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AN EPIDEMIOLOGICAL GROWTH MODEL: DERIVATION, PROPERTIES, AND PARAMETER ESTIMATION

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ABSTRACT. The focus of this paper is the formulation of a new logistic growth model. The model has possible applications in epidemiology, psychology, and many other scientific areas. The model is first derived. Then, the model is described analytically, with special attention paid to computations relevant to mechanical application. Lastly, the model is applied to a set of epidemiological data in a real-world example using nonlinear least squares parameter estimation methods in *R*.

Keywords: nonlinear modeling, logistic growth, nonlinear parameter estimation

1. INTRODUCTION

A number of epidemiological models exist that were derived with the intended goal of describing disease spread, evolution, and control (Waltman, 1974; A. G. Ladde and G. S. Ladde, 2012, 2013). The current model is of the SI-type, where individuals are classified as either being *susceptible* to infection or currently *infected*. It is assumed that the population is well-mixed and is confined to a limited territory – as to not have to account for differences in geography.

More generally, models of the current kind are know as *logistic growth models* (Bates and Watts, 1988). Logistic growth models are non-decreasing sigmoidal functions that can be used to model the growth of an object or entity over time or some other variable of interest. Functions of this kind have been used in a number of scientific settings to model a plethora of different phenomena (A. G. Ladde and G. S. Ladde, 2012, 2013). An early example of the use of a logistic growth model comes from the field of ecology, where Pierre Verhulst (1838) used the curve to model population growth.

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2. MODEL CHARACTERISTICS

2.1. **Model Formulation.** Let us consider the following scalar hereditary nonlinear differential equation under probabilistic and stochastic process varying coefficients:

$$dI = \pi(\xi(t))(S^* - I)(a + bI + c\int_{-\tau}^{0} I(t+s)d\eta(s))dt, I_{t_0} = \phi_0, \quad \text{for } t \geq t_0 \tag{2.1.1}$$

where S^* and I respresent the sizes of ultimate susceptible and infective agent/node /species of a dynamic process with past history, respectively; $\phi_0 \in C[[-\tau, 0], R]$; $I_t(s) = I(t+s)$, $s \in [-\tau, 0]$. obviously, the integral in (2.1.1) is the Riemann-Stieltjes integral with respect to η, a delay distribution (incubation process) with a finite incubation period, $\tau > 0$; $\xi(t)$ is a right-continuous stochastic process; $N(t)$ is a non-homogeneous Poisson process; $\xi(t)$ and $N(t)$ are defined on the complete probability space $(\Omega, \mathcal{F}, P)$; $\pi(t)$ is an intensity rate for the non-homogeneous Poisson process $N(t)$; $a\pi(\xi(t), k(t))\Delta t$, $b\pi(\xi(t), k(t))\Delta t$, and $c\pi(\xi(t), k(t))\Delta t$ are probabilistic rates exerted by external, internal, and hereditary influences, respectively, to a change of infective state size (dI) over a time interval of length $\Delta t \approx dt$. Moreover, it is well-known that the probability distribution of a non-homogeneous Poisson process also characterizes the response/adaptation time delay (Baker, Scarf, and Wang, 1997); $\xi(t)$ characterizes a single node level dynamic structural perterbation; a, b, and c are positive constants exhibiting the existence of external, internal, and hereditary dynamic influences of a single node process, respectively. This model can be modified to accomodate other natural time delay processes (communication, contact, preparation, transportation, etc.).

By setting $x = \frac{I}{S^*}$ and $x_{t_0} = \frac{I_{t_0}}{S^*}$, the original dynamic model (2.1.1) is equivalent the following state-normalized form of the differential equation:

$$dx = \pi(\xi(t))(1 - x)(a + bS^* + cS^*\int_{-\tau}^{0} x(t+s)d\eta(s))dt, x_{t_0} = \varphi_0 \tag{2.1.2}$$

It is a well-known fact that the complete set of closed-form solutions to the scalar linear delay differential equation: $dy = by(t - \tau)$, for $\tau > 0$, is not feasible. Obviously, its characteristic equation: $\mu = be^{-\tau\mu}$ has infinitely many roots (real and complex). This forces one to utilize either analytic or numerical approaches to obtain information about solutions. We also note that (2.1.2) has a unique non-negative solution (Ladde, 1981), whenever $\phi_0(s) \geq 0$, on $[-\tau, 0]$. Moreover, from the nature of the rate functional in (2.1.2), we conclude that the solution of (2.1.2) is non-decreasing and hence, we obtain the following inequality:

$$\begin{cases} 0 \leq \pi(\xi(t))(1 - x)(a + bS^*x + cS^*\int_{-\tau}^{0} x(t+s)d\eta(s)) \\ \quad \leq \pi(\xi(t))(1 - x)(a + (b + \tau c)S^*x) \\ |x_{t_0}(s)|_0 = \max(x(t_0 + s)) \leq x(t_0), \text{ a.s.} \end{cases} \tag{2.1.3}$$

Using (2.1.3), theory of differential inequalities, and the well-known comparison therem in the context of Lyapunov-like functions ($V(x) = x$) with a minimal class of functions for functional differential equations (Ladde, 1976; Lakshmikantham and Leela, 1969), we obtain an estimate on the solution of (2.1.1) by using the following scalar nonlinear ordinary comparison differential equation with stochastic process varying coefficients:

$$du = \pi(\xi(t))(1-u)(a+(b+\tau c)S^*u)dt, \quad u(t_0) = x(t_0) = r_0 \tag{2.1.4}$$

The closed-form maximal solution process $r(t, t_0, u_0)$ (due to uniqueness; Lakshmikantham and Leela, 1969) of ordinary comparison differential equation with stochastic process varying coefficients (2.1.4) is given by:

$$r(t) \equiv r(t, t_0, r_0) = \frac{\gamma_0 \exp[\int_{t_0}^{t} \beta(s)ds] - \alpha}{1 + \gamma_0 \exp[\int_{t_0}^{t} \beta(s)ds]}, \quad \text{for } t \geq t_0 \tag{2.1.5}$$

where $\alpha = \frac{a}{(b+\tau c)S^*}$, $\beta(t) = [a+(b+\tau c)S^*]\pi(\xi(t))$, $r_0 = \frac{I_0}{S^*}$, $\gamma_0 = \frac{r_0+\alpha}{1-r_0}$, and $0 \leq r_0 < 1$.

Thus, the maximal solution of comparison differential equation (2.1.4) is an upper estimate for the solution process of (2.1.2); that is:

$$x(t, t_0, x_0) \leq r(t, t_0, r_0), \quad \text{for } t \geq t_0 \text{ a.s.} \tag{2.1.6}$$

which implies that:

$$I(t, t_0, x_0) \leq S^* r(t, t_0, r_0), \quad \text{for } t \geq t_0 \text{ a.s.} \tag{2.1.7}$$

where:

$$S^* r(t, t_0, r_0) = S^* \frac{\gamma_0 \exp[\int_{t_0}^{t} \beta(s)ds] - \alpha}{1 + \gamma_0 \exp[\int_{t_0}^{t} \beta(s)ds]}, \quad \text{for } t \geq t_0 \tag{2.1.8}$$

Remark 2.1.1: If $a = c = 0$, $b = \frac{\beta}{S^*}$, $\pi(\xi(t)) = \gamma\lambda(\lambda t)^{\gamma-1}$, then $\alpha = 0$, $\gamma_0 = \frac{r_0}{1-r_0}$, and (2.1.5) reduces to:

$$r(t) \equiv r(t, t_0, r_0) = \frac{\frac{r_0}{1-r_0} \exp[\beta[(\lambda t)^\gamma - (\lambda t_0)^\gamma]]}{1 + \frac{r_0}{1-r_0} \exp[\beta[(\lambda t)^\gamma - (\lambda t_0)^\gamma]]}, \quad \text{for } t \geq t_0 \tag{2.1.9}$$

which is equal to:

$$r(t) \equiv r(t, t_0, r_0) = \frac{1}{1 + \frac{1-r_0}{r_0} \exp[-\beta[(\lambda t)^\gamma - (\lambda t_0)^\gamma]]}, \quad \text{for } t \geq t_0 \tag{2.1.10}$$

In this case, (2.1.7) and (2.1.8) combine to become:

$$I(t, t_0, x_0) \leq S^* r(t, t_0, r_0) = \frac{S^*}{1 + \frac{1-r_0}{r_0} \exp[-\beta[(\lambda t)^\gamma - (\lambda t_0)^\gamma]]}, \quad \text{for } t \geq t_0 \tag{2.1.11}$$

Remark 2.1.2: As noted before, the closed-form solution process of (2.1.2) is not feasible. However, we do have its analytic estimate (2.1.7). Therefore, our approach

of shedding light on the dynamic model (2.1.1) depends on the corresponding comparison dynamic model described in (2.1.4). This idea is used in the qualitative study of nonlinear differential equations (Ladde and Lakshmikantham, 1980; Ladde and Sambandham, 2004; Lakshmikantham and Leela, 1969). In addition, except the incubation-period parameter, $\tau > 0$, almost all parameters of the comparison model (2.1.4) are the parameters of (2.1.1). We further note that the solution process $r(t, t_0, r_0)$ of (2.1.4) can be considered as a stochastic process varying dynamic growth model. In the following, we demonstrate that $r(t, t_0, r_0)$ includes the existing dynamic growth models (Abraham and Ledolter, 2006; Myers, 1989) in a systematic and unified way. In the following, we present a few more special cases of (2.1.4).

Moreover, in the absense of *Internal Influence* ($b = c = 0$), and if $a = 1$, $r_0 = 0$, $t_0 = 0$, and $\pi(t) = \gamma\lambda(\lambda t)^{\gamma-1}$, then the solution process of (2.1.4) is the well-known Weibull distribution: $(1 - \exp[-(\lambda t)^{\gamma}])$, and in the case where $\gamma = 1$, the Weibull distribution becomes the exponential distribution: $(1 - \exp[-\lambda t])$ (Abraham and Ledolter, 2006; Parzen, 1962; Ross, 1972).

The underlying state $r(t)$ is application dependent and interpretation ranging from cumulative amount of information to resource allocation of distribution over an interval of time $[0, t]$. These special cases also provide tools to investigate the dynamic (Ladde and Siljak, 1983) and statistical reliability (Ascher and Feingold, 1984).

2.2. **The Model.** In this paper, we initiate our long-range plan for focusing the study of (2.1.11), by utilizing the model below:

$$\tilde{I}(t, t_0, R_0) \equiv S^* r(t, t_0, R_0) = \frac{S^*}{1 + R_0 \exp[-\beta[(\lambda t)^{\gamma} - (\lambda t_0)^{\gamma}]]} \tag{2.2.1}$$

where t represents time (or some other response variable); t_0 is the initial time; r_0 is the initial proportion of infected individuals ($R_0 = \frac{1-r_0}{r_0}$); and β, γ, λ, and S^* are parameters. S^* is known as the *saturation point* — the horizontal asymptote in the range of $\tilde{I}(t)$. The parameter vector is given by $\theta = (\beta, \gamma, \lambda, s^*)' \in \Theta = \{\theta \in \Re^4 : \theta > \mathbf{0}\}$. Lastly, t is in the set of positive real numbers, such that $t \geq t_0$.

2.3. **Model Limits.** A number of limits are given below for the model (2.2.1). In each section below, we assume that everything but the respective variable is fixed and finite. Using the comparison theorem (Lakshmikantham and Leela, 1969), the limits of the infective size of the population, $\tilde{I}$, are obtained as a function of time and the parameters.

For $t \in [0, \infty)$:

$$\lim_{t \to 0} \tilde{I}(t) = 0 \text{ and } \lim_{t \to \infty} \tilde{I}(t) = S^* \tag{2.3.1}$$

iFor $\beta \in (0, \infty)$:

$$\lim_{\beta \to 0} \tilde{I}(t) = \frac{S^*}{1 + R_0} = S^* r_0 \text{ and } \lim_{\beta \to \infty} \tilde{I}(t) = S^* \tag{2.3.2}$$

For $\gamma \in (0, \infty)$:

$$\lim_{\gamma \to 0} \tilde{I}(t) = S^* r_0 \tag{2.3.3}$$

$$\lim_{\gamma \to \infty} \tilde{I}(t | \lambda t, \lambda t_0 \in (0, 1]) = S^* r_0 \tag{2.3.4}$$

$$\lim_{\gamma \to \infty} \tilde{I}(t | \lambda t \in (1, \infty), \lambda t_0 \in (0, 1]) = S^* \tag{2.3.5}$$

$$\lim_{\gamma \to \infty} \tilde{I}(t | \lambda t_0 \in (1, \infty)) = \text{Does Not Exist} \tag{2.3.6}$$

For $\lambda \in (0, \infty)$:

$$\lim_{\lambda \to 0} \tilde{I}(t) = \frac{S^*}{1 + R_0} = S^* r_0 \text{ and } \lim_{\lambda \to \infty} \tilde{I}(t) = S^* \tag{2.3.7}$$

2.4. **Model Derivatives.** Letting $u = \beta[(\lambda t)^\gamma - (\lambda t_0)^\gamma]$ and $\phi = \frac{R_0 \exp[-u]}{(1 + R_0 \exp[-u])^2}$, the first partial derivatives of the model (2.2.1), with respect to the parameters, are given by:

$$\frac{\partial \tilde{I}}{\partial S^*} = \frac{1 - \exp[-u]}{(1 + R_0 \exp[-u])^2} \tag{2.4.1}$$

$$\frac{\partial \tilde{I}}{\partial \beta} = S^* \frac{1}{\beta} u \phi \tag{2.4.2}$$

$$\frac{\partial \tilde{I}}{\partial \gamma} = S^* \beta [ln(\lambda t)(\lambda t)^\gamma - ln(\lambda t_0)(\lambda t_0)^\gamma] \phi \tag{2.4.3}$$

$$\frac{\partial \tilde{I}}{\partial \lambda} = S^* \frac{\gamma}{\lambda} u \phi \tag{2.4.4}$$

We note that the partial derivatives above are all non-negative for $t \geq t_0$, which is reflected in the graph of the model (2.2.1) in Figure 1 below.

2.5. **Point of Inflection/Maximum Growth.** While there is no closed-form expression for the point of inflection/maximum growth for the model (2.2.1), certain inequalities can be derived. By setting $\frac{\partial^2 \tilde{I}}{\partial t^2} = 0$, we have:

$$\frac{\partial^2 \tilde{I}}{\partial t^2} = S^* \phi \left[\left(\frac{\partial^2 u}{\partial t^2} \right) + \left(\frac{\partial u}{\partial t} \right)^2 \left(\frac{R_0 \exp[-u] - 1}{R_0 \exp[-u] + 1} \right) \right] = 0 \tag{2.5.1}$$

which implies that:

$$S^* \phi \beta \gamma \lambda^\gamma t^{\gamma - 2} \left[(\gamma - 1) + \beta \gamma \lambda^\gamma t^\gamma \left(\frac{R_0 \exp[-u] - 1}{R_0 \exp[-u] + 1} \right) \right] = 0 \tag{2.5.2}$$

which further implies that:

$$(1-\gamma) = \beta\gamma\lambda^{\gamma}t^{\gamma}\left(\frac{R_0\exp[-u]-1}{R_0\exp[-u]+1}\right) \tag{2.5.3}$$

Therefore, if $\gamma = 1$, the point of inflection becomes:

$$t_I = \left(\frac{ln(R_0)}{\beta\lambda} + t_0\right) = \left(\frac{ln(R_0)}{\beta\lambda^{\gamma}} + t_0^{\gamma}\right)^{1/\gamma} = \tilde{I}^{-1}\left(\frac{S^*}{2}\right) \tag{2.5.4}$$

and given that $\beta\gamma\lambda^{\gamma}t^{\gamma}$ and $(R_0\exp[-u]+1)$ are always positive, we have:

$$\begin{cases} t_I < \left(\frac{ln(R_0)}{\beta\lambda^{\gamma}} + t_0^{\gamma}\right)^{1/\gamma} = \tilde{I}^{-1}\left(\frac{S^*}{2}\right), & \text{for } \gamma < 1 \\ t_I > \left(\frac{ln(R_0)}{\beta\lambda^{\gamma}} + t_0^{\gamma}\right)^{1/\gamma} = \tilde{I}^{-1}\left(\frac{S^*}{2}\right), & \text{for } \gamma > 1 \end{cases} \tag{2.5.5}$$

The model (2.2.1) is graphed below for various parameter values.

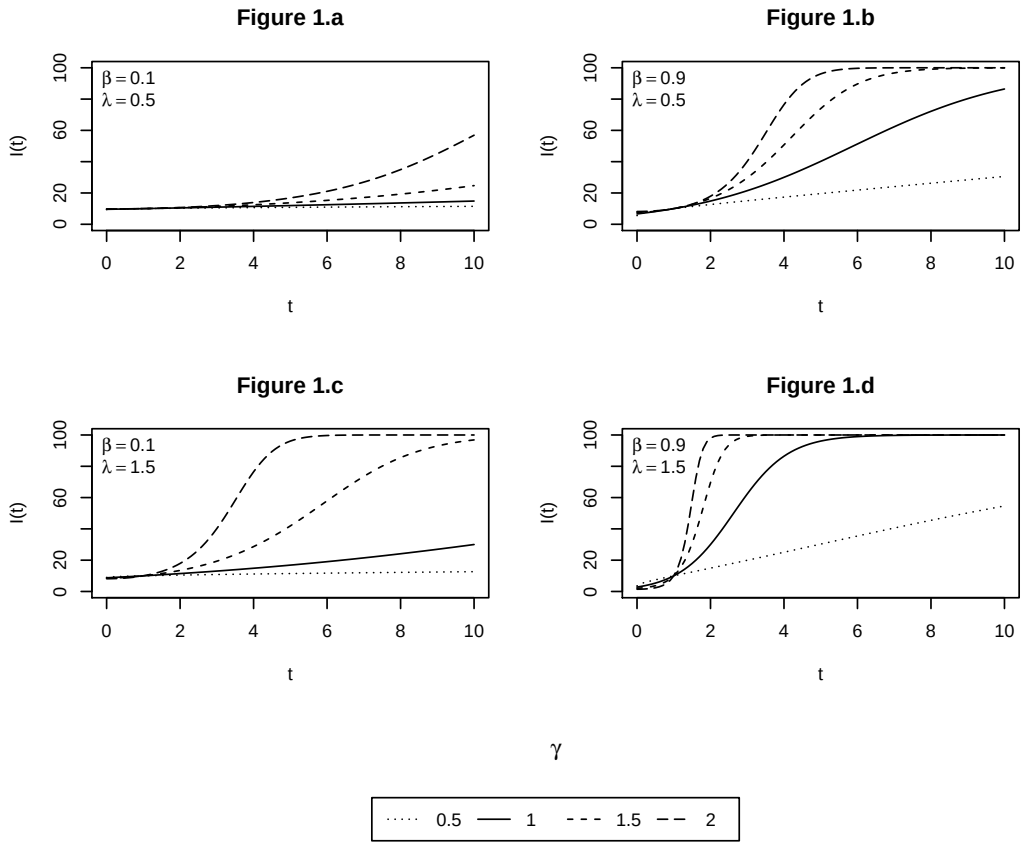

FIGURE 1. Model Plot for Various Parameter Values

In the figure above, $t_0 = 1, r_0 = 0.10$, and $S^* = 100$. One will note from Figure 1 that increases in β, γ, or λ correspond to an increase in the speed with which growth reaches the saturation point S^*.

3. MODEL APPLICATION

The model (2.2.1) was fit to data on HIV prevalence (available at http://data.worldbank.org/indicator/SH.DYN.AIDS.ZS). The "Small State" (SST; a collection of countries with a population below 1.5 million each) location classification was used, mainly for its standard sigmoidal curve appearance when plotted (see Figure 2). First, starting estimates for the parameters were obtained. Next, the model (2.2.1) was fitted using the *nls* ("Nonlinear Least Squares"; R Core Team, 2013) function in *R*. The response variable was HIV prevalence (as a % of the population ages 15-49), and the explanatory variable was time (ranging from 1990 to 2011).

3.1. **The Data.**

TABLE 1. Percentage of Infected Individuals for the Small States (1990-2011)

Year	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000
Infected (%)	1.23	1.65	2.19	2.87	3.72	4.63	5.53	6.32	6.92	7.37	7.69
Year	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Infected (%)	7.86	7.93	7.92	7.87	7.79	7.70	7.62	7.60	7.56	7.56	7.56

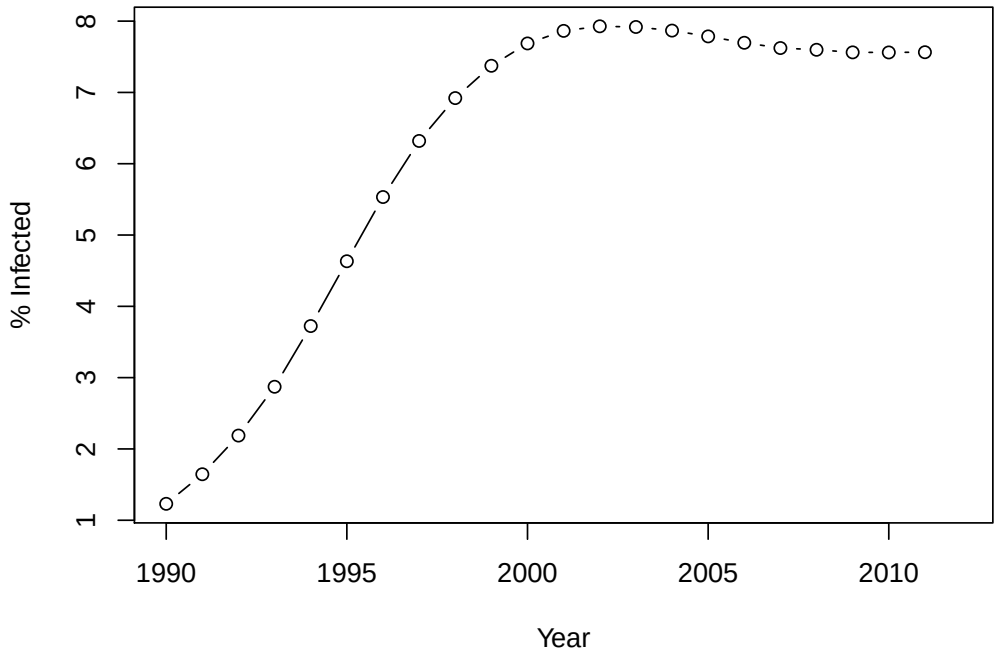

FIGURE 2. Percentage of Infected Individuals for the Small States by Year

3.2. **Starting Parameter Estimates.** Good starting parameter estimates often facilitate convergence to the least-squares minimum when using iterative techniques for nonlinear parameter estimation (G. A. F Seber and C. J. Wild, 1989). As S^* is the carrying capacity, a natural starting value for this parameter is the maximum infected percentage, which is 7.93% found in 2002. As β and λ are not uniquely identifiable, due to the structural nature of the model (2.2.1), the parameters are *reparameterized* as $\eta = \beta\lambda^\gamma$. A starting value of 1 for is chosen for γ, as at $\gamma = 1$, the comparison model reduces to a standard logistic model with rate parameter η; this is done mainly for computational ease. After starting estimates have been chosen for S^* and γ, we can transform the data to get a starting estimate for η using the linear least squares method. Let $y_i = ln(R_0/R_i)$, where $R_i = (s^{*0} - \tilde{I}_i)/\tilde{I}_i$ and R_0 is defined as above (r_0 set to the minimum infected percentage value). Also, let $x_i = t_i - t_0$ (since $\gamma^0 = 1$). When using $s^{*0} = \max(\tilde{I}_i)$, one must omit the infinity created when $R_i = 0$ ($\tilde{I}_i = \max(\tilde{I}_i)$). Using the transformations above, we can run a linear regression of the form $y_i = 0 + \eta x_i$ ($i = \{1, 2, \ldots, n\}$), to obtain a starting estimate for η. Using the data in Table 1, we get $\eta^0 = 0.3388106$. The time variable is constructed by mapping Year to the set of natural numbers. In other words, $t = \{1, 2, \ldots, n\}$. Lastly, t_0 is set to t_1 from the data.

3.3. **The Gauss-Newton Algorithm.** Once starting values are obtained for the parameter vector, we can start the process of obtaining the nonlinear least squares estimates. This can be done in R using the *nls* function, with the default algorithm option – the Gauss-Newton.

The results of the Gauss-Newton Algorithm are provided below in Table 2. The procedure converged in nine iterations, with a residual standard error of 0.1414 on 19 degrees of freedom. A plot containing the fitted model is provided in Figure 3.

TABLE 2. Parameter Estimation Results

Parameter	Initial Values	Estimates	Standard Error	t value	Correlations		
S^*	7.928	7.74853	0.04429	174.969	1.00		
η	0.339	0.17629	0.02848	6.189	0.32	1.00	
γ	1.000	1.42423	0.07992	17.820	-0.37	-0.99	1.00

3.4. **Parameter Identifiability.** As stated above, the model (2.2.1) must be *reparameterized*, as β and λ are not uniquely identifiable. Therefore, in the analysis above, the parameter $\eta = \beta\lambda^\gamma$ was utilized. Using the estimates obtained in the analysis above, the relationship between β and λ is plotted below in Figure 4.

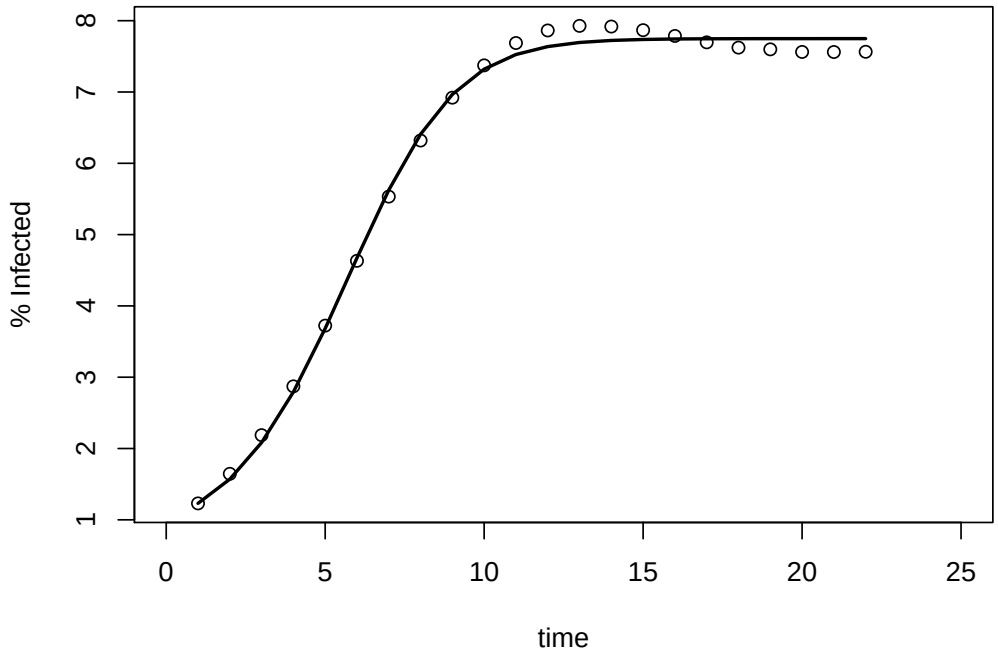

FIGURE 3. Plot of the Model Fit

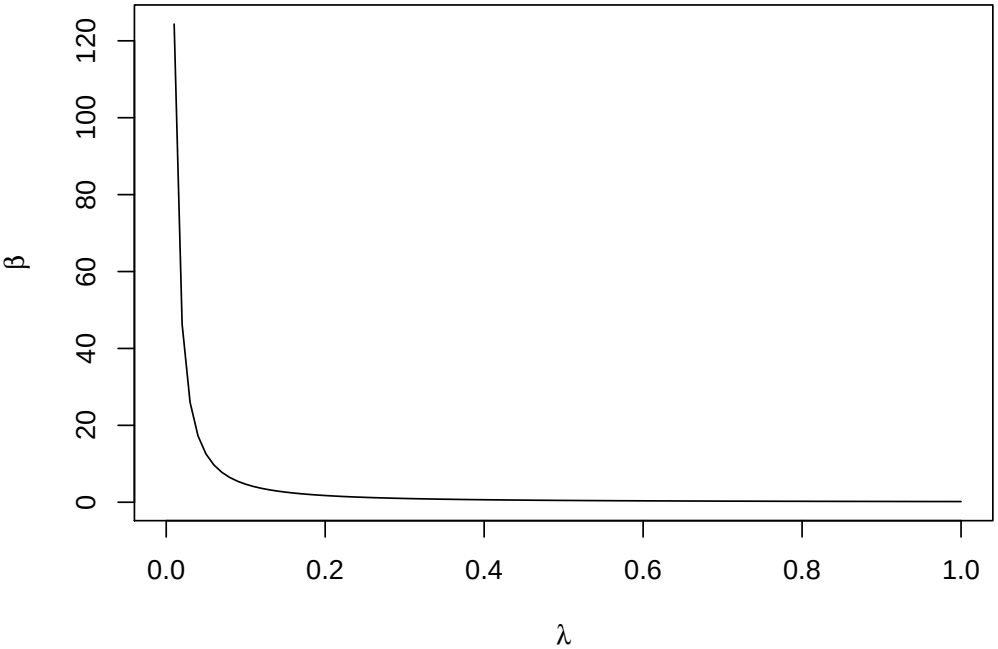

FIGURE 4. Relationship between β and λ for $\hat{\eta} = \beta\lambda^{\hat{\gamma}}$

4. **CONCLUSION**

In the absense of a closed-form solution to the presented mathematical model, we utilized the comparison method and the idea of a minimal class of functions to obtain an analytic estimate for the solution process of (2.1.1). The parameter estimation problem of the original mathematical model was recasted into the parameter

estimation problem of the comparison dynamic model. In the future, we propose to explore the development of parameter estimation techniques for a more general class of problems; the results of which will be published elsewhere.

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REFERENCES

[1] P. Waltman (1974). *Deterministic Threshold Models in the Theory of Epidemics*. Springer-Verlag, New York.

[2] A. G. Ladde and G. S. Ladde (2012). *Deterministic Modeling, Methods, and Analysis*. World Scientific, New Jersey.

[3] A. G. Ladde and G. S. Ladde (2013). *Stochastic Modeling, Methods, and Analysis*. World Scientific, New Jersey.

[4] D. M. Bates and D. G. Watts (1988). *Nonlinear Regression Analysis and Its Applications*. Wiley, New York.

[5] R. D. Baker, P. A. Scarf, and W. Wang (1997). A Delay-time model for repairable machinery: maximum likelihood estimation of optimum inspection intervals, IMA J. of Math. Appl. in Business and Industry, Vol. 8, pp. 83–92.

[6] G. S. Ladde (1981). Competitive Processes and Comparison Differential Systems II. *Journal of Mathematical and Physical Sciences*, v.15, pp. 435–454.

[7] G. S. Ladde (1976). Stability of Large-Scale Hereditary Systems under Structural Perturbations. *Large-Scale Systems Theory and Applications*, (Editors: G. Guardabassi and A. Locatelli), Unin, Italy, The publication of IFAC, pp. 215–226.

[8] V. Lakshmikantham and S. Leela (1969). Differential and Integral Inequalities: Theory and Applications, Vol. 1 and Vol. 2, Academic Press, New York.

[9] G. S. Ladde and V. Lakshmikantham (1980). Random Differential Inequalities, Academic Press, New York.

[10] G. S. Ladde and M. Sambandham (2004). Stochastic Versus Deterministic Systems of Differential Equations, Marcel Dekker, Inc., New York.

[11] B. Abraham and J. Ledolter (2006). Introduction to Regression Modelling, Thompson, Brooks/Cole.

[12] R. H. Myers (1989). Classical and Modern Regression with Applications, Duxbury Press.

[13] E. Parzen (1962). Stochastic Processes, Holden-Day, Inc., San Francisco.

[14] S. M. Ross (1972). Introduction to Probability Models, Academic Press, New York.

[15] G. S. Ladde and D. D. Siljak (1983). Multiplex Control Systems: Stochastic Stability and Dynamic Reliability, Inter. J. of Contr., Vol. 28, pp. 515–524.

[16] H. Ascher and H. Feingold (1984). Repairable Systems Reliability, Marcel Dekker, Inc., New York.

[17] R Core Team (2013). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/.

[18] G. A. F. Seber and C. J. Wild (1989). *Nonlinear Regression*. Wiley, New York.