BIOST/STAT 578 C
Statistical Methods in Infectious Diseases
Lecture 2
January 8, 2009

Reed-Frost model, Greenwood model, chain-binomial model

Today’s Lecture

- History (with pictures and movies)
- Derivation of the model (traditional way)
- Extensions and points about the model

Course Website

- Department Biostat: http://courses.washington.edu/b578a/
- Courses
- BIOS 578A

Reed-Frost Model History

- P. D. En'ko (1889)
- L. Reed & W.H. Frost (1930)
- M. Greenwood (1931)
- H. Abbey (1952)
- L. Elveback, J.P. Fox, E. Ackerman (1960)

Reed-Frost Model

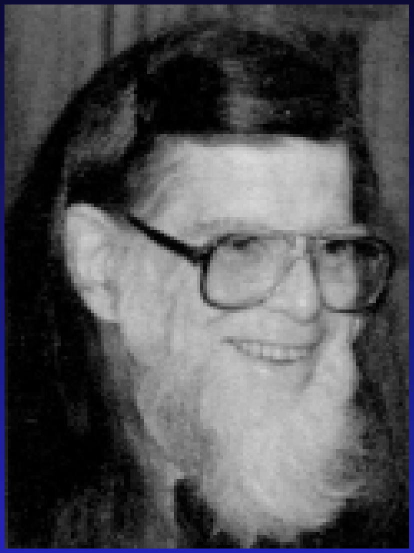
Lowell Reed

1886 - 1966

Wade Hampton Frost
1880–1938

Both Former Deans: Johns Hopkins School of Public Health

Helen Abbey
1915 - 2001

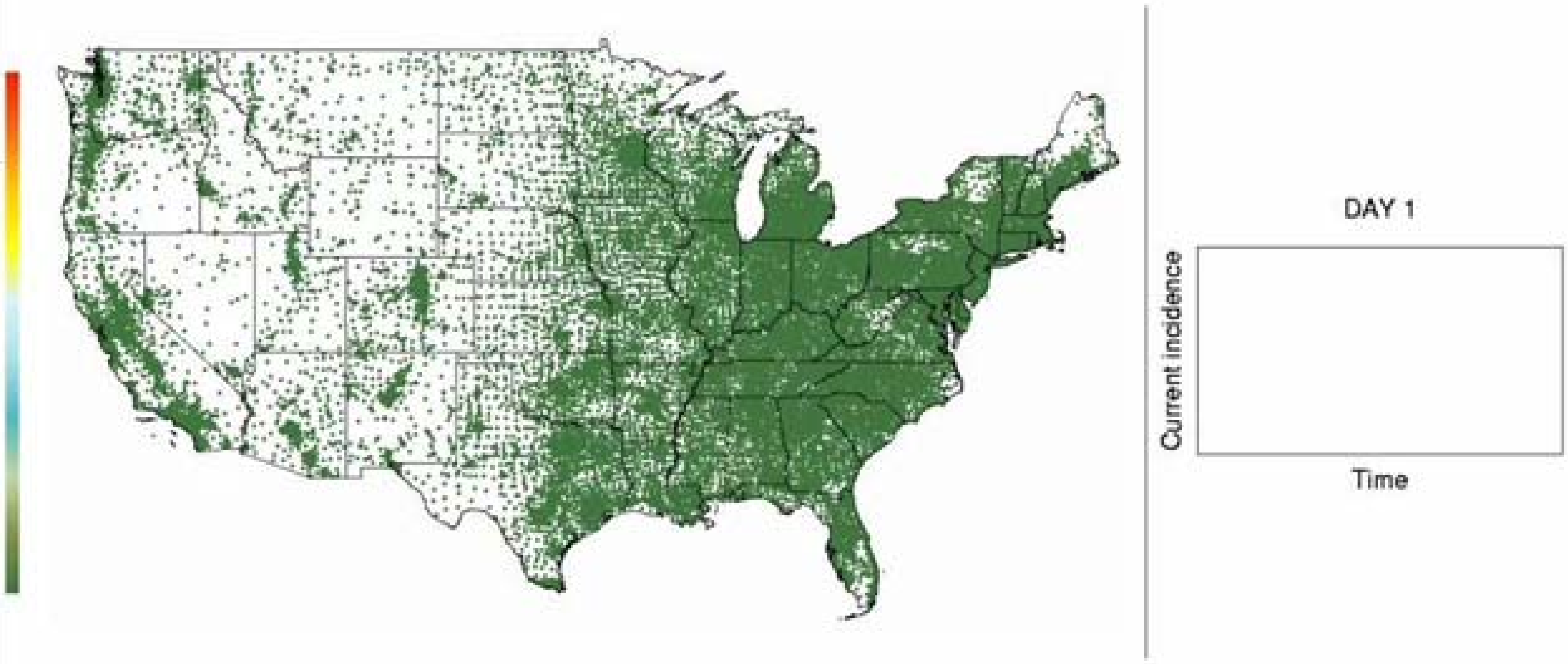


Eugene Ackerman
1920 -

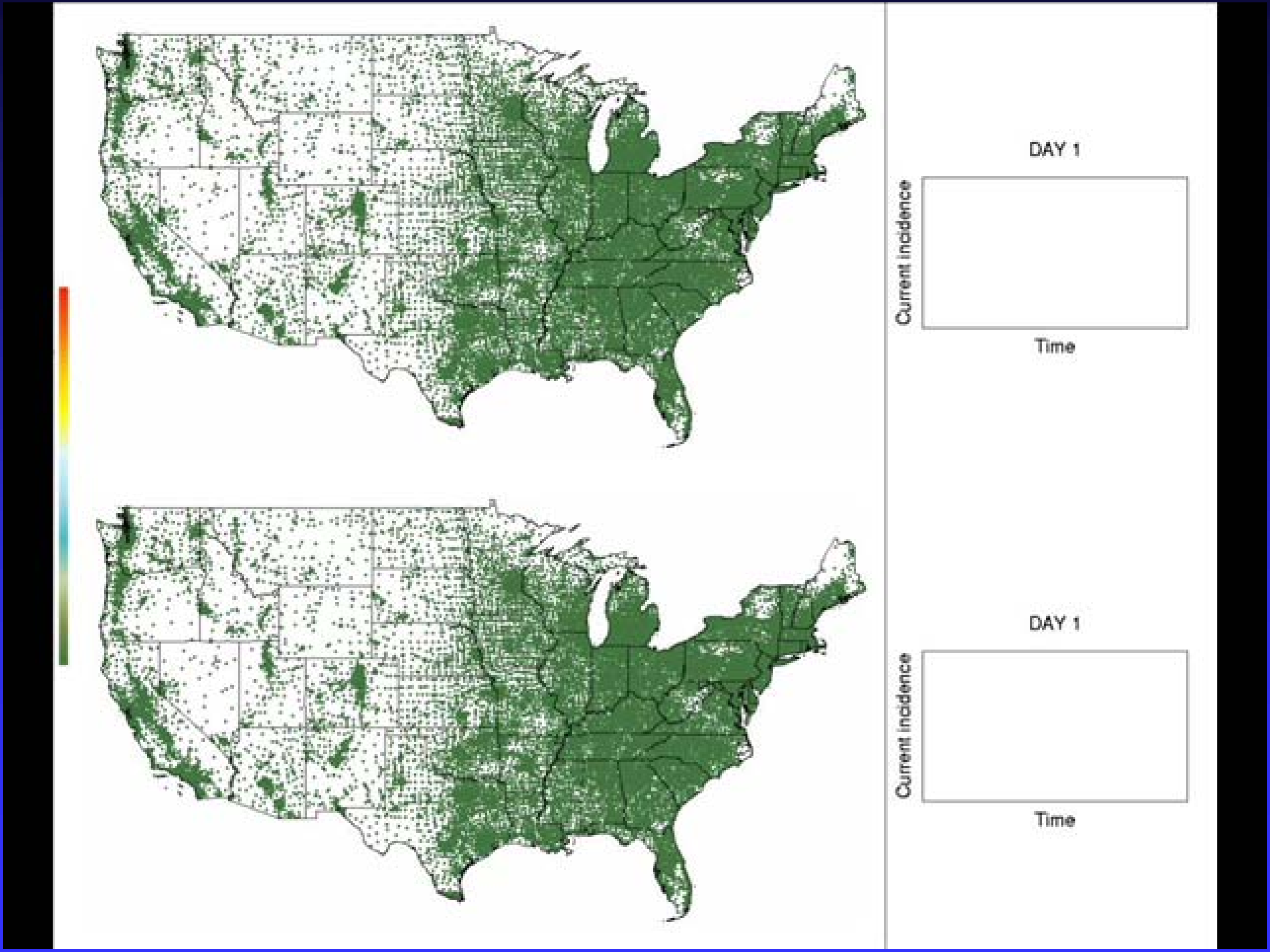
Extensions of the Reed-Frost Model

- Pandemic influenza in entire US
- Containment of pandemic influenza at the source
- Control of endemic cholera in Bangladesh with killed oral vaccines

Pandemic Influenza in the US , $R_0 = 1.9$
Logical Outcome of Reed-Frost Model



Vaccination post-alert; 10M doses/week for 25 weeks of low-efficacy vaccine, R_0 = 1.9

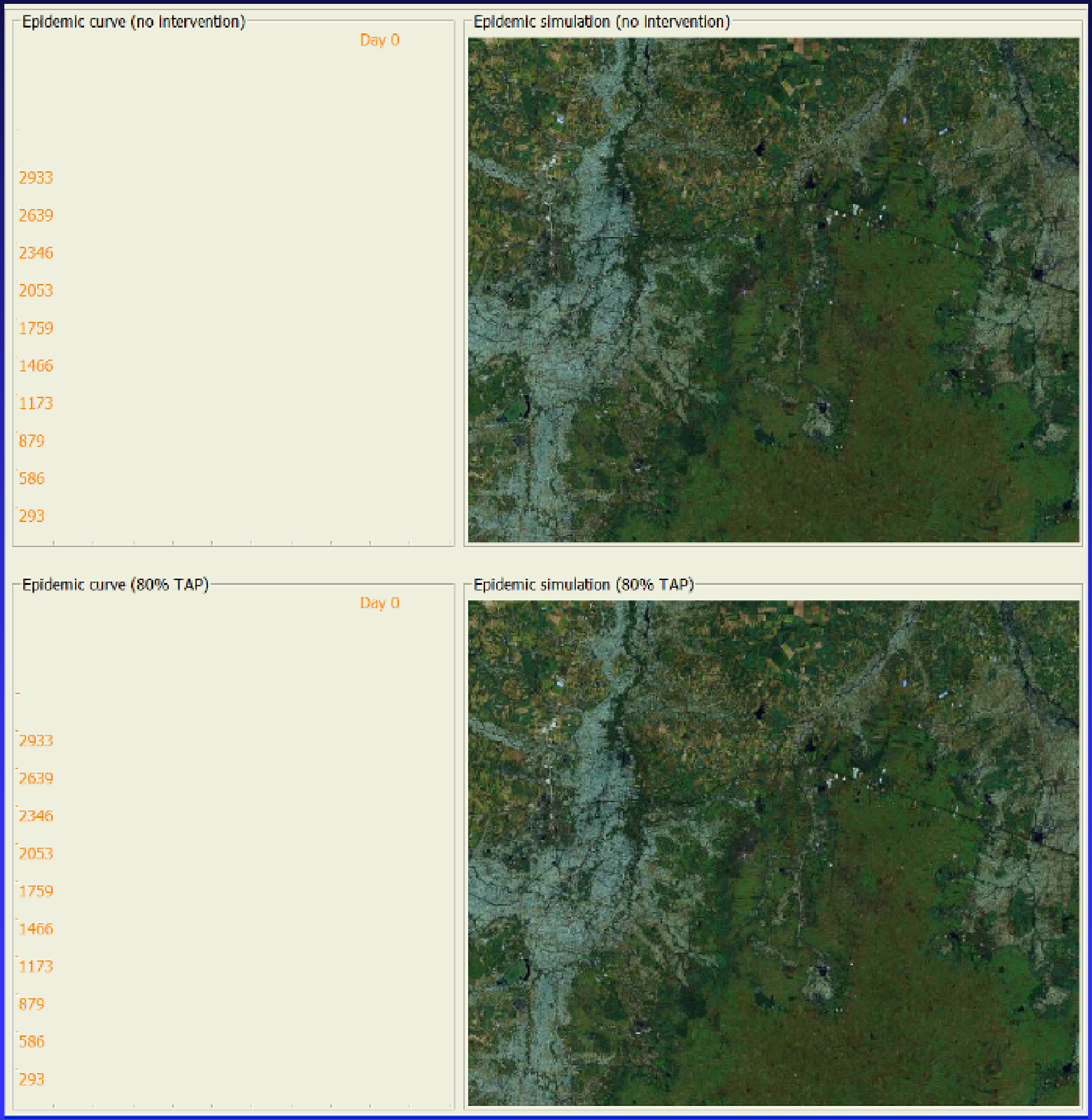


Containment of Pandemic Influenza in SE Asia

Simulated pandemic influenza outbreak $R_0 = 1.4$

Without intervention

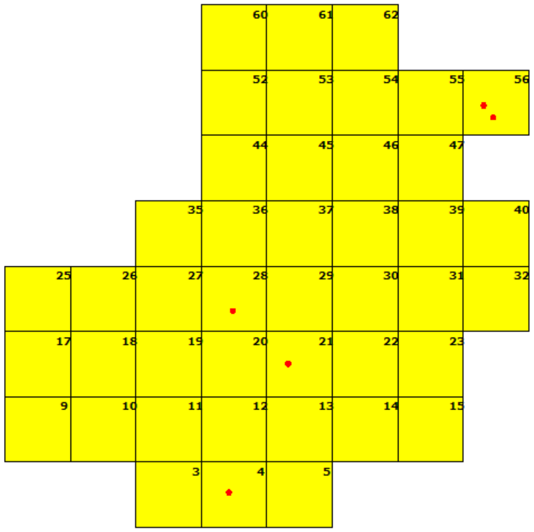
80% TAP



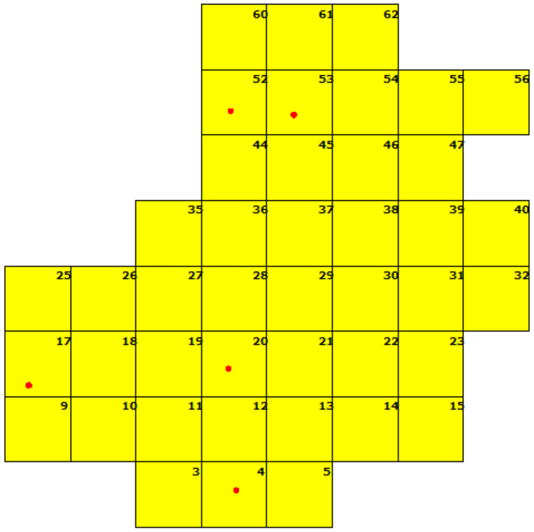
Longini et al. Science 2005; 309: 1083-1087

Cholera in Bangladesh
Control with Killed Oral Vaccine

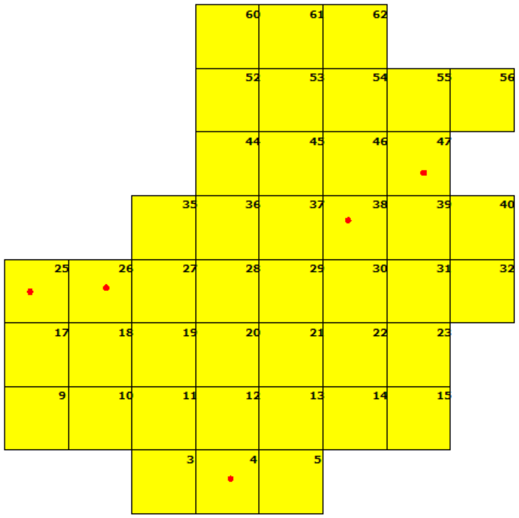
Mass Vaccination: 0 %
Day:1
Red: Infected Blue: Ill

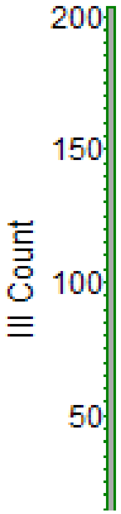


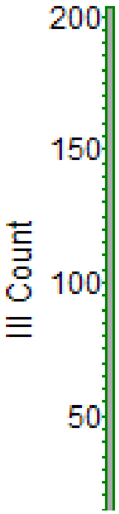
Mass Vaccination: 38 %
Day:1
Red: Infected Blue: Ill

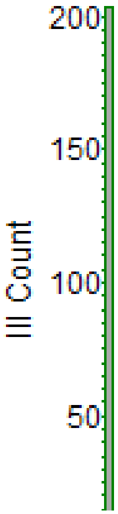


Mass Vaccination: 58 %
Day:1
Red: Infected Blue: Ill









Reed-Frost Model

Stochastic process: discrete state space and time t_0, t_1, t_2 ….

- Infectious agent natural history
  - Infectious for one time unit
- Social contact structure
  - Random mixing
  - $p = 1 - q$, probability two people make contact sufficient to transmit
- $R_0 = (n-1)p$

Reed-Frost Model

$$P(I_{t+1}|S_t, I_t) = \binom{S_t}{I_{t+1}}(1-q^{I_t})^{I_{t+1}} q^{I_t(S_t - I_{t+1})}, S_t \geq I_{t+1},$$

$$S_{t+1} = S_t - I_{t+1},$$

$$R_{t+1} = R_t + I_t,$$

$$S_t + I_t + R_t = n, \forall t,$$

$$P[S(0) = n-1] = 1, P[I(0) = 1] = 1, P[R(0) = 0] = 1$$

$$\{S_t, I_t\}_{t=0,1,\ldots} \ is\ a\ Markov\ chain$$

See chain binomial chapter in the *Encyclopedia Biostat., Vol 1,* 593-7

Greenwood Model

$$P(I_{t+1} \mid S_t, I_t) = \binom{S_t}{I_{t+1}} (1 - q^{I_t})^{I_{t+1}} q^{I_t (S_t - I_{t+1})}, S_t \geq I_{t+1},$$

$$S_{t+1} = S_t - I_{t+1},$$

$$R_{t+1} = R_t + I_t,$$

$$S_t + I_t + R_t = n, \forall t,$$

$$P[S(0) = n - 1] = 1, P[I(0) = 1] = 1, P[R(0) = 0] = 1$$

$$\{S_t, I_t\}_{t=0,1,\ldots} \quad is\ a\ Markov\ chain$$

A Chain

$$I_0 \longrightarrow I_1 \longrightarrow I_2 \longrightarrow \cdots \longrightarrow I_r$$

$$\begin{aligned} P(I_0, I_1, I_2, \cdots, I_r) &= \\ P(I_1 &\mid S_0, I_0) P(I_2 \mid S_1, I_1) \cdots \\ P(I_r &\mid S_{r-1}, I_{r-1}) \end{aligned}$$

$$T = \inf_{t \geq 0} \{t : S_t I_t = 0\}.$$

Example

Possible individual chains when $S_0 = 3,\ I_0 = 1$

Chain $\{i_0, i_1, i_2, ..., i_T\}$	Probability	Final Size R_T
$\{1\}$	q^3	1
$\{1,1\}$	$3pq^4$	2
$\{1,1,1\}$	$6p^2q^4$	3
$\{1,2\}$	$3p^2q^3$	3
$\{1,1,1,1\}$	$6p^3q^3$	4
$\{1,1,2\}$	$3p^3q^2$	4
$\{1,2,1\}$	$3p^3q\,(1+q)$	4
$\{1,3\}$	p^3	4

Reed-Frost Model

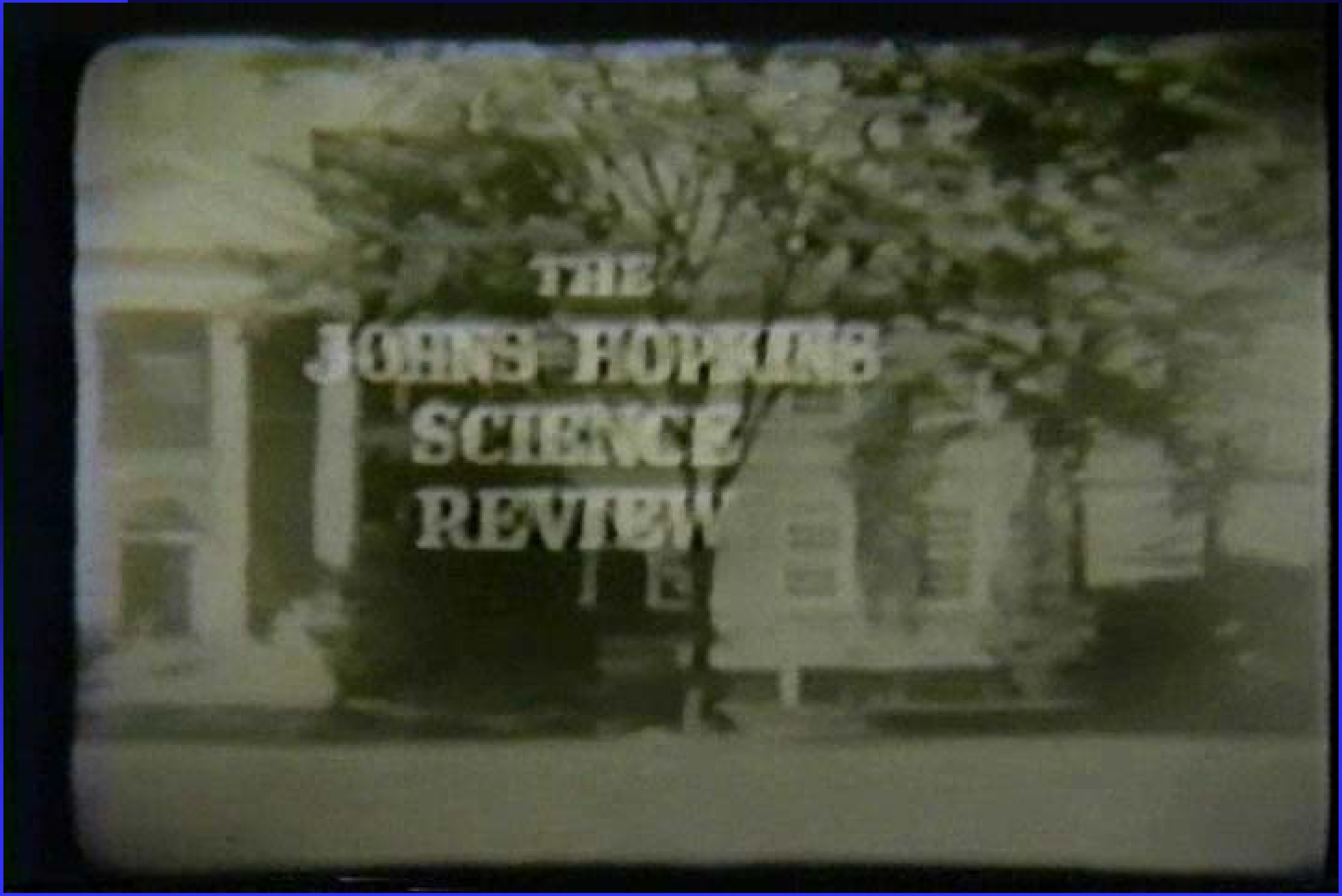
$$\boxed{R_0 = (n-1)p}$$

Threshold theorem:

When $R_0 \leq 1$, then no epidemic,

When $R_0 > 1$, then epidemic with probability $\boxed{\approx 1 - \left(\frac{1}{R_0}\right)^{I_0}}$

Lowell Reed, 1950's



Simulated Reed-Frost Model*

- Start with (S_0,$I_0 \geq 1$)
- For each S_0, generate random number $x \in [0,1]$
- If $x \geq q^{I_o}$, then person becomes infected
- Repeat for next generation and update states
- Stop when $S_0 = 0$ or $I_0 = 0$

*First done by Elveback and Varma (1965)

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                                    CHNBIN.OUT

REED-FROST MODEL

PROBABILITY OF INFECTION =  .200

   1 INITIAL INFECTIVES

   9 INITIAL SUSCEPTIBLES

BASIC REPRODUCTION NUMBER = 2.00

REPRODUCTION NUMBER = 1.80

PROBABILITY OF NO SPREAD =  .134

EPIDEMIC   INFECTED        CHAIN
---------------------------------------
    1         10         1  4  5
    2          3         1  1  1  0
    3          8         1  2  1  2  2  0
    4         10         1  2  4  2  1
    5          5         1  1  2  1  0
    6         10         1  2  3  2  2
    7          1         1  0
    8          8         1  1  2  1  2  1  0
    9         10         1  2  2  1  1  1  1  1
   10          9         1  2  3  3  0
--------------------------------------


DISTRIBUTION OF NO. INFECTED

INFECTED   FREQUENCY   PROPORTION
---------------------------------
    1           1         .100
    3           1         .100
    5           1         .100
    8           2         .200
    9           1         .100
   10           4         .400
---------------------------------

MEAN NUMBER OF INFECTED =   7.40
```

```
                                    CHNBIN.OUT

GREENWOOD MODEL

PROBABILITY OF INFECTION =  .200

   1 INITIAL INFECTIVES

   9 INITIAL SUSCEPTIBLES

BASIC REPRODUCTION NUMBER = 2.00

REPRODUCTION NUMBER = 1.80

PROBABILITY OF NO SPREAD =  .134

EPIDEMIC   INFECTED        CHAIN
---------------------------------------
    1          9         1  1  3  3  1  0
    2          6         1  3  1  1  0
    3          7         1  1  1  2  2  0
    4          1         1  0
    5          5         1  1  1  1  1  0
    6          8         1  1  4  2  0
    7          3         1  1  1  0
    8          2         1  1  0
    9          4         1  3  0
   10          5         1  3  1  0
--------------------------------------


DISTRIBUTION OF NO. INFECTED

INFECTED   FREQUENCY   PROPORTION
---------------------------------
    1           1         .100
    2           1         .100
    3           1         .100
    4           1         .100
    5           2         .200
    6           1         .100
    7           1         .100
    8           1         .100
    9           1         .100
---------------------------------

MEAN NUMBER OF INFECTED =  5.00
```

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                                    CHNBIN.OUT

REED-FROST MODEL

PROBABILITY OF INFECTION =  .200

   1 INITIAL INFECTIVES

   9 INITIAL SUSCEPTIBLES

BASIC REPRODUCTION NUMBER = 2.00

REPRODUCTION NUMBER = 1.80

PROBABILITY OF NO SPREAD =  .134

EPIDEMIC   INFECTED         CHAIN
---------------------------------------
    1         10         1  4  5
    2          3         1  1  1  0
    3          8         1  2  1  2  2  0
    4         10         1  2  4  2  1
    5          5         1  1  2  1  0
    6         10         1  2  3  2  2
    7          1         1  0
    8          8         1  1  2  1  2  1  0
    9         10         1  2  2  1  1  1  1
   10          9         1  2  3  3  0
--------------------------------------


DISTRIBUTION OF NO. INFECTED

INFECTED   FREQUENCY   PROPORTION
---------------------------------
    1           1          .100
    3           1          .100
    5           1          .100
    8           2          .200
    9           1          .100
   10           4          .400
---------------------------------

MEAN NUMBER OF INFECTED =  7.40
```

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                                  CHNBIN.OUT
GREENWOOD MODEL

PROBABILITY OF INFECTION =  .200

   1 INITIAL INFECTIVES

   9 INITIAL SUSCEPTIBLES

BASIC REPRODUCTION NUMBER = 2.00

REPRODUCTION NUMBER = 1.80

PROBABILITY OF NO SPREAD =  .134

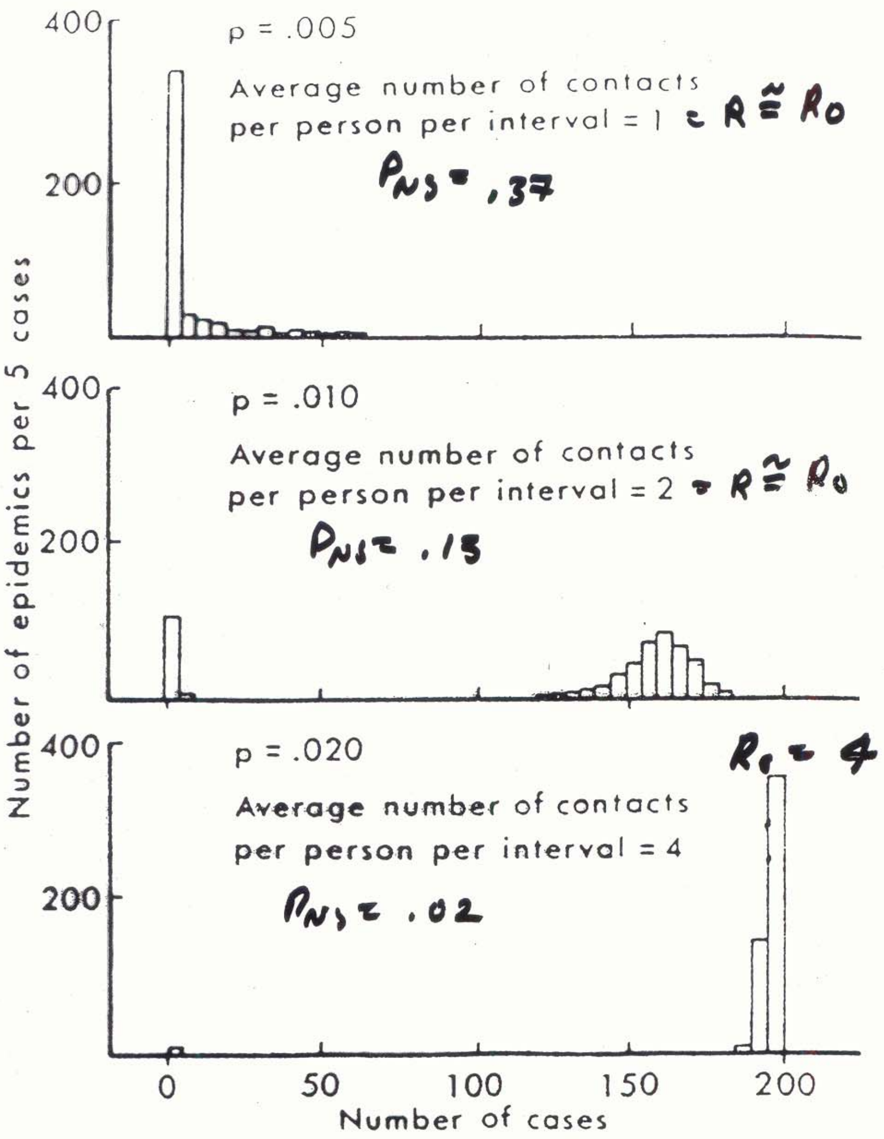
EPIDEMIC   INFECTED         CHAIN
-------------------------------------
    1          9        1  1  3  3  1  0
    2          6        1  3  1  1  0
    3          7        1  1  1  2  2  0
    4          1        1  0
    5          5        1  1  1  1  1  0
    6          8        1  1  4  2  0
    7          3        1  1  1  0
    8          2        1  1  0
    9          4        1  3  0
   10          5        1  3  1  0
------------------------------------


DISTRIBUTION OF NO. INFECTED

INFECTED   FREQUENCY   PROPORTION
-------------------------------
    1           1        .100
    2           1        .100
    3           1        .100
    4           1        .100
    5           2        .200
    6           1        .100
    7           1        .100
    8           1        .100
    9           1        .100
-------------------------------

MEAN NUMBER OF INFECTED =  5.00
```

Figure 3.* Size of epidemics in population of 200 susceptibles in 500 epidemics for each of 3 contact rates



*Source: Elveback and Varma (1965)

Reed-Frost-Greenwood Simulation CHNBIN

- Put CHNBIN.EXE and CHNBIN.OUT in same directory
- Click on CHNBIN.EXE
  - Enter values
- Output will be in CHNBIN.OUT

Inference

Data are usually in the form of observed chains, $\{i_0, i_1, ..., i_r\}$, for one or more populations. Suppose that we have N populations and let $\{i_{k0}, i_{k1}, ..., i_{kr}\}$ be the observed chain for the k^{th} population. Then, the likelihood function for estimating $p = 1 - q$ is

$$\mathsf{L}(p) = \prod_{k=1}^{N} \prod_{t=0}^{r-1} \binom{s_{kt}}{i_{kt+1}} \left(1 - q^{i_{kt}}\right)^{i_{kt+1}} q^{i_{kt}\left(s_{kt}-i_{kt+1}\right)}$$