Optimal Vaccination Strategies for the Control of Epidemics in Highly Mobile Populations

Petter Ögren [1]
Division of Optimization and Systems Theory
Department of Mathematics
Royal Institute of Technology
S-100 44 Stockholm, Sweden

Clyde F. Martin [2]
Department of Mathematics
Institute of Environmental and Human Health
Texas Tech University
Lubbock, 79409 Texas

Abstract

Our goal is to calculate optimal vaccination patterns for a rapidly spreading disease in an urbanized highly mobile population. The goal being to determine if vaccination can effect a disease for which there is low immunity in the population. Different types of structured SIR models are investigated. We construct a model appropriate for a traveling urbanized population and introduce a control in terms of a vaccination program. Linear constraints, a quadratic cost on the control and a linear cost on the number of infected are imposed. In this setting we calculate optimal vaccination patterns using the maximum principle of Pontryagin.

1 Introduction

The classical model for the spread of an infectious disease is the SIR model introduced by Kermack and McKendrick [1]. It is in the form of three coupled ordinary differential equations corresponding to the three states susceptible, infected and immune. The model has been extended in many ways to incorporate e.g. mortality and fertility or population structure by age, sex and spatial distribution. In this text we will concentrate on one such extension, although the theory is equally well applicable to the other ones. We divide the population into smaller groups that have something in common that makes them influence other groups in a similar way. The situation we are mainly interested in is the spread of a disease from city to city by means of travelers. We investigate four different versions of modeling the spread and find one that seems to fit our setting. In this model we introduce a control in terms of a vaccination program.

This project was motivated by the need to understand how an epidemic progresses through a nation or through the world using the air routes as the primary means of transport. Within the next two decades we will almost surely see a new version of a highly infectious influenza virus originate in the Orient. The scenario which we might face is the following. A passenger boards a Boeing 777 in Hong Kong bound for Los Angles knowing that he has a slight fever and the aches and pains associated with the common cold. During the flight he develops a cough and an intestinal disturbance. In the 15 hours that the plane is in the air he visits the toilets many times. By coughing he is spreading virus particles throughout the plane. By the time the plane lands in Los Angles 350 passengers have been exposed to a new strain of virus and because it is new 90% will become infectious within 36 hours. More than half board flights to cities throughout the Untied States. 48 hours after landing the original passenger becomes very ill and reports to a local hospital. Standard symptomatic treatment is begun but to no avail. The passenger dies 96 hours after landing. An alert physician notes that the disease appears to be influenza and sends samples to the Center for Disease Control in Atlanta, Georgia. At the same time the CDC is receiving reports of hundreds of new cases

[1] Corresponding author. email: petter@math.kth.se; fax: +46 8 22 53 20. Supported in part by the Bernt Järmark Foundation

[2] Supported in part by grants from the National Science Foundation, ECS 9705312 and 9720357

of an influenza like disease in widespread cities in the United States and the World Health Organization is receiving reports of widespread deaths around the world. It is determined that the influenza strain is close to a known strain and an existing vaccine might be partially effective. Can we institute a vaccination program that will slow the spread and minimize the number of dead from this epidemic?

Our task is to find an optimal vaccination strategy for our model. In order to make the question of optimization meaningful we have to agree on a cost function. We put a linear cost on the total time spent sick and a quadratic cost on the number of vaccine doses used. Furthermore we allow general linear constraints on the vaccination, i.g. limited maximal vaccination per group or a limited supply shared by a number of groups. With the help of the Maximum Principle of Pontryagin we can then find an optimal control strategy.

This paper is organized as follows: In section 2 we find and investigate a model for the spread of the disease. In section 3 we apply the maximum principle to our equations and finally, in section 4 we display simulation results.

2 Structured SIR Models

A natural way of taking into account the differences between individuals in a population model is to introduce subpopulations of some kind. That is subgroups of individuals with some common factor that makes them influence other subgroups in a similar way. Examples are age and location. The general subpopulation SIR model takes the following form [2], with the differences accounted for in different forces of infection.

$$\begin{aligned} \dot{S}(i) &= (-\lambda(i) - \frac{q(i)}{N_i})S(i) \\ \dot{I}(i) &= \lambda(i)S(i) - \gamma I(i) \\ \Big(\dot{R}(i) &= \gamma I(i) + \frac{q(i)}{N_i}S(i)\Big) \end{aligned}$$

where:

$S(i)$ – is number of Susceptibles in i'th group
$I(i)$ – is number of Infected in i'th group
$R(i)$ – is number of Removed in i'th group
$\lambda(i)$ – is force of infection, (see below)
$q(i)$ – is vaccination rate (or isolation rate)
γ – is recovery rate (or death rate)

Since the population in every subgroup is constant the last equation is redundant. Note that the vaccination could equally well be isolation and that recovery could be death. The important thing is that in these cases the recovered/dead/vaccinated/isolated are *removed* from the system.

2.1 Forces of infection

There are some different ways to model the way the subpopulations influence each other. The ones below all have the nice property that in case of just one subpopulation they simplify to $\lambda = \frac{\alpha I}{N}$ i.e. the same as the unstructured SIR model. The first three below are standard models. They all seem to be somewhat inappropriate when the subgroups differ significantly in population size. Therefore we use a fourth to model an urbanized situation with different population sizes.

$$\begin{aligned} \lambda_1(i) &= \alpha \sum_{j=1}^{n} \frac{c_{i,j} I(j)}{N_i} \\ \lambda_2(i) &= \alpha \sum_{j=1}^{n} \frac{c_{i,j} I(j)}{N_j} \\ \lambda_3(i) &= \alpha \sum_{j=1}^{n} \frac{c_{i,j} I(j)}{N_{Tot}} \\ \lambda_4(i) &= \alpha \sum_{j=1}^{n} (\frac{M_{i,j}}{N_i} \frac{I(j)}{N_j}) \end{aligned}$$

Where:

N_i – is size of subgroup
α – is infectiousness
$c_{i,j}$ – is a contact rate between the subgroups
$M_{i,j}$ – is number of travelers between subgroups

Lets look at the different forces of infection in detail:

λ_1 (From [2]) The force is independent of the actual population size and depends only on the number of sick. This could correspond to doctors being contacted by infected people while the uninfected mind there own business.

λ_2 (Proportions, from [4]) Each individual is in contact with a certain number of others from each subgroup, independently of the subgroups size. In other words, a subgroup influences other groups independently of it's size.

λ_3 (Scaled Mass Action) This is a decent model when all subpopulations are equally mixed, e.g in an age structured model. But if we're looking for a model where adjacent subgroups influence each other a lot and others not at all its still inadequate.

λ_4 (New) None of the above three forces of infection take into account the sizes of both the influenced and the influencing populations disregarding the rest. This is a reasonable such force. Since we are aiming for a traveler type of contact rate we replace the ordinary and vague rate $c_{i,j}$ with the actual number of travelers: $M_{i,j}$. In this way the influence of another population is proportional to both the fraction of infected in that population and how big the number of travelers are compared to the whole population being influenced.

To evaluate and compare these four λ's we simulate the spread of the disease in a graph with four nodes corresponding to two major cities and two smaller ones (fig 1).

The subpopulations are connected in a hub fashion with one in the middle. The population sizes are 1000 for the two big and 100 for the two small populations. The contact rates and number of travelers reflect the graph and can be found in table: 1.

The initial conditions are 10% infected in one of the cities (Subpopulation 1) and 100% susceptibles in the rest. The results are seen in (Figure 2-5). When viewing the plots, remember that the

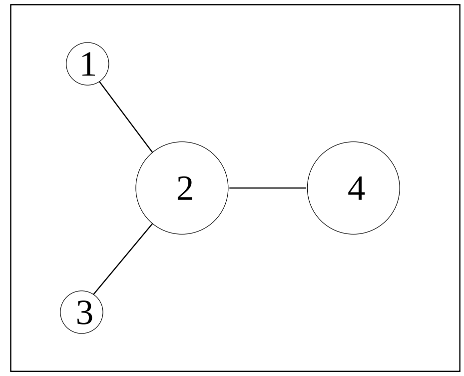

Figure 1: The 4 city setting in which to evaluate the different λ_i's.

	$c_{i,j}$	$M_{i,j}$
i,j adjacent	0.1	10
i,j not adjacent	0	0
$i=j$	1	$N_i - \sum_{i \neq j} M_{i,j}$

Table 1: Contact Rates and Travelers in evaluation setting

susceptibles are monotonically decreasing, the removed are increasing and the infected usually display a local maximum.

A reasonable order of infection is 1,2,3 and 4. As can be seen λ_4 is the only alternative yielding such a result and is therefore used from now on.

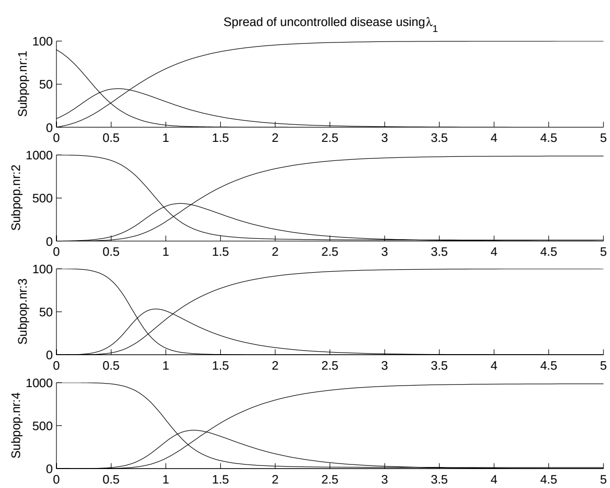

Figure 2: λ_1: Note that the spread in subgroup 3 is faster than in subgroup 2

2.2 Airport Graph Structure

Now lets look at the model applied to some real traveling and population data. In a paper by Longini, [3] we find such air travel statistics. Al-

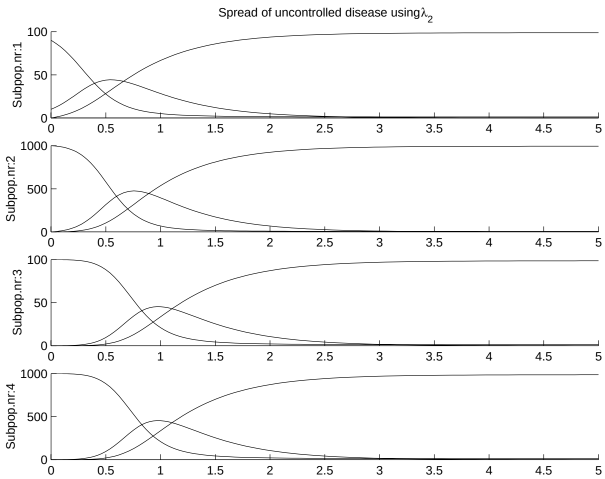

Figure 3: λ_2: Note that the spread in subgroup 3 is identical to subgroup 4

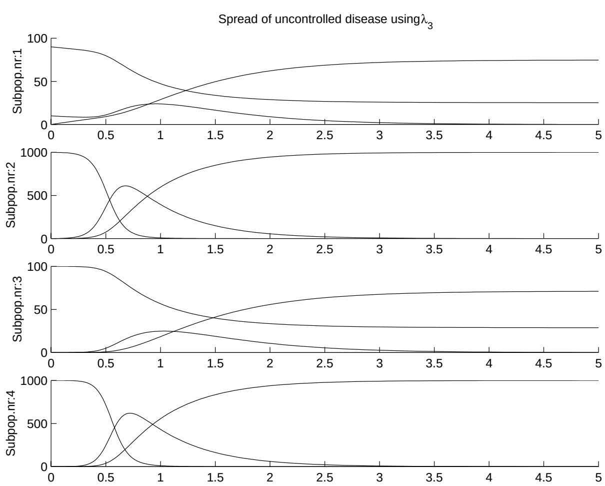

Figure 4: λ_3: Note how the mass action saves the smaller populations

though the numbers are a little bit old (1969) they will serve our purposes well. We choose six European and six American cities with the following data: (tables 2, 3).

Using λ_4 an epidemic starting in San Francisco spreads like this: (fig 6) Note how the intense air traffic in the US propagates the disease, while the less evolved traveling of Europe delays it. Still, with no vaccination there is only a question of time until the majority of the population is contaminated.

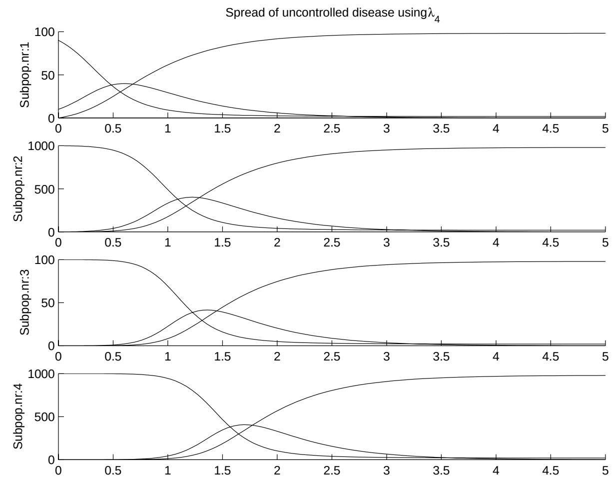

Figure 5: λ_4: Note how the disease spreads in a reasonable order

City	Population	Travelers per day			
London	7400000	L	980	110	40
Paris	8200000		P	150	30
Rome	2800000			R	2
Berlin	3200000				B
Madrid	2900000				
Stockholm	970000				
New York	11570000				
Los Angeles	7000000				
Houston	1230000				
Chicago	7800000				
San Francisco	3700000				
Atlanta	1260000				

Table 2: Population statistics from 1969

3 The Optimization Problem

A natural thing to minimize is $\int_0^T I(t)dt$ e.g the total time spent sick in the population. This is a good measure of the population inconvenience and it's also proportional to costs for time spent in a hospital or time not on the job. Since $\gamma I(i)$ is a term in $\dot{R}$ it is also proportional to the total number of people who endured the disease. Thus it is a good measure in the case of a deadly disease as well. This approach would obviously lead to a maximal vaccination effort at all times. But suppose the vaccine is expensive, then you must make

Average number of travelers per day							
M	S	NY	LA	H	C	SF	A
170	120	420	130	40	80	6	40
200	50	220	30	7	20	6	0
70	11	120	50	0	50	0	0
5	8	10	0	0	0	5	0
M	14	140	40	0	0	0	0
	S	50	0	0	0	0	0
		NY	1780	450	1340	1090	1020
			LA	340	1900	3500	1370
				H	450	220	790
					C	1520	1240
						SF	910
							A

Table 3: Airline statistics from 1969

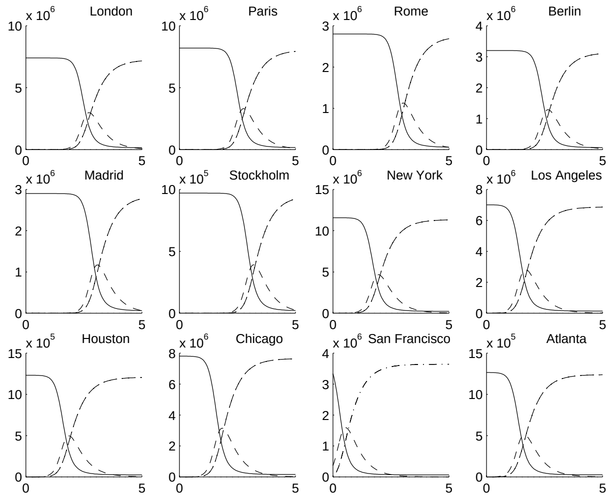

Figure 6: Spread through Airports, note the jump from the USA to Europe

a tradeoff between the two costs. This is realized in terms of adding a function of u in the integral above.

We choose a quadratic cost on the control or a combination of quadratic and linear. A pure linear cost would lead to bang-bang control i.e. jumps in vaccinations between subpopulations.

Thus the problem is as following. Minimize:

$$\int_{t_0}^{t^1} \Big(\frac{1}{2}q^T Aq + q^T b + \sum_{i=1}^{n} I(i)g(i)\Big)dt$$

when: $\dot{S}(i) = (-\lambda(i) - \frac{g(i)}{N_i})S(i)$, $\dot{I}(i) = \lambda(i)S(i) - \gamma I(i)$ and $x(0) = x_0$, $x(T) = \text{free}$, $A -$ positive semi definite nxn matrix, $q \in Q$, the admissible set of controls.

3.1 The Optimal Control

The control q is given by

$$\min_{q\in Q}\Big(\frac{1}{2}q^T Aq + q^T b + \sum_i -y_S(i)S(i)\frac{q(i)}{N_i}\Big),$$

where $y_S(i)$ are the costates. We can thus allow linear constraints on the control vector and still have it a continuous function of the states and costates. Linear constraints can either be a maximum on each control term or, more interesting, a limit on the joint resources of vaccines. Thus more vaccination in one place means less in another. With such a limit we also have to make the positivity constraint explicit. If we choose the unconstrained case on the other hand, any optimal control will contain only positive values.

4 Results

Now lets see some results of applying the algorithm. When viewing the graphs, remember that the susceptibles are monotonically decreasing, marked by undashed lines. The removed are marked by dash-dotted lines and increase. The dashed lines are the infected and they usually display a hump. Finally, the vaccination intensity is dotted. To emphasize the effect of vaccination we draw two curves for the removed. One for only those recovered from the disease and one for the total number of removed (i.e. including the vaccinated).

4.1 The four subpopulations example

We first look at the setting we used to compare the different forces of infection. With a max constraint on each control term, $q_i \leq 200$ we get the following result: (fig 7). Note the difference in numbers of recovered and vaccinated respectively. The 200 maximum penalizes the larger populations and subpopulation number 3 is the only one where a majority never gets infected. If we instead have a common supply to the four populations in terms of a linear constraint: $\Sigma q_i \leq 500$ we get:(fig 8). Notice how subpopulation 1 is almost instantly abandoned in favor of the other ones where there is still time. We see a bimodal nature in pop.3 and 4 when resources are released from pop.2. Up until about 1.5 time units the ≤ 500 constraint is still active. After that the vaccination becomes less useful as the susceptibles decay further.

4.2 Airport Graph Structure

With a epidemic started in San Francisco we observe the following unconstrained optimal vaccination pattern (fig 9). With a maximal common resource of 8000000 and a start in New York we get (fig 10). As can be seen, the bimodal structure of fig 8 is present here as well in the less exposed cities.

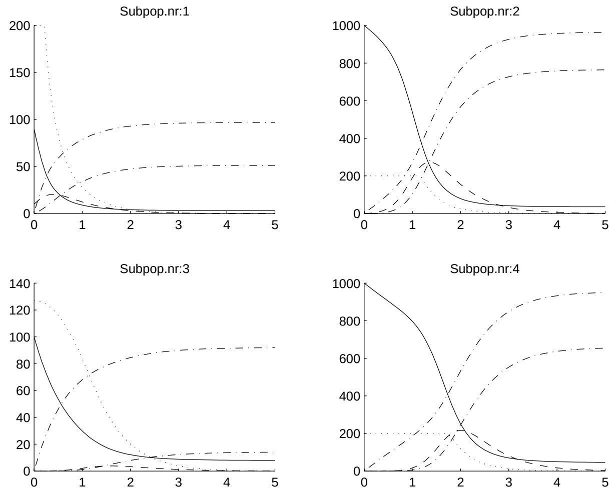

Figure 7: Optimal Control with individual ≤ 200 constraint

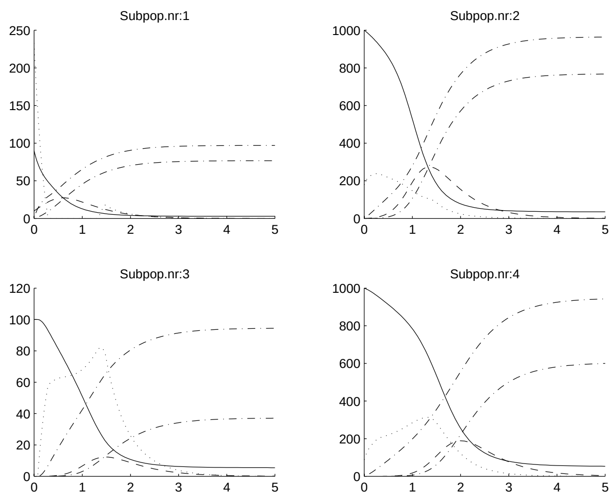

Figure 8: Optimal Control with common resources ≤ 500

5 Conclusion

We have shown a model for rapidly spreading diseases in urbanized populations. By applying the maximum principle to this model we have found optimal vaccination patterns. Improvements remain to be done on both model and numerics to make this kind of considerations applicable but the issue only grows in importance in the light of the biological warfare threat.

References

[1] W. Kermack and A. McKendrick. *A contribution to the mathematical theory of epidemics.* Proc. Roy. Soc., Ser. A, 115:700-721,1927

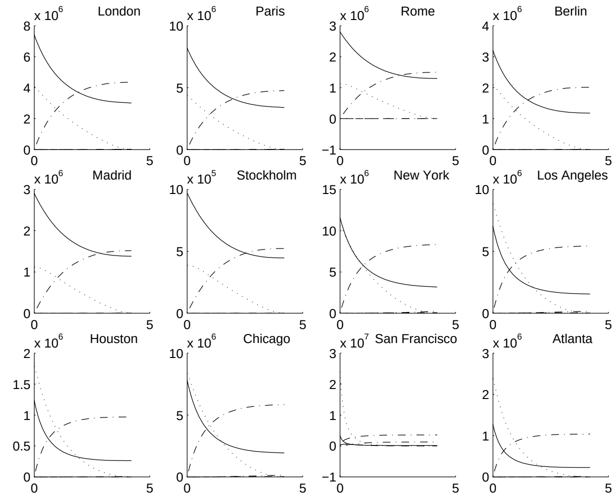

Figure 9: Unconstrained control, Airports, note the difference between Europe and the USA

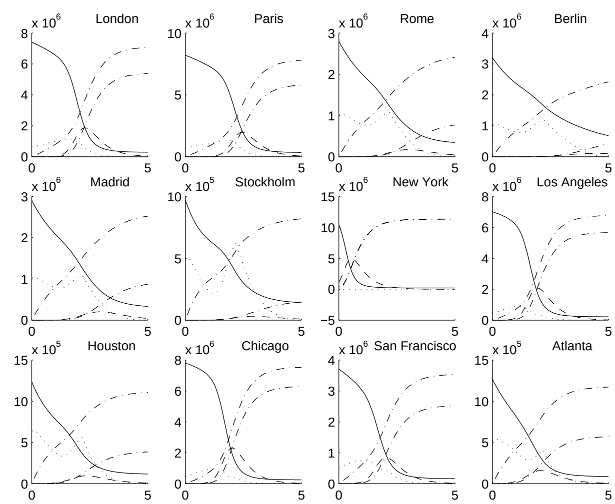

Figure 10: Common resources, Airports, $\Sigma \leq 8000000$

[2] Linda J.S. Allen *Some Discrete-Time SI, SIR, and SIS Epidemic Models* Math. Biosciences 124(1994):83-105

[3] Leonid A. Rvachev and Ira M. Longini,jr *A Mathematical Model for the Global Spread of Influenza* Math. Biosciences 75(1985):3-22

[4] Linda J.S. Allen and David B. Thrasher *The Effects of Vaccination in an Age-Dependent Model for Varicella and Herpes Zoster* IEEE Transactions on automatic control, VOL. 43, NO. 6, June 1998

[5] Wayne M. Getz *Optimal Control and Principles in Population Management* Proceedings of Symposia in Applied Mathematics, Vol. 30, 1984

[6] Baoming Ma *An Improved Algorithm for Solving Constrained Optimal Control Problems* Thesis Report Ph.D, University of Maryland, 1994