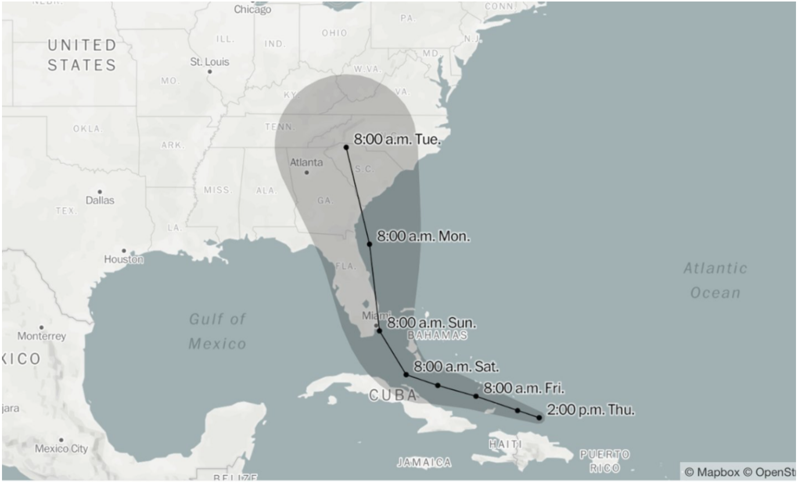
Decision making in case of uncertainties



Bayesian Analysis

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  - uncertainty is presented with probabilities
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- 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

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- 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

- Epistemic uncertainty due to lack of knowledge

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  - 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

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- $p(\theta|\text{y} = \text{red}, \text{yellow}, \text{red}, \text{red}, \ldots) =?$
- 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

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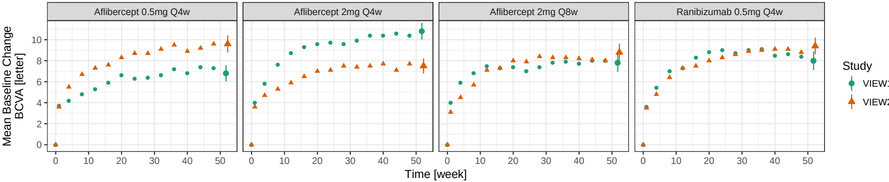
- Likelihood: $p(y|\theta)$ as a function of θ given fixed y provides information about epistemic uncertainty, but is not a probability distribution
- Bayes rule combines the likelihood with prior uncertainty $p(\theta)$ and transforms them to updated posterior uncertainty

Example application

wet age-related macular degeneration (wetAMD)



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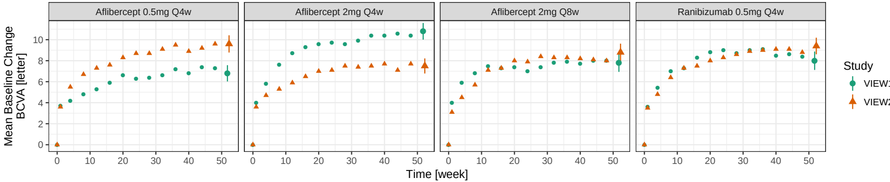

Pharmacometric with ordinal differential equations

$$\frac{dR_j(t)}{dt} = k_j^{\text{in}} - k_j^{\text{out}} \left[R_j(t) - E_{\max j}\, S_j(C_j(t)) \right] .$$

Combining results from different studies

The art of probabilistic modeling

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- 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
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Bayesian data analysis

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  - 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

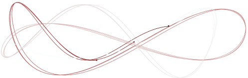
Computation

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

$$\mathrm{E}_{\theta|y}\left[g(\theta)\right] = \int p(\theta|y)g(\theta)d\theta$$

- 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

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  - 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

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Questions

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- Is the quantum uncertainty aleatoric or epistemic?

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- 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

$\ln p(y|\theta)$

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In $p(y|\theta)$

- y can be variable or value

    we could clarify by using $p(Y|\theta)$ or $p(y|\theta)$

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- Due to the sloppines 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