Smallpox Epidemiology

Determining Important Parameters in Response ot Smallpox Outbreaks

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Epidemiology

Modeling spread of diseases

- Population Models
- Epidemic Aversion

Epidemiology

SIR Model

Basic Model for Population Epidemiology

$$\frac{dS}{dt} = -\beta I S$$

$$\frac{dI}{dt} = \beta I S - \nu I$$

$$\frac{dR}{dt} = \nu I$$

Epidemiology

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- Each variable S, I, R is a percentage of the total population, and thus are non-dimensional.

Epidemiology

SIR Model

Basic Model for Population Epidemiology

$$\frac{dS}{dt} = -\beta IS$$

$$\frac{dI}{dt} = \beta IS - \nu I$$

$$\frac{dR}{dt} = \nu I$$

- Each variable S, I, R is a percentage of the total population, and thus are non-dimensional.
- The only stable solution is trivial (nobody is sick).

Sensitivity Analysis

Goal

To evaluate sensitivy of a model to the parameters describing it, i.e. to determine the amount that the entire model changes when each parameter is altered.

Used in models for which traditional analysis is impossible or inconclusive.

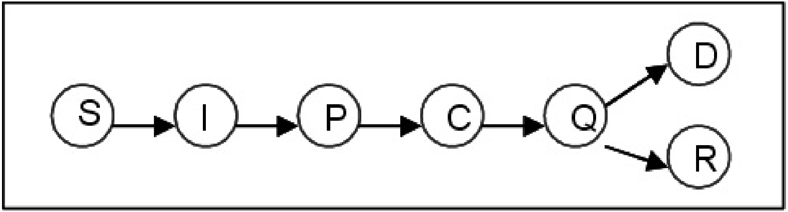
Smallpox Epidemic

Stages of Smallpox

1. Incubation (12-14 days after infection) - not contagious
2. Prodrome (2-4 days) - early symptoms and negligible infectivity
3. Fulminant- rashes appear and the patient is infectious within the next 7-10 days

Scabs fall off after 3 weeks but are still infectious.

Smallpox Epidemic



[1]

[1] Chen, Li-Chiou, et al. "Aligning simulation models of smallpox outbreaks." Intelligence and Security Informatics. Springer Berlin Heidelberg, 2004. 1-16.

Smallpox Epidemic

Base Model

$$\frac{dS}{dt} = -\beta SC$$

$$\frac{dI}{dt} = \beta SC - \sigma I$$

$$\frac{dP}{dt} = \sigma I - \alpha P$$

$$\frac{dC}{dt} = \alpha P - \gamma C$$

$$\frac{dQ}{dt} = \gamma C - \nu Q$$

$$\frac{dD}{dt} = \lambda \nu Q$$

$$\frac{dR}{dt} = (1 - \lambda)\nu Q$$

Smallpox Epidemic

Nondimensionalized Model

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

$$\frac{dI}{dt} = SC - r_0 I$$

$$\frac{dP}{dt} = r_0 I - r_1 P$$

$$\frac{dC}{dt} = r_1 P - r_2 C$$

$$\frac{dQ}{dt} = r_2 C - r_3 Q$$

$$\frac{dD}{dt} = \lambda r_3 Q$$

$$\frac{dR}{dt} = (1 - \lambda) r_3 Q$$

Variables and Parameters

Eight Variables

S - Susceptible
I - Incubating
P - Prodrome
C - Contagious
Q - Quarantined
D - Dead
R - Recovered
t - Time

One Constant

N - Total Population

Note:

$$N = S + I + P + C + Q + D + R$$

Variables and Parameters

Six Base Parameters

β - Rate of Transmission
σ - Frequency of Incubation State
α - Frequency of Prodrome State
γ - Rate of Quarantine
ν - Frequency of the Course of the Disease
λ - Death Rate

Five Nondimensionalized

r_0 - $\frac{\sigma}{\beta}$
r_1 - $\frac{\alpha}{\beta}$
r_2 - $\frac{\gamma}{\beta}$
r_3 - $\frac{\nu}{\beta}$
λ

Numeric Approximation of Solutions

System of ODEs numerically integrated using Matlab from $t = 0$ to $t = 75$.

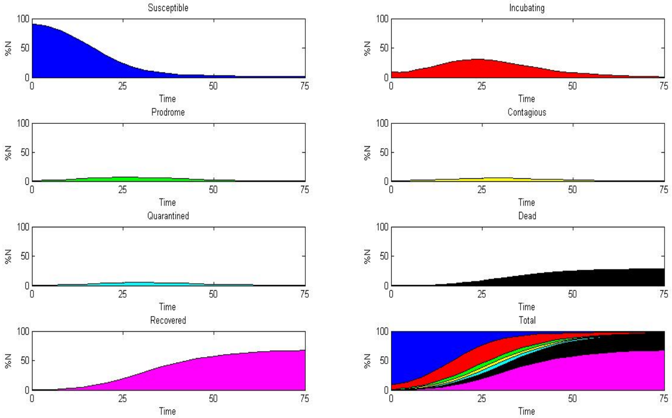
Initial Conditions

$S = 0.9$
$I = 0.1$
All other state vectors zero.
I.E., 10% of population gets infected.

$r_0 = 4.5$
$r_1 = 20$
$r_2 = 25$
$r_3 = 25$
$\lambda = 0.3$

Numeric Approximation of Solutions

System of ODEs numerically integrated using Matlab from $t = 0$ to $t = 75$.



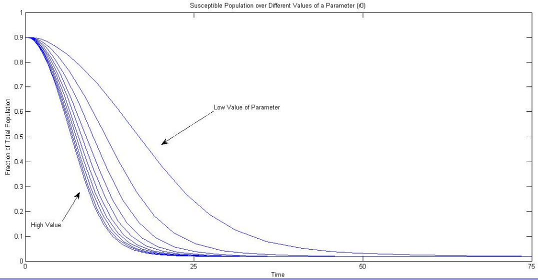
Introducing Discrete Analysis

Solutions of system as one parameter is changed, all others held constant.

Example

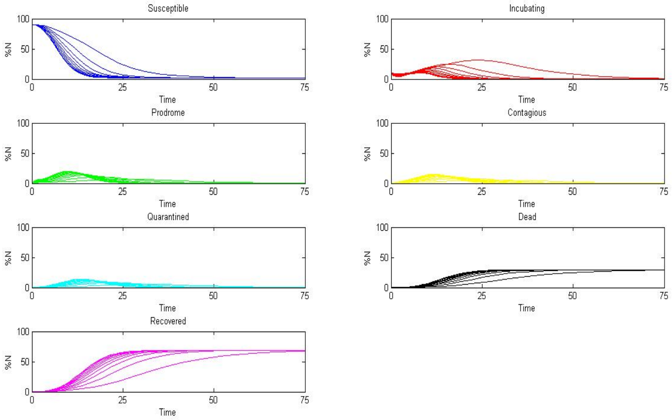
Plots of S, integrated from $t = 0$ to $t = 75$, as r_0 is iterated 10 times greater than its initial value.

S as a function of time at different values of r_0



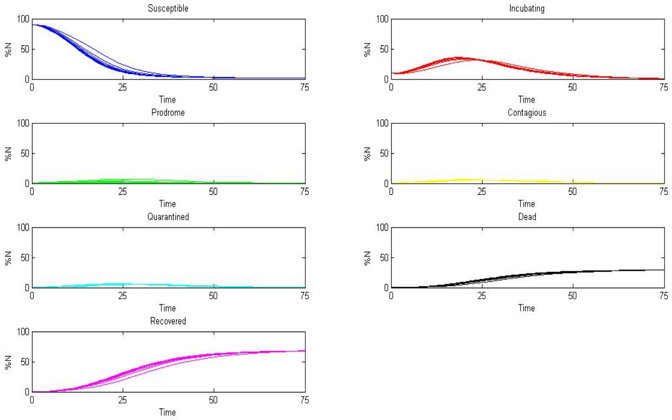
Discrete Graphical Analysis

Change in system as r_0 varies, integrated from $t = 0$ to $t = 75$.



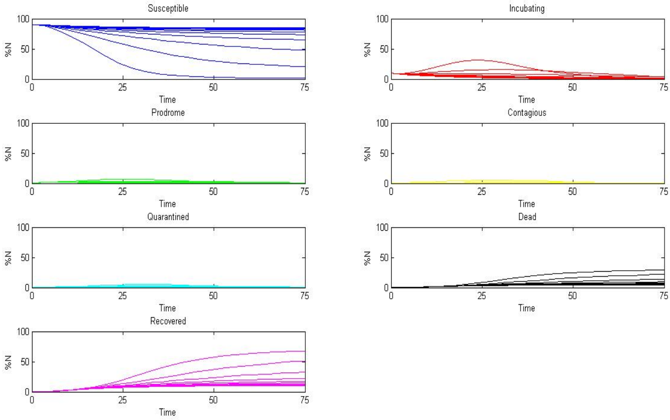
Discrete Graphical Analysis

Change in system as r_1 varies, integrated from $t = 0$ to $t = 75$.



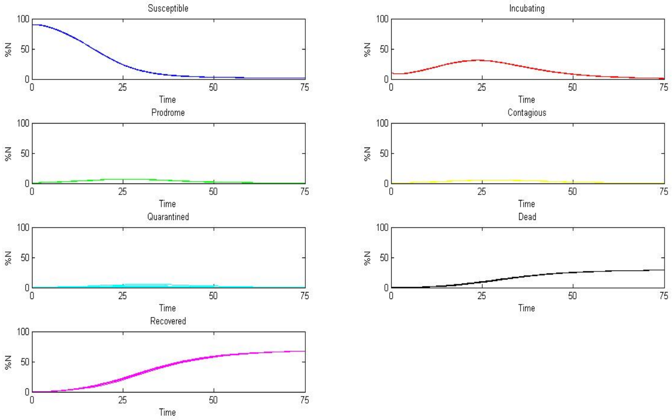
Discrete Graphical Analysis

Change in system as r_2 varies, integrated from $t = 0$ to $t = 75$.



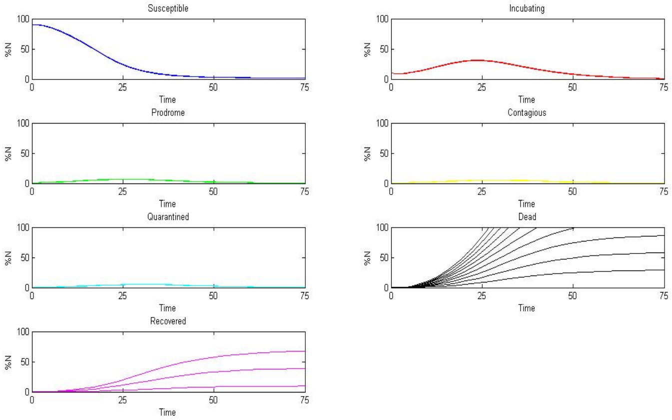
Discrete Graphical Analysis

Change in system as r_3 varies, integrated from $t = 0$ to $t = 75$.



Discrete Graphical Analysis

Change in system as λ varies, integrated from $t = 0$ to $t = 75$.



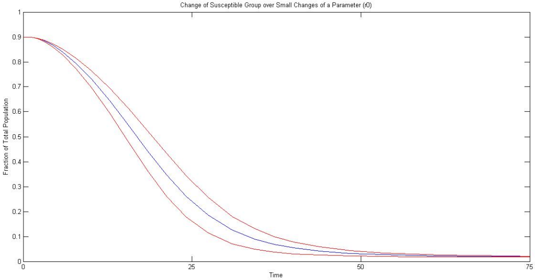
Introducing Continuous Analysis

Analytical bounds determined using numeric solution for $\frac{\partial y}{\partial p}$.

Example

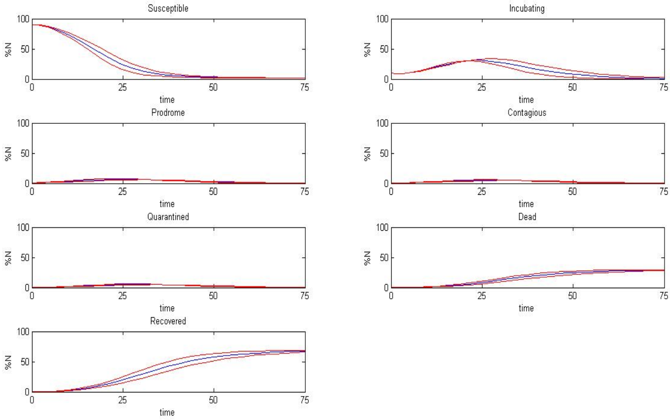
Plot of S, integrated from $t = 0$ to $t = 75$, together with plots of $S \pm \frac{\partial S}{\partial r_0}$.

S as a function of time with bounds for perturbations of r_0.



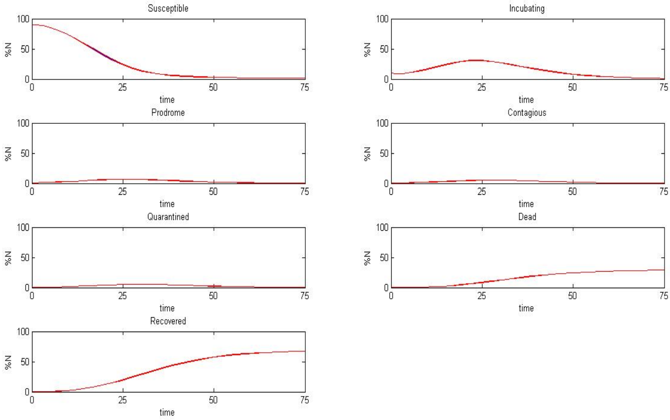
Continuous Graphical Analysis

System with analytic bounds due to perturbations of r_0.



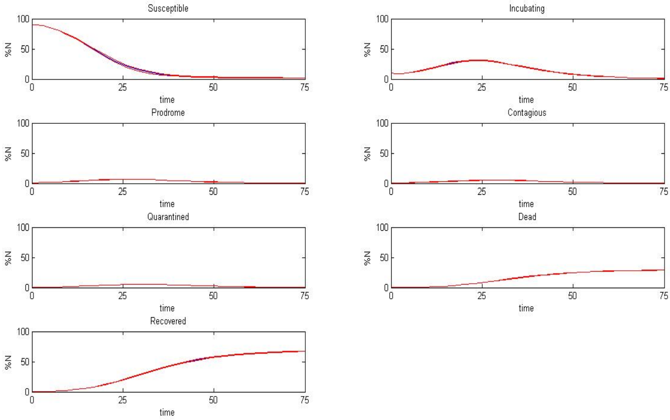
Continuous Graphical Analysis

System with analytic bounds due to perturbations of r_1.



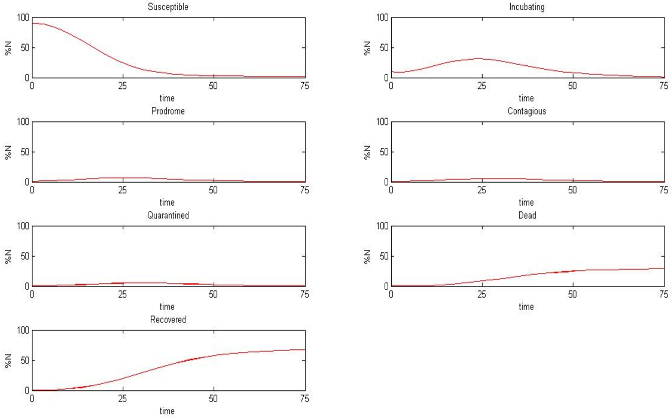
Continuous Graphical Analysis

System with analytic bounds due to perturbations of r_2.



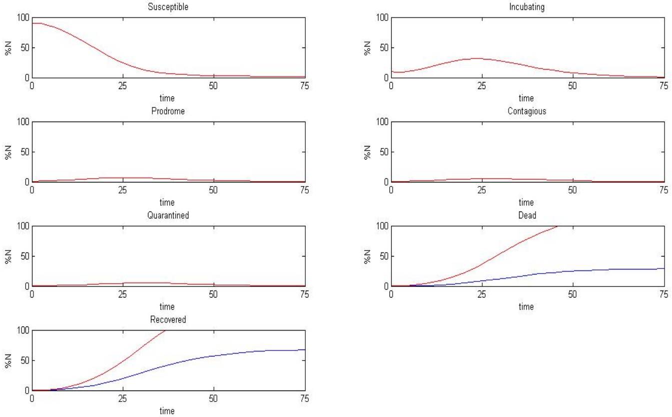
Continuous Graphical Analysis

System with analytic bounds due to perturbations of r_3.



Continuous Graphical Analysis

System with analytic bounds due to perturbations of λ.



Continuous Numerical Analysis

Forward Sensitivity Analysis

Provides analytical bounds to state variables fluctuations with respect to small perturbations in parameter values.

Sensitivity to small perturbations in parameter values is captured using a sensitivity index, η, of a variable y that depends on a parameter p by

$$\eta = \frac{\partial y}{\partial p} \frac{p}{y}$$

Continuous Numerical Analysis

Maximum values over time of η calculated for each variable-parameter pair.

Table : Maximum η Values

	r_0	r_1	r_2	r_3	λ
S	-1.1104	-0.3978	1.5911	-	-
I	-1.7429	0.3199	-0.8148	-	-
P	1.0839	-1.1469	-0.7684	-	-
C	1.159	0.468	-1.6656	-	-
Q	1.0961	0.4444	-0.6916	-0.9844	-
D	0.851	0.3565	-0.412	0.1215	1
R	0.851	0.3565	-0.412	0.1215	-0.4286

Summary

- Picked smallpox model and determined factors affecting transmission.
- Nondimensionalized model, developed code to simulate and solve numerically.
- Determined values for sensitivity index.
- System sensitive to small and large changes of $r_o = \frac{\sigma}{\beta}$.
- System sensitive to large changes of $r_2 = \frac{\gamma}{\beta}$, but not small ones.
- Only D and R are sensitive to λ.

Summary

What does it mean?

- The disease spreads slowest when rates of transmission are low, and when periods of illness are quick.
- Lots of quarantine can significantly slow the spread of infection.
- Progress of the illness after quarantine is inconsequential to the spread of the disease.

Summary

Recommendations

- Medical care should be emphasized for those in initial stages of the disease.
- Rate of transmission should be lowered: vaccination.
- If a quarantine is to be enacted, it should be over a vast majority of the population.