ON STABLE PARAMETER IDENTIFICATION IN AVIAN INFLUENZA

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ABSTRACT

When it comes to infectious diseases, one of the most important tasks is to evaluate the transmission rate accurately so that the government agencies could develop adequate control strategies and safety measures. The transmission rate of the virus is equal to the product of transmission probability and the number of contacts with infected individuals. However, measuring the probability of a contact to result in a disease is extremely difficult, since it depends on a number of factors such as age, genetics, immunity, etc. For avian influenza, also known as "bird flu", this probability varies in time due to temperature fluctuations, wild birds migration, and other environmental changes [1], [2].

In our study of avian influenza, instead of directly measuring the probability of the transmission, we propose to use the information available on human and poultry highly pathogenic avian influenza (HPAI) outbreaks, as well as other related data, to approximate a bird-to-human transmission rate by solving the underlying inverse problem [3]. Up until recently, models developed with annualized data primarily used constant transmission rates. With the advent of more timely and frequent reporting, the data can be seen to ebb and swell over time. Following Martcheva and Tuncer, we represent the transmission rate as a time-dependent function [1], [2]. To that end, the avian influenza dynamics are described by the SI-model, according to which the human population is divided into two classes: susceptible humans, $S(t)$, and infected humans, $I(t)$. The rate of change in the number of susceptible humans is given by the following equation

$$\frac{dS}{dt} = \Lambda - \beta(t) I_b(t) S(t) - \mu S(t). \tag{1}$$

Similarly, the domestic bird population is divided into susceptible birds, $S_b(t)$, and birds infected with high pathogenic avian influenza, $I_b(t)$. It is assumed that for susceptible humans, μ and $\beta(t)$ are the natural death rate and the bird-to-human HPAI transmission rate, respectively, which results in the force of infection being $\beta(t) I_b(t) S(t)$. The remaining parameter Λ is the birth rate of humans. Integrating $\beta(\tau) I_b(\tau) S(\tau)$ from the initial time 0 to time equal to t, one obtains the cumulative number of HPAI human cases over the period from 0 to t:

$$C(t) = \int_0^t \beta(\tau) S(\tau) I_b(\tau) d\tau, \quad t \in (0, T).$$

The inverse problem of practical importance is to evaluate the time dependent transmission rate, $\beta(t)$, given the number of birds infected with HPAI, $I_b(t)$, the number of confirmed H5N1 human cases, $C(t)$, and the constant parameters Λ, μ, and $S(0)$. The above equation for $C(t)$ combined with (1) implies

$$\frac{dS}{dt} = \Lambda - \mu S - \frac{dC}{dt}. \tag{2}$$

Since $C(t)$ is known, we can view (2) as a linear ODE with respect to $S = S(t)$ (susceptible humans). Solving (2) analytically, one gets

$$S(C(t), t) = \left(S_0 - \frac{\Lambda}{\mu} \right) \mathrm{e}^{-\mu t} + \frac{\Lambda}{\mu} - C(t) + \mu \int_0^t C(\tau) \mathrm{e}^{-\mu(t-\tau)} \, d\tau. \tag{3}$$

Using (3), one can find $\beta(t)$ from the following linear Volterra integral equation of the first kind:

$$\int_0^t K(C(\tau), \tau) \beta(\tau) \, d\tau = C(t), \quad K(C(\tau), \tau) := S(C(\tau), \tau) I_b(\tau), \quad t \in (0, T). \tag{4}$$

Problem (4) is unstable [4]. Hence a numerical algorithm for solving (4) is to be combined with a suitable regularization procedure, especially considering the fact that in our case the noise is not in the right-hand side only, but also in the operator itself.

In [3], a local regularization procedure [5] for solving (4) in the framework of the general regularization theory of Volterra integral equations of the first kind was used , and the benefits of the approach that naturally incorporates the structure into the regularizing strategy have been examined. However, since the kernel in (4) is time-independent, one can view (4) as a numerical differentiation problem and try to apply, say, finite difference formulas along with sampled data smoothing or a finite combination of Legendre polynomials to solve (4) numerically in a stable manner. Alternatively, one can obtain $S = S(\beta(t), t)$ from (1) and write the kernel in (4) as a nonlinear function of $\beta(t)$. This will result in a nonlinear Volterra equation of the first kind, which can be solved with an iteratively regularized algorithm. While it will introduce an error of the numerical method in addition to the errors due to regularization scheme and discrete approximation, this approach leads to a noise-free kernel as opposed to (3)-(4), where the kernel is noise contaminated.

The goal of our current research is to perform a very careful comparison of these three approaches. As in [3], theoretical analysis is illustrated with numerical simulations on real data. We experiment with two different data sets. In the first case, we work with data obtained from all countries where highly pathogenic avian influenza (HPAI) of subtype H5N1 is observed. In the second case, we focus on Indonesia, one of the countries where most of cases are seen, and use data for Indonesia only. In both experiments, we estimate the time-dependent transmission rate of the avian influenza model using cumulative number of infected H5N1 human cases and the number of infected poultry [3].

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