

# DOSE RESPONSE CURVES: A WORKFLOW WALKTHROUGH

(I MADE THIS IN LATEX USING A TEMPLATE!)

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AUGUST 11, 2020



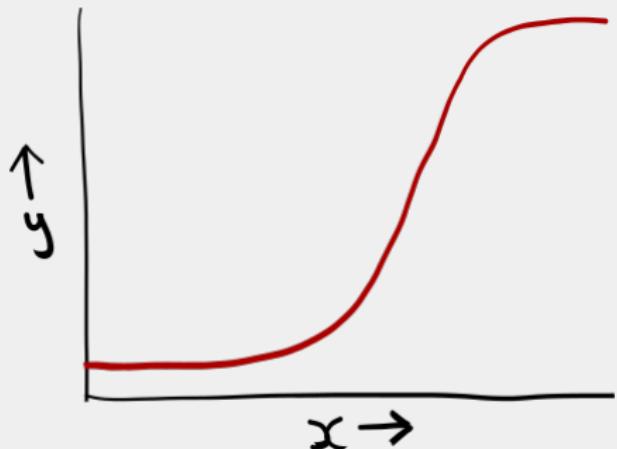
# **WHAT ARE RESPONSE CURVE MODELS?**

# INTRODUCTION

Non linear model

Maximum and minimum asymptotes.

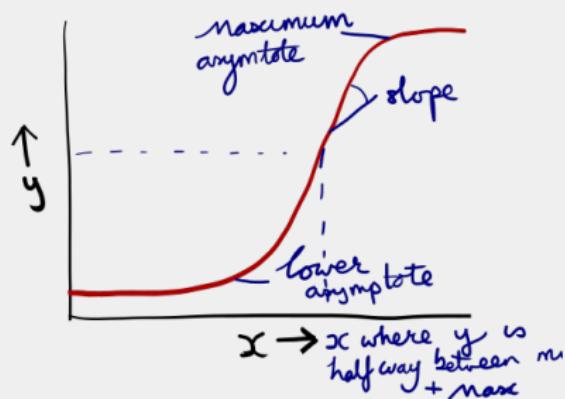
Often used for poison/medicine safety thresholds



# DOSE RESPONSE PARAMETERS

Different parameterizations

Todays has: minimum asymptote, maximum asymptote, rate, 50% effective dose

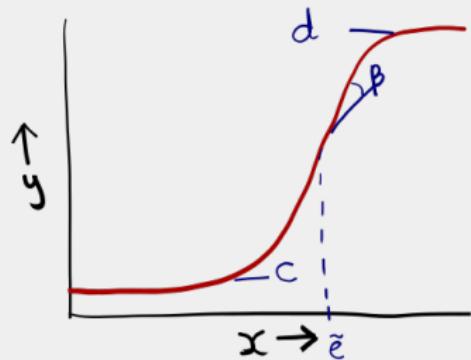


# DOSE RESPONSE PARAMETERS

Different parameterizations

Todays has:  $c, d, \beta, \tilde{e}$

$(\tilde{e})$  is  $\log(e)$



# THE EQUATION

Basic curve:

$$\mu = f(x, (b, c, d, e)) = c + \frac{d - c}{1 + e^{\beta(\log(x) - \tilde{e})}}$$

$x$  is the concentration of the dose (amount of winter cold)

$\beta$  is the response rate (slope)

$d$  is the upper asymptote of the response (maximum hardiness)

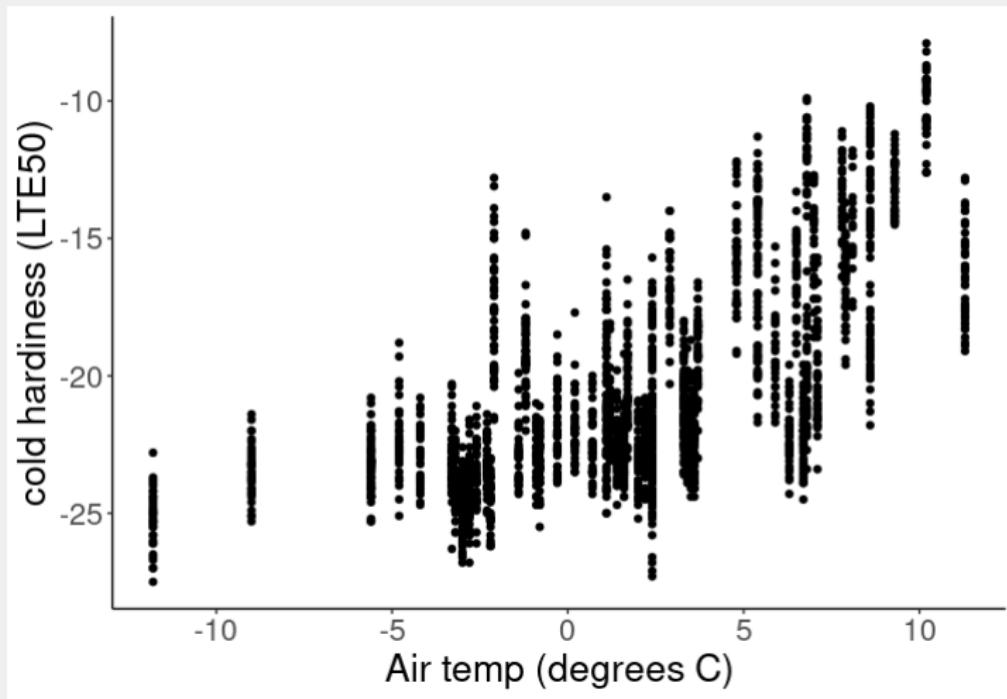
$c$  is the lower asymptote of the response (minimum hardiness)

$e$  is the effective dose ED50 (winter temperature where cold hardiness is half way between min and max)

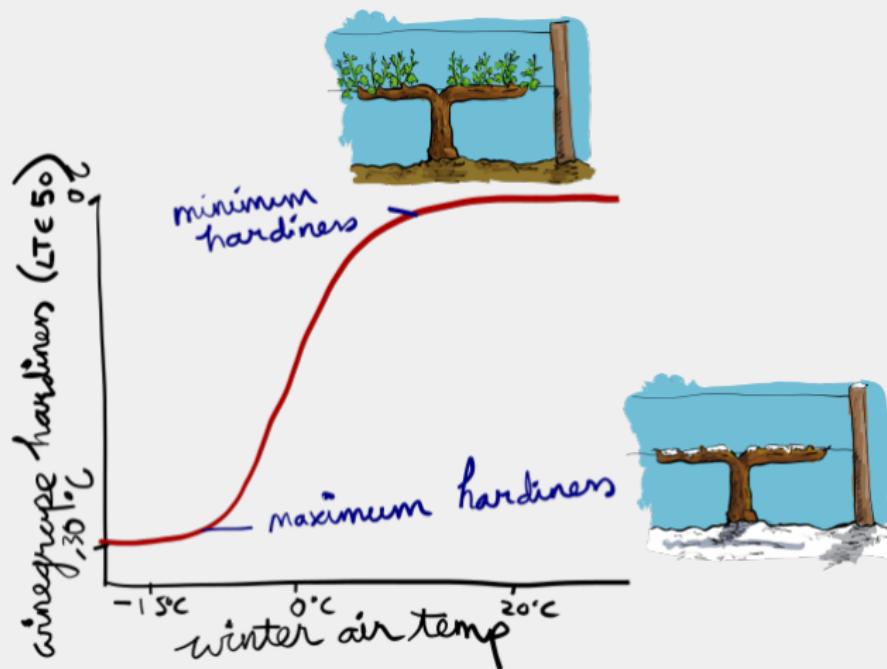
$\tilde{e}$  is the log of the effective dose ED50

# **DRCs AND WINEGRAPE WINTER HAR- DINESS**

# MY DATA - A REMINDER



# WINEGRAPE HARDINESS AS A DRC



# **BUILDING THE MODEL**

# **BUILDING THE MODEL**

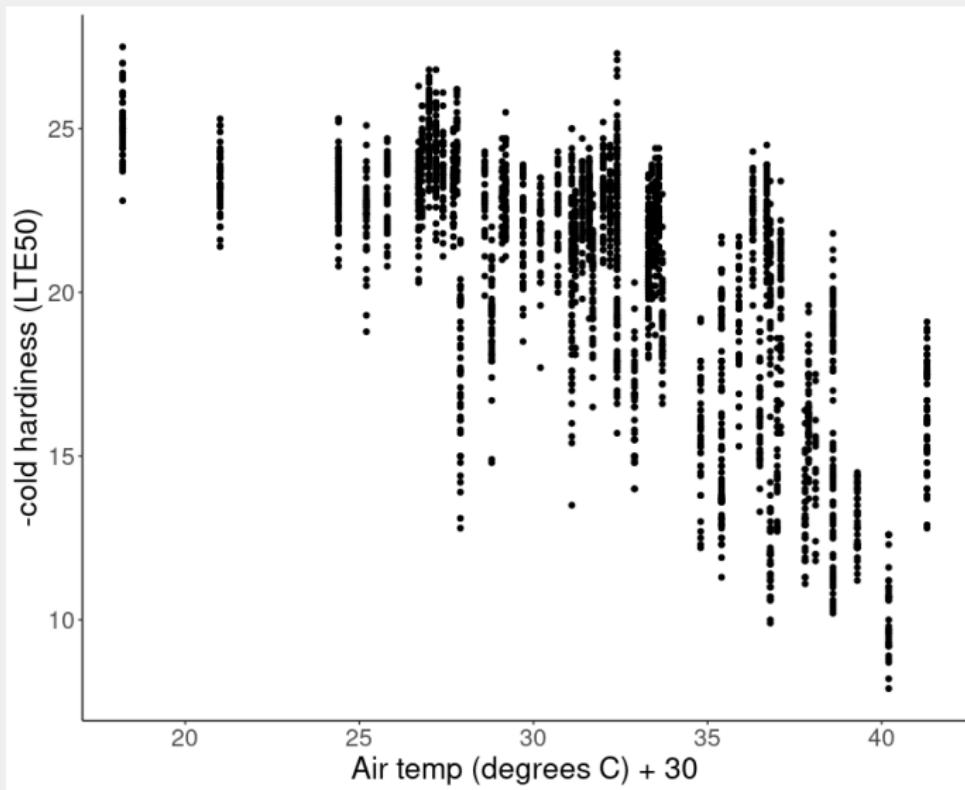
**FIRST STEP FOR PRIOR DESIGN**

## DOMAIN SPECIFIC KNOWLEDGE - DATA

Air temperature - need to be positive. Add 30.

Hardiness - highest hardiness smallest value. Make positive.

## DOMAIN SPECIFIC KNOWLEDGE - DATA



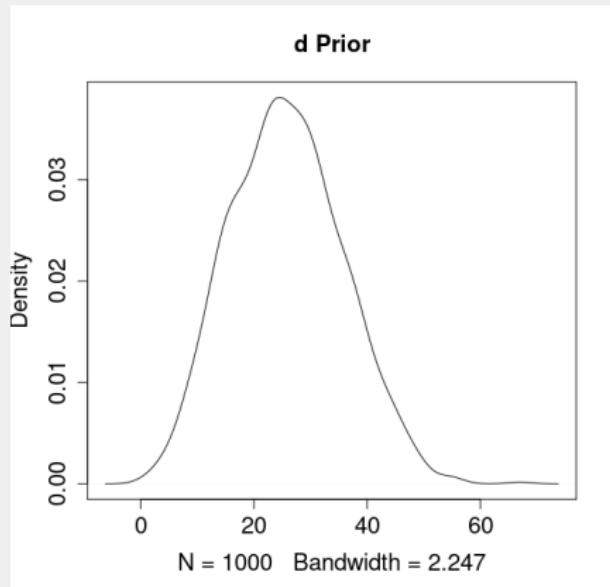
# DOMAIN SPECIFIC KNOWLEDGE - PARAMETERS

d

The higher asymptote.

Should be between 10 and 50  
(10 and 50).

Mean 30,  $\sigma$  of 10. Must be  
positive



# DOMAIN SPECIFIC KNOWLEDGE - PARAMETERS

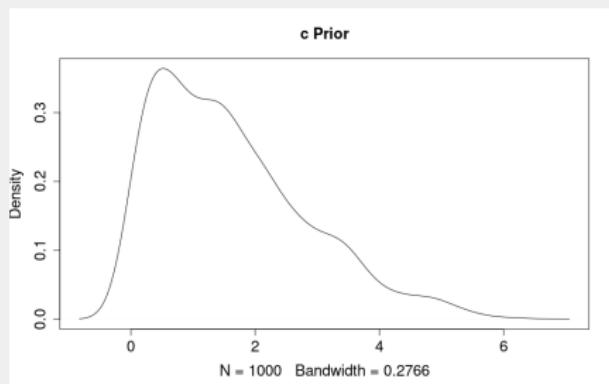
C

The lower asymptote.

Should be between 0 and 5 - must be positive.

Mean 0, half normal,  $\sigma$  of 2.

Narrow prior because more knowledge but less data.

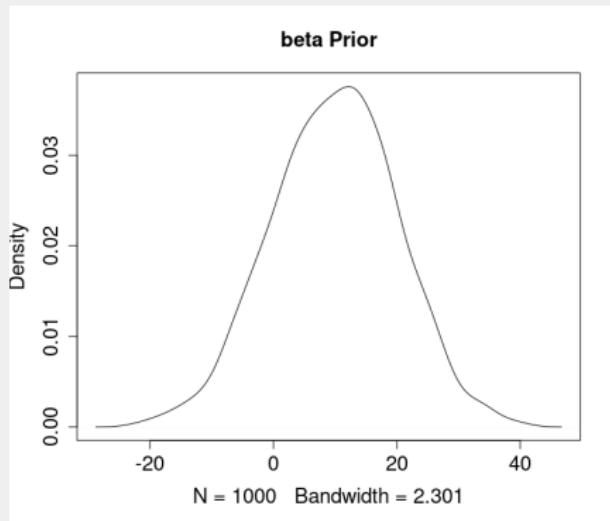


# DOMAIN SPECIFIC KNOWLEDGE - PARAMETERS

$\beta$

The response intensity.

From playing with values I'm going to try 10 plus/minus  $\sigma$  of 5.



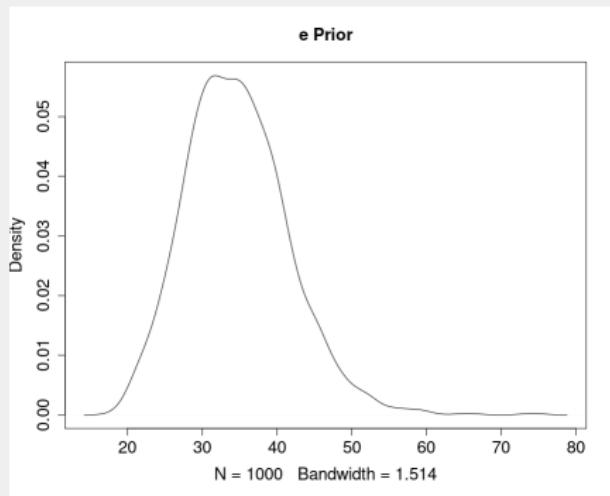
# DOMAIN SPECIFIC KNOWLEDGE - PARAMETERS

$e$

$x$  where  $y$  is half way between  $c$  and  $d$ . Should be centred around mean of  $x$ ,  $\sigma$  of 10. But

goes in as  $\log e$ , so need to consider that!

Pushforwards.

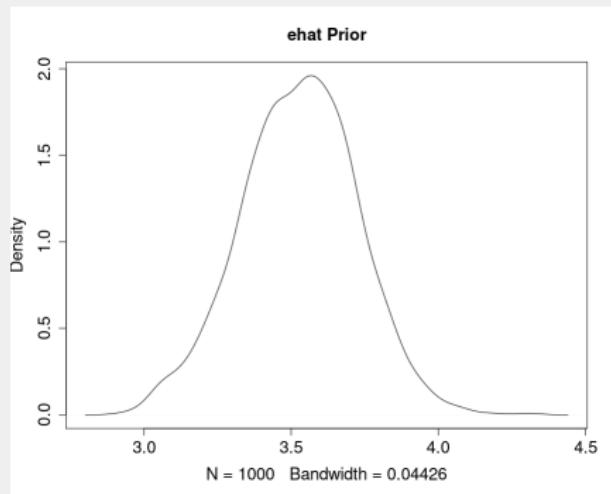


# DOMAIN SPECIFIC KNOWLEDGE - PARAMETERS

$x$  where  $y$  is half way between  $c$  and  $d$ . Should be centred around mean of  $x$ , plus/minus 10. But goes in as  $\log e$ , so need

to consider that!

Pushforwards.

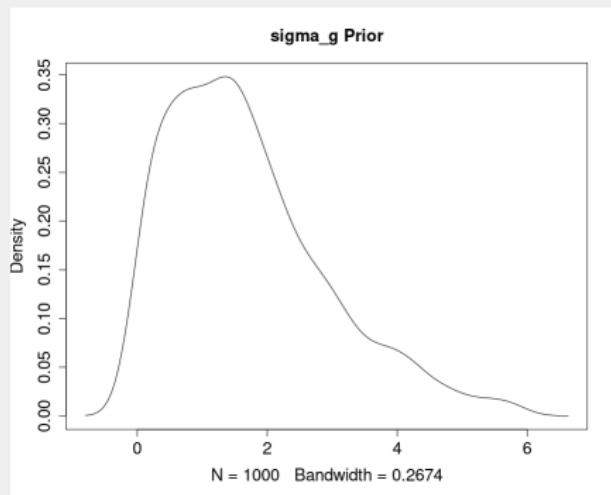


# DOMAIN SPECIFIC KNOWLEDGE - PARAMETERS

$\sigma_g$

Observation error from the Gaussian process model.

Not sure, but probably plus/minus 10 degrees?



# **BUILDING THE MODEL**

## **PRIOR PREDICTIVE CHECKS**

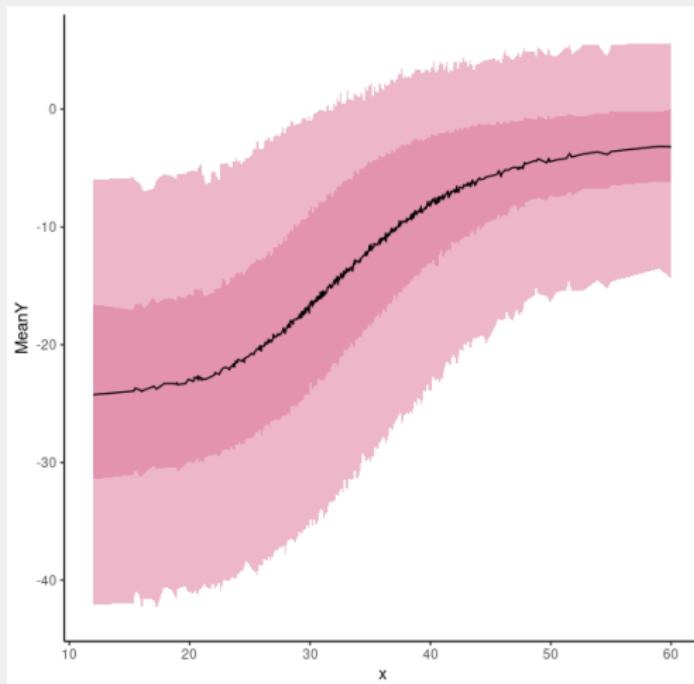
# STAN CODE

doseResponse\_priorCheck\_1.stan

generated quantities

algorithm "Fixed\_param"

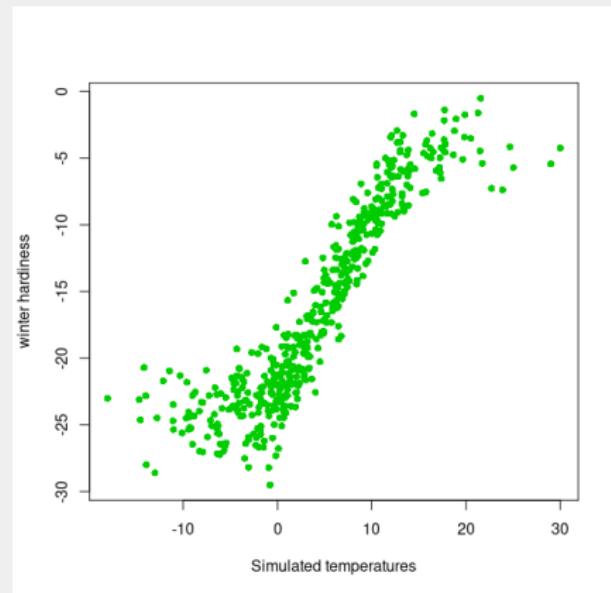
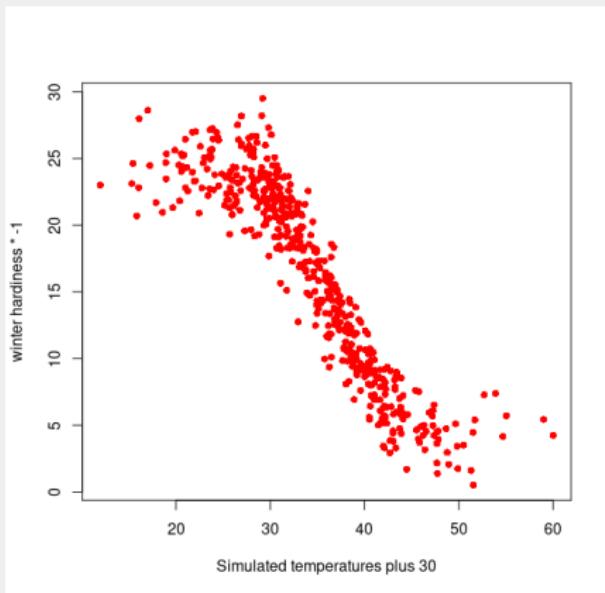
# PREDICTION



# **BUILDING THE MODEL**

## **SIMULATED DATA**

# MY DATA



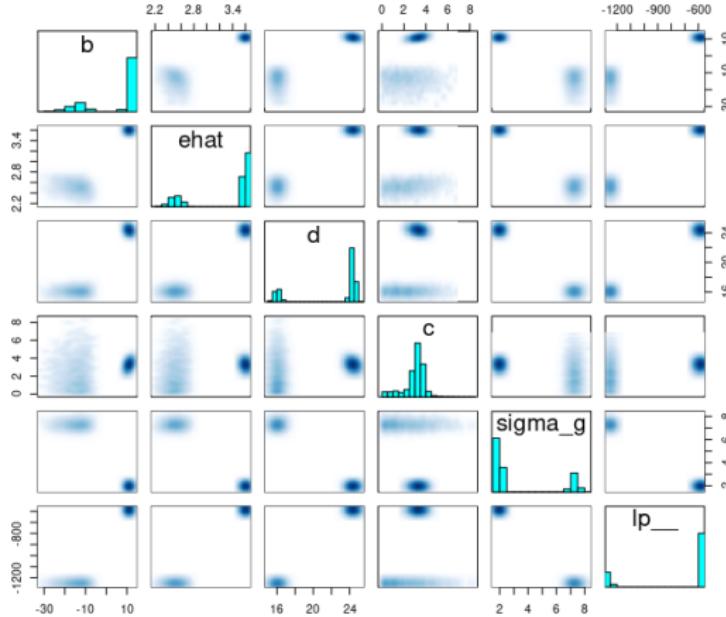
# STAN CODE

See doseResponseSimple2\_oldPriors.stan

# **BUILDING THE MODEL**

**WAS IT A GOOD MODEL???**

# PROBLEMS



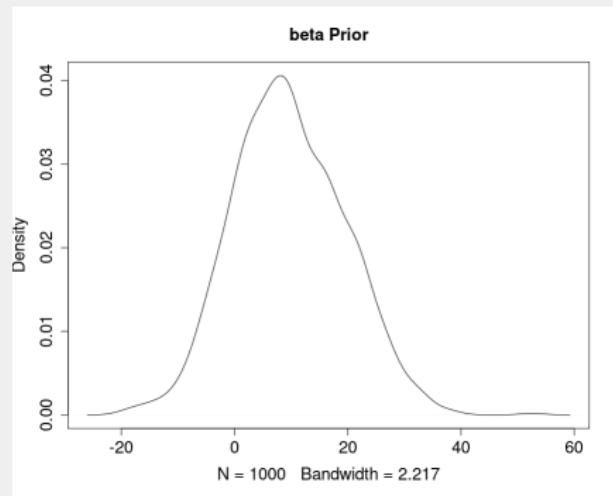
Weird distributions happening - when beta drops below 0?

# **BUILDING THE MODEL**

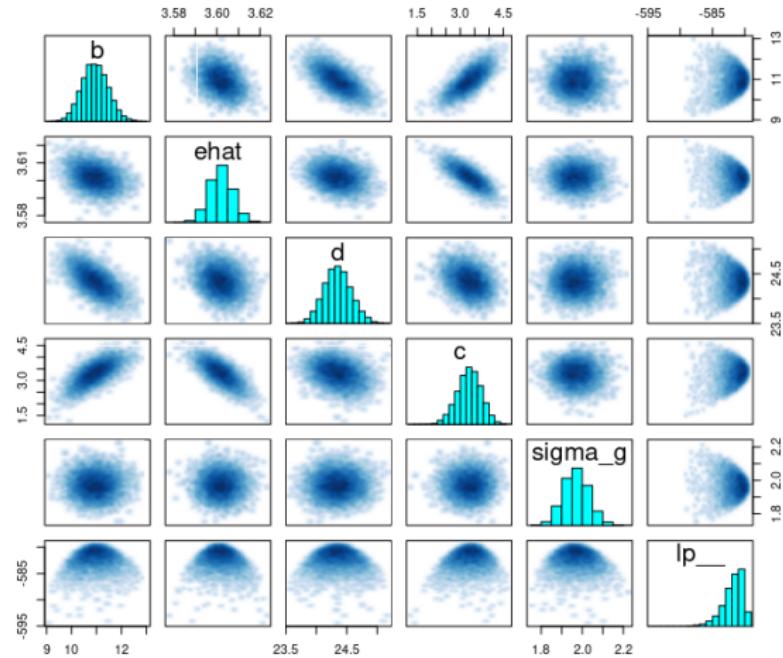
**NEXT ATTEMPT**

# POSITIVE BETA

$\beta \sim truncNormal(10, 10)$

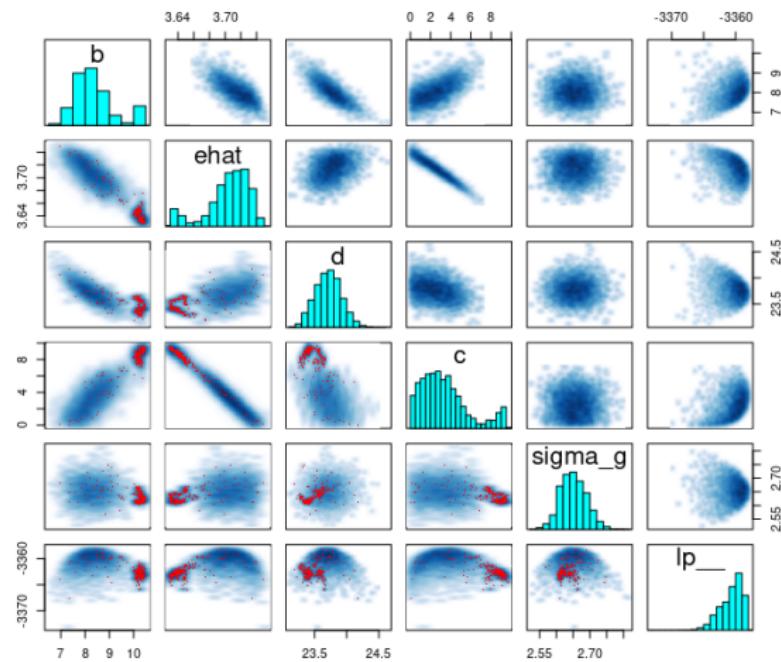


# BETTER...



Better, but still  
some suggestions  
of collinearity.

# REAL DATA



Big problems still -  
large c's, small e's  
and large b's

# **BUILDING THE MODEL**

**VARIOUS ATTEMPT**

# TROUBLESHOOTING

I tried various combinations of priors

Inspecting pairs plots

Eventually tried gamma distributions to avoid zero  
Need domain knowledge to do this though.

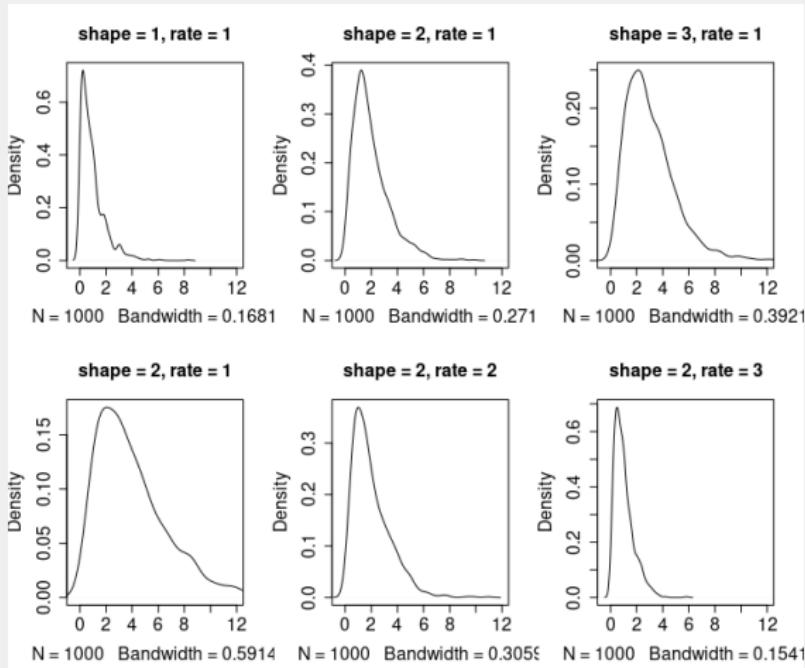
## GAMMA DISTRIBUTION

Gamma is positive only, and has a shape and a rate function

Not as intuitive as a normal for setting priors.

Can use stan, but I used plots because easier.

# GAMMA DISTRIBUTION

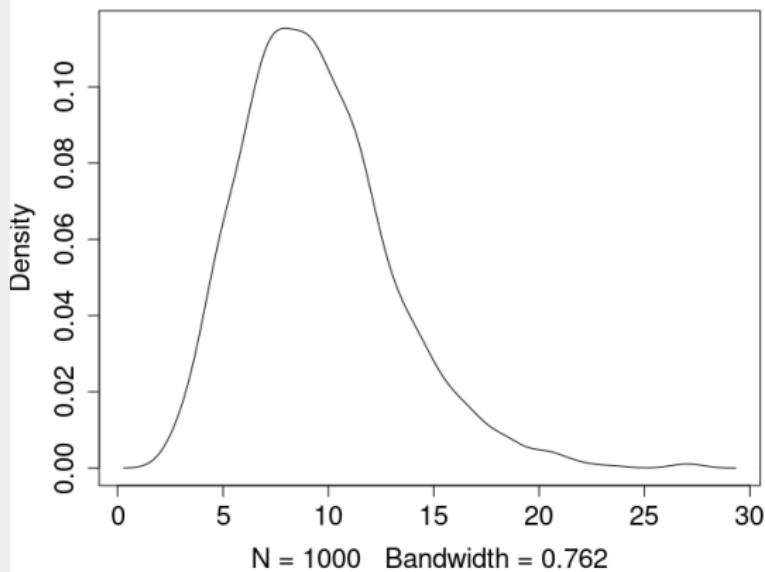


# **BUILDING THE MODEL**

**CURRENT MODEL**

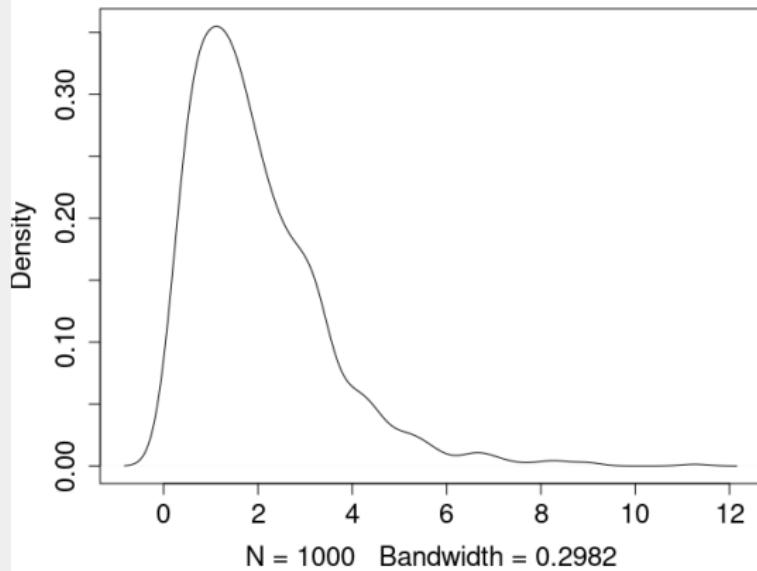
# CURRENT PRIORS

beta Prior (gamma) shape = 7, scale = 0.75

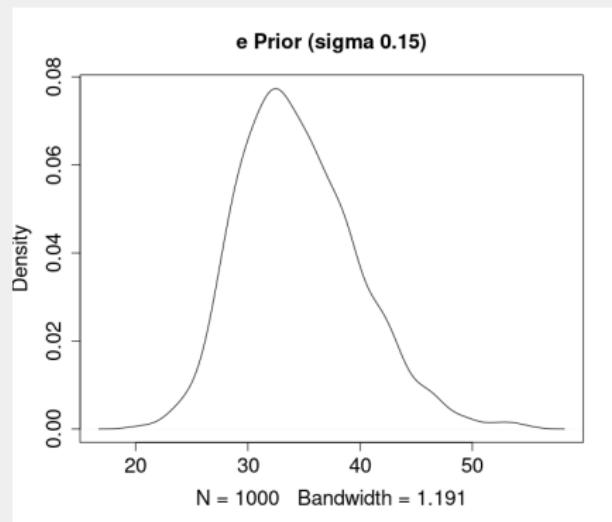
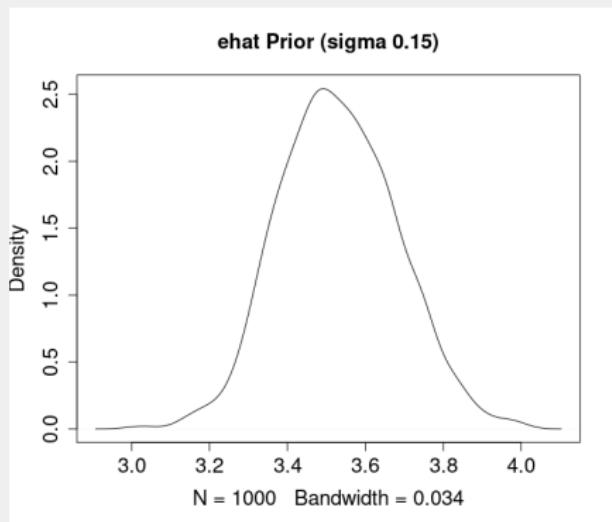


# CURRENT PRIORS

c Prior (gamma) shape = 3, rate = 1



# CURRENT PRIORS

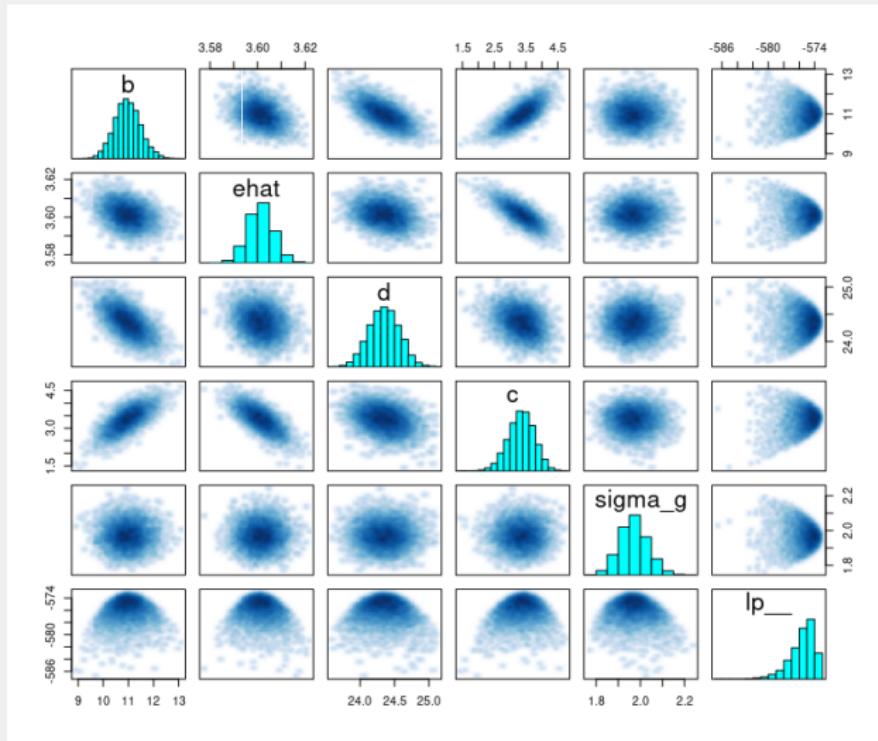


## STAN CODE

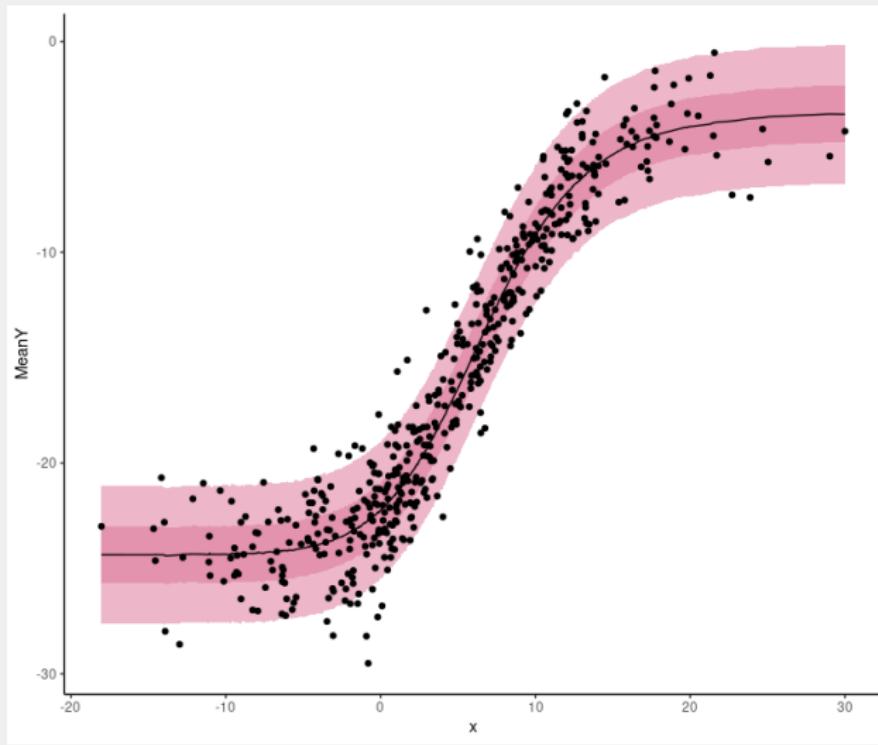
See doseResponse\_priorCheck.stan

doseResponseSimple2.stan

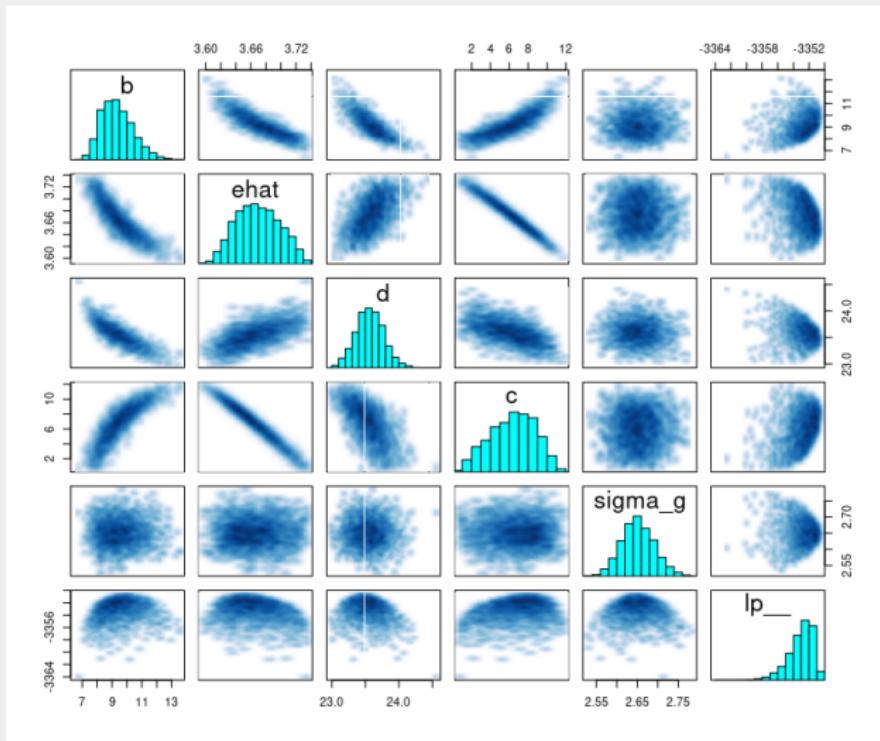
# CURRENT MODEL FIT SIMULATED DATA



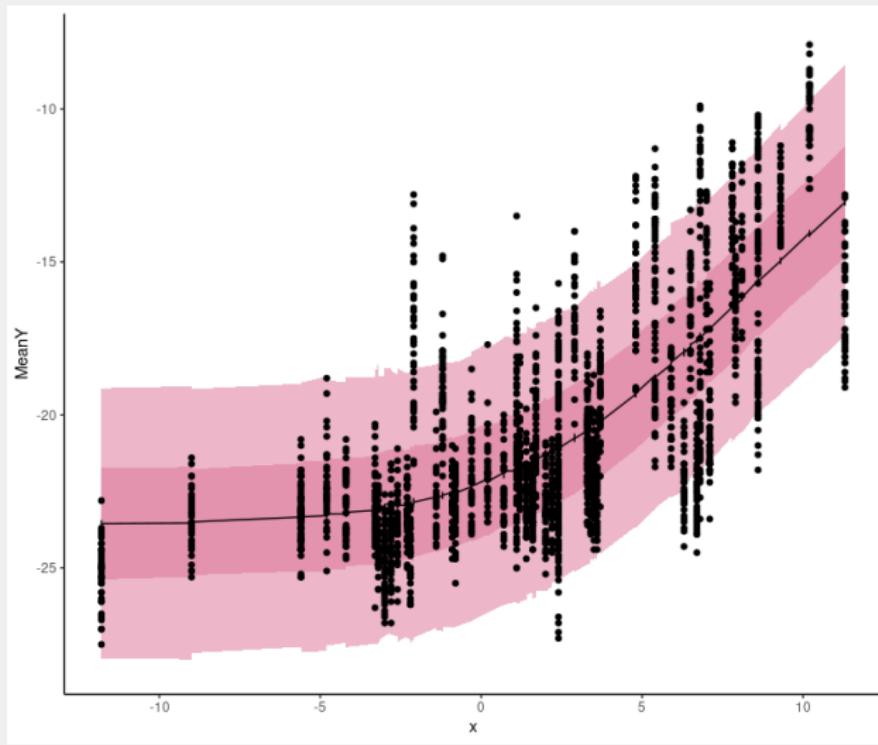
# CURRENT MODEL FIT SIMULATED DATA



# CURRENT MODEL NOT FIT REAL DATA



# CURRENT MODEL NOT FIT REAL DATA



# NEXT STEPS

# FIRST STEP

More prior tweaking

## OTHER OPTIONS

Try a different parameterization that is supposed to be easier to fit?

Or set c to zero?

# ONE DAY....

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Hierarchical elements!

Start on d? Then include  $\beta$ ?

# QUESTIONS?