Integral equation approach for modeling age-dependent infectiousness of diseases

RGUI Meththananda[1], NC Ganegoda[2] and SSN Perera[3]

[1]*Department of Spatial Sciences, General Sir John Kotelawala Defence University - Southern Campus, Sri Lanka, umamethananda@gmail.com*
[2]*Department of Mathematics, University of Sri Jayewardenepura, Nugegoda, Sri Lanka, naleencg@gmail.com*
[3]*Research & Development Centre for Mathematical Modeling, Department of Mathematics, University of Colombo, Sri Lanka, ssnp@maths.cmb.ac.lk*

Abstract- Many mathematical models have been developed through differential equations to understand age-dependent infectiousness of diseases. These models face the complexity of heterogeneity of disease transmission in different age groups which leads to complicated parameter estimation. Proposed model in this paper conveys the applicability of integral equations to interpret the age dependency on general behavior of infectiousness. Acquired immunity and mobility of hosts are considered here as main influencing factors. The degenerated kernel plays a major role in this proposed structure allowing time-dependent influences too.

Keywords: Age-dependent, Integral equation, Infectiousness, Degenerated Kernel, Acquired Immunity, Mobility

1 Introduction

The chronological age of an individual is a vital factor in assessing the transmission and morbidity of infectious diseases. By the infectiousness of such a disease, we understand the state or condition of being infectious. Age-dependent characteristics of infectiousness occur due to biological factors of hosts and vectors, environmental factors dominated by exposure to weather conditions, and behavioral factors of infected and susceptible individuals [3]. Time-dependent characteristics of infectiousness are also influenced by some of these factors, for instance seasonal weather patterns may affect to the rate of infection. The diseases like influenza, mumps, smallpox, river blindness, tuberculosis, malaria, filariasis and dengue have the potential of being a pandemic disease due to different types of influences as biological, environmental and behavioral. Mathematical models can be used to link these influences to observe emergent dynamics of infection.

The main aim of this paper is to mimic the infectiousness according to the age-scale of an individual via a dependent variable catering the risk of being infectious. Two main influential factors based on age, acquired immunity and mobility are considered here. Acquired immunity is a biological factor while mobility is a behavioral factor. Day-to-day mobilization of humans affects the transmission as more interaction between infected and susceptible individuals occur. Middle-age is more vulnerable in that sense. The time-scale is also incorporated via the proposed integral equation approach.

Often mathematical models via systems of differential equations are developed to incorporate age-dependency on infectiousness [1]. More advanced models are with partial differential equations catering both time and age as independent variables [2], [8]. These models require many data for parameter estimation to model heterogeneity of disease spread in different age groups. In addition, systems with integro-differential equations have also been developed [6]. However, proposed integral equation approach simply requires only one type of equation infusing acquired immunity and mobility along with some time-dependent incorporations too. It would easily illustrate general behavior of infectiousness against age according to a given behaviors of acquired immunity and mobility.

2 Model formulation and solution

At its simplest, the effect of morbidity can be described by enumerating the risk of being infectious in different age groups. It is observed that this risk is accumulated with the mobility patterns of each individual influenced by environmental conditions too. Thus, a model can be established by taking excessive risk due to mobility proportional to past experience of the risk. Here in Eq. (1), we take $f(a)$ as a function of age a representing the risk level according to acquired immunity. Next, $u(a)$ represents the overall risk level and then $u(a)-f(a)$ is the excessive risk.

$$u(a)-f(a) \propto \int_0^b K(a,t)u(t)dt \tag{1}$$

where $K(a,t)=\sum_{k=1}^{n} a_k(a)b_k(t)$

By introducing a proportional constant λ, model equation becomes;

$$u(a)-f(a)=\lambda \int_0^b K(a,t)u(t)dt$$

$$u(a)=f(a)+\lambda \int_0^b K(a,t)u(t)dt \tag{2}$$

The proportional constant shows the incorporation of the accumulation given by the integral over the lifespan a_1 to the difference $u(a)-f(a)$. It is clear that this excessive risk is influenced by the accumulation of environmental and behavioral influences. The behavioral infectiousness that depends on the contact patterns of an infected is generally boosted with environmental impact such as weather factors.

We propose here a term called kernel $K(a,t)$, to cater both age-scale a and time-scale t. Note that t also runs in a same way as a in its domain. Its general composition $\sum_{k=1}^{n} a_k(a)b_k(t)$ incorporates interactive effect of risk levels given by age-dependant influences via a_k's and time-dependant influences via b_k's. In our approach, we take simply that a_k's represent mobility data and b_k's represent weather data.

As Eq. (2) falls under the classification of the Fredholm integral equations, it owes several attributes in solving depending on the characteristics of kernel $K(a,t)$ [4]. The structure of $K(a,t)$ used in Eq. (2) is called degenerated kernel. The solving technique is based on transforming the equation into a system of linear equations as follows.

$$u(a)=f(a)+\lambda \int_0^b \sum_{k=1}^{n} a_k(a)b_k(t)u(t)dt$$
$$u(a)-f(a)=\lambda \sum_{k=1}^{n} a_k(a) \int_0^b b_k(t)u(t)dt$$

Letting $c_k=\int_0^b b_k(t)u(t)dt$,

$$u(a)=f(a)+\lambda \sum_{k=1}^{n} a_k(a)c_k \tag{3}$$

The solution to the original equation Eq. (2) counts on c_k values which can be figured out by converting Eq. (3) into a system of n linear equations given below.

$$c_m=f_m+\lambda \sum_{k=1}^{n} a_(mk)c_k; \quad m=1,2,...,n \tag{4}$$

Finally, the solution for $u(a)$ is obtained through back substitution on Eq. (3) by the c_k values obtained from the n linear equations in (4).

3 Results and sensitivity analysis

We implement model equation (2) using hypothetical curves for biological, behavioral and environmental influences. As a fundamental illustration, $f(a)$ represents the risk according to acquired immunity and only one influential function $a_k(a); k=1$is considered for mobility and one function $b_k(t)$; $k=1$ is used for weather influences. The model output $u(a)$ adequately describes the general dynamics of the age-dependency of infectiousness.

In the following illustration in Figure 1, $f(a)$ depicts a situation of high risk in younger ages and later saturated in lower risk with maturity. Risk level due to mobility is shown by $a_1(a)$, carrying higher risk in middle ages, which is evident in many host populations. The function $b_1(t)$ is merged to the model as a periodic function with one peak per year simply representing a possible rainfall effect ultimately on infectiousness. We set the lifespan into 80 years and hypothetical curves within the range $[0,1]$ allowing an easier base for comparisons.

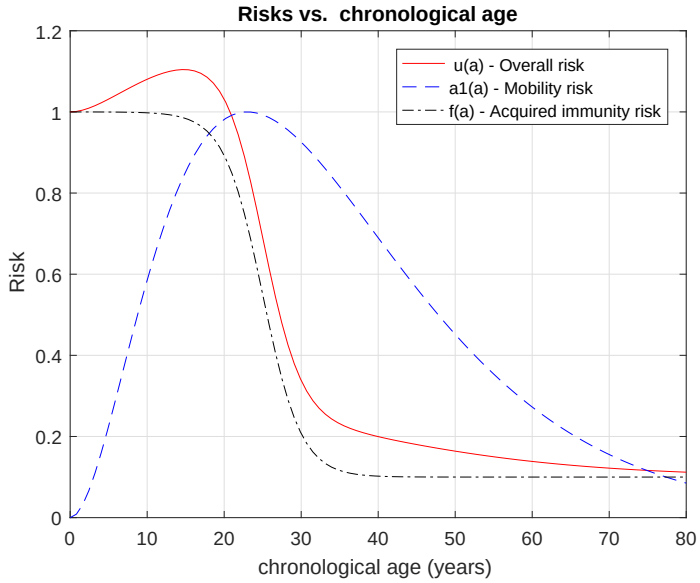

Fig. 1: Age-dependent risk of infectiousness due to mobility, acquired immunity and weather influence

Figure 1 shows a general validity as overall risk level indicated by $u(a)$ is higher than $f(a)$, indicating the increase in risk due to mobility. Moreover, overall $u(a)$ has approached a peak between 20 and 30 years and latter part settles with a saturation. These two attributes are not observable simultaneously in either $f(a)$ or $a_1(a)$. The two influential functions $f(a)$ or $a_1(a)$ are carrying either a peak (in $a_1(a)$) or a saturation (in $f(a)$), but not both phenomena.

These type of different situations can be simulated by changing the proportional rate λ accordingly. The Figure 2 depicts a sensitivity analysis with different λ. What readily observable is that peaks slightly move towards higher ages and saturation may vanish with higher λ.

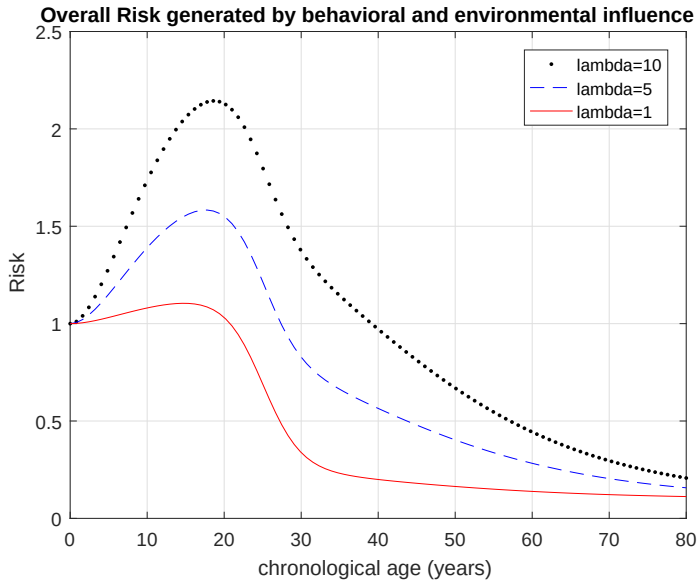

Fig. 2: Sensitivity analysis on age-dependent risk of infectiousness

For further interpretations, Figure 3 illustrates excessive risk given by $u(a) - f(a)$. This analysis indirectly paves the way to estimate suitable λ for a host population by comparing with another population. In that purpose, the risk level can be mimiced via the prevalence of the disease by age. Such observational and experimental findings are available for some diseases in literature supporting this claim [9].

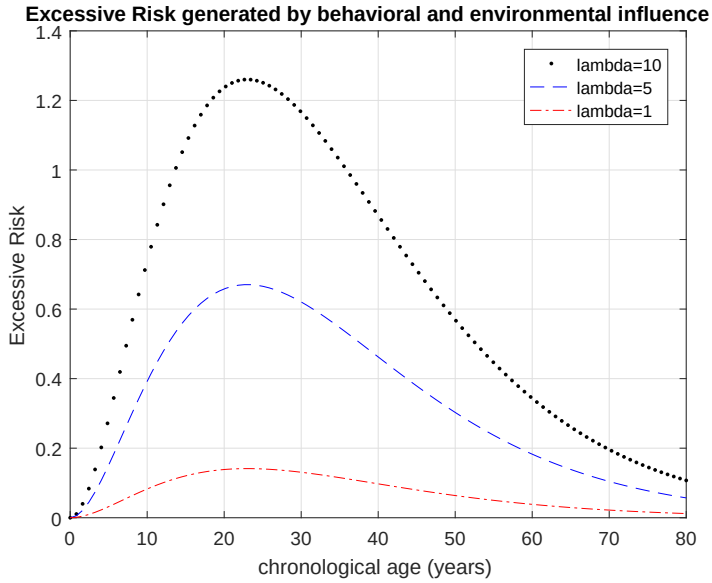

Fig. 3: Excessive risk on age-dependent infectiousness

4 Discussion and Conclusion

When the parsimonious modeling perspective is concerned, the proposed integral equation approach has a reasonable ability of expressing heterogeneity of biological, behavioral and environmental influences on age-dependent infectiousness of a disease. At the end, model accuracy is a matter of choosing suitable curves for each influencing function.

Furthermore, this model can be used as a guide to formulate hypotheses and data collection strategies to measure the risk of a disease. For instance, when different immunity mechanisms play in different ages, $f(a)$ curve can be tested with different options. One motivation towards this is the fact that some diseases accountable with innate immunity in early ages and subsequently with acquired immunity. Different options on mobility related influences can be brought via a_k functions. The degenerate kernel facilitates any finite number of such functions. Moreover, time-scale connections with such a_k functions can be produced by different $b_k$functions.

It is evident that integral approach reduce the inconvenience of many parameter estimations required in models with systems of differential equations. Here in this model, the proportional constant λ is the only visible parameter to be estimated as all the other evaluations can be incorporated with general functions proposed for any influential factor. As depicted in sensitivity analysis and excessive risk analysis, model based experiments can be carried out to estimate λ according to a selected set of influential functions. Next, reliable predictions can be made using those models.

References

[1] M. Chan, E. Michael, S. Pani, R. Norman, D. Bundy, P. Vanamail, K. Ramaiah,P. Das, and A.Srividya, "Epifil: a dynamic model of infection and disease in lymphatic filariasis," *The American Journal of Tropical Medicine and Hygiene*, vol. 59, no. 4, pp. 606–614, 1998.

[2] M. Gambhir, and E. Michael, "Complex Ecological Dynamics and Eradicability of the Vector Borne Macroparasitic Disease," *Lymphatic Filariasis. PLoS ONE*, vol. 3, no. 8, pp. 100–110, 2008.

[3] N. Grassly, and C. Fraser, "Mathematical models of infectious disease transmission," *Nature Reviews Microbiology*, vol. 6, no. 6, pp. 477–487, 2008.

[4] A. Jerri, *Introduction to integral equations with applications*. New York: Dekker, 1985.

[5] M. Li and X. Liu, "An SIR Epidemic Model with Time Delay and General Nonlinear Incidence Rate," *Abstract and Applied Analysis*, pp. 1-7, 2014.

[6] J. Murray, *An Introduction to Mathematic Biology*. New York: Springer, 2001.

[7] R. Norman, M. Chan, A. Srividya, S. Pani, K. Ramaiah,P. Vanamail,E. Michael, P. Das and D. Bundy, "EPIFIL: The development of an age-structured model for describing the transmission dynamics and control of lymphatic filariasis," *Epidemiology and Infection*, vol. 124, no. 3, pp. 529–541, 2000.

[8] E. Shim, Z. Feng,M. Martcheva and C. Castillo-Chavez, "An age-structured epidemic model of rotavirus with vaccination," *Journal of Mathematical Biology*, vol. 53, no. 4, pp. 719–746, 2006.

[9] W.A. Stolk, "Lymphatic Filariasis: Transmission, Treatment and Elimination." *(Ph.D. Thesis), Erasmus University Rotterdam, Netherlands*, 2005.