Epidemic Modeling: SIRS Models

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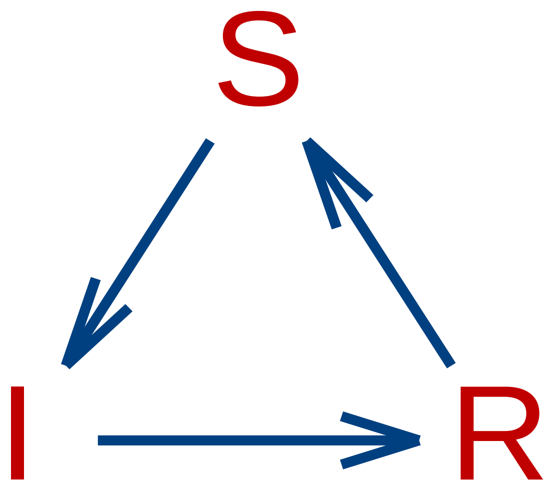
Threshold Phenomena in Epidemic Models

- Epidemic models often exhibit threshold phenomena. Below criticality the major epidemic is impossible or unlikely, whereas when the *reproductive number* is above one, a major epidemic is possible.

- The final outcome of the infection spread for simple epidemic models, SIRS and SIS, in both subcritical and supercritical cases as well as critical and near critical is of interest.

SIRS Epidemic Models



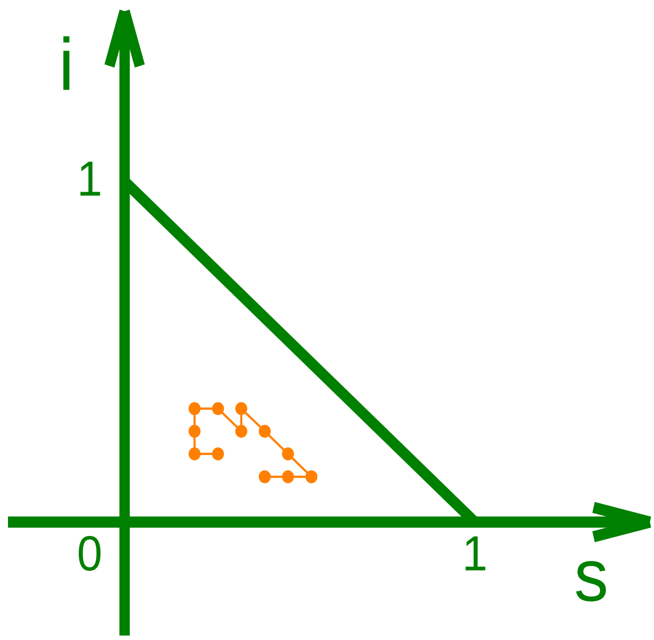
$S_t = \#$ susceptible at time t
$I_t = \#$ infected at time t
$R_t = \#$ recovered (immune) at time t

SIRS Epidemic Models

$$N \equiv S_t + I_t + R_t = \text{ population size}$$

$$s_t = S_t/N, \;\; i_t = I_t/N$$
$$r_t = R_t/N = 1 - s_t - i_t$$

$$\gamma_t = (s_t, i_t)^T$$



SIRS Epidemic Model

MCs indexed by N with transition rates:

$$\rho\,(s \to i) = S \cdot \theta I/N = N\theta si$$
$$\rho\,(i \to r) = \rho I = N\rho i$$
$$\rho\,(r \to s) = R = Nr$$

Questions:

- *Establishment:* Will the infection spread?
- *Spread:* How does it develop with time?
- *Persistance:* When does it disappear and what is the final outcome?

Deterministic Approximation

Fix N, $h > 0$

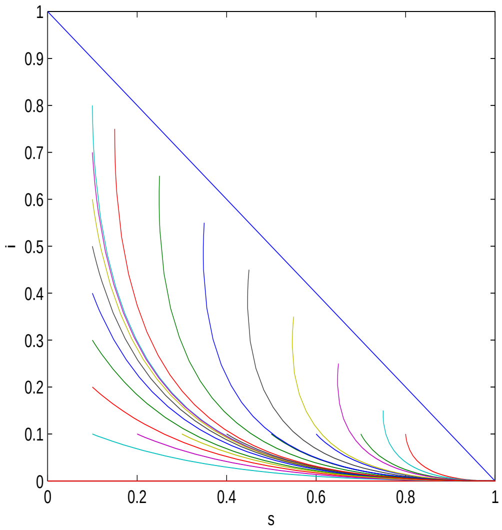
$$\mathbf{E}_t(s_{t+h}) = s_t + r_t h - \theta i_t s_t h + o(h)$$
$$\mathbf{E}_t(i_{t+h}) = i_t + \theta i_t s_t h - \rho i_t h + o(h)$$

Get "mean field approximation" as $h \to 0$

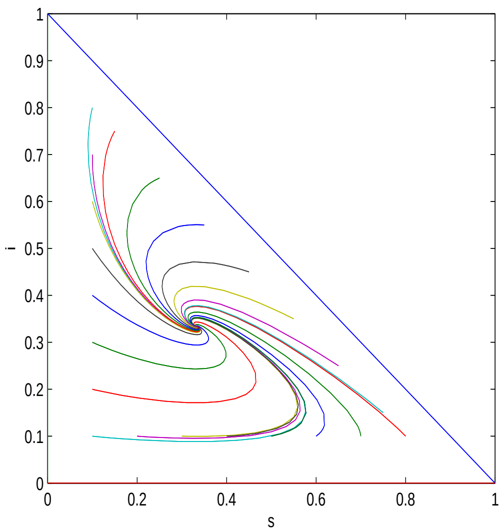
$$\left\{ \begin{array}{rcl} \dfrac{ds_t}{dt} & = & r_t - \theta i_t s_t \\ \dfrac{di_t}{dt} & = & \theta i_t s_t - \rho i_t \end{array} \right. \quad := F(\gamma_t)$$

Deterministic Approximation

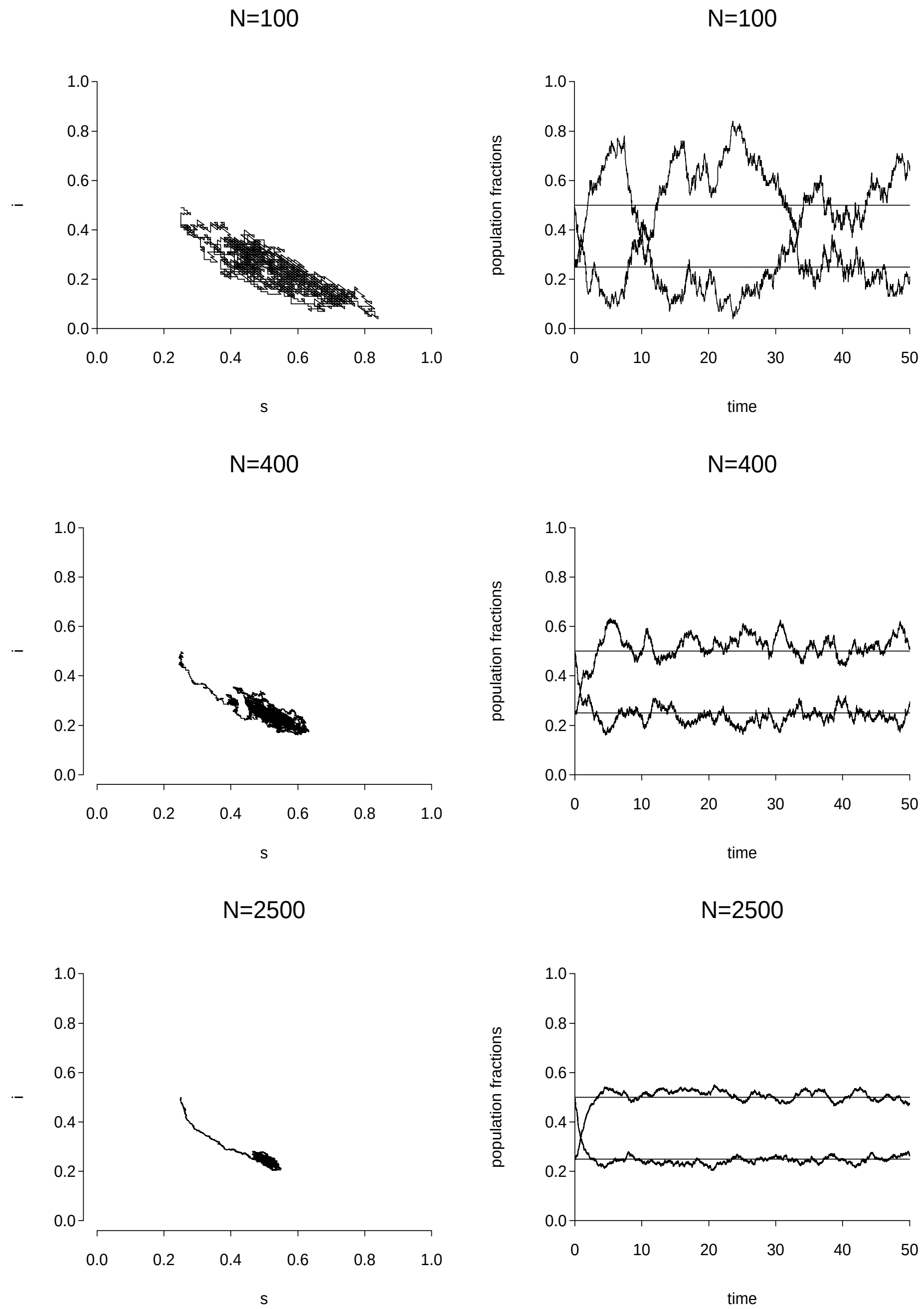
Subcritical Epidemic: $\theta < \rho$



Supercritical Epidemic: $\theta > \rho$



Supercritical Epidemic



Deterministic Approximation

$(\bar{\gamma}_t)_{t\geq 0}$ - solution of mean path ODE,
i.e. $\dot{\gamma} = F(\gamma)$

$\left(\gamma_t^N\right)_{t\geq 0}$ - random path

Theorem 1. *If $\gamma_0^N \to \bar{\gamma}_0$ as $N \to \infty$ then for any $T > 0$*

$$\lim_{N\to\infty} \sup_{t\leq T} |\gamma_t^N - \bar{\gamma}_t| = 0 \quad \textit{a.s.}$$

Supercritical Epidemic

Fluctuations around (s_∞, i_∞)

$$X_t^N := \begin{cases} x_t^1 = \sqrt{N}(s_t^N - s_\infty) \\ x_t^2 = \sqrt{N}(i_t^N - i_\infty), \end{cases}$$

so that

$$\begin{cases} s_t^N = s_\infty + \dfrac{x_t^1}{\sqrt{N}} \\ i_t^N = i_\infty + \dfrac{x_t^2}{\sqrt{N}} \end{cases}$$

Theorem 2. *If* $X_0^N \to_{\mathcal{D}} X_0$ *as* $N \to \infty$ *then* $X^N \Rightarrow X$ *in* $D_{\mathbb{R}^2}[0, \infty)$.

Supercritical Epidemic

Fluctuations around (s_∞, i_∞)

X is generated by $\mathcal{G}$

$$\mathcal{G} = \sum_{i=1}^{2} \mu_i(x) \, \frac{\partial}{\partial x_i} + \frac{1}{2} \sum_{i,j=1}^{2} \sigma_{ij} \, \frac{\partial^2}{\partial x_i \partial x_j},$$

where

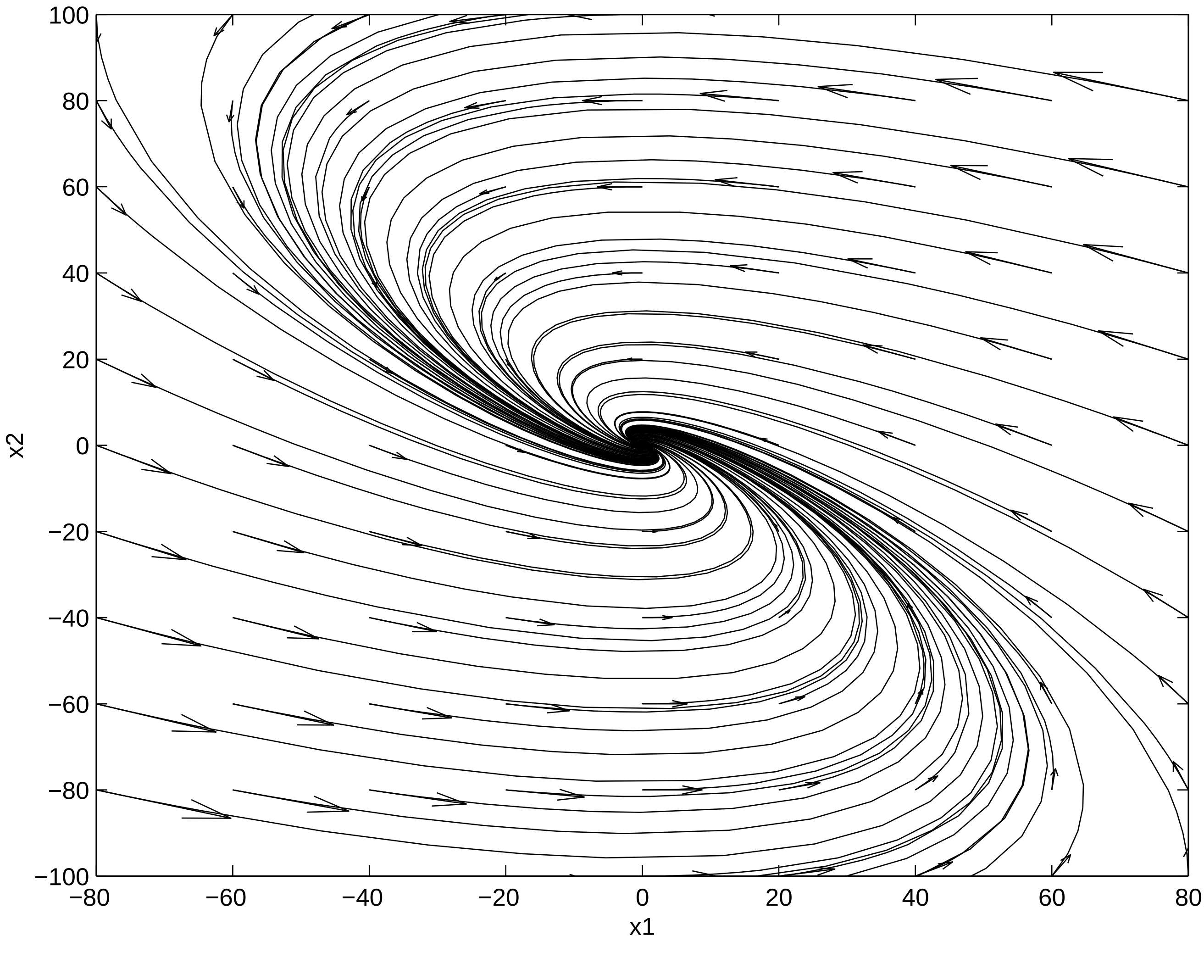
$$\begin{pmatrix} \mu_1(x) \\ \mu_2(x) \end{pmatrix} = \begin{pmatrix} -\frac{1+\theta}{1+\rho} & -(1+\rho) \\ \frac{\theta-\rho}{1+\rho} & 0 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \end{pmatrix},$$

$$\begin{pmatrix} \sigma_{11} & \sigma_{12} \\ \sigma_{12} & \sigma_{22} \end{pmatrix} = \begin{pmatrix} \frac{2\rho(\theta-\rho)}{\theta(1+\rho)} & -\frac{\rho(\theta-\rho)}{\theta(1+\rho)} \\ -\frac{\rho(\theta-\rho)}{\theta(1+\rho)} & \frac{2\rho(\theta-\rho)}{\theta(1+\rho)} \end{pmatrix}.$$

Supercritical Epidemic

Fluctuations around (s_∞, i_∞)

Mean Field

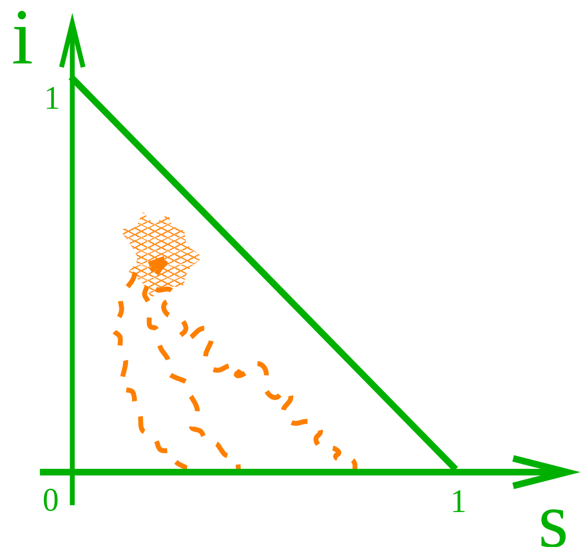


Supercritical Epidemic

Time to Extinction

For all N, infection dies out with prob.1.

How long until this happens?



- If $Y \sim$ Geometric(q) then $\mathbf{E}(Y) = \frac{1}{q}$.

- Connection to "most likely" path.

- Large Deviations for exit paths (LDP).

Large Deviations Principle

Def. Family μ^N satisfy *LDP* on $\mathcal{X}$ with rate function I if

$$
\begin{aligned}
-\inf_{x\in F^\circ} I(x) &\leq \underline{\lim}_{N\to\infty}\frac{1}{N}\log\mu^N(F) \\
&\leq \overline{\lim}_{N\to\infty}\frac{1}{N}\log\mu^N(F) \leq -\inf_{x\in\bar{F}} I(x)
\end{aligned}
$$

for $F\subset\mathcal{X}$.

$Y_t =$ Poisson processes rate m

$y_t^N = N^{-1}Y_{Nt}$ satisfy LDP with rate function

$$
\begin{aligned}
I(y) &= \int_0^T \dot{y}_t \log\left(\frac{\dot{y}_t}{m}\right) - \dot{y}_t + m\,dt \\
&:= \int_0^T f(\dot{y}_t, m)\,dt
\end{aligned}
$$

Time Changed Poisson Processes

$Y_1(t)$, $Y_2(t)$, $Y_3(t)$ are rate 1 PPs

$y_k(t) = y_k^N(t) = N^{-1} Y_k(Nt)$ for $k = 1, 2, 3$

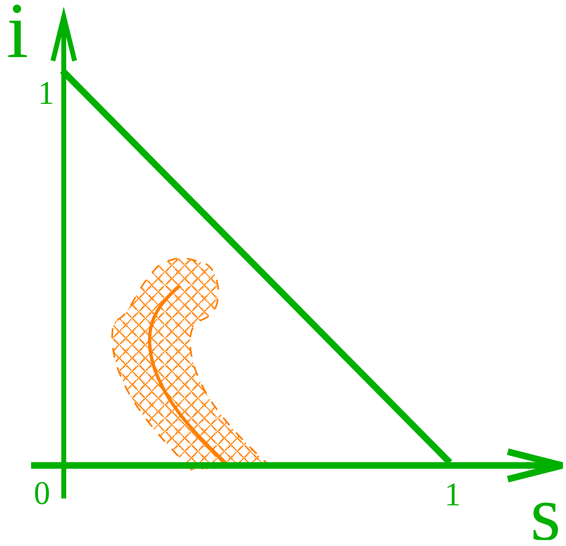
$$s_t = s_0 - y_1\left(\int_0^t \theta s_u i_u \, du\right) + y_3\left(\int_0^t r_u \, du\right)$$
$$i_t = i_0 + y_1\left(\int_0^t \theta s_u i_u \, du\right) - y_2\left(\int_0^t \rho i_u \, du\right).$$

Exit Path LDP

- Why standard methods don't work
  - Contraction Principle

    Cont. $f : \mathcal{X} \to \mathcal{Y}$ & LDP for μ^N on $\mathcal{X}$
    $\Rightarrow$ LDP for $\mu^N \circ f^{-1}$ on $\mathcal{Y}$.
  - Wentzell and Freidlin
- Dangers of diffusion approximations

Exit path LDP



Fix $\gamma = (s_t, i_t)_{t \geq 0} \in \mathcal{AC}[0, T]$

Let $\lambda, \mu, \nu \geq 0$ s.t.

$$\begin{cases} \dfrac{ds_t}{dt} = \nu_t - \lambda_t \\ \dfrac{di_t}{dt} = \lambda_t - \mu_t \end{cases}$$

Exit path LDP

For $\gamma \in \mathcal{AC}[0, T]$

$$I(\gamma) = \inf_{\lambda,\mu,\nu} \int_0^T f(\lambda_t, \theta s_t i_t) + f(\mu_t, \rho i_t) + f(\nu_t, r_t) dt,$$

where

$$f(x, m) = x \log\left(\frac{x}{m}\right) - x + m, \quad x, m \geq 0.$$

Theorem 3. *SIRS processes γ^N satisfy LDP with good rate function $I(\gamma)$,*

i.e.

$$\mathbf{P}^N\left(||\gamma - \tilde{\gamma}||_T < \delta\right) \approx e^{-NI(\tilde{\gamma})}.$$

Time until extinction

$$\tau^N = \text{inf}\{t : i_t = 0\} = \text{time to extinction}$$

$$\bar{I} = \text{inf}_\gamma\, I_\tau(\gamma) = \text{“minimal cost” of exit}$$

In fact,for any $\epsilon > 0$

$$\lim_{N\to\infty} \mathbf{P}^N \left(e^{N(\bar{I}-\epsilon)} \le \tau^N \le e^{N(\bar{I}+\epsilon)} \right) = 1.$$

Conjecture.

$$\lim_{N\to\infty} \frac{1}{N} \log \mathbf{E}\, \tau^N = \bar{I}.$$

SIS Stochastic Epidemic

$$S \longrightarrow I \longrightarrow S$$

- $I_t = \#$ infected at time t,
  $S_t = \#$ susceptible at time t,
  $S_t + I_t \equiv N =$ population size.

- $I_t =$ state of the chain at time t;
  $[N] = \{0, 1, \ldots, N\} =$ state space.

- Continuous time Markov Chain
  with infinitesimal transition probabilities

  $$\mathbf{P}_t^x\Big\{I_{t+h} = x + 1\Big\} = \beta x(1 - x/N)h + o(xh),$$
  $$\mathbf{P}_t^x\Big\{I_{t+h} = x - 1\Big\} = xh + o(xh).$$

Branching Envelope

- When the number of individuals infected is small the epidemic evolves $\approx$ branching process Z_t with infinitesimal transition probabilities

$$\mathbf{P}_t^x\Big\{Z_{t+h} = x+1\Big\} = \beta xh + o(xh),$$
$$\mathbf{P}_t^x\Big\{Z_{t+h} = x-1\Big\} = xh + o(xh).$$

- The death rate x is the same as for the SIS epidemic, but the the birth rate βx dominates the birth rate $\beta x(1-x/N)$ of the SIS process.

- The difference $\beta x^2/N$ = *attenuation rate*.

Noncritical SIS Epidemic

Final Outcome

- Again, LLN
$$\frac{dI}{dt} = \beta I\Big(1 - I/N\Big) - I.$$

- Below criticality $\beta < 1$ and
$$\frac{dI}{dt} = I\left(\beta\Big(1 - I/N\Big) - 1\right) < 0,$$
and the epidemics dies out in finite time.

- Above criticality $\beta > 1$ and if $I = o(N)$
$$\frac{dI}{dt} = I\left(\beta\Big(1 - I/N\Big) - 1\right) > 0 \text{ for large } N,$$
and the epidemic lasts an exponentially long time in N.

Critical Scaling for Branching Envelope

- A near critical branching process when properly renormalized, behaves approximately as a solution of the stochastic differential equation

$$dY_t = \lambda Y_t \, dt + \sqrt{Y_t} dW_t, \tag{1}$$

  where W_t is a standard Wiener process.

- **Feller's theorem (1951).** If $\beta = 1 + \lambda/m$

$$Z^m = Z_{mt}/m \xrightarrow{\mathcal{D}} Y_t \quad \text{as } m \to \infty.$$

Critical Scaling for SIS Epidemic

- The epidemic is *critical* when $\beta = 1$, and *near-critical* when $\beta = 1 + \lambda/\sqrt{N}$.

- Near-critical SIS process $\prec$ by its branching envelope. The corresponding SIS started with $I_0 \sim bN^{\alpha}$ infected individuals cannot have duration longer than $\mathbf{O}_P(N^{\alpha})$ time units.

Critical Scaling for SIS Epidemic

- If the attenuation rate, divided by the scale factor N^α and integrated to time N^α, is $o_P(1)$ then the limiting behavior of $I_{N^\alpha t}/N^\alpha$ should be no different from that of the branching envelope $Z_{N^\alpha t}/N^\alpha$.

  Can show that when $\alpha < 1/2$ it is the case.

- When $\alpha = 1/2$, the accumulated attrition over the duration of the branching envelope will be on the same order of magnitude as the fluctuations, and so the rescaled SIS process should have a genuinely different asymptotic behavior from the branching envelope.

Diffusion Limit for Critical SIS Epidemic

Theorem. If for some constants $\alpha < 1/2$ and $b > 0$ the number of individuals initially infected satisfies $I_0^N \sim bN^\alpha$, and $\beta = 1 + \lambda/N^\alpha$, then

$$I^N_{N^\alpha t}/N^\alpha \xrightarrow{\mathcal{D}} Y_t \text{ as } N \to \infty$$

where Y_t is a Feller diffusion(1) with drift λ and $Y_0 = b$.

If $I_0^N \sim bN^{1/2}$ for some constant $b > 0$ and if $\beta = 1 + \lambda/\sqrt{N}$ then

$$I^N_{\sqrt{N}t}/\sqrt{N} \xrightarrow{\mathcal{D}} Y_t \text{ as } N \to \infty,$$

where Y_t is an *attenuated Feller diffusion* with drift λ and $Y_0 = b$, that is, Y_t is a solution to the stochastic differential equation

$$dY_t = (\lambda Y_t - Y_t^2)\, dt + \sqrt{Y_t} dW_t.$$

Critical SIS Epidemic

Final Outcome

- The size of an epidemic is the total number ξ of new infections during its entire course. Alternatively,
$$S = S^N = \int_0^T I_t \, dt.$$
Can show that the two quantities have the same asymptotic behavior.

- Because the integral above is a continuous functional of the path I_t^N the theorem implies that if $I_0 \sim b\sqrt{N}$ and $\beta = 1 + \lambda/\sqrt{N}$ then
$$S^N/N \xrightarrow{\mathcal{D}} \int_0^{\tau_0} Y_t \, dt,$$
where Y_t is the attenuated Feller diffusion with initial state $Y_0 = b$ and τ_0 is the first passage time to 0 by Y_t.

Critical SIS Epidemic

Final Outcome

- The instantaneous rate $Y_t\, dt$ at which infection time accrues coincides with the rate of change in accumulated quadratic variation of the semimartingale Y_t.

- This suggests the natural time change to a new time scale $s = s(t)$

$$ds = Y_t\, dt,$$

so that $\int Y_t\, dt = \int ds$ is the limit of the rescaled epidemic sizes S^N/N.

Critical SIS Epidemic

Final Outcome

The time-changed process $V_s = Y_{t(s)}$ satisfies the SDE

$$dV_s = (\lambda - V_s)\,ds + d\tilde{W}_s,$$

where $\tilde{W}_s$ is again a standard Wiener process. Setting $U_s = V_s - \lambda$, one gets the SDE for the Ornstein-Uhlenbeck process:

$$dU_s = -U_s\,ds + d\tilde{W}_s.$$

Corollary. If $I_0 \sim b\sqrt{N}$ and $\beta = 1 + \lambda/\sqrt{N}$ then

$$S^N/N \xrightarrow{\mathcal{D}} \tau(b - \lambda; -\lambda),$$

where $\tau(x; y)$ is the time of first passage to y by a standard O-U process started at x.