What influences model results

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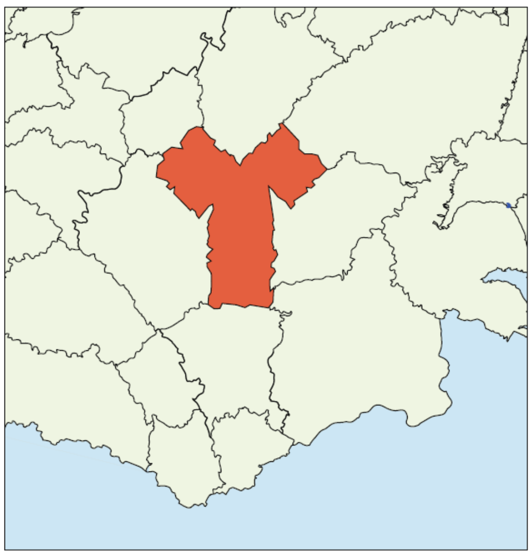
2020-07-20 19:44:43

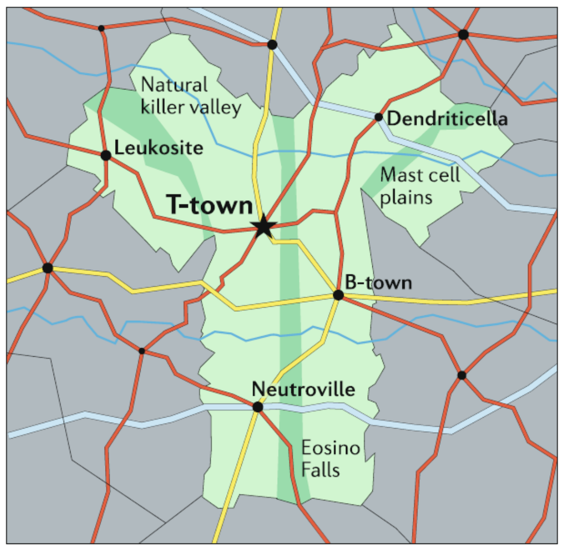
Uncertainty in model results

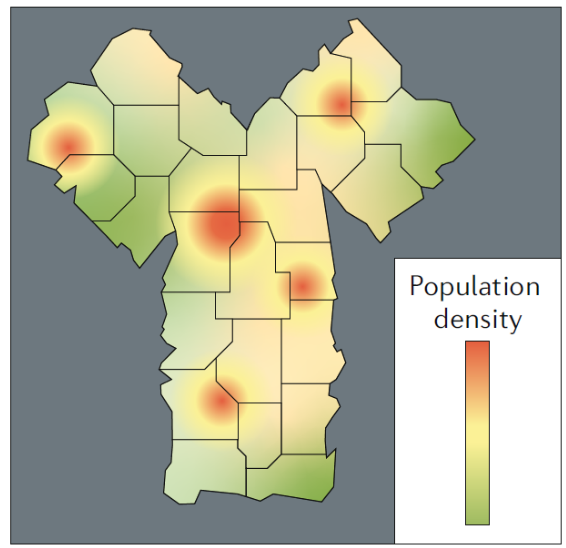
- Model results have different sources of uncertainty attached to them.
- Not all types of uncertainty are always explicitly acknowledged.
- That's true not only for mathematical/computer models.

Structural Uncertainty

- Models are simplifications and abstractions of the real world.
- Specific assumptions lead to different models.
- Every model is ‘wrong’ in some sense, but some might be useful.
- We need to decide which variables and processes to include and which to exclude.







Structural Uncertainty

- Include certain variables/components not?
- How to formulate mechanisms/processes?
- What type of model? (ODE, IBM, etc.)

Example variants of specific processes

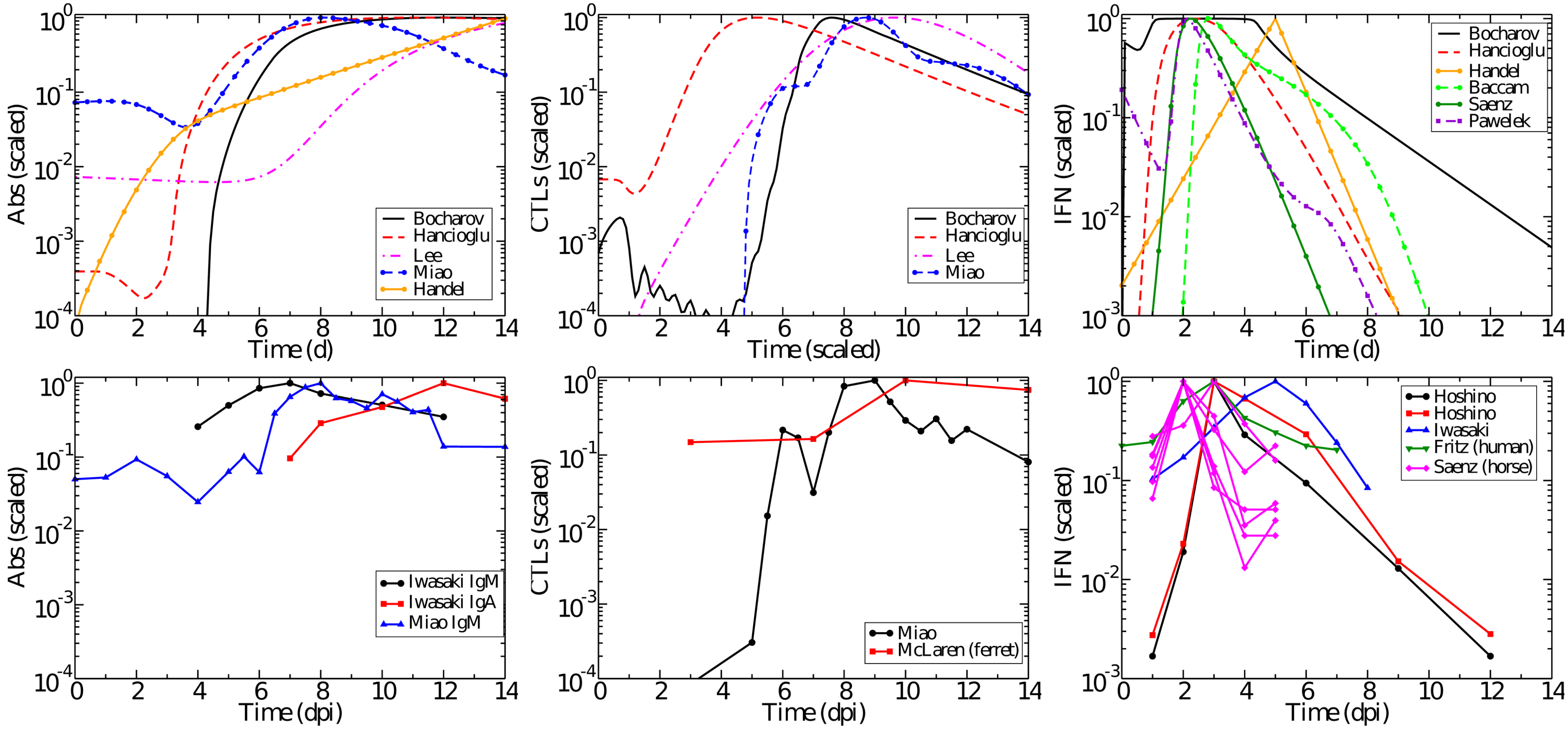
Exponential or Linear growth? Mass-action or saturating killing?

$$\begin{aligned}\dot{B} &= gB - d_B B - kBI \\ \dot{I} &= rBI - d_I I\end{aligned}$$

$$\begin{aligned}\dot{B} &= g - d_B B - k\frac{B}{B+s}I \\ \dot{I} &= rBI - d_I I\end{aligned}$$

Structural Uncertainty Example

Dobrovolny et al. (2013 PLoS One) compared different influenza models and assessed how they matched experimental data.



Top: models, bottom: data

Structural Uncertainty - Summary

- The biggest source of variability in outcomes.
- No systematic way to deal with it.
- Often discussed/addressed the least. Comparison of results across models is rare.
- Topical example: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/forecasting-us.html

Structural Uncertainty - Practice

- The *Model variant exploration* app in DSAIRM explores the impact of different model formulations.

Parameter Uncertainty

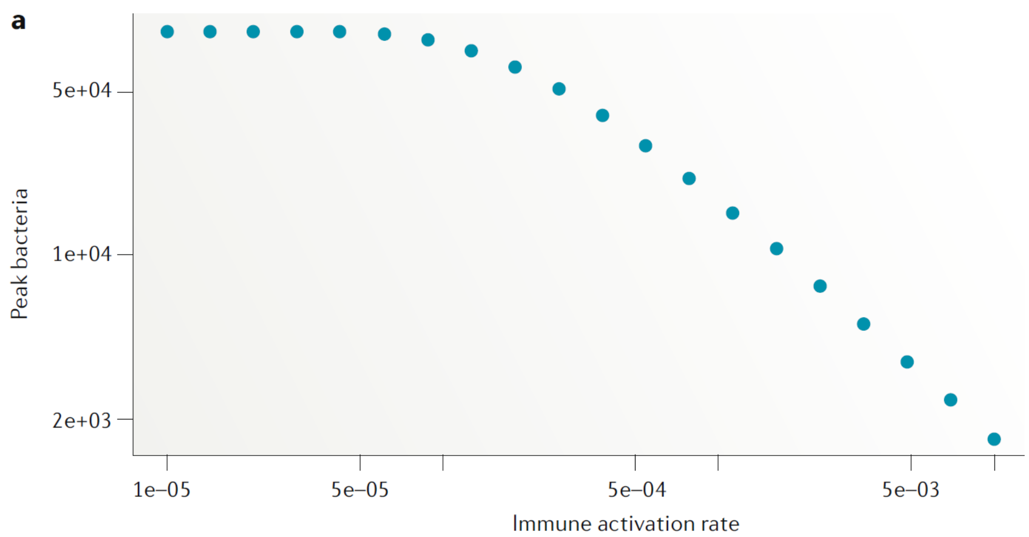
Parameter Uncertainty

- Assume we chose a certain structure for our model and built it (e.g. a certain set of ordinary differential equations).
- To explore the model or make predictions, we need to supply it with values for the model parameters (and starting conditions).
- Often, we do not know the values for the model parameters very well.

$$
\begin{aligned}
\dot{B} &= gB - d_B B - kBI \\
\dot{I} &= rBI - d_I I
\end{aligned}
$$

Exploring the impact of model parameters

- Sometimes we can obtain estimates for parameter values from fitting to data, but the right data is often not available.
- Instead of running our model for just one set of parameter values, we could run it using different values that are within reasonable ranges.
- If we have a small model, we could systematically explore model behavior for each parameter.



Exploring the impact of model parameters

- Once models get big, it would take too long to thoroughly scan over all parameters.
- Often we can get reasonable ranges from the literature, but not exact values.
- Sometimes, we might be *mainly* interested in how results change as we vary one parameter, but we also want to know how uncertainty in other parameters affect our outcome.
- Other times, we might want to use our model to make predictions. We need to figure out how uncertainty in parameters affects our predictions.

Uncertainty & Sensitivity Analysis

Varying multiple inputs/parameters over a usually broad range is called a (global) uncertainty & sensitivity analysis.

- **Uncertainty Analysis:** Given uncertainty in the inputs (parameters), how much uncertainty is there in the outputs/results?
- **Sensitivity Analysis:** How much do individual inputs contribute to the uncertainty in outputs/results?

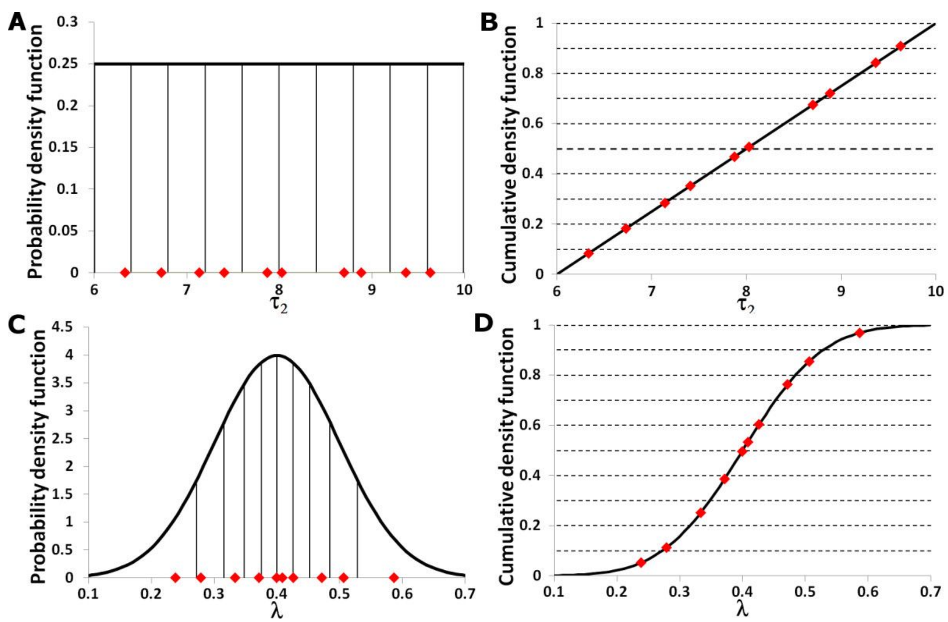
Doing Uncertainty & Sensitivity Analysis

- Determine ranges of uncertainty for each input (parameter and initial conditions).
- Repeatedly draw samples of parameter values from the specified distributions.
- Run model for each parameter sample, record outcomes.

Parameter ranges

For each parameter, specify its distribution:

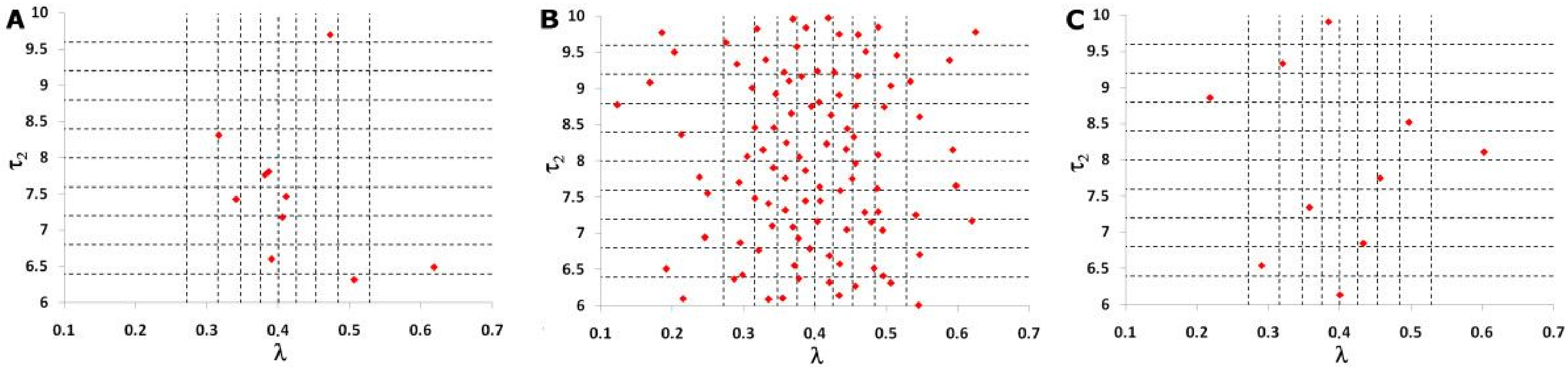
- Single value if we are very certain.
- Uniform distribution between some min and max values if we know very little.
- A ‘peaked’ distribution (e.g. gamma, log-normal) if we are fairly certain about some parameters.



Hoare et al 2008 TBMM

Parameter sampling

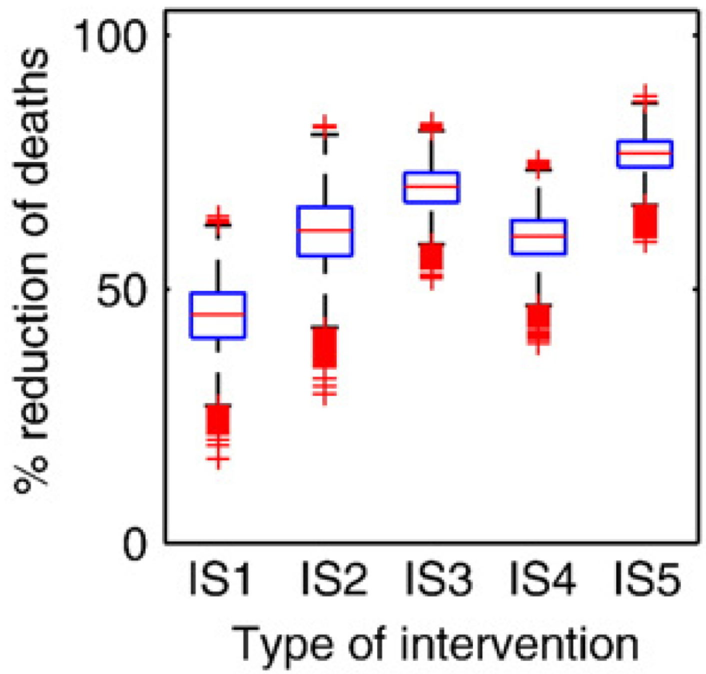
- Exhaustively trying all parameter value combinations takes too long.
- Randomly sampling is not efficient, it might leave areas of parameter space unexplored.
- A method called Latin Hypercube Sampling creates samples that efficiently span the parameter space.



Hoare et al 2008 TBMM

Uncertainty Analysis

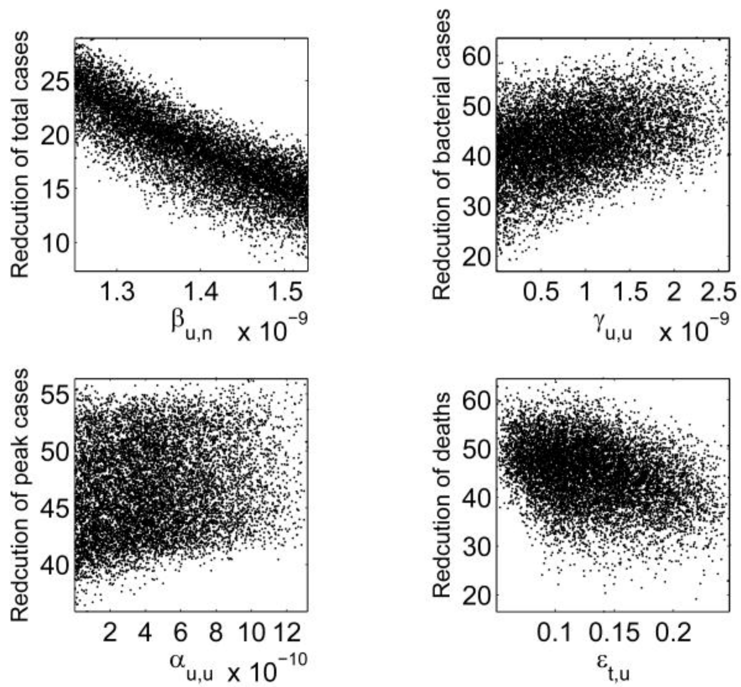
- Sample over parameters, record outcomes for each sample.
- Show the uncertainty in outcomes due to uncertainty in parameters with e.g. a boxplot



Example of a boxplot for some U/S analysis. For different intervention strategies (along the x-axis), samples are run and some outcome is recorded.

Sensitivity Analysis

- Uncertainty analysis tells us how uncertainty in inputs affects uncertainty in outputs.
- If we want to know in more detail how a specific input affects a specific output, we can move on to sensitivity analysis.
- Using the same simulation results, we now plot scatterplots for income/outcome pairs of interest instead of boxplots.



Handel et al (2009), Epidemics

Sensitivity Analysis

- If the scatterplot shows a monotone relation, we can summarize it with a single number, a correlation coefficient
- Correlation Coefficients (CC) indicate how correlated a given output is with a given input.
- CC are between -1 and 1. Large CC means strong (negative) correlation, CC ≈ 0 means no correlation.
- Input-output relations are often nonlinear, therefore computing the linear correlation is often not the best measure.
- Using a Rank CC is usually more suitable.
- Partial Rank Correlation Coefficients (PRCC) are even better if multiple inputs/parameters are changed at the same time.

U/S Analysis - Summary

- Uncertainty in parameters can be fairly easily quantified.
- By sampling over parameters, one can obtain confidence intervals or similar measures of uncertainty.
- **This does not account for structural or inherent uncertainty!**

Parameter uncertainty - Practice

- The *U/S analysis* app explores the concept in more detail.

Inherent/Stochastic Uncertainty

Introduction

- Deterministic models (both continuous and discrete-time) give you the same result for a set of parameters and starting conditions no matter how often you run them.
- Real systems are stochastic/random, which means they have some inherent variability.
- The words Stochasticity, Randomness, Noise, Variability are often used interchangably.

Sources of Stochasticity

- Random (external) noise (e.g. measurement error).
- Fluctuations in parameters (e.g. due to temperature or circadian rythms).
- Unpredictability of event occurence (e.g. births, deaths).

When is stochasticity important

- For small numbers.
- When we want to answer questions such as “What is the probability that X will happen?”

Stochastic compartmental models

We can fairly easily formulate any compartmental model (e.g. and ODE model) as a stochastic model.

- All variables take on discrete values (0,1,2,…).
- Increases or decreases are dicated by inflows and outflows.
- At each time step, one of the possible inflows/outflows occurs, with probability based on the size of the term.

Some terminology

- The events that happen are often called reactions or transitions.
- The inflow and outflow terms are called propensities, multiplied by the time step they are probabilities.

Example

$$\begin{aligned} \text{Uninfected Cells} \qquad \dot{U} &= n - d_U U - bUV \\ \text{Infected Cells} \qquad \dot{I} &= bUV - d_I I \\ \text{Virus} \qquad \dot{V} &= pI - d_V V - bUV \end{aligned}$$

Event type	Transitions	Propensity
Production of U	U => U+1	n
death/removal of U	U => U-1	d_UU
infection	U => U-1, V => V-1, I => I+1	bUV
death if I	I => I-1	d_II
production of V	V => V+1	pI
removal of V	V => V-1	d_VV

Comments

- Stochastic models are not much harder to implement, but they require more computational time since we need to run ensembles.
- One can fit stochastic models to data, but that's tricky and takes a long time.
- The `adaptivetau` package in R makes implementing stochastic models easy.
- The `pomp` package in R is a good tool for fitting stochastic models.

Stochastic uncertainty - Practice

- The apps in the *Stochastic models* section of DSAIDE provide more details.
- The *Stochastic Model* and *Influenza antivirals and resistance* apps in DSAIRM illustrate stochastic models.

Summary

- Uncertainty in modeling results can come from different sources.
- Structural uncertainty is arguably the most important but rarely explored. (Similar problems exist outside of modeling, e.g. how good a model are mice or elite undergrad students for the general population?)
- Parameter uncertainty is increasingly included in modeling projects and should be explored if a model is used for prediction.
- Stochastic models are also becoming more common but are still somewhat harder to work with.