Sensitivity Analysis of Deterministic Models

Introduction to Latin Hypercube Sampling

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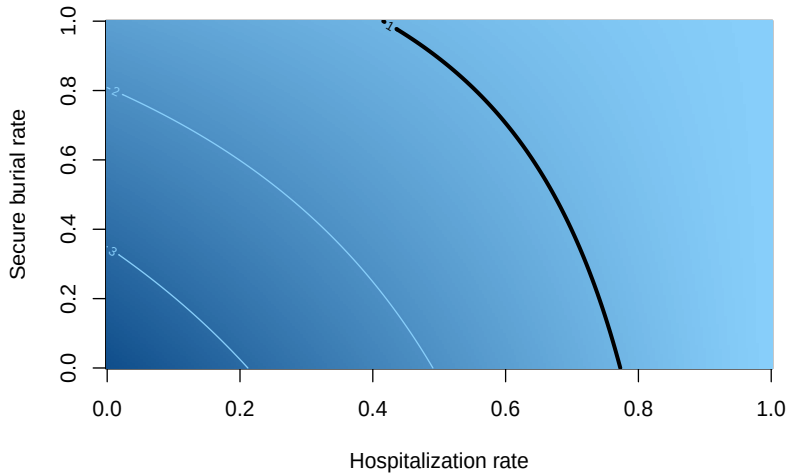
Sensitivity analysis

Key questions about uncertainty:

- Which factors are most important to determining model behavior?
- How much will my result change if the conditions (parameters, initial state) change?
- What range of outcomes are consistent with my knowledge of the parameters?
- What processes do I need more information about and how much information do I need

Simple models

In simple, deterministic models with few state variables and few parameters we can often produce model visualizations to answer such questions.

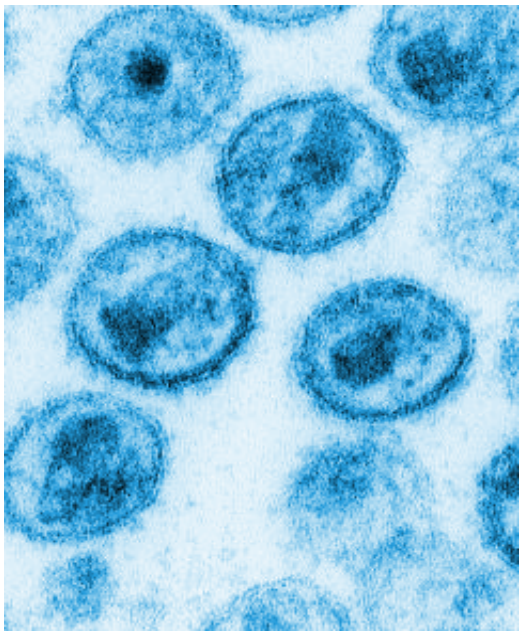


Invasion boundary for a model of Ebola virus transmission

But, what do we do with more complicated models?

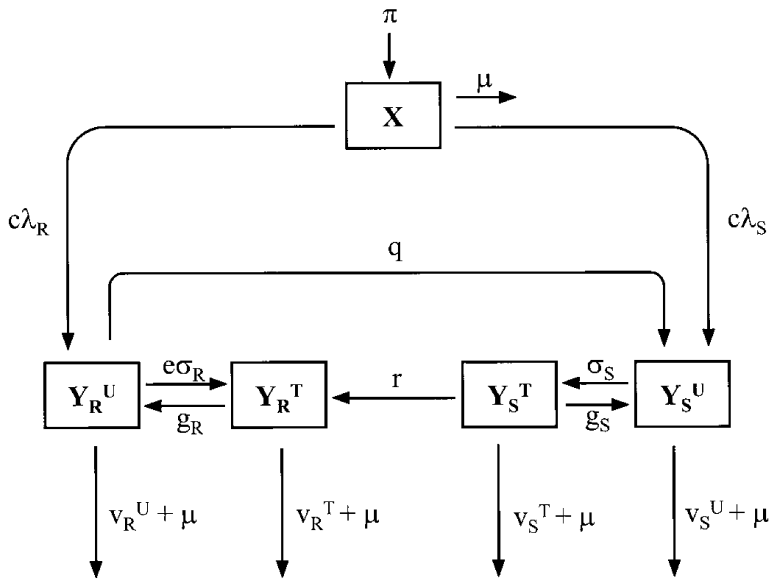
Motivating example: A model for the transmission of HIV among homosexual men

- In 2000, $\approx 30\%$ of gay men in San Francisco were infected with HIV, $\approx 50\%$ of these were taking combination antiretroviral therapy (ART)
- ART was effective at reducing AIDS death rate, but does not completely eliminate infectivity
- It was unclear whether the net effects of increased distribution of ART would increase or decrease HIV



Motivating example: A model for the transmission of HIV among homosexual men

What is the effect of antiretroviral therapy on incidence of HIV?



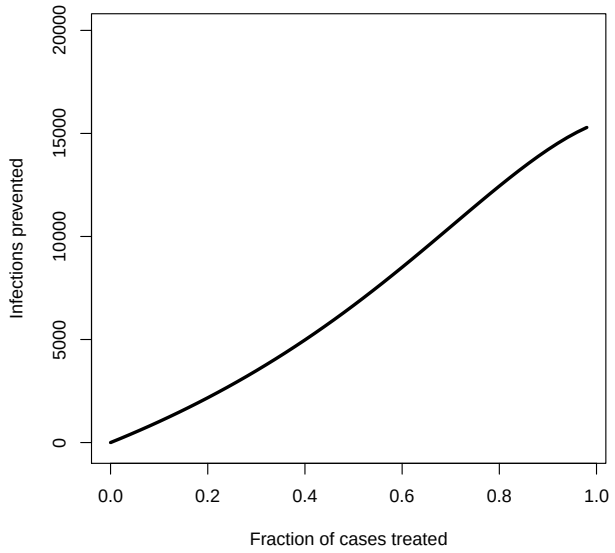
Blower, S.M., *et al.* 2000. A tale of two futures: HIV and antiretroviral therapy in San Francisco. *Science* 287:650-654.

Motivating example: A model for the transmission of HIV among homosexual men

X	Susceptible
Y	Infected (R=resistant, S=sensitive; U=untreated, T=treated)
π	Rate at which gay men join the sexually active community
μ^{-1}	Average time during which new partners are acquired
c	Average number of new partners per year
p	Probability of a drug-resistant case transmitting drug-sensitive viruses
q^{-1}	Average time for a drug-resistant infection to revert to drug-sensitive infection
σ	Per capita effective treatment rate
e	Relative efficacy of ART in treating drug-resistant infections
r	Rate of emergence of resistance due to acquired infection
g	Proportion of cases that give up ART per year
ν	Average rate of disease progression

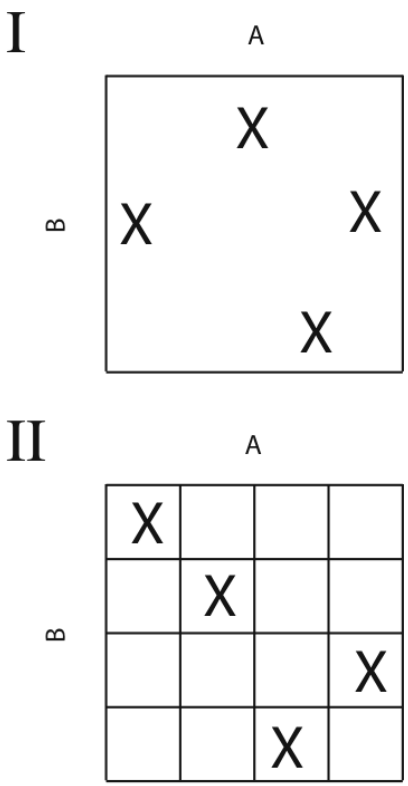
Motivating example: A model for the transmission of HIV among homosexual men

- It appears that ART could prevent $\approx 15,000$ cases over 20 years
- How reliable is this result?
- Model has 20 parameters but none is known exactly



Number of infections prevented as a function of the fraction of cases treated

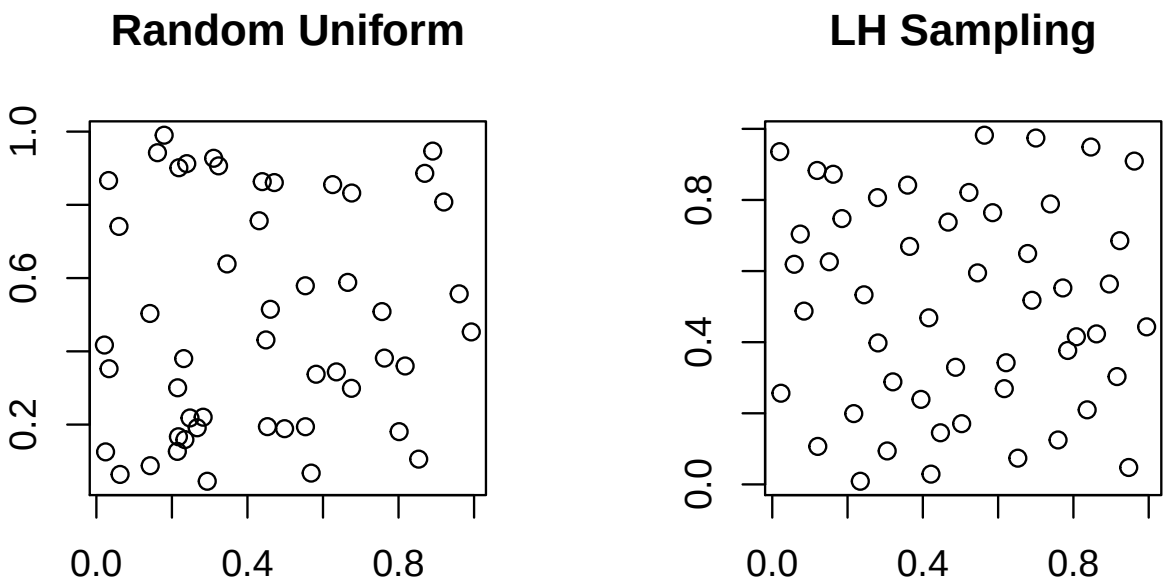
Latin hypercube sampling



- To determine robustness of model predictions, we require a way of exploring the output of a family of parameterized models
- Realistic models will often have many parameters so that high resolution exploration of its parameter space is computationally intractable
- Latin hypercube sampling is a scheme for simulating random parameter sets that adequately cover the parameter space.

Latin hypercube sampling in R

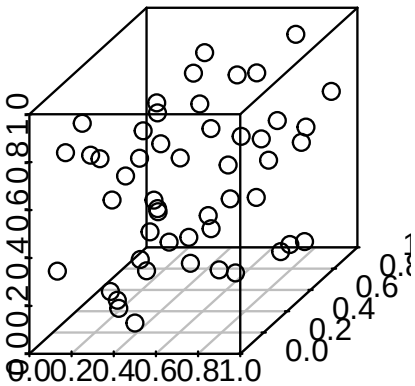
```
> require(lhs)
> x <- runif(50)
> y <- runif(50)
> h <- 50
> lhs<-maximinLHS(h,2)
> par(mfrow=c(1,2))
> plot(x,y,type='p', main='Random Uniform', xlab='', ylab='')
> plot(lhs, type='p', main='LH Sampling', xlab='', ylab='')
```



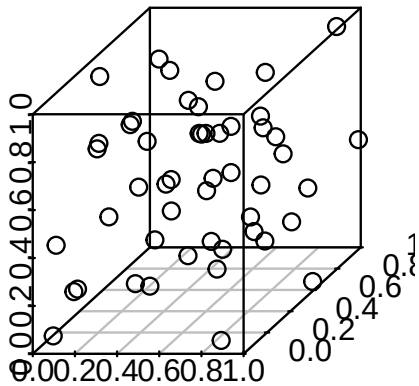
Latin hypercube sampling in R (3-D)

```
> require(scatterplot3d)
> x <- runif(50); y <- runif(50); z <- runif(50)
> h <- 50
> lhs<-maximinLHS(h,3)
> par(mfrow=c(1,2))
> scatterplot3d(x,y,z, type='p', main='Random Uniform', xlab='', ylab='', zlab='
> scatterplot3d(lhs, type='p', main='LH Sampling', xlab='', ylab='', zlab='')
```

Random Uniform



LH Sampling



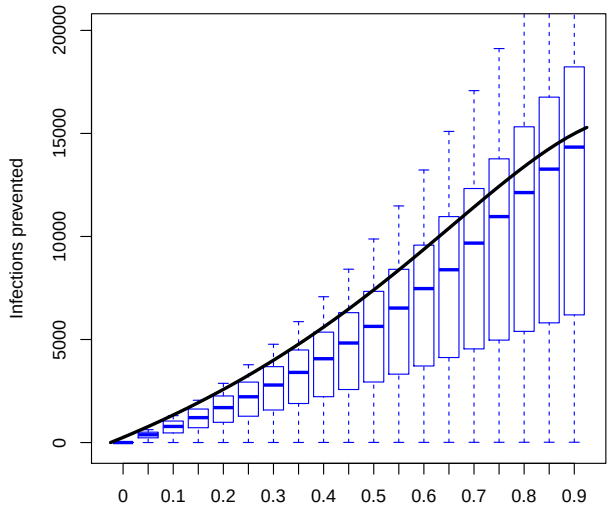
Rescaling interval sample

- Need to re-scale the random point (a number in the interval [0,1]) to an interval from α_{min} to α_{max} where α is some parameter.
- This can be done by "stretching" the interval using the following formula

$$\alpha_0 = U(\alpha_{max} - \alpha_{min}) + \alpha_{min}$$

Motivating example: A model for the transmission of HIV among homosexual men

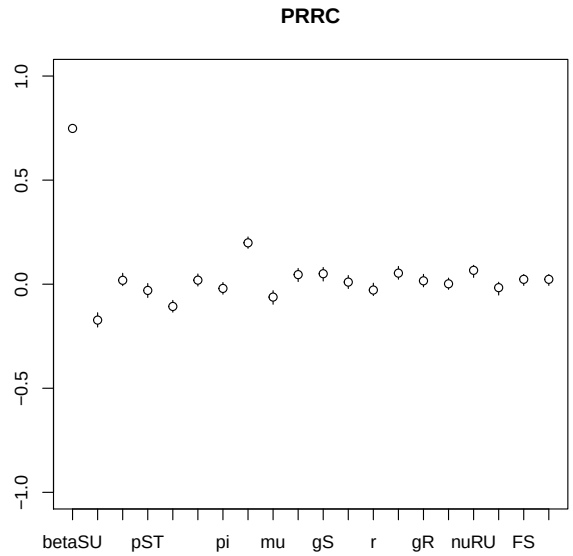
- Evidently, our best guesses are rather optimistic compared with the range of scenarios we believe to be plausible
- At least ART was found never to be counter-productive (an open question at the time of this study)



Range of outcomes as a function of fraction treated

Which parameters are important

- Correlation analysis can be used to investigate how model output is related to input parameters (but does not account for covariances among parameters, if there are any)
- Partial rank correlation coefficients partition effects to each input variable



Partial rank correlation coefficients of 20 parameters

Summary

- A key problem is to distiguish variability that arises from intrinsic stochasticity and uncertainty that can be mitigated through the acquisition of better information
- The effect of uncertainty in model parameters can be identified through Latin Hypercube Sampling coupled with Partial Rank Correlation analysis
- Other methods (e.g. Sobol's Index, Sensitivity Heat Map) may be used to determine the effects of parameter interactions or direction of effect

For further reading: Wu et al. 2013. Sensitivity analysis of infectious disease models: methods, advances and their application. *Journal of the Royal Society Interface* 10:20121018.