Understanding Renewal Equations for Epidemiological Modeling

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This document serves as a reference to interpreting multiple epidemiological models frameworks and their development using renewal equations. We'll seek to motivate the details from either an application or mathematical perspective for each approach to better understand how these frameworks may be translated for our application(s).

See References for further access/details than denoted by the sections.

Important Definitions

Renewal Equations: a form of integral equation used to define renewal processes, conditioned on time of first arrival for which the process restarts at each arrival independently of the past

Renewal Process: an idealized stochastic model for "events" which occur randomly in time. For our application, an example of a temporal renewal/arrival could be exposure to or infection of a disease for an individual (we will specify to occur at time τ)

Delay ODEs: rule for extending a function of time towards the future on the basis of known or assumed past; time derivative at a current time t depend on the solution (and potentially it's derivatives) at previous times

probably need more background mathy stuff here especially depending on the audience..

Useful Resources for Reference

1. `https://www.randomservices.org/random/renewal/Equations.html`
2. `http://galton.uchicago.edu/~lalley/Courses/383/Renewal.pdf`

1 Breda et al. 2012

Title: **On the formulation of epidemic models (an appraisal of Kermack and McKendrick)**

"The aim of the present paper is to take up 'the problem of endemicity' and to show that, actually, one can formulate it in a way that is very reminiscent of the general epidemic model of 1927, provided one takes the force of infection as the primary unknown. In particular, we show that one can derive a scalar nonlinear renewal equation for the force of infection under rather general assumptions on both the demographic turnover and the waning of immunity."

1.1 Epidemic in a closed population, permanent immunity

This is considerable as a base/simple case from which we will build upon. Our assumptions in this case include the population is closed (meaning no individual leaves or joins), immunity is permanent so individuals do not become reinfected or rejoin the susceptible population (more thoroughly, this means $S(t)-$ monotonically decreasing), the population is static relative to time of infection, Keeping in mind the following definitions: $F(t)$ - force of infection (probability of transmission) at time t, $S(t)$ - density of susceptibles at time t (per unit area), incidence $= F(t)S(t)$ (number of new cases per unit time and area). Note that area defines a proximity of individuals to enforce a definition of contact ($\leq \epsilon$). Given our assumptions, the susceptible population will only change by how often individuals become infected so we may define the derivative and solve for the function of susceptibles (to reduce unknowns in future equations) as follows:

$$\dot{S}(t) = -F(t)S(t) \implies S(t) = S(-\infty)e^{-\int_0^t F(\sigma)d\sigma} \tag{1}$$

We want to understand the force of infection at our current time t based on historical prevalence defined by an individual infected at time τ. Where $A(\tau)$ is the contribution to the current force of infection ($F(t)$) from an individual (singular member of the population) infected at time τ, we define the following as $F(t)$ is composed of the continuous incidence with contribution from made by the individual

$$F(t) = \int_0^\infty F(t-\tau)S(t-\tau)A(\tau)d\tau \tag{2}$$

From our given we found a solution (Equation 1) that may be implemented into the structure for the force of infection (Equation 2) such that our scenario is contained in a nonlinear scalar renewal equation, defined below.

$$F(t) = \int_0^\infty F(t-\tau)\left(S(-\infty)e^{-\int_0^{t-\tau} F(\sigma)d\sigma}\right)A(\tau)d\tau \tag{3}$$

This breaks down into the incidence at time $t-\tau$ dependent upon the change of susceptibles defined by Equation 1 multiplied by the influence an individual infected at time τ contributes. This is utilized as a setup as we need to further inspect cumulative force of infection, R_0 and final endemic size.

Remark: On selecting $A(\tau)$ and Linear Chain Trickery

We make the following assumptions which correspond to an individual having strictly positive or no effect on the force of infection and integrability

$$A(\tau) \geq 0$$

$$A : [0, \infty) \to [0, \infty)$$

Generally, we can understand $A(\tau)$ to depend upon contact intensity and infectiousness, the later we hope medicine can provide insight for. This function plays a crucial role, as the mathematics will emphasize, in severity indicators such as final size and R_0.

Present framework exists for common compartmental models, including but not limited to

$$A(\tau) = \beta e^{-\alpha\tau} \iff SIR$$

$$A(\tau) = \beta \frac{\gamma}{\gamma - \alpha} \left(e^{-\alpha\tau} - e^{-\gamma\tau} \right) \iff SEIR$$

The general idea that delay equations with kernels defined in terms of matrix exponentials correspond to systems of ODEs is called 'Linear Chain Trickery' ... need to work on these proofs... motive for sharing them? might be helpful as a check so could put at the end...

End of Remark

We now introduce the cumulative force of infection ($y(t)$) to draw conclusions from Equations 1-3.

$$y(t) = \int_{-\infty}^{t} F(\sigma) d\sigma$$

Furthermore, using our previous definition of force of infection (Equation 2) we may construct the cumulative force of infection. To perform the integral, we will switch the order of integration and employ the fact

$$-\dot{S}(t-\tau) = F(t-\tau)S(t-\tau)$$

which yields the following derivation procedure, note leaving in terms of $S(t-\tau)$ for simplicity:

$$\int_{-\infty}^{t} \left(\int_{0}^{\infty} F(t-\tau)S(t-\tau)A(\tau)d\tau \right) d\sigma$$

$$\implies \int_0^\infty \left(\int_{-\infty}^t F(t-\tau)S(t-\tau)A(\tau)d\sigma \right) d\tau$$

Because $A(\tau)$ does not depend on σ, it can be pulled from the integral and the remaining incidence can be rewritten as follows

$$\implies \int_0^\infty A(\tau) \left(\int_{-\infty}^t -\dot{S}(t-\tau)d\sigma \right) d\tau$$

$$\implies \int_0^\infty -A(\tau) \left(S(t-\tau) - S(-\infty) \right) d\tau$$

By plugging in our definition for $S(t-\tau)$ from Equation 1 we can conclude our formulation of the cumulative force of infection as a scalar nonlinear renewal equation of convolution type:

$$y(t) = \int_0^\infty (1 - e^{-y(t-\tau)})S(-\infty)A(\tau)d\tau \tag{4}$$

Properties of these functions allow us to interpret the long-term behavior analytically. Because the force of infection can only be positive ($F \geq 0$), then the cumulative force of infection should be increasing and is preserved s.t. y increasing on $(-\infty, 0) \implies y$ increasing on $(0, \infty)$. Additionally we find y bounded as $1 - e^{-y} \leq 1$ for $y \geq 0$ and A integrable condition. Therefore,

$$y(\infty) = \lim_{t \to \infty} y(t) \implies y(\infty) = \lim_{t \to \infty} \int_0^\infty (1 - e^{-y(t-\tau)})S(-\infty)A(\tau)d\tau$$

$$\implies y(\infty) = R_0(1 - e^{-y(\infty)})$$

Thus we may define the reproduction number R_0 as the susceptible density at $t = -\infty$ multiplied by the contributions to the force of infection of individuals infected at time $\tau \in [0, \infty)$.

$$R_0 = S(-\infty) \int_0^\infty A(\tau)d\tau \tag{5}$$

We may draw two major conclusions from this in terms of possible solutions to Equation 5.

1. $R_0 > 1 \implies$ introduction of infection produces an outbreak of final size defined by Equation 6, for $y(\infty)$ the unique strictly positive solution of $y(\infty) = R_0(1 - e^{-y(\infty)})$

$$1 - \frac{S(\infty)}{S(-\infty)} = 1 - e^{-y(\infty)} = \frac{1}{R_0} y(\infty) \tag{6}$$

2. $R_0 \leq 1 \implies$ introduction of infection produces an outbreak of final size approximately zero. We can elaborate on this as the relevant solution is the zero solution. Thus, to analytically capture the introduction of a small number of infected, we can redefine the cumulative force of infection for a given $f(t)$ as

$$y(t) = \int_0^{\infty} (1-e^{-y(t-\tau)})S(-\infty)A(\tau)d\tau + f(t) \implies y(\infty) = R_0(1-e^{-y(\infty)}) + f(\infty)$$

Therefore, we may reemphasize the positive solution $y(\infty)$ goes to zero as $f(\infty) \to 0$.