 from Murray chapters 19 & 20

6. Models for the spreading of diseases

6.1. An epidemic model (SIR model)

Consider disease which upon recovery gives rise to immunity.
Divide population (size N) into three classes

susceptibles	$S(t) \geq 0$
infectives	$I(t) \geq 0$
removed (recovered and immune, recovered and isolated, or dead)	$R(t) \geq 0$

$$S \rightarrow I \rightarrow R$$

Assumptions concerning transmission of infection and incubation period:

① gain in I is given by rSI with $r>0$ a constant (infection rate)

② rate of $I \to R$ is αI with $\alpha > 0$ a constant (removal rate of infectives)
α^{-1} is average infectious period

③ incubation period sufficiently short to be ignored

Rate equations

$$\frac{dS}{dt} = -rSI \qquad (*)$$

$$\frac{dI}{dt} = rSI - \alpha I \qquad (**)$$

$$\frac{dR}{dt} = \alpha I \qquad (***)$$

Kermack-McKendrick (1927)

Initial conditions

$$S(0) = S_0, \quad I(0) = I_0, \quad R(0) = 0$$

Conservation law

$$\frac{d}{dt}(S+I+R) = 0$$

So

$$S(t) + I(t) + R(t) = \text{const.} = N$$

Question: given r, α, S_0, I_0 will infection spread or not? Show that $I_0 > I(t) \to 0$ if population of susceptibles at $t=0$ is below a critical value.

$$\left.\frac{dI}{dt}\right|_{t=0} = (rS_0 - \alpha) I_0 \begin{cases} <0 & \text{if } S_0 < \frac{\alpha}{r} = \rho \\ >0 & \text{if } S_0 > \rho \end{cases}$$

The parameter ρ is called relative removal rate, and $\sigma = \rho^{-1}$ is called the infection's contact rate. Write

$$\boxed{r_0 = \frac{rS_0}{\alpha} = \sigma \cdot S_0 = \frac{S_0}{\rho}}$$

which is called reproductive rate (of the infection).

From $(*)$

$$\frac{dS}{dt} \leq 0 \quad \rightsquigarrow \quad S(t) \leq S_0$$

So if $S_0 < \frac{\alpha}{r}$ (i.e. $\frac{S_0}{\rho} < 1$ or $r_0 < 1$) then

$$\frac{dI}{dt} = (rS - \alpha)I \leq (rS_0 - \alpha)I < 0.$$

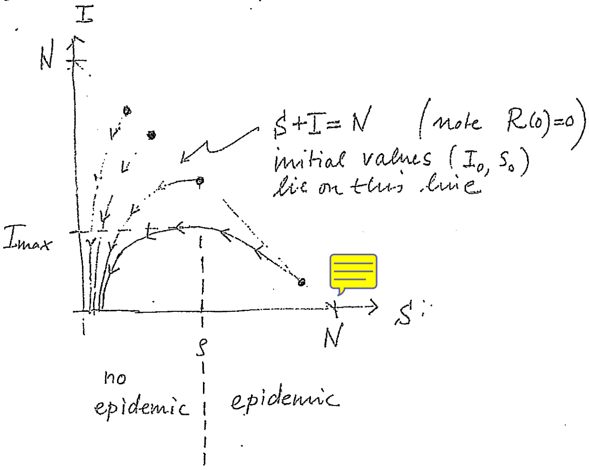
In this case

$$I_0 > I(t) \longrightarrow 0 \quad \text{as } t \to \infty,$$

infection does not spread.

If by contrast $r_0 > 1$ have an epidemic: $I(t)$ initially increases so that for some $t>0$ find $I(t) > I_0$.

Phase-space diagram. Equation for R is slaved to eqns. for S and I. Consider dynamics in phase plane (S, I).



Ⓐ Dynamics doesn't leave triangular region

Use same trick as for Lotka-Volterra model (→p. 81): divide (**) by (***)

[assume $I \neq 0$]

$$\frac{dI}{dS} = \frac{\frac{dI}{dt}}{\frac{dS}{dt}} = -\left(\frac{rS}{rS-\alpha}\right)^{-1} = \frac{\rho}{S} - 1$$

Integrate

$$I + S - \rho \log S = \text{const.}$$
$$= I_0 + S_0 - \rho \log S_0$$

So

$$I + S = I_0 + S_0 + \rho \log \frac{S}{S_0}$$
$$\leq I_0 + S_0 = N$$

Since $S < S_0$ have $\log \frac{S}{S_0} \leq 0$

So phase-plane dynamics never leaves triangular region sketched on previous page.

Ⓑ Determine maximal number of infectives

Find I_{max} for given initial conditions (S_0, I_0) by determining value of S for which

$$\frac{dI}{dt} = 0$$

Since $\frac{dI}{dt} = (rS - \alpha) I$ this occurs for

$S = \rho$. I_{max} at ρ [$\rho = \frac{\alpha}{r}$]

From $I + S = I_0 + S_0 + \rho \log \frac{S}{S_0}$ obtain

$$I_{max} = I_0 + S_0 - \rho + \rho \log \frac{\rho}{S_0}$$
$$= N - \rho + \rho \log \frac{\rho}{S_0}$$

Ⓒ Time to reach $I=0$

As $I \to 0$, $\frac{dI}{dt} \to 0$ and $\frac{dS}{dt} \to 0$. So it takes infinitely long to reach $I = 0$.

Ⓓ Total # of susceptibles infected

What is the total number of susceptibles infected during epidemic?

$$I_{tot} = I_0 + (S_0 - S(\infty))$$

So to answer this question need to determine $S(\infty)$. Divide (*) by (***)

$$\frac{dS}{dR} = \frac{\frac{dS}{dt}}{\frac{dR}{dt}} = -\frac{rS}{\alpha} = -\frac{S}{\rho}$$

$$\Rightarrow S(t) = S_0 e^{-\frac{R(t)}{\rho}} \geq S_0 e^{-\frac{N}{\rho}} > 0$$

So $0 < S(\infty)$. The figure on p. 244 shows $S(\infty) < \rho$. In summary

$$0 < S(\infty) < \rho.$$

Since $I(\infty) = 0$, $S(t) + I(t) + R(t) = N$ implies

$$R(\infty) = N - S(\infty)$$

So $S(\infty)$ is the positive root $0 < z < \rho$ of

$$z = S_0 e^{-\frac{N-z}{\rho}} \qquad z = S(\infty)$$

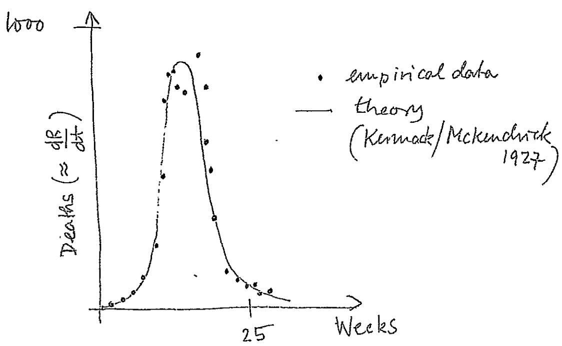
This determines I_{tot}.

Have as $t \to \infty$

$$I(t) \to 0$$
$$S(t) \to S(\infty) > 0$$

So epidemic dies out due to lack of infectives and not due to lack of susceptibles.

Public health records record rate $\frac{dR}{dt}$ at which infectives are removed, due to death for example (Bombay plague epidemic of 1905/06).



Theory. Take

$$\frac{dR}{dt} = \alpha I = \alpha\left(N - R - \underset{\substack{\uparrow \\ S = S_0 e^{-\frac{R}{\rho}}}}{S}\right)$$

$$= \alpha\left[N - R - S_0 \exp\left(-\frac{R}{\rho}\right)\right]$$

Solution can be found numerically.
Instead assume $R/\rho \ll 1$ and expand

$$\exp\left(-\frac{R}{\rho}\right) \approx 1 - \frac{R}{\rho} + \frac{R^2}{2\rho^2}$$

to get

$$\frac{dR}{dt} = \alpha\left(N - S_0 + \left(\frac{S_0}{\rho} - 1\right)R - \frac{S_0 R^2}{2\rho^2}\right)$$

Obtain

$$R(t) = \frac{\rho^2}{S_0}\left[\left(\frac{S_0}{\rho} - 1\right) + \beta \tanh\left(\frac{\beta\alpha t}{2} - \phi\right)\right],$$

$$\beta = \left[\left(\frac{S_0}{\rho} - 1\right)^2 + \frac{2S_0(N - S_0)}{\rho^2}\right]^{1/2},$$

$$\phi = \frac{1}{\beta}\tanh^{-1}\left(\frac{S_0}{\rho} - 1\right).$$

Check by differentiating $R(t)$.

In particular

$$\frac{dR}{dt} = \frac{\alpha\beta^2\rho^2}{2S_0}\operatorname{sech}^2\left(\frac{\alpha\beta t}{2} - \phi\right)$$

Fitting parameters

$$\left.\begin{aligned} A_1 &= \frac{\alpha\beta^2\rho^2}{2S_0} \approx 890 \\ A_2 &= \frac{\alpha\beta}{2} \approx 0.2 \\ A_3 &= \phi \approx 3.4 \end{aligned}\right\} \text{for plot on p. 8}$$

Problems:

1. if duration of epidemic is too long must include birth & death terms,
2. incubation period
3. age classes
4. Spatial spreading

6.2 A model for the spatial spread of an epidemic

Consider model from section 6.1,

$$\frac{dI}{dt} = (rS - \alpha)I$$

$$\frac{dS}{dt} = -rSI$$

α^{-1} life expectancy of an infective
r measures transmission efficiency
Assume diffusive spreading with diffusion constant D

Note: same D for I and for S

$$\frac{\partial I}{\partial t} = (rS - \alpha)I + D\Delta I \qquad \Delta = \partial_x^2 + \partial_y^2$$

$$\frac{\partial S}{\partial t} = -rSI + D\Delta S$$

$I = I(\underline{r}, t)$ and $S = S(\underline{r}, t)$ with $\underline{r} = \binom{x}{y}$.

Consider one-dimensional case to keep algebra simple. Proceed in usual fashion: dimensionless variables

$$I' = \frac{I}{S_0}, \quad S' = \frac{S}{S_0},$$

$$t' = rS_0 t, \quad \lambda = \frac{\alpha}{rS_0},$$

$$x' = \sqrt{\frac{rS_0}{D}}\, x$$

Now drop primes for notational convenience

$$\frac{\partial S}{\partial t} = -IS + \frac{\partial^2 S}{\partial x^2} \qquad (*)$$

$$\frac{\partial I}{\partial t} = IS - \lambda I + \frac{\partial^2 I}{\partial x^2}$$

Only one dimensionless parameter remains. Note $\lambda^{-1} = \frac{rS_0}{\alpha}$ is reproductive rate of the infection (p. 3).

$$r_0 = \frac{S_0}{\rho}$$

Travelling wave of infections ?

Ansatz (→ p.158)

$$I(x,t) = I(z), \quad S(x,t) = S(z) \quad \text{with } z = x - ct$$

c: wave speed

Substituting into (*)

$$\frac{d^2 I}{dz^2} + c\frac{dI}{dz} + I(S-\lambda) = 0$$

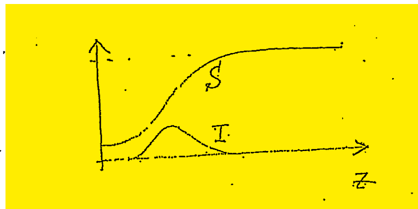
$$\frac{d^2 S}{dz^2} + c\frac{dS}{dz} - IS = 0$$

Boundary conditions

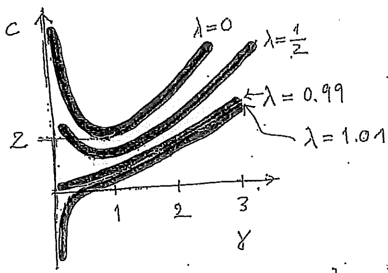
$$I(-\infty) = I(\infty) = 0,$$

$$0 \leq S(-\infty) < S(\infty) = 1,$$

Constraint $I(z) \geq 0, \quad S(z) \geq 0.$



Also $\sqrt{1-\lambda}$ must be real and >0. Thus $\lambda < 1$



singularity in dispersion relation

Conditions for existence of travelling wave

$$c \geq 2\sqrt{1-\lambda}$$

minimum wave speed $c_{min} = 2\sqrt{1-\lambda}$

$$\lambda < 1.$$

Go back to dimensional variables:

$$\lambda = \frac{\alpha}{rS_0} = \frac{\rho}{S_0}$$

So $\lambda < 1$ corresponds to $S_0 > \rho$ which is the condition for an epidemic found on p. 3.

Do not use approach from section 4.8 here because phase space is four-dimensional here (two second-order equations). Instead linearise equations near leading edge of wave $(S \approx 1, I \approx 0)$:

$$\frac{d^2 I}{dz^2} + c\frac{dI}{dz} + (1-\lambda) I \approx 0$$

Ansatz: $I(z) = I_0 e^{-\gamma z}$. Find

$$\gamma^2 - c\gamma + (1-\lambda) = 0$$

$$\gamma^2 - c\gamma + \frac{c^2}{4} = \frac{c^2}{4} - (1-\lambda)$$

$$\gamma = \frac{c \pm \sqrt{c^2 - 4(1-\lambda)}}{2}$$

So

$$I(z) = I_0 \exp\left(-\frac{c \pm \sqrt{c^2-4(1-\lambda)}}{2}\, z\right)$$

Take $\lambda < 1$.
Must have $c > 2\sqrt{1-\lambda}$ otherwise $I(z) < 0$ for some z (because $I(z)$ would be oscillatory).

Minimum wave speed

$$V=\sqrt{rS_0D}\,c = 2\sqrt{rS_0D\left(1-\frac{\alpha}{rS_0}\right)}$$

$$\frac{\alpha}{rS_0}<1$$

The preceeding analysis is valid near leading edge of wave.
The figure on p. 14 shows that $I(z)$ has in fact a maximum.

$S(z)$ cannot have a local maximum
At a maximum would have $\frac{dS}{dz}=0$
and at that point

$$\frac{d^2S}{dz^2}=IS>0$$

which is the condition for a minimum, in contradiction with the assumption.

$S(z)$ is a monotonically increasing function of z. Linearise

$$\frac{d^2S}{dz^2}+c\frac{dS}{dz}-IS=0$$

by putting $S=1-\sigma$: $\quad 0<\sigma\ll 1$

$$\frac{d^2\sigma}{dz^2}+c\frac{d\sigma}{dz}-\underset{\uparrow\ \text{small}}{I}=0$$

Together with (*) find $\sigma(z)=O(e^{-\beta z})$ with $\beta>0$, so $S(z)$ approaches unity exponentially as $z\to\infty$.

Discussion:

epidemic
$$\boxed{\frac{rS_0}{\alpha}\equiv\frac{S_0}{\rho}>1}$$

① minimum critical population density

$$S_c=\frac{\alpha}{r}\equiv\rho$$

for travelling wave to occur.

② for a given population S_0 minimum critical transmission coefficient (for disease to spread)

$$r_c=\frac{\alpha}{S_0}$$

③ given r and S_0 obtain threshold mortality rate.

$$\alpha_c=rS_0$$

Control strategies: reduce S_0 by vaccination, reduce r by isolation. Discuss possible implications of sudden influx of susceptibles in near-threshold population.

6.3 Dynamics of diseases in large but finite populations

1. SIS model (infinite population, $N\to\infty$)

S susceptibles
I infectives

$$S \xrightarrow{\frac{\beta}{N}SI} I \xrightarrow{\gamma I} S$$

Infectives can recover (at rate γ) and become susceptible again.

$$\frac{dI}{dt}=\frac{\beta}{N}SI-\gamma I$$

$$\frac{dS}{dt}=-\frac{\beta}{N}SI+\gamma I$$

Find $S+I=$ constant. Write $S+I=N$ where N is population size.
Eliminate S from first equation

$$\frac{dI}{dt}=\frac{\beta}{N}(N-I)I-\gamma I = \beta\left(1-\frac{I}{N}\right)I-\gamma I \qquad (*)$$

the disease is called <u>endemic</u> if Eq. (*) can sustain a finite number of infectives, that is when Eq. (*) has a linearly stable steady state $I^* > 0$.

Find

$$I^* = N\left(1-\frac{\gamma}{\beta}\right) \equiv N\left(1-\frac{1}{r_0}\right)$$

where

$$r_0 = \frac{\beta}{\gamma}$$

is the <u>reproductive value</u> (also referred to as <u>reproductive ratio</u> or <u>reproductive rate</u>, see p. 3).

Conclusion: the disease is endemic provided

$$r_0 > 1,$$

and the disease will disappear if

$$r_0 < 1.$$

→ J.R. Chasnov „Mathematical Biology"

Biological interpretation of reproductive value r_0:

> If a single infective individual introduced into a susceptible population produces more than one secondary infection before recovering, then $r_0 > 1$, the disease is endemic.

Show this by computing the expected number of secondary infections. To this end require the probability that an individual infective at $t=0$ is still infective at time t.

$$p_{\text{infective}}(t+\delta t) = p_{\text{infective}}(t)\,(1-\gamma\delta t)$$

recovery rate

$$\frac{dp_{\text{infective}}}{dt} = -\gamma\, p_{\text{infective}}$$

Initial condition $p_{\text{infective}}(0) = 1$.

$$p_{\text{infective}}(t) = e^{-\gamma t}.$$

Now compute expected number of secondary infections produced by one primary infective

$$\int_0^\infty p_{\text{infective}}(t)\, \frac{\beta}{N} S(t)\, dt$$

prob. that primary infective still infectious

expected number of secondary infections produced by single infective in time dt

Assume that total number of secondary infections is small compared to N, $S(t) \approx N$.

$$\approx \beta \int_0^\infty dt\, p_{\text{infective}} = r_0 .$$

Note: dimensionless variables

$$I' = \frac{I}{N} \qquad r_0 = \frac{\beta}{\gamma}$$

$$t' = t\gamma$$

Drop primes:

$$\frac{dI}{dt} = r_0 I(1-I) - I$$

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2. Stochastic dynamics in large but finite population

Write a gain-loss equation for the probability $\varrho_n(t)$ to observe n infectives at time t.

non-linearity compare simple branching process

		rate
infection	$n-1 \to n$	$\lambda_{n-1} = \beta\left(1-\frac{n-1}{N}\right)(n-1)$
recovery	$n+1 \to n$	$\mu_{n+1} = \gamma\,(n+1)$

population size

Change in ϱ_n in small time intervall δt due to infection

$$\left(\lambda_{n-1}\varrho_{n-1} - \lambda_n \varrho_n\right)\delta t$$

and due to recovery

$$\left(\mu_{n+1}\varrho_{n+1} - \mu_n \varrho_n\right)\delta t \,.$$

Together

$$\frac{d\varrho_n}{dt} = \lambda_{n-1}\varrho_{n-1} + \mu_{n+1}\varrho_{n+1} - (\mu_n+\lambda_n)\varrho_n$$

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This gain-loss equation is also referred to as a <u>Master equation</u> (van Kampen, 1981).

Master equations of the form (*), corresponding to one-dimensional, one-step birth-death processes can be solved exactly (van Kampen).

In several dimensions (e.g. SIR model, p. 241) no exact solution in general. Must resort to approximate methods.

Plan: describe approximate method for solving (*) despite the fact that (*) is exactely soluble. The approximate method generalises to multi-species models.

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<u>Questions</u>

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Convenient representation of Master equation in terms of step operators $\mathbb{E}^{\pm}$ (van Kampen, 1981). The operators are defined by their actions on functions g of n:

$$\mathbb{E}^{\pm} g_n = g_{n\pm 1}\,.$$

In terms of $\mathbb{E}^{\pm}$, the Master equation (*) takes the form

$$\frac{d\varrho_n}{dt} = (\mathbb{E}^{-}-1)\lambda_n\varrho_n + (\mathbb{E}^{+}-1)\mu_n\varrho_n\,.$$

3. Expansion of Master equation in N^{-1}

Consider large but finite values of N.
Introduce the variable

$$I = \frac{n}{N}$$

compare I' on p. 24.
Define functions $\lambda(I)$ and $\mu(I)$ by

$$\lambda_n = N\lambda(I) \quad \sim \quad \lambda(I) = \beta I(1-I)$$

$$\mu_n = N\mu(I) \quad \sim \quad \mu(I) = \gamma I$$

Expect that $\rho(I,t)$ is a smooth function of I in the limit of large values of N.
Represent action of $E^{\pm}$ on smooth function $g(I)$ in terms of derivatives:

$$\mathbb{E}^{\pm}\, g(I) = g(I \pm \tfrac{1}{N}) = \sum_{k=0}^{\infty} \frac{(\pm\frac{1}{N})^k}{k!} \frac{d^k g}{dI^k} \equiv e^{\pm\frac{1}{N}\frac{d}{dI}}\, g(I).$$

Now expand Master equation to lowest order in N^{-1}.

$$\frac{\partial \rho}{\partial t} = \left(e^{-\frac{1}{N}\frac{\partial}{\partial I}} - 1\right) N\lambda(I)\rho(I) + \left(e^{\frac{1}{N}\frac{\partial}{\partial I}} - 1\right) N\mu(I)\rho(I)$$

$$\approx \frac{\partial}{\partial I}\big(\mu(I) - \lambda(I)\big)\, \rho(I)$$

This is a transport equation of the form

$$\frac{\partial \rho}{\partial t} + \frac{\partial}{\partial I}\big(v(I)\rho\big) = 0 \quad \rightarrow \text{p.}$$

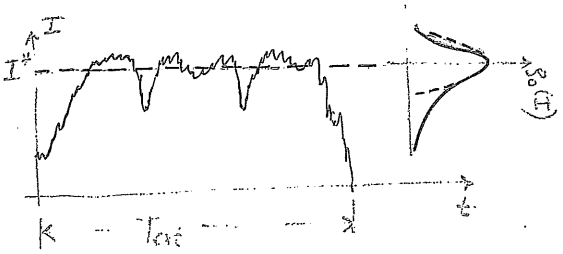
It corresponds to deterministic dynamics of the form

$$\frac{dI}{dt} = v(I) = \big(\lambda(I) - \mu(I)\big) = \beta I(1-I) - \gamma I$$

Up to a rescaling of I with a factor of N this is the deterministic SIS model (*) on p. 20, Dimensionless variables, p. 24.

4. Quasi-steady state

Fundamental dichotomy:
epidemic must eventually become extinct due to fluctuations. But deterministic limit predicts it lasts ad infinitum.



Can show: $T_{ext} \sim e^N$ for large N.

Quasi-steady state.

Expect long-lived quasi-steady state in the limit of large values of N.

Try to compute quasi-steady state distribution ρ_0 given by

$$\frac{\partial \rho_0}{\partial t} \approx 0.$$

Ansatz

$$\rho_0(I) = e^{-NS_0(I) - S_1(I) + \frac{1}{N}S_2(I) + \ldots}$$

(compare WKB ansatz to describe quantum-mechanical tunneling. N^{-1} plays the rôle of $\hbar$).

Insert into

$$0 \approx \left(e^{-\frac{1}{N}\frac{\partial}{\partial I}} - 1\right) N\lambda(I)\rho_0(I) + \left(e^{\frac{1}{N}\frac{\partial}{\partial I}} + 1\right) N\mu(I)\rho_0(I)$$

and expand in N^{-1}.

Write $S_0' \equiv \frac{dS_0}{dI}$.

Now

$$e^{\pm\frac{1}{N}\frac{\partial}{\partial I}}\left(e^{-NS_0(I)-S_1(I)-\dots}\right) = e^{-N\left(S_0\pm\frac{S_0'}{N}+\dots\right)-\left(S_1\pm\frac{S_1'}{N}+\dots\right)}$$

$$\approx \rho_0(I)\,e^{\mp S_0'}\left(1+\text{corrections in } N^{-1}\right)$$

Insert into equation for $\rho_0(I)$ on p. 31

$$0\approx \rho_0(I)\left[N\lambda(I)\left(e^{S_0'}-1\right)+N\mu(I)\left(e^{-S_0'}-1\right)\right]$$

Write this differential equation for $S_0(I)$ as

$\boxed{H(I,p)=0}$ with $p=S_0'$ and

$$H(I,p)=\lambda(I)\left(e^{p}-1\right)+\mu(I)\left(e^{-p}-1\right)$$

The condition $H=0$ implies

$$S_0'(I) = -\log\frac{\lambda(I)}{\mu(I)}$$

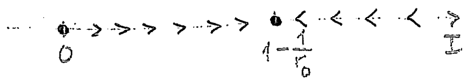
Now integrate to get $S_0(I)$.

Boundary conditions? Recall that the deterministic dynamics (p. 24)

$$\frac{dI}{dt} = \lambda(I)-\mu(I) = \beta I(1-I)-\gamma I$$

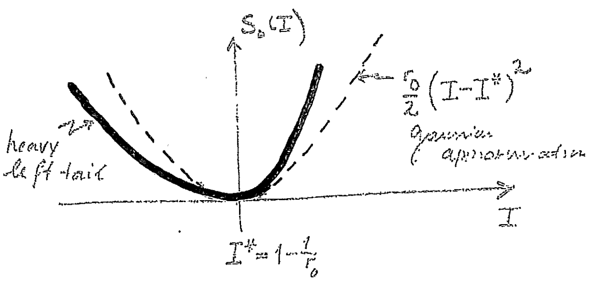
has two fixed points:

$$\left.\begin{array}{ll} I^*=0 & \text{unstable} \\ I^*=1-\frac{\gamma}{\beta}\equiv 1-\frac{1}{r_0} & \text{stable} \end{array}\right\} \text{ for } r_0=\frac{\beta}{\gamma}>1$$



Expect $\rho_0(I)$ has maximum at $I^*=1-\frac{1}{r_0}$,
so $S_0(I)$ has a minimum there.
Set $S_0(I^*)=0$ (this defines normalization constant)

$$S_0(I)=\int_{I^*}^{I}dy\,S_0'(y) = -\int_{1-\frac{1}{r_0}}^{I}dy\,\log\left[r_0(1-y)\right].$$



Distribution non-Gaussian.

Gaussian approximation

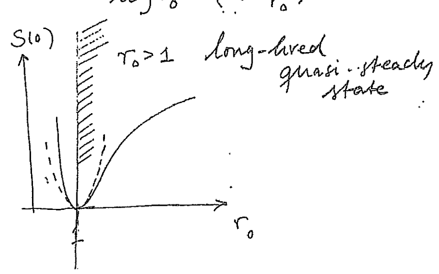
$$S_0(I) = \frac{r_0}{2}(I-I^*)^2+\dots \qquad \mathrm{var}(I)\sim\frac{1}{r_0 N}$$

does not capture heavy tail for small I

Time to extinction of epidemy ($r_0>1$)
(this time and the possibility to affect it are of great interest)

$$T_{ext}\sim e^{NS(0)}$$

$$S(0) = -\int_{1-\frac{1}{r_0}}^{0}dI\,\log\left[r_0(1-I)\right] = \log r_0-\left(1-\frac{1}{r_0}\right)$$



$\boxed{\text{Extinction of disease in finite time}}$