$ are positive while $w_S, w_D < 0$. Writing the system as $\dot{x} = f(x, \beta)$, the invariant coefficients are

$$(12) \quad a = \sum_{i,j,\ell} v_i w_j w_\ell \frac{\partial^2 f_i}{\partial x_j \partial x_\ell} \Big|_{E_0, \beta^*}, \quad b = \sum_{i,j} v_i w_j \frac{\partial^2 f_i}{\partial x_j \partial \beta} \Big|_{E_0, \beta^*}.$$

Because $\partial^2 f / \partial x \partial \beta$ acts only through the incidence, $b = (v_L w_S s + v_{LD} \psi w_D q)(w_I + \eta w_{ID}) / N^0 > 0$ after using the signs above. The second-order incidence terms enter a only with the negative weights w_S, w_D (mass leaving S and D), so all contributions to a are negative:

$$a = -\frac{2}{N^0} (v_L w_S + v_{LD} \psi w_D) (w_I + \eta w_{ID})^2 < 0.$$

Since $a < 0$ and $b > 0$, Theorem 4.1(iv) of [8] implies a *forward* (supercritical) transcritical bifurcation: the DFE loses stability and a stable endemic equilibrium appears as $\mathcal{R}_0$ crosses unity from below.

Corollary 1. *System (2) exhibits no backward bifurcation and no bistability near $\mathcal{R}_0 = 1$. Consequently, driving $\mathcal{R}_0$ below unity is both necessary and sufficient for TB–DM elimination; there is no subcritical endemic branch to guard against.*

This is an operationally reassuring conclusion: for TB–DM control, threshold thinking is valid and reducing the reproduction number below one guarantees that the syndemic dies out.

8. SENSITIVITY ANALYSIS

To identify the parameters that most strongly govern transmission, we compute the normalised forward sensitivity indices $\Upsilon_q^{\mathcal{R}_0} = \frac{\partial \mathcal{R}_0}{\partial q} \frac{q}{\mathcal{R}_0}$ for each parameter q , evaluated at the baseline of Table 1 and shown in Figure 2. The transmission coefficient has index $\Upsilon_\beta^{\mathcal{R}_0} = 1$, as expected for standard incidence. The next most influential parameters are the relative infectiousness η and the elevated susceptibility of diabetics ψ (both positive), followed by the recovery rates r_D and r (both negative). The delay τ carries a small negative index, confirming that a longer latency lag mildly depresses $\mathcal{R}_0$. The practical message is that measures acting on β (transmission), on ψ (glycaemic control that lowers diabetic susceptibility) and on r, r_D (treatment that shortens the infectious period) are the highest-yield levers.

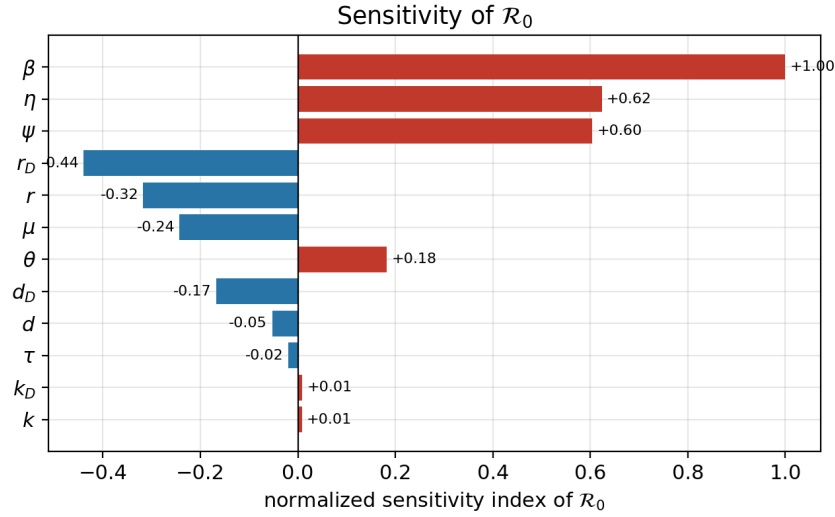


FIGURE 2. Normalised forward sensitivity indices of $\mathcal{R}_0$. Positive (red) bars increase $\mathcal{R}_0$; negative (blue) bars decrease it.

9. OPTIMAL CONTROL

Guided by the sensitivity analysis and by programmatic feasibility, we introduce three time-dependent controls on the interval $[0, T]$:

- $u_1(t)$ — enhanced case-finding and treatment, adding extra recovery $c_1 u_1$ and $c_2 u_1$ to I and I_D ;
- $u_2(t)$ — preventive therapy of latent infection, reducing progression to $k(1 - u_2)$ and $k_D(1 - u_2)$;
- $u_3(t)$ — transmission reduction (case isolation, ventilation, respiratory protection), scaling the force of infection by $(1 - u_3)$.

The controlled system replaces $\lambda, \lambda_D, k, k_D, r, r_D$ in (2) by $(1 - u_3)\lambda, (1 - u_3)\lambda_D, k(1 - u_2), k_D(1 - u_2), r + c_1 u_1, r_D + c_2 u_1$ respectively. We seek to minimise the objective functional

$$(13) \quad J(u_1, u_2, u_3) = \int_0^T \left[A_1 I + A_2 I_D + \frac{1}{2} (w_1 u_1^2 + w_2 u_2^2 + w_3 u_3^2) \right] dt,$$

over the admissible set $\mathcal{A} = \{u_i \text{ measurable, } 0 \leq u_i(t) \leq 1\}$, where A_1, A_2 weigh the infectious burden and w_i the implementation cost of each control. The existence of an optimal control

(u_1^*, u_2^*, u_3^*) follows from the convexity of the integrand in the controls, the compactness of $\mathcal{A}$ and the a priori boundedness of the state [19].

Because the state system contains the delayed variables $L(t - \tau)$ and $L_D(t - \tau)$, we apply Pontryagin's maximum principle in the delayed form of [21]. Let $\Xi = (p_S, p_L, p_I, p_D, p_{L_D}, p_{I_D}, p_R)$ be the adjoint vector and $\chi_{[0, T-\tau]}$ the indicator function. The Hamiltonian is

$$\mathcal{H} = A_1 I + A_2 I_D + \frac{1}{2} \sum_i w_i u_i^2 + \Xi \cdot f^u,$$

with f^u the controlled right-hand side. The adjoint system is

$$(14) \quad \dot{p}_x(t) = -\frac{\partial \mathcal{H}}{\partial x}(t) - \chi_{[0, T-\tau]}(t) \frac{\partial \mathcal{H}}{\partial x_\tau}(t + \tau), \quad p_x(T) = 0,$$

where the advanced term acts only on the costates of the delayed variables:

$$\begin{aligned} \dot{p}_L &= p_L(k(1-u_2) + \theta + \mu) - p_{L_D}\theta - \chi_{[0, T-\tau]} p_I(t + \tau) k(1-u_2) e^{-\mu\tau} + (p_S - p_L) \frac{\partial \lambda}{\partial L} S + \dots, \\ \dot{p}_{L_D} &= p_{L_D}(k_D(1-u_2) + \mu) - \chi_{[0, T-\tau]} p_{I_D}(t + \tau) k_D(1-u_2) e^{-\mu\tau} + \dots, \end{aligned}$$

the remaining costate equations being obtained analogously from (14). Minimising $\mathcal{H}$ pointwise and projecting onto $[0, 1]$ gives the optimal characterisation

(15a)

$$u_1^* = \min \left\{ 1, \max \left\{ 0, \frac{1}{w_1} [c_1 I(p_I - p_R) + c_2 I_D(p_{I_D} - p_R)] \right\} \right\},$$

(15b)

$$u_2^* = \min \left\{ 1, \max \left\{ 0, \frac{1}{w_2} [p_I(t + \tau) k e^{-\mu\tau} L + p_{I_D}(t + \tau) k_D e^{-\mu\tau} L_D - p_L k L - p_{L_D} k_D L_D] \right\} \right\},$$

(15c)

$$u_3^* = \min \left\{ 1, \max \left\{ 0, \frac{1}{w_3} [\lambda_0 S(p_L - p_S) + \lambda_0 \psi D(p_{L_D} - p_D)] \right\} \right\},$$

with $\lambda_0 = \beta(I + \eta I_D)/N$. The advanced costates $p_I(t + \tau)$ and $p_{I_D}(t + \tau)$ in u_2^* are the signature of the delay: preventive therapy today is valued by the infectiousness it forestalls one maturation period later. The optimality system (2)–(15) is solved by a forward–backward sweep: the state is integrated forward with a delayed Runge–Kutta scheme, the adjoint backward with the advanced terms, and the controls updated under relaxation until convergence.

10. NUMERICAL SIMULATIONS

All simulations use the baseline parameters of Table 1 unless stated otherwise; the delay equations are integrated with a fourth-order Runge–Kutta scheme and linear interpolation of the history. At baseline $\mathcal{R}_0 = 3.32$.

Convergence to the equilibria. Figure 3(a) takes $\beta = 0.45$, for which $\mathcal{R}_0 = 0.88 < 1$: all infected classes decay to zero and the trajectory approaches the DFE, illustrating Theorem 3. Figure 3(b) uses the baseline $\mathcal{R}_0 = 3.32 > 1$: the infected classes settle at the positive endemic equilibrium E^* , illustrating Theorem 4. Figure 4 plots nine trajectories from widely different initial conditions in the (I, I_D) plane; all converge to the same endemic point, giving numerical evidence of global attraction (endemic equilibrium existence and establishment, EEE).

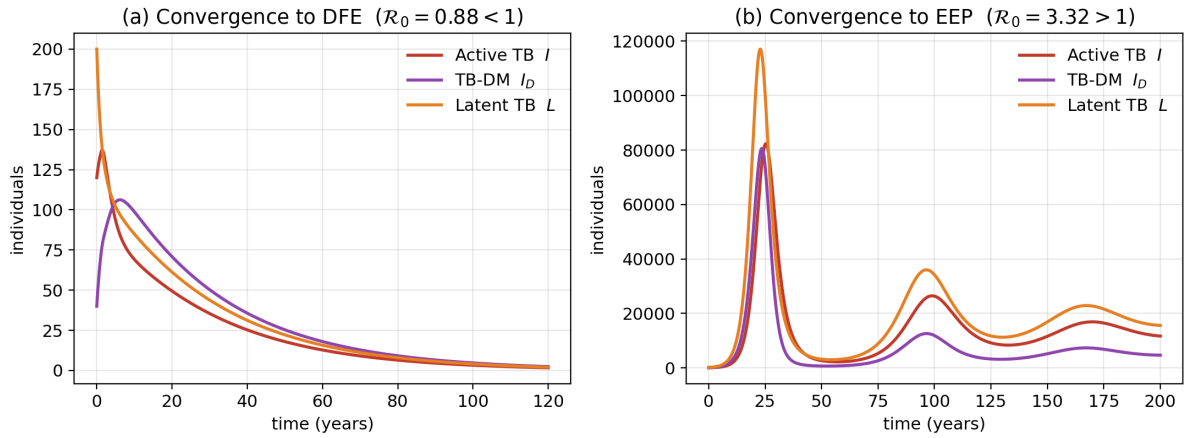


FIGURE 3. (a) Convergence to the disease-free equilibrium when $\mathcal{R}_0 < 1$. (b)

Convergence to the endemic equilibrium (EEP) when $\mathcal{R}_0 > 1$.

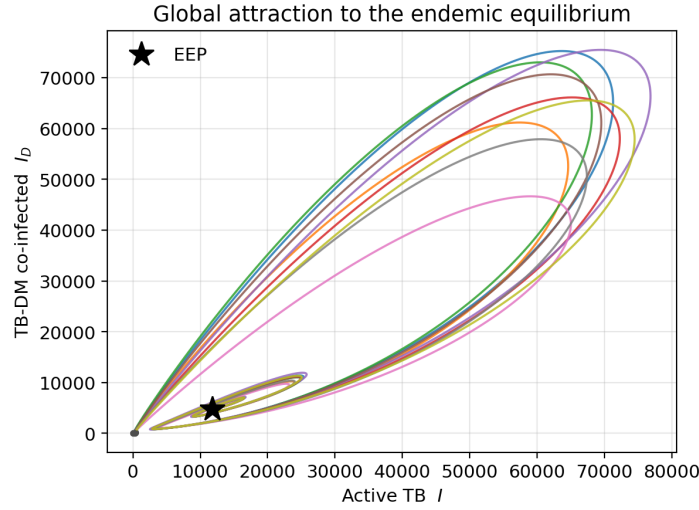


FIGURE 4. Global attraction to the endemic equilibrium: trajectories from nine initial conditions in the (I, I_D) plane all reach the same point E^* .

Effect of the maturation delay. Figure 5 varies $\tau \in \{0, 1.2, 2.5, 4.0\}$ years. Increasing the delay slows the epidemic build-up and lowers the peak of active TB, and it slightly reduces the endemic level, consistent with the monotone dependence of $\mathcal{R}_0$ on $e^{-\mu\tau}$ in (8). The delay therefore reshapes the transient dynamics that matter for programme planning even though it does not by itself cross the elimination threshold at the baseline transmission level.

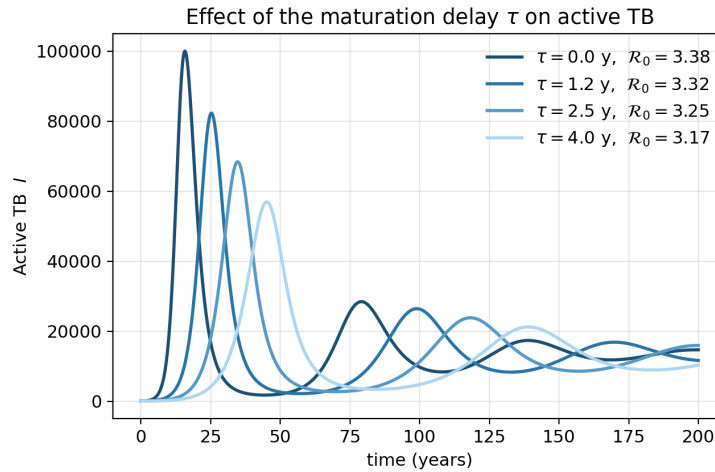


FIGURE 5. Active-TB dynamics for increasing maturation delay τ . Longer lags flatten and postpone the epidemic peak.

Bifurcation. Figure 6 traces the total infectious burden $I^* + I_D^*$ against $\mathcal{R}_0$ (varied through β). The endemic branch emanates continuously and stably from $\mathcal{R}_0 = 1$ while the DFE loses stability there, confirming the forward transcritical bifurcation of Section 7 and the absence of bistability.

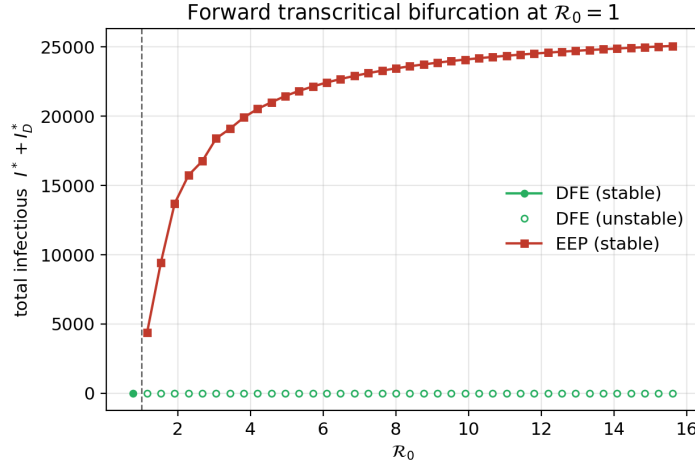


FIGURE 6. Forward transcritical bifurcation at $\mathcal{R}_0 = 1$: the stable endemic equilibrium appears exactly as the DFE loses stability.

Optimal control. With $A_1 = A_2 = 1$, $w_1 = w_2 = w_3 = 4 \times 10^3$, $c_1 = 0.6$, $c_2 = 0.5$ and $T = 20$ years, the forward–backward sweep yields the profiles of Figure 7(b) and the state response of Figure 7(a). The integrated strategy collapses both I and I_D far below their uncontrolled trajectories and reduces the objective functional by more than an order of magnitude. Transmission reduction u_3 carries the largest sustained effort, treatment u_1 a moderate effort that tapers as prevalence falls, and preventive therapy u_2 a smaller but non-negligible role whose value derives from the advanced costates in (15). Figure 8 displays the cumulative infectious burden averted, which grows steadily over the horizon.

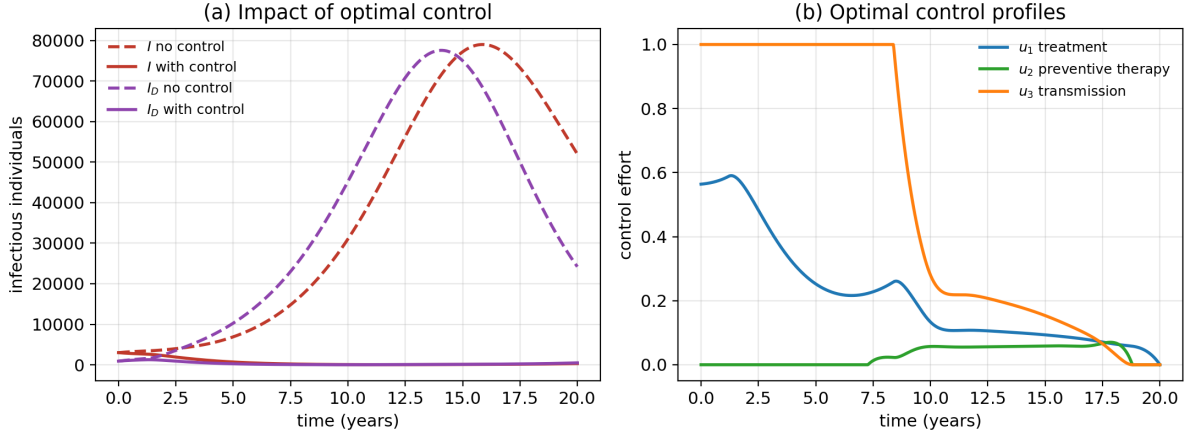


FIGURE 7. (a) Active TB I and co-infection I_D with and without control. (b) Optimal control profiles u_1 (treatment), u_2 (preventive therapy) and u_3 (transmission reduction).

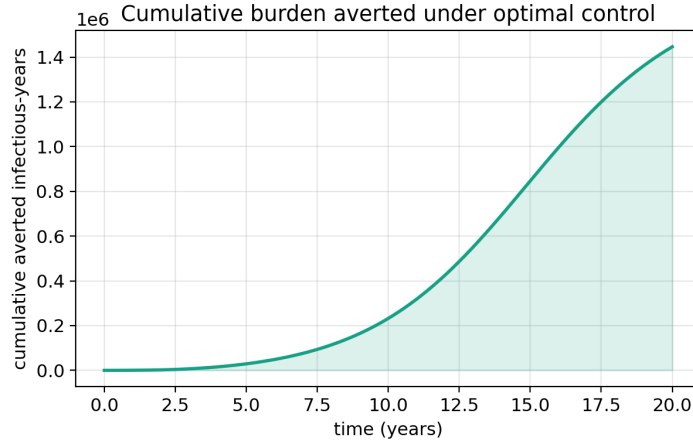


FIGURE 8. Cumulative infectious burden (infectious-years) averted by the optimal control programme relative to the uncontrolled dynamics.

11. DISCUSSION AND IMPLICATIONS FOR PRACTICE

The analysis yields a clear and clinically actionable picture. The single threshold $\mathcal{R}_0$ governs the fate of the TB–DM syndemic, and the forward bifurcation guarantees that pushing $\mathcal{R}_0$ below one is sufficient for elimination without the hidden endemic reservoir that a backward bifurcation would create. The sensitivity ranking then tells practitioners *where* to push. Three levers

dominate. First, transmission control (β, u_3): prompt diagnosis, case isolation and infection prevention in clinics and congregate settings. Second, glycaemic control (ψ): because diabetes raises susceptibility, integrating diabetes management into TB services lowers the effective reproduction number, not merely individual risk. Third, treatment and preventive therapy (r, r_D, u_2): shortening the infectious period and treating latent infection in people with diabetes both reduce onward transmission, and the delayed optimal-control structure shows that preventive therapy is valued precisely for the future infectiousness it forestalls.

These findings reinforce the WHO recommendation of *bidirectional screening*: testing people with TB for diabetes and screening people with diabetes for TB. In the model this corresponds to coupling the D and L_D pathways to case-finding and to preventive therapy, and the optimal-control experiment confirms that the combined programme outperforms any single measure. The maturation delay, often omitted, matters for operational planning: it postpones and flattens epidemic peaks, so programmes calibrated on instantaneous models may misjudge the timing of demand for diagnostic and treatment capacity.

Limitations. The model uses a single fixed delay rather than a distributed latency distribution, aggregates diabetes into a single class without glycaemic strata, and omits drug resistance, HIV co-infection and age structure. Standard incidence and homogeneous mixing are simplifying assumptions. Parameter values are plausible but illustrative; fitting to programmatic surveillance data in a specific high-burden setting is the natural next step. These extensions would refine quantitative predictions without altering the qualitative threshold structure established here.

12. CONCLUSION

We analysed a delayed model of TB–diabetes co-infection that makes the latency between infection and infectiousness explicit. We proved well-posedness, derived a reproduction number in which the delay appears through a survival factor, and established the local and global stability of both equilibria; the disease-free state by a matrix-theoretic Lyapunov function and the endemic state by the graph-theoretic method, each augmented with a Krasovskii functional to absorb the delay. A centre-manifold analysis showed the bifurcation at $\mathcal{R}_0 = 1$ to be forward, and an optimal-control formulation with delayed adjoints identified a cost-effective combination

of treatment, preventive therapy and transmission reduction. The results give health practitioners a threshold-based rationale for integrated, bidirectional TB–DM programmes and quantify the payoff of acting on the parameters to which transmission is most sensitive.

DATA AND CODE AVAILABILITY

The Python source code implementing the delayed model, the equilibrium and bifurcation experiments, the sensitivity analysis and the forward–backward sweep for optimal control accompanies this manuscript and reproduces every figure.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this paper.

REFERENCES

- [1] World Health Organization, Global Tuberculosis Report 2024, WHO, Geneva, 2024.
- [2] International Diabetes Federation, IDF Diabetes Atlas, 11th ed., International Diabetes Federation, Brussels, 2025.
- [3] C.Y. Jeon, M.B. Murray, Diabetes mellitus increases the risk of active tuberculosis: A systematic review of 13 observational studies, *PLoS Med.* 5 (2008), e152.
- [4] B.I. Restrepo, Diabetes and tuberculosis, *Microbiol. Spectr.* 4 (2016).
- [5] E.M. Musyoki, W.N. Mutuku, N.M. Imbusi, E.O. Omondi, Mathematical modelling of tuberculosis and diabetes co-infection using the non-standard finite difference scheme, *Pan-Amer. J. Math.* 2 (2023), 16.
- [6] E.M. Musyoki, W.N. Mutuku, N.M. Imbusi, E.O. Omondi, A model of tuberculosis and diabetes co-infection with optimal control, *Asian Res. J. Math.* 19 (2023), 80–108.
- [7] P. van den Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, *Math. Biosci.* 180 (2002), 29–48.
- [8] C. Castillo-Chavez, B. Song, Dynamical models of tuberculosis and their applications, *Math. Biosci. Eng.* 1 (2004), 361–404.
- [9] C. Castillo-Chavez, Z. Feng, W. Huang, On the computation of R_0 and its role in global stability, *Mathematical Approaches for Emerging and Reemerging Infectious Diseases: An Introduction*, Springer, New York, 2002, 229–250.
- [10] Z. Shuai, P. van den Driessche, Global stability of infectious disease models using Lyapunov functions, *SIAM J. Appl. Math.* 73 (2013), 1513–1532.

- [11] M.Y. Li, Z. Shuai, Global-stability problem for coupled systems of differential equations on networks, *J. Differential Equations* 248 (2010), 1–20.
- [12] H. Guo, M.Y. Li, Z. Shuai, Global stability of the endemic equilibrium of multigroup SIR epidemic models, *Canad. Appl. Math. Q.* 14 (2006), 259–284.
- [13] K.L. Cooke, P. van den Driessche, Analysis of an SEIRS epidemic model with two delays, *J. Math. Biol.* 35 (1996), 240–260.
- [14] J.K. Hale, S.M. Verduyn Lunel, *Introduction to Functional Differential Equations*, Springer, New York, 1993.
- [15] Y. Kuang, *Delay Differential Equations with Applications in Population Dynamics*, Academic Press, Boston, 1993.
- [16] Z. Feng, C. Castillo-Chavez, A.F. Capurro, A model for tuberculosis with exogenous reinfection, *Theor. Popul. Biol.* 57 (2000), 235–247.
- [17] S.M. Blower, A.R. McLean, T.C. Porco, P.M. Small, P.C. Hopewell, M.A. Sanchez, A.R. Moss, The intrinsic transmission dynamics of tuberculosis epidemics, *Nat. Med.* 1 (1995), 815–821.
- [18] C. Dye, B.G. Williams, The population dynamics and control of tuberculosis, *Science* 328 (2010), 856–861.
- [19] S. Lenhart, J.T. Workman, *Optimal Control Applied to Biological Models*, Chapman & Hall/CRC, Boca Raton, 2007.
- [20] L.S. Pontryagin, V.G. Boltyanskii, R.V. Gamkrelidze, E.F. Mishchenko, *The Mathematical Theory of Optimal Processes*, Interscience, New York, 1962.
- [21] L. Göllmann, D. Kern, H. Maurer, Optimal control problems with delays in state and control variables subject to mixed control–state constraints, *Optimal Control Appl. Methods* 30 (2009), 341–365.
- [22] J.P. LaSalle, *The Stability of Dynamical Systems*, SIAM, Philadelphia, 1976.