Hey Kids, Wanna Model Some Drugs?

A Light Primer on Bayesian Pharmacometrics

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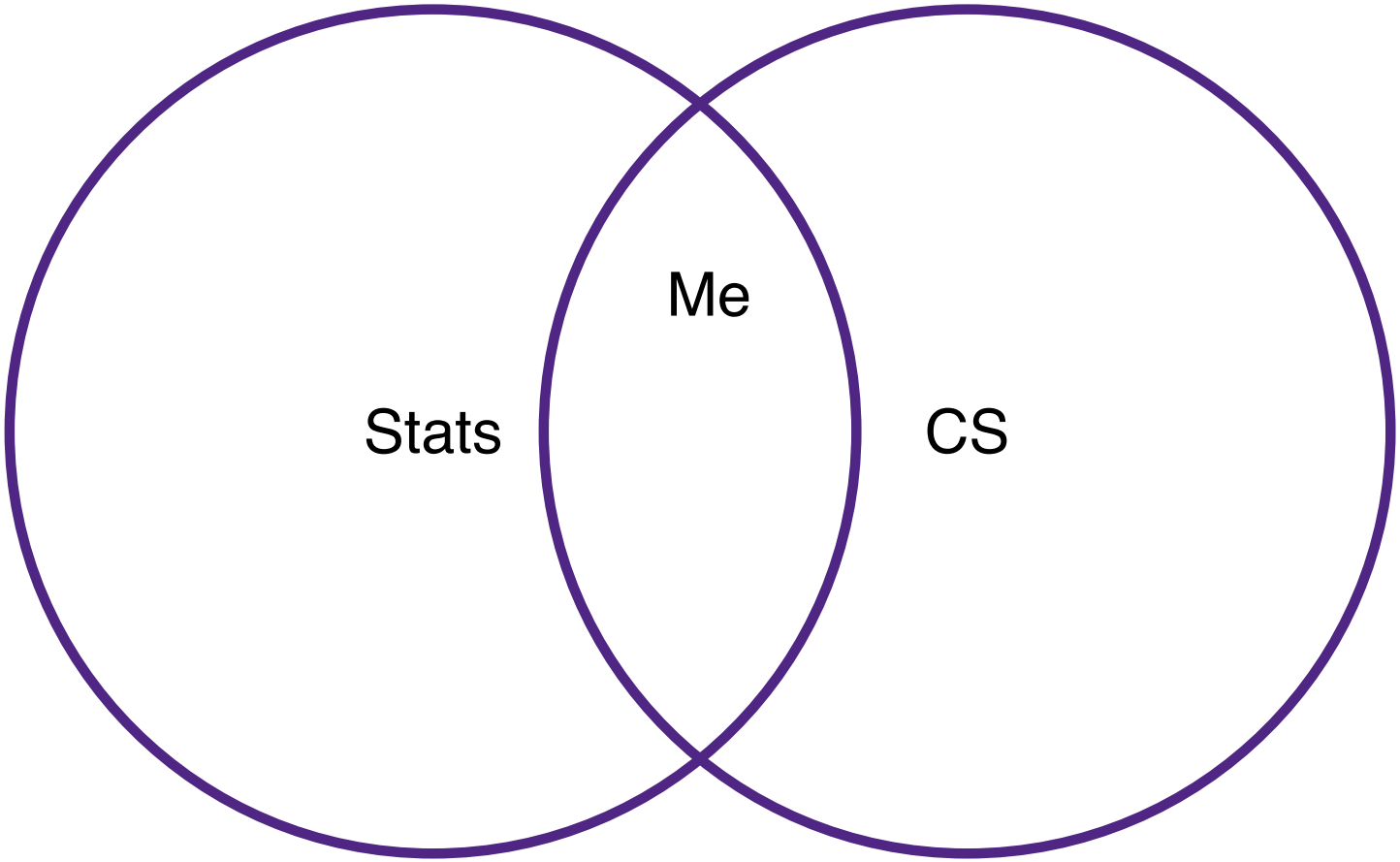
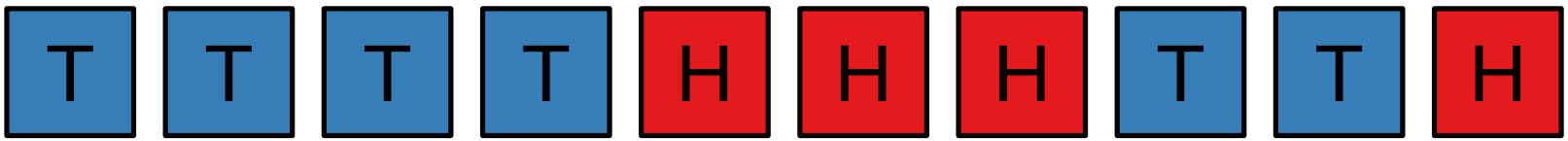
About Me



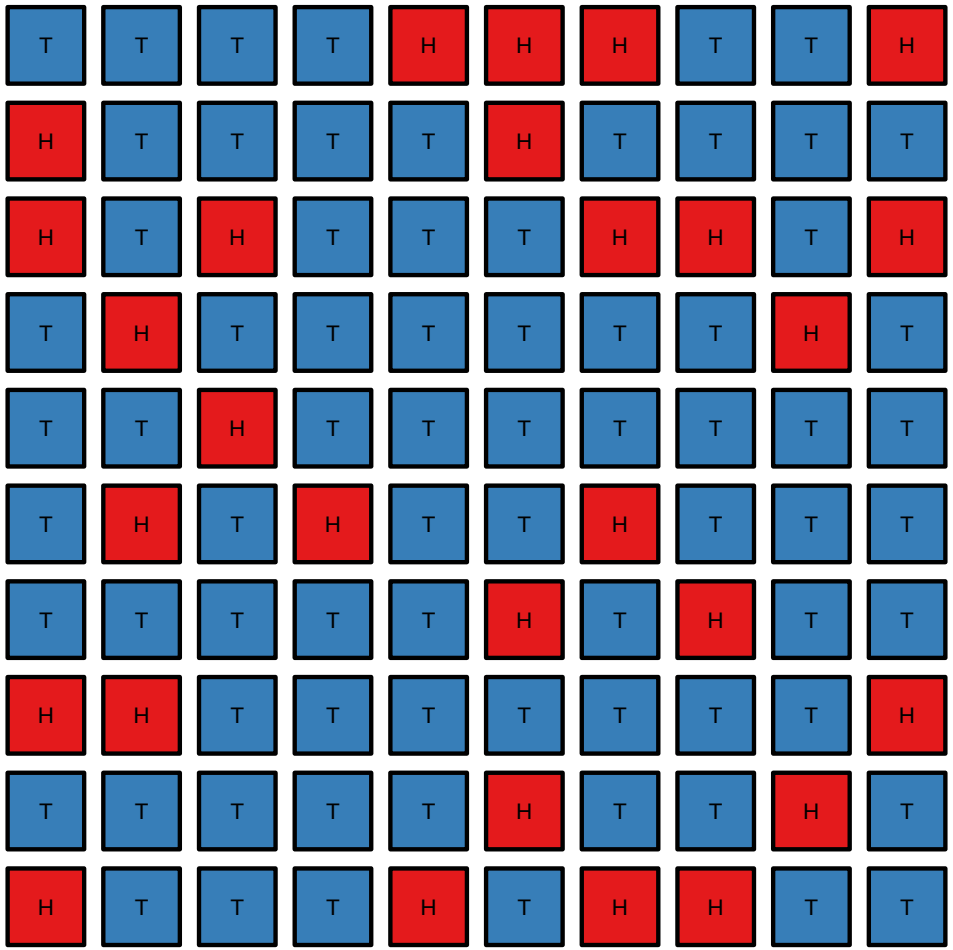
What is the bias of this coin?

Figure 1:A potentially biased quarter

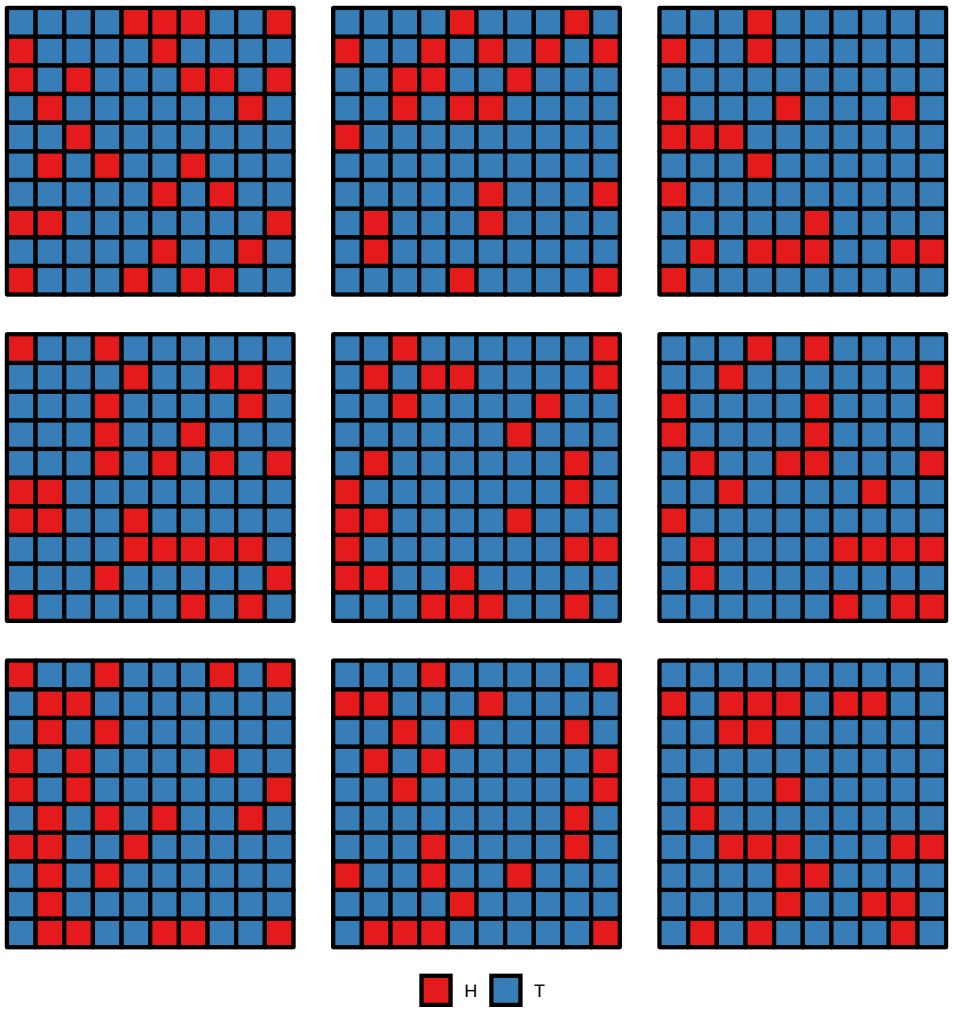
Maybe No Bias?



Looks Like a Bias Towards Tails?



Almost Certainly Biased Towards Tails



Without Putting Words in Your Mouth...

- You have a belief based on prior experience
- You observed new coin flips
- Those new flips changed your belief

Bayesian Statistics

- Prior Belief
- Observe Evidence/Data
- Update Belief
- Repeat!

Bayesian Statistics

Encode your prior belief as a probability distribution $p(\theta)$. Allow the data to change your belief through the likelihood $p(\boldsymbol{y}|\theta)$. Your posterior belief is obtained via Bayes' rule

$$p(\theta|\boldsymbol{y}) \propto p(\boldsymbol{y}|\theta)p(\theta)$$

I've Left A Lot Out

I've left out a lot because Bayesian Statistics in 10 minutes is near herculean.

Personalized Medicine & Pharmacometrics

- Some patients metabolize drugs improperly due to genetic variations
- They still need these drugs, but dosing is incredibly tricky
- Warfarin is a good example

Pie in the Sky

- Predict a future patient's drug metabolism based on clinical/demographic/genetic covariates before they are given a script

Why Even Go Bayesian

- Aren't there Frequentist methods to do this
  - Yes (e.g. R's `nlmeODE`).
- Why learn all this?
  - Leverage prior studies/information, especially when n is small.
  - Be honest about variance of estimates
  - Sequential improvement of model

What Are My Priors

- Need prior information to do any of this
  - PK/PD models
  - Physical understanding of what is possible, what is not
  - Lots of literature re: genetics and drugs to be incorporated into model

Prior Information: PK models

We know how drugs *should* be metabolized. The dynamics are given by ODE models.

$$\frac{d\mu}{dt} = k_a \frac{D}{V} \mathrm{e}^{-k_a t} - k\mu\,, \quad \mu(0) = 0$$

Gives a curve conditional on k and k_a.

$$\mu(t) = \frac{D \cdot k_a}{V \cdot (k - k_a)} \Big(\exp(-k_a t) - \exp(-kt) \Big)$$

We can get further information on k and k_a from literature, expert opinion, or empirically.

(One Possible) Full Model

$$\log(Y_t)|\mu(t),\sigma \sim \mathcal{N}(\mu(t),\sigma)$$

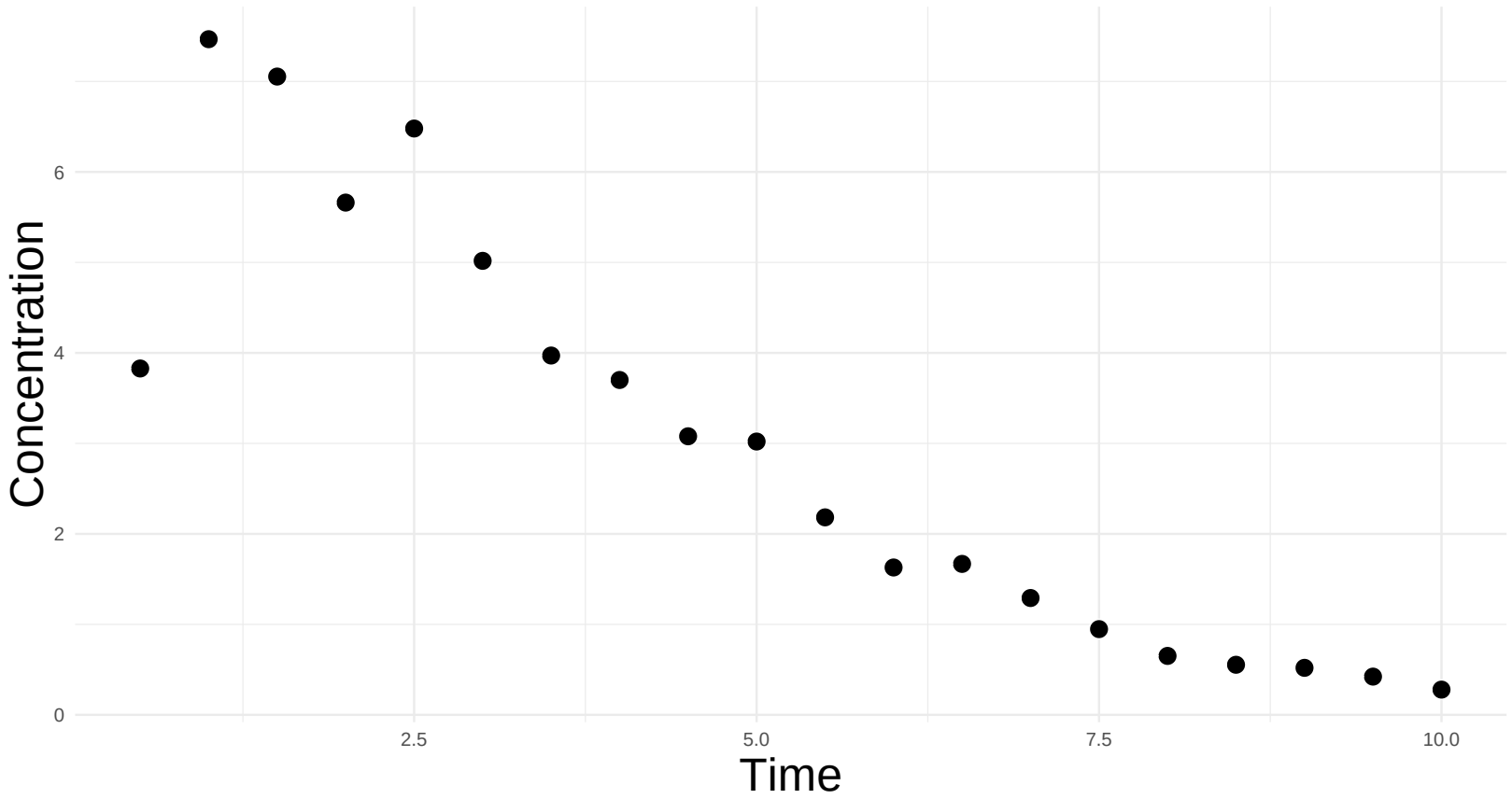
$$\mu(t)|k_a,k = \frac{D \cdot k_a}{V \cdot (k - k_a)}\Big(\exp(-k_a t) - \exp(-kt)\Big)$$

$$\sigma \sim \text{Half} - \text{Cauchy}(0,1)$$

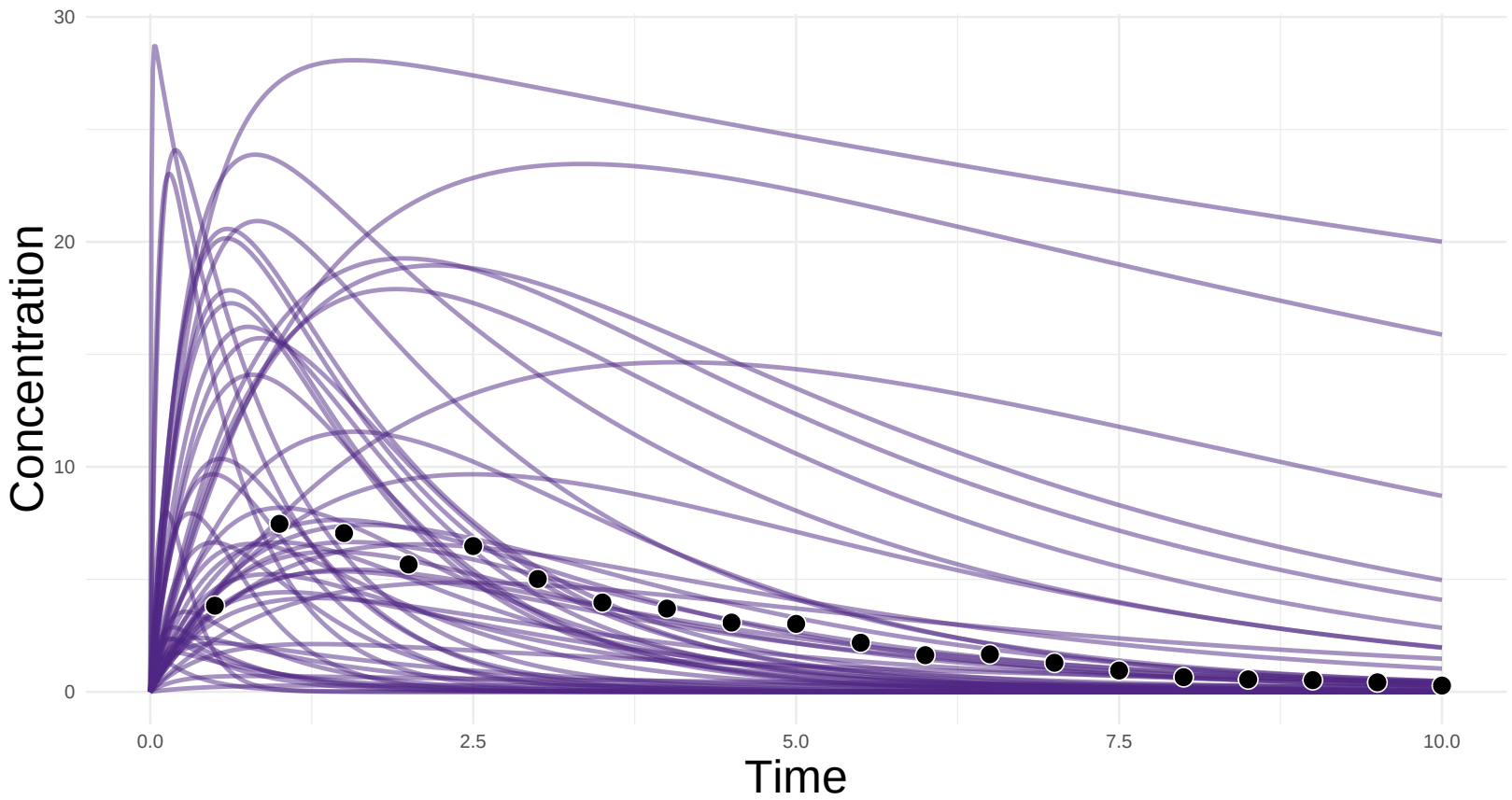
$$k \sim \text{Half} - \text{Cauchy}(0,1)$$

$$k_a \sim \text{Half} - \text{Cauchy}(0,1)$$

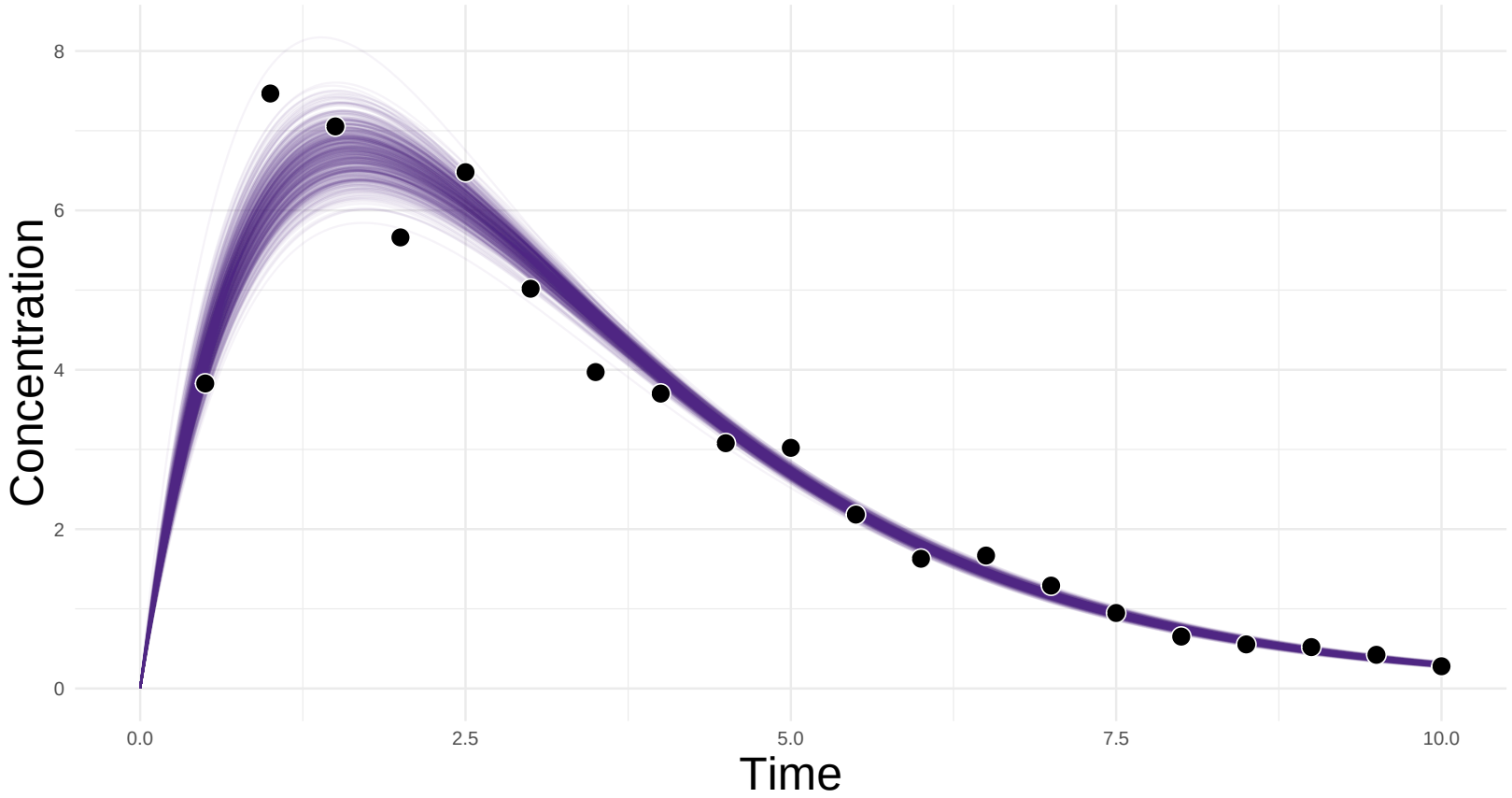
More Concretely



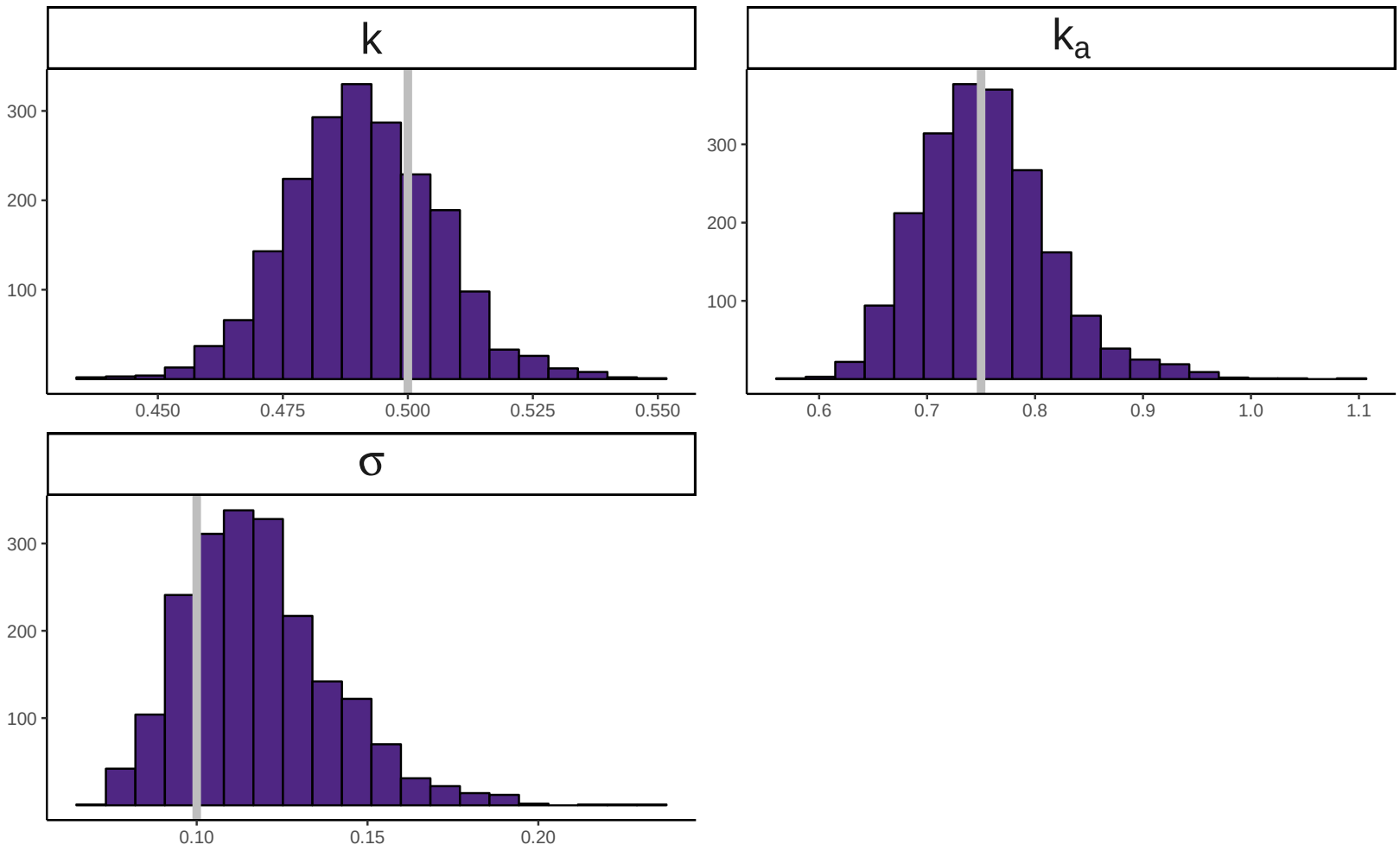
Draws from $p(\theta)$



Draws from $p(\theta|\boldsymbol{y})$



Marginal Posterior Distributions



This is Just the Begining

Still need to...

- Meet with stakeholders/scientists. Understand which population we are studying and indentify potential sources of bias/confounding
- Construct good priors from data/expert knowledge
- Construct a theoretical model
- Code in `Stan`

Please Join Us!

The slides, plots, and computations for this presentation were all done in R!

Questions