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THIRD AUTUMN COURSE ON MATHEMATICAL ECOLOGY

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"Infectious Disease Models with Infectivity Depending on Age of Infection "

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These are preliminary lecture notes, intended only for distribution to participants.

Infectious Disease Models with Infectivity depending on Age of Infection

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The first stage is to generalize the classical simple models which admit an endemic equilibrium

S-I-S [Kermack & McKendrick (1932)]

$$S' = -\beta S I + \frac{1}{\tau} I$$
$$I' = \beta S I - \frac{1}{\tau} I \qquad [S + I = K]$$

S-I-R [Hethcote (1974)]

$$S' = -\beta S I + \mu (K - S)$$
$$I' = \beta S I - \frac{1}{\tau} I - \mu I$$
$$R' = \frac{1}{\tau} I - \mu R \qquad [S + I + R = K]$$

in three directions:

(1) nonlinear density-dependent population dynamics

(2) rate of contact per infective depending on total population size

(3) arbitrary distribution of lengths of infective period

Specific assumptions: (1) Per capita birth rate $B(N)$ and per capita death rate $D(N)$ depend on total population size $N = S + I + R$. All births are in class S and death rates (other than from disease) are proportion to size of class. Population has carrying capacity K : $B(K) = D(K)$, $B'(K) < D'(K)$, $B'(N) \leq 0$, $[NB(N)]' = B(N) + NB'(N) \geq 0$, $0 \leq D'(N) \leq \frac{D(N)}{N}$

(2) Number of contacts per infective in unit time is $C(N)$

$$C(N) > 0, \quad C'(N) \geq 0, \quad \left[\frac{C(N)}{N}\right]' \leq 0$$

Define $\hat{C}(N) = \frac{C(N)}{N}$, so that $\hat{C}'(N) \leq 0$ and $\beta = \hat{C}(K)$. Rate of new infections in unit time is

$$I\, C(N) \cdot \frac{S}{N} = \hat{C}(N)\, S I$$

(3) Fraction of infectives remaining infective a time s after becoming infective is $P(s)$, with

$$P(s) \geq 0, \quad P(0) = 1, \quad P \text{ non-increasing}$$

$$\int_0^\infty P(s)\,ds = \tau < \infty$$

$$P_1(s) = P(s)\, e^{-D(N)s}$$

$$\hat{P}_1(\lambda) = \int_0^\infty e^{-\lambda s} P_1(s)\, ds$$

S-I-S model

$$I(t) = \int_0^t \hat{C}\{N(x)\}\,[N(x)-I(x)]\, I(x)\, P(t-x)\, e^{-\int_x^t D\{N(y)\}dy}\, dx$$

$$N' = N[B(N) - D(N)] \qquad [S = N - I]$$

Contact number $\beta K \hat{P}_1(0)$. If $\beta K \hat{P}_1(0) > 1$ there is an endemic equilibrium with $I = I_\infty > 0$, $N = K$. Characteristic equation at endemic equilibrium

$$\beta(K - 2I_\infty)\hat{P}_1(\lambda) = 1,$$

stability condition $\beta K \hat{P}_1(0) > 1$

S-I-R model (with recovery)

$$S' = NB(N) - SD(N) - \hat{C}(N)\, S I$$

$$I(t) = \int_0^t \hat{C}\{N(x)\}\, S(x)\, I(x)\, P(t-x)\, e^{-\int_x^t D\{N(y)\}dy}\, dx$$

$$N' = N[B(N) - D(N)] \qquad [R = N - I - S]$$

Contact number $\beta K \hat{P}_1(0)$. If $\beta K \hat{P}_1(0) > 1$ there is an endemic equilibrium with $S = S_\infty < K$, $I = I_\infty > 0$, $N = K$. Characteristic equation at endemic equilibrium

$$b\hat{P}_1(\lambda) = \frac{\lambda + a}{\lambda + c} = 1 + \frac{a - c}{\lambda + c}$$

with $b = \frac{1}{\hat{P}_1(0)}$, $a = \beta I_\infty + D(K)$, $c = D(K) < a$

If $\mathcal{R}\lambda \geq 0$, $|b\hat{P}_1(\lambda)| \leq 1$, $\mathcal{R}\left[1 + \frac{a-c}{\lambda + c}\right] \geq 1$

S-I-R model (fatal)

$$S' = NB(N) - SD(N) - \hat{C}(N)SI$$
$$I(t) = \int_0^t \hat{C}\{N(x)\}S(x)I(x)P(t-x)e^{-\int_x^t D\{N(y)\}dy}dx$$

or replace $NB(N)$ by $SB(S)$ if appropriate or, for diseases with short infective periods so deaths not caused by disease occur only in susceptible class and infectives do not contribute to birth rate

$$S' = g(S) - \hat{C}(S+I)SI$$
$$I(t) = \int_0^t \hat{C}\{S(x)+I(x)\}S(x)I(x)P(t-x)dx$$
$$[N = S+I]$$

Contact number $\beta K\hat{P}(0) = \beta K\int_0^\infty P(s)ds = \beta K\tau$

If $\beta K\tau > 1$, disease-free equilibrium is unstable and there is an endemic equilibrium (S_∞, I_∞), $S_\infty = \dfrac{1}{\tau\hat{C}(S_\infty+I_\infty)} < K$, $I_\infty > 0$, having characteristic equation

$$b\hat{P}(\lambda) = 1 + \frac{a-c}{\lambda+c},$$

$$a = I_\infty\hat{C}(S_\infty+I_\infty) + S_\infty I_\infty\hat{C}'(S_\infty+I_\infty) - g'(S_\infty)$$
$$b = S_\infty\hat{C}(S_\infty+I_\infty) + S_\infty I_\infty\hat{C}'(S_\infty+I_\infty) \le S_\infty\hat{C}(S_\infty+I_\infty) =$$
$$c = -g'(S_\infty) < a$$

If $g'(S_\infty) < 0$, just like recovery model, but if $g'(S_\infty) > 0$ instability is possible – happens for fixed infective period but not for exponential distribution with large contact number

Age of infection models

Let $\pi(s)$ $[0 \le \pi(s) \le 1]$ be probability of infection in a contact with an infective who has been infected for a period s at time t

$i(t,s)$ number of infectives at time t who have been infected for period s

$J(t) = \int_0^t i(t,s)\,ds$ number of infected members

$\Phi(t) = \int_0^t \pi(s)\, i(t,s)\,ds$ total infectivity

Then rate of new infections is $\hat{C}(N) S \Phi$

S-I-S model

$$\Phi(t) = \int_0^t \hat{C}\{N(x)\} S(x) \Phi(x) \pi(t-x) P(t-x) e^{-\int_x^t D\{N(y)\}dy} dx$$

$$J(t) = \int_0^t \hat{C}\{N(x)\} S(x) \Phi(x) P(t-x) e^{-\int_x^t D\{N(y)\}dy} dx$$

$$N' = N[B(N) - D(N)] \qquad [S = N - J]$$

Consider special case $D(N) \equiv d$, and let

$P_1(s) = e^{-ds}P(s)$, $R(s) = \pi(s)P(s)$, $R_1(s) = e^{-ds}R(s)$

$$\Phi(t) = \int_0^t \hat{C}\{N(x)\} S(x) \Phi(x) R_1(t-x)\,dx$$

$$J(t) = \int_0^t \hat{C}\{N(x)\} S(x) \Phi(x) P_1(t-x)\,dx$$

$$N' = N[B(N) - d]$$

Contact number $\beta K \hat{R}_1(0)$. If $\beta K \hat{R}_1(0) > 1$ there is an endemic equilibrium with $S = S_\infty < K$, $\Phi = \Phi_\infty > 0$, $J = J_\infty > 0$, $N = K$ and characteristic equation

$$\beta S_\infty \hat{R}_1(\lambda) = 1 + \beta \Phi_\infty \hat{P}_1(\lambda),$$

$$\beta S_\infty = \frac{1}{\hat{R}_1(0)}, \quad \beta \Phi_\infty = \frac{\beta K \hat{R}_1(0) - 1}{\hat{P}_1(0)}$$

Endemic equilibrium is asymptotically stable for some choices of $P(s)$, e.g. if $P(s) \geq 0$, $P'(s) \leq 0$, $P''(s) \geq$ but instability is conceivable - especially if $\pi(s)$ is concentrated near $s = 0$

S-I-R model (with recovery)

$$S' = NB(N) - SD(N) - \hat{C}(N) S \Phi$$

$$\Phi(t) = \int_0^t \hat{C}\{N(x)\} S(x) \Phi(x) R_1(t-x) dx$$

$$J(t) = \int_0^t \hat{C}\{N(x)\} S(x) \Phi(x) P_1(t-x) dx$$

$$N' = N[B(N) - D(N)] \qquad [R = N - S - J]$$

Just like model without age of infection (I replaced by Φ, P_1 replaced by R_1) and same analyses and results.

S-I-R model (fatal)

$$S' = g(S) - \hat{C}(N) S \Phi$$

$$\Phi(t) = \int_0^t \hat{C}\{N(x)\} S(x) \Phi(x) R(t-x) dx$$

$$J(t) = \int_0^t \hat{C}\{N(x)\} S(x) \Phi(x) P(t-x) dx$$

$$[N = S + J]$$

Contact number $\beta K \hat{R}(0)$. Characteristic equation at endemic equilibrium $S = S_\infty = \frac{1}{\hat{C}(N_\infty)\hat{R}(0)} < K$, $J = J_\infty > 0$, $\Phi = \Phi_\infty > 0$ if $\beta K \hat{R}(0) > 1$ is

$$S_\infty \hat{C}(N) \hat{R}(\lambda) + S_\infty \Phi_\infty \hat{C}'(N_\infty) \hat{P}(\lambda) = 1 + \frac{[\hat{C}(N_\infty) + S_\infty \hat{C}'(N_\infty)] \Phi_\infty}{\lambda - g'(S_\infty)}$$

Same instability possibilities as model without age of infection and if $\hat{C}'(N) \not\equiv 0$, can also have instability with $g'(S_\infty) < 0$ [Thieme & Castillo-Chavez, to appear]