Determining Important Parameters in Response to Smallpox Outbreaks

Project Description

- This study is motivated by the danger of a potential smallpox outbreak in an event of biological warfare.
- Both agent-based and continuous dynamical systems are used to model smallpox transmission [1].
- Parameter analysis is well-documented in studies modeling other diseases [2].
- The goal of this project is finding important factors which can be used to slow the spread of smallpox.

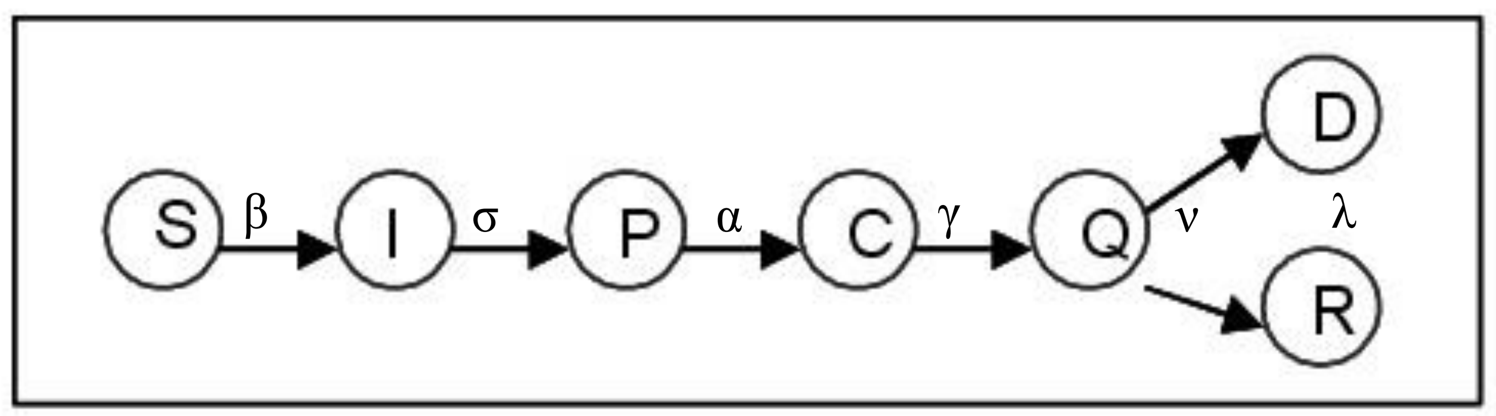

Figure 1. Box diagram of epidemiological model, with population partitions for **S**usceptible, **I**ncubating, **P**rodrome, **C**ontagious, **Q**uarantined, **D**ead, and **R**ecovered [1]. Transition parameters are located between state variables.

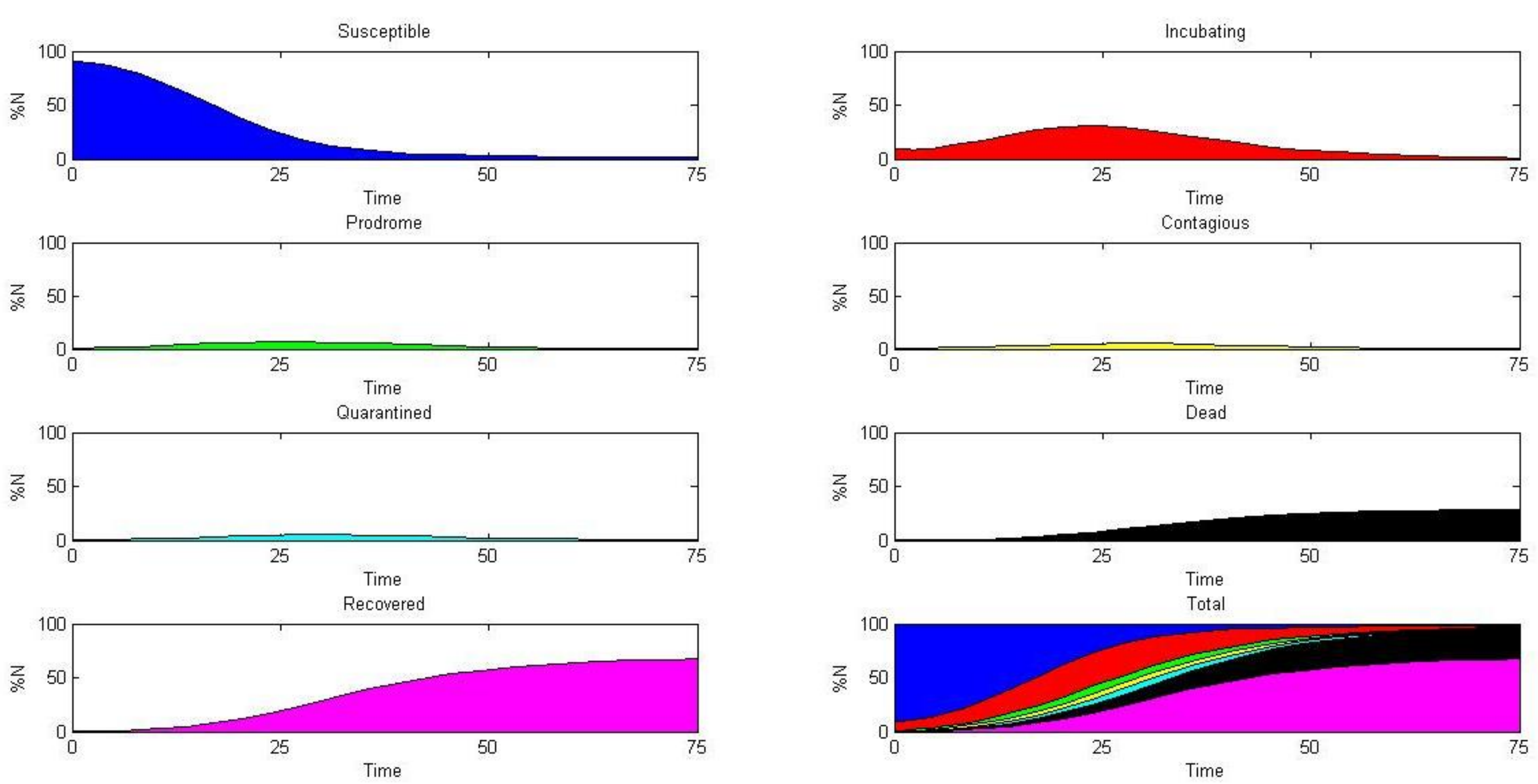

Figure 2. Example of entire model graphed over 75 days, using an initial value of 10% infection. All seven state variables sum to the total population, N, as depicted in the lower-right subplot.

Scientific Challenges

- Forward sensitivity analysis provides analytical bounds to state variables' fluctuations with respect to small perturbations in parameter values.
- Except in rare cases where a closed-form solution to a system is available, sensitivity analysis must be performed numerically.

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Methodology

1. Forward sensitivity analysis is performed on the continuous epidemiological model from Chen et. Al [1] (Fig 1).

2. The stages of smallpox infection determined the parameter values in the model.

3. The non-dimensionalized system of equation is numerically integrated using the ode45 module in Matlab (Fig 2).

4. First, discrete graphical sensitivity analysis is performed using various values for each parameter (Fig. 3).

5. Analytical bounds on fluctuations on the state variables are determined by differentiating the system with respect to a given parameter (Fig 4).

6. Sensitivity to small perturbations in parameter values is captured using a sensitivity index of a variable *u*, that depends on a parameter *p* by $\Upsilon = \frac{\partial u}{\partial p} \cdot \frac{p}{u}$. Maximum values are reported in Table 1.

Results

1. The variables are most sensitive to small changes in R_0. The system is also sensitive to large changes in R_2, but not small ones.

2. Intervention strategies for control of smallpox should focus on slowing transition from incubation, and decreasing rates of transmission.

3. Quarantine can have a significant affect on the spread of the disease, but only if undertaken in a large percentage of the population.

	R_0 (σ / β)	R_1 (α / β)	R_2 (γ / β)	R_3 (ν / β)	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

Table 1. Sensitivity indices of Parameters for smallpox model shown relative to the stages in the process of smallpox transition. Higher values correspond to higher sensitivity; dashes represent no dependence on a particular parameter.

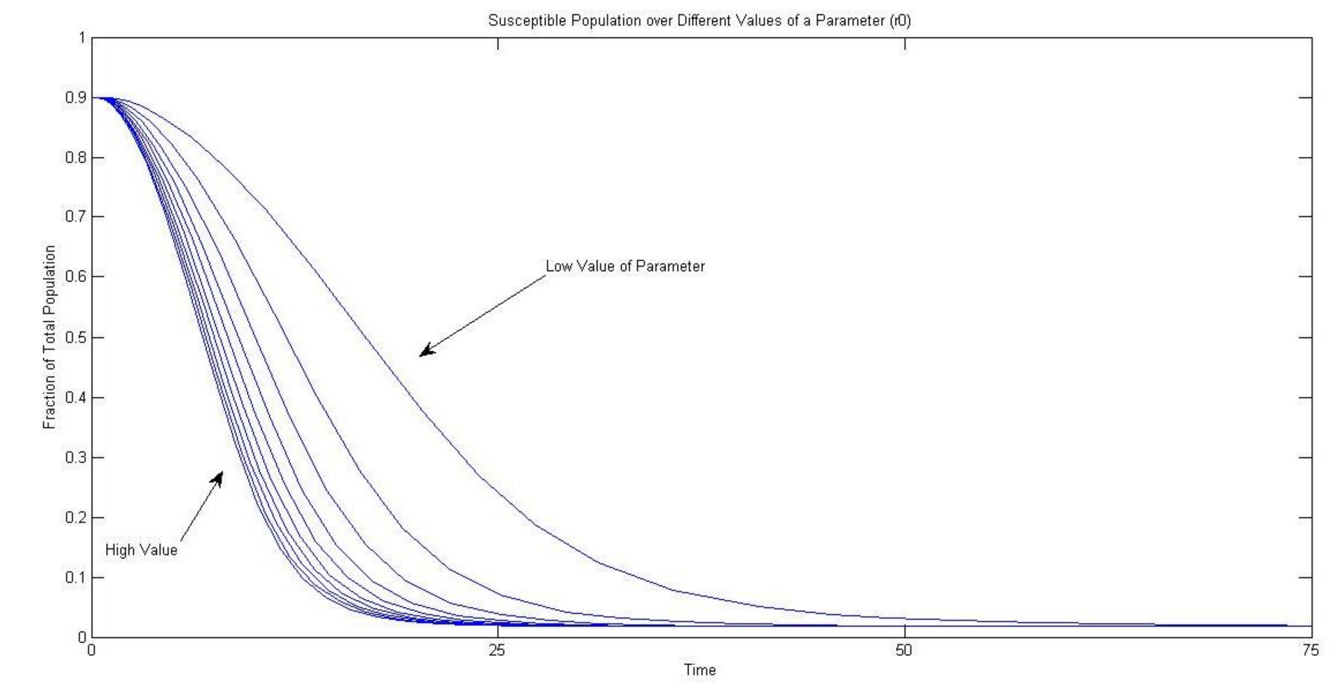

Figure 3. Discrete analysis of a state variable (S) as it changes with various values of a parameter (R_0).

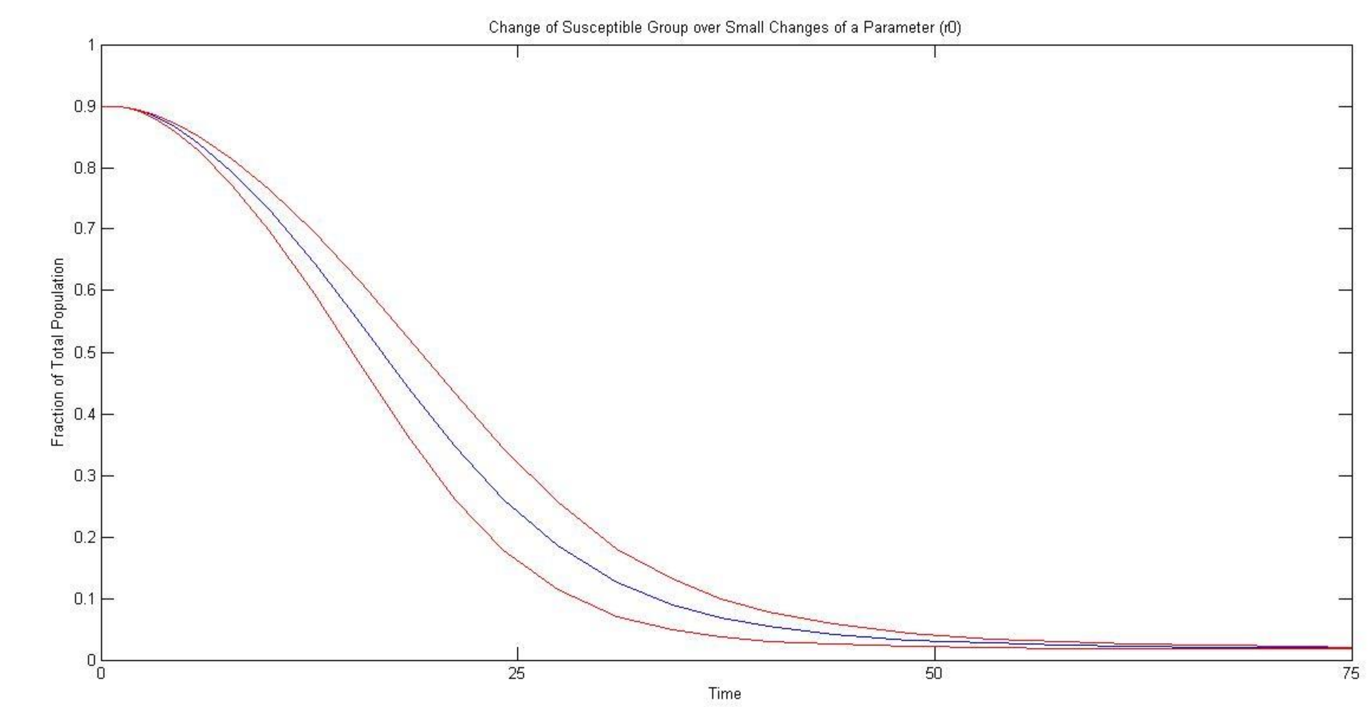

Figure 4. Dynamics of one variable (S) with maximum and minimum effect as a parameter (R_0) changes.

Potential Applications

- This study can be used to determine optimal quarantine procedure and treatment of infected individuals.

References

1. Chen, L. et. al. Aligning Simulation Models of Smallpox Outbreaks. Lecture Notes in Computer Science. 3073 (2004) 1-16.
2. Nakul Chitnisa, James M. Hyman, Jim M. Cushing, Determining Important Parameters in the Spread of Malaria Through the Sensitivity Analysis of a Mathematical Model, Bulletin of Mathematical Biology (2008) 70: 1272–1296

Acknowledgments

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