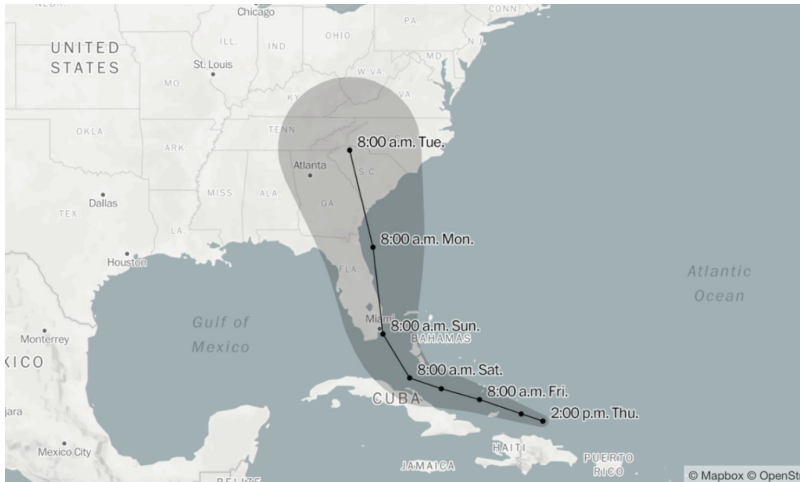


Decision making in case of uncertainties



Bayesian Analysis

- ▶ Based on Bayesian probability theory
 - ▶ uncertainty is presented with probabilities
 - ▶ probabilities are updated based on new information
- ▶ Thomas Bayes (170?–1761)
 - ▶ English nonconformist, Presbyterian minister, mathematician
 - ▶ considered the problem of *inverse probability*
 - ▶ significant part of the Bayesian theory
- ▶ Bayes did not invent all, but was first to solve problem of inverse probability in special case
- ▶ Modern Bayesian theory with rigorous proofs developed in 20th century

Term Bayesian used first time in mid 20th century

- ▶ Earlier there was just "probability theory"
 - ▶ concept of the probability was not strictly defined, although it was close to modern Bayesian interpretation
 - ▶ in the end of 19th century there were increasing demand for more strict definition of probability (mathematical and philosophical problem)
- ▶ In the beginning of 20th century frequentist view gained popularity
 - ▶ accepts definition of probabilities only through frequencies
 - ▶ does not accept inverse probability or use of prior
 - ▶ gained popularity due to apparent objectivity and "cook book" like reference books
- ▶ R. A. Fisher used in 1950 first time term "Bayesian" to emphasize the difference to general term "probability theory"
 - ▶ term became quickly popular, because alternative descriptions were longer

Uncertainty and probabilistic modeling

- ▶ Two types of uncertainty: aleatoric and epistemic
- ▶ Representing uncertainty with probabilities
- ▶ Updating uncertainty

Two types of uncertainty

- ▶ Aleatoric uncertainty due to randomness
 - ▶ we are not able to obtain observations which could reduce this uncertainty
- ▶ Epistemic uncertainty due to lack of knowledge
 - ▶ we are able to obtain observations which can reduce this uncertainty
 - ▶ two observers may have different epistemic uncertainty

Updating uncertainty

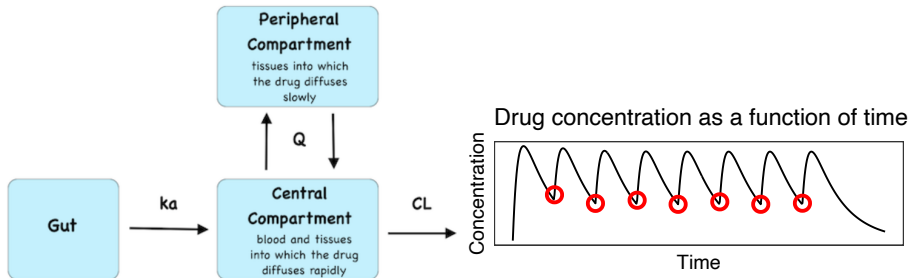
- ▶ Probability of red $\frac{\#red}{\#red + \#yellow} = \theta$
- ▶ $p(y = \text{red}|\theta) = \theta$ aleatoric uncertainty
- ▶ $p(\theta)$ epistemic uncertainty
- ▶ Picking many chips updates our uncertainty about the proportion
- ▶ $p(\theta|y = \text{red, yellow, red, red, } \dots) = ?$
- ▶ Bayes rule $p(\theta|y) = \frac{p(y|\theta)p(\theta)}{\int p(y|\theta)p(\theta)d\theta}$

Model vs. likelihood

- ▶ Bayes rule $p(\theta|y) \propto p(y|\theta)p(\theta)$
- ▶ Model: $p(y|\theta)$ as a function of y given fixed θ describes the aleatoric uncertainty
- ▶ Likelihood: $p(y|\theta)$ as a function of θ given fixed y provides information about epistemic uncertainty, but is not a probability distribution
- ▶ Bayes rule combines the likelihood with prior uncertainty $p(\theta)$ and transforms them to updated posterior uncertainty

Example application: Drug dosage for liver transplant¹

- ▶ Everolimus is immunosuppressant to prevent rejection of organ transplants
- ▶ Pharmacokinetic model of drug and body, optimal dosage depends on weight



- ▶ Model fitted with 500 adults, extrapolation to children?
- ▶ Maturation effect, 17 observations from children

¹with E. Siivola, Aalto and S. Weber, Novartis Pharma

The art of probabilistic modeling

- ▶ The art of probabilistic modeling is to describe in a mathematical form (model and prior distributions) what we already know and what we don't know
- ▶ “Easy” part is to use Bayes rule to update the uncertainties
 - ▶ computational challenges
- ▶ Other parts of the art of probabilistic modeling are, for example,
 - ▶ model checking: is data in conflict with our prior knowledge?
 - ▶ presentation: presenting the model and the results to the application experts

- ▶ Galaxy clusters for cosmology
- ▶ Coagulation of blood
- ▶ Gene regulation
- ▶ Pharmacokinetics and -dynamics
- ▶ Decision support
- ▶ Effects of nutrition for diabetes
- ▶ Evolutionary anthropology
- ▶ Clinical trial designs
- ▶ Daily demand for gas
- ▶ Brain structure trees
- ▶ School enrollment
- ▶ Sports
- ▶ Product demand
- ▶ Cocoa bean fermentation
- ▶ Marine propulsion power
- ▶ Alcohol consumption trends
- ▶ Flood probability
- ▶ Instantaneous heart rate distributions
- ▶ Drug dosing regimens in pediatrics
- ▶ Human T stem cell memory cells
- ▶ Fairness in university admission policies
- ▶ Destruction of bacteria and bacterial spores under heat

Bayesian data analysis

Example analyses

- ▶ Treatment/control
 - ▶ randomize patients to treatment or control
 - ▶ is the treatment effective?
- ▶ Continuous valued treatment
 - ▶ randomize patients with different dosages
 - ▶ which dosage is sufficient without too many side effects?
- ▶ Different effects for different patients?
 - ▶ Is the treatment effect different for male/female, child/adult, light/heavy, ...

Bayesian approach

- ▶ Benefits of Bayesian approach
 - ▶ integrate over uncertainties to focus to interesting parts
 - ▶ use relevant prior information
 - ▶ hierarchical models
 - ▶ model checking and evaluation

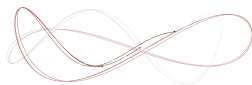
Computation

We need to be able to compute expectations with respect to posterior distribution $p(\theta|y)$

$$E_{\theta|y} [g(\theta)] = \int p(\theta|y)g(\theta)d\theta$$

- ▶ Analytic
 - ▶ only for very simple models
- ▶ Monte Carlo, Markov chain Monte Carlo
 - ▶ generic
- ▶ Distributional approximations
 - ▶ e.g. Laplace, variational, expectation propagation
 - ▶ less generic, but can be much faster with sufficient accuracy

Probabilistic programming



Enables agile workflow for developing probabilistic models

language – automated inference – diagnostics



`mc-stan.org`

Binomial model for treatment/control comparison

- ▶ Two groups of patients: treatment and control
 - ▶ Binary outcome
 - ▶ Is the treatment useful?

Binomial model for treatment/control comparison

```
data {  
  int<lower=0> N1;  
  int<lower=0> y1;  
  int<lower=0> N2;  
  int<lower=0> y2;  
}  
parameters {  
  real<lower=0,upper=1> theta1;  
  real<lower=0,upper=1> theta2;  
}  
model {  
  theta1 ~ beta(1,1);  
  theta2 ~ beta(1,1);  
  y1 ~ binomial(N1,theta1);  
  y2 ~ binomial(N2,theta2);  
}  
generated quantities {  
  real oddsratio;  
  oddsratio = (theta2/(1-theta2))/(theta1/(1-theta1));  
}
```


Binomial model for treatment/control comparison

RStanARM

```
fit_bin2 <- stan_glm(y/N ~ grp2, family = binomial(),  
                    data = d_bin2, weights = N)
```

Modeling nature

- ▶ Drop a ball from different heights and measure time
 - ▶ Newton
 - ▶ air resistance, air pressure, shape and surface structure of the ball
 - ▶ relativity
- ▶ Taking into account the accuracy of the measurements, how accurate model is needed?
 - ▶ often simple models are adequate and useful
 - ▶ *All models are wrong, but some of them are useful*, George P. Box

Reminder: Uncertainty and probabilistic modeling

- ▶ Two types of uncertainty: aleatoric and epistemic
- ▶ Representing uncertainty with probabilities
- ▶ Updating uncertainty

Questions

- ▶ Pick a number between 1–5
 - ▶ raise as many fingers
 - ▶ is the number of fingers raised random (by you or by others)?
- ▶ If we build a robot with very fast vision which can observe the rotating coin accurately, is the throw random for the robot?
- ▶ Is the quantum uncertainty aleatoric or epistemic?
- ▶ What is your own example with both aleatoric and epistemic uncertainty?

Rest of the course

- ▶ Basic models which can be used as building blocks
- ▶ Basic computation
- ▶ Typical simple scientific data analysis cases
 - ▶ e.g. comparison of treatments
- ▶ Presentation of the results

Some important terms

- probability
- probability density
- probability mass
- probability density function (pdf)
- probability mass function (pmf)
- probability distribution
- discrete probability distribution
- continuous probability distribution
- cumulative distribution function (cdf)
- likelihood

Ambiguous notation in statistics

In $p(y|\theta)$

- y can be variable or value
we could clarify by using $p(Y|\theta)$ or $p(y|\theta)$
- θ can be variable or value
we could clarify by using $p(y|\Theta)$ or $p(y|\theta)$
- p can be a discrete or continuous function of y or θ
we could clarify by using P_Y , P_Θ , p_Y or p_Θ
- $P_Y(Y|\Theta = \theta)$ is a probability mass function, sampling distribution, observation model
- $P(Y = y|\Theta = \theta)$ is a probability
- $P_\Theta(Y = y|\Theta)$ is a likelihood function (can be discrete or continuous)
- $p_Y(Y|\Theta = \theta)$ is a probability density function, sampling distribution, observation model
- $p(Y = y|\Theta = \theta)$ is a density
- $p_\Theta(Y = y|\Theta)$ is a likelihood function (can be discrete or continuous)
- y and θ can also be mix of continuous and discrete
- Due to the sloppiness sometimes likelihood is used to refer $P_{Y,\theta}(Y|\Theta)$, $p_{Y,\theta}(Y|\Theta)$

Chapter 1

Reading instructions

- ▶ 1.1-1.3 important terms
- ▶ 1.4 a useful example
- ▶ 1.5 foundations
- ▶ 1.6 & 1.7 examples (can be skipped, but may be useful to read)
- ▶ 1.8 & 1.9 background material, good to read before doing the exercises
- ▶ 1.10 a point of view for using Bayesian inference