# Modeling Glaucoma Progression Using Partial Differential Equations and Regression

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# Background on Glaucoma

- A sight-threatening disorder marked by an increase in intraocular pressure that leads to complete blindness if untreated.

- Affects 1-2% of the US population.

- The number of persons estimated to be blind as a result of glaucoma is 4.5 million.

# Objectives and Research Questions

- Model progression of glaucoma
- Can we predict how quickly the disease is spreading?
- Can we see if the eyesight is deteriorating at a faster-than-normal rate?
- Can we determine whether patients are diseased based on some mathematical model?

# Data Collection



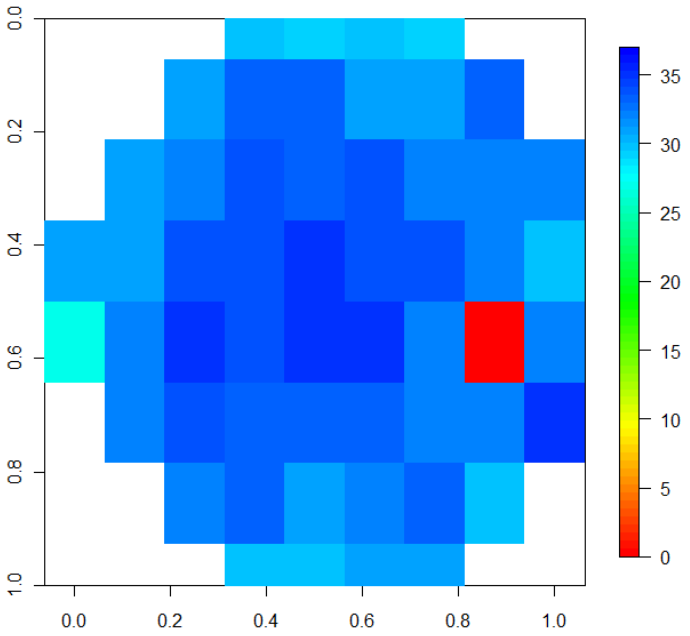
| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | 30 | 29 | 29 | 29 | | |
| | 30 | 31 | 30 | 31 | 31 | 30 | |
| 33 | 32 | 31 | 32 | 32 | 31 | 30 | 30 |
| 29 | 32 | 32 | 32 | 33 | 33 | 33 | 27 | 31 |
| 30 | 30 | 33 | 34 | 33 | 33 | 31 | | 30 |
| | 29 | 30 | 31 | 32 | 34 | 32 | 32 | 32 |
| | | 27 | 27 | 32 | 32 | 32 | 33 | |
| | | | 27 | 31 | 31 | 33 | | |

# Study Data

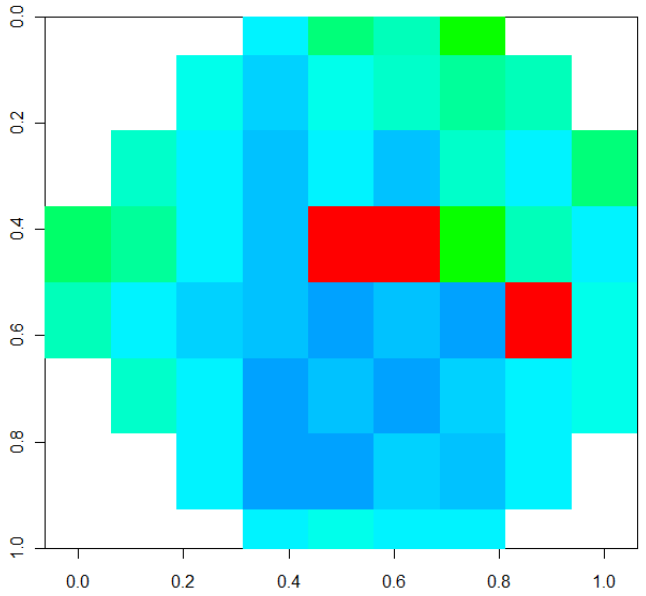
- 120 patients with glaucoma
- 60 normal patients
- 10 visits each.  One every 6 months.
- Missing data

# Normal versus Diseased Eyes

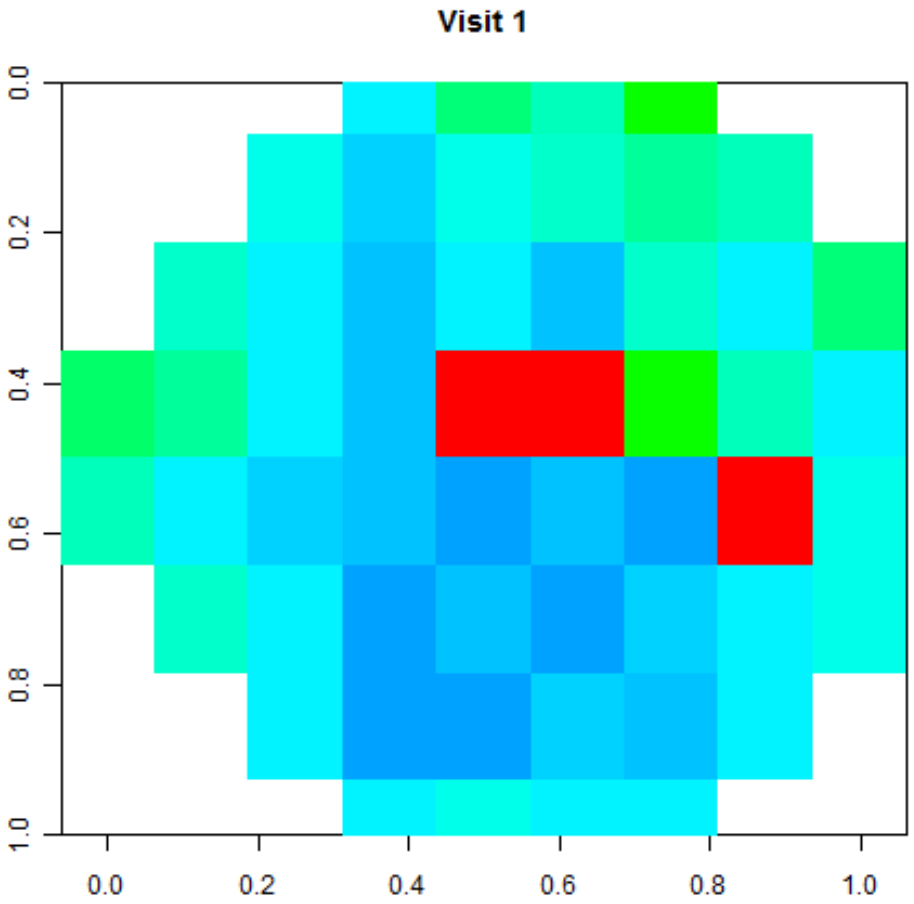
## Normal Patient




## Diseased Patient



# Animated Progression of Disease



# Partial Differential Equations

Theoretical Reaction-Diffusion Model:

$$\delta/\,\delta t\; z_t(x,y) = \beta[\delta^2/\,\delta x^2 + \delta^2/\,\delta y^2\,] + \alpha^*\, z_t(x,y)$$

Approximate model based on discrete study data:

$$z_{t+1}(x,y) = \beta[z_t(x+1,y) - 2^* z_t(x,y) + z_t(x-1,y) + z_t(x,y+1) - 2^* z_t(x,y) + z_t(x,y-1)] + (\alpha+1)\, z_t(x,y)$$

- $\beta$ is the rate of spatial change

- $\alpha$ is the rate of temporal change

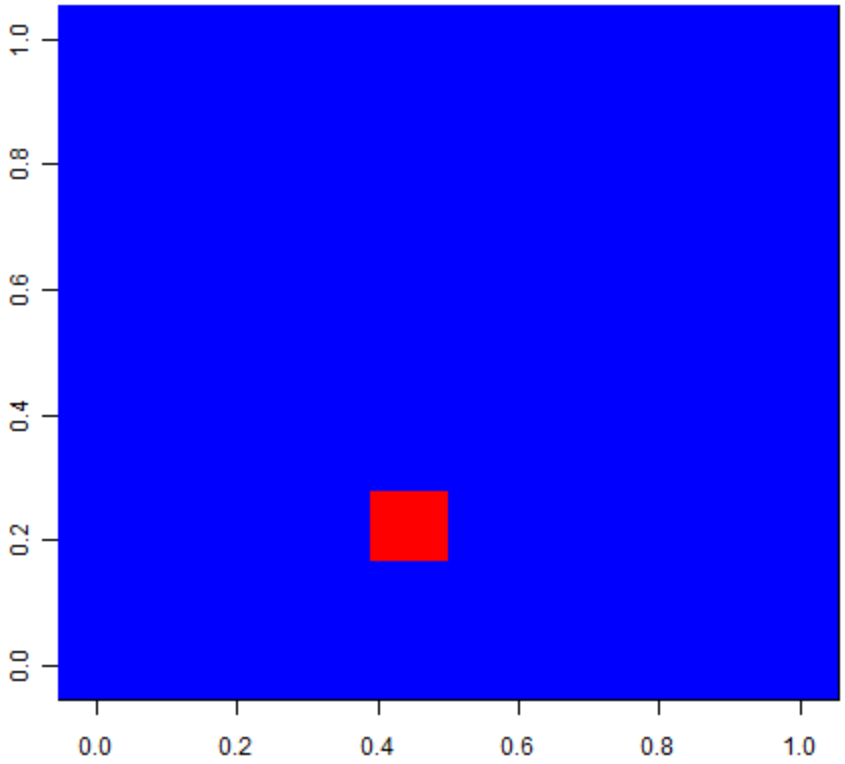
# Challenges with Differential Equations

Boundary points

-We assumed there was no change in vision beyond boundary points

-Theoretical simulations suggested this was the most appropriate way to model the spread of the disease.

# Simulation of Disease Spread



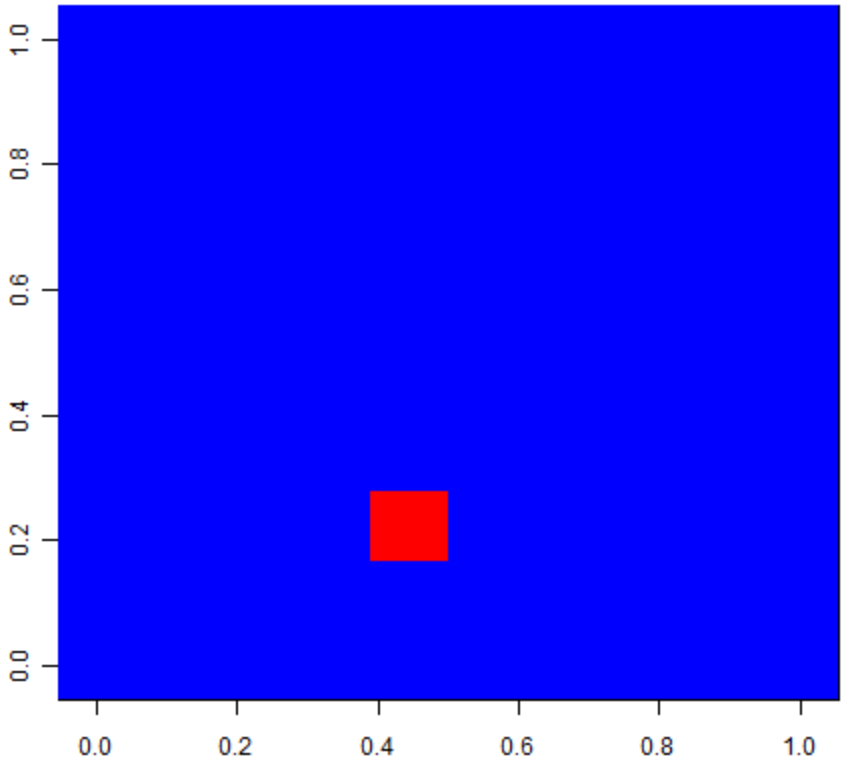
# Linear Regression Model

- Response: Measurement at time t+1 at (x,y)
- Predictors:
  - -Measurement at time t at location (x,y)
  - -Sum of partial derivatives at time t at location (x,y)

$$z_{t+1}(x,y)=\beta[z_t(x+\Delta x,y)-2*z_t(x,y)+z_t(x-\Delta x,y)+z_t(x,y+\Delta y)-2*z_t(x,y)+z_t(x,y-\Delta y)]+(\alpha+1)z_t(x,y)+\varepsilon$$

$$\text{Error}\sim N(0,\sigma^2)$$

# Simulation data with noise



# Results

$$z_{t+1}(x,y)=\beta[z_t(x+\Delta x,y)-2^*z_t(x,y)+z_t(x-\Delta x,y)+z_t(x,y+\Delta y)-2^*z_t(x,y)+z_t(x,y-\Delta y)]+(\alpha+1)z_t(x,y)+\varepsilon$$

| Patient # | α | α p-value | β | β p-value |
|---|---|---|---|---|
| 1 | 0.001485 | 0.8131 | 0.030078 | < 0.0001 |
| 2 | -0. 001842 | 0.6538 | 0.031128 | < 0.0001 |
| 3 | -0.004483 | 0.5861 | 0.048816 | < 0.0001 |

# Confidence intervals

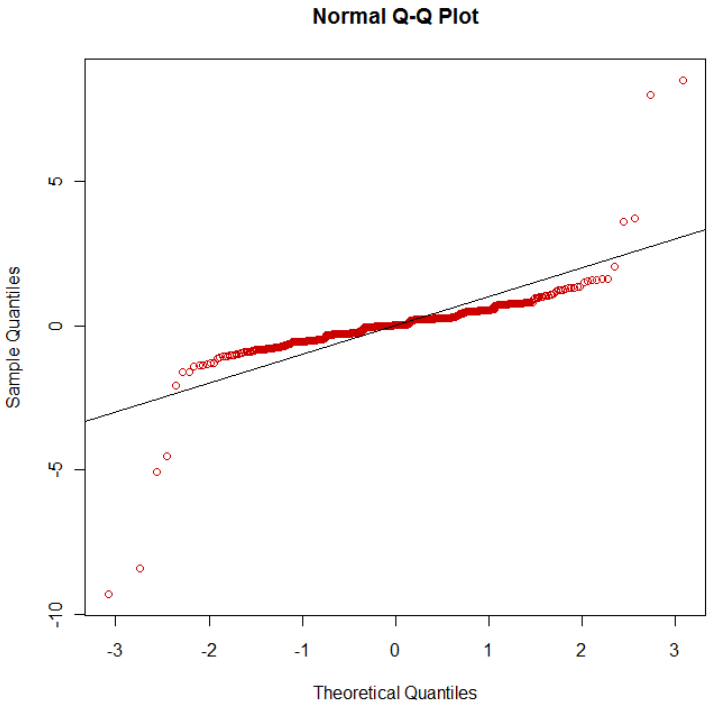
Patient 1

95% confidence interval for $\alpha$
(-0.01084420, 0.01381332)

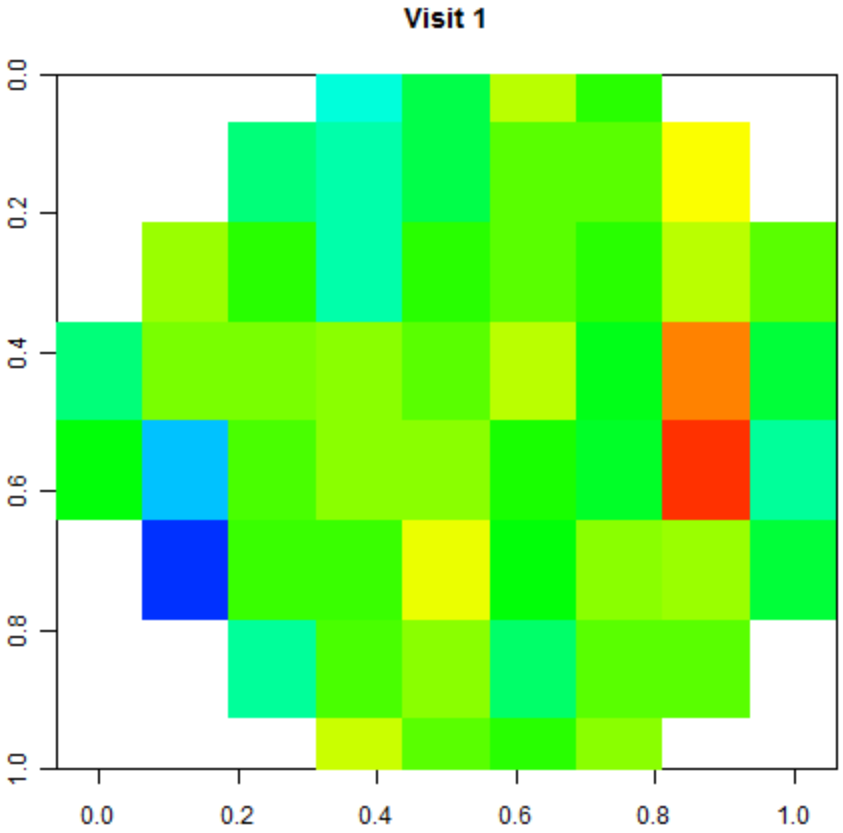
95% confidence interval for $\beta$
(0.01793912, 0.04221690)

# Regression Assumptions

- Regression assumes that error terms are normally distributed

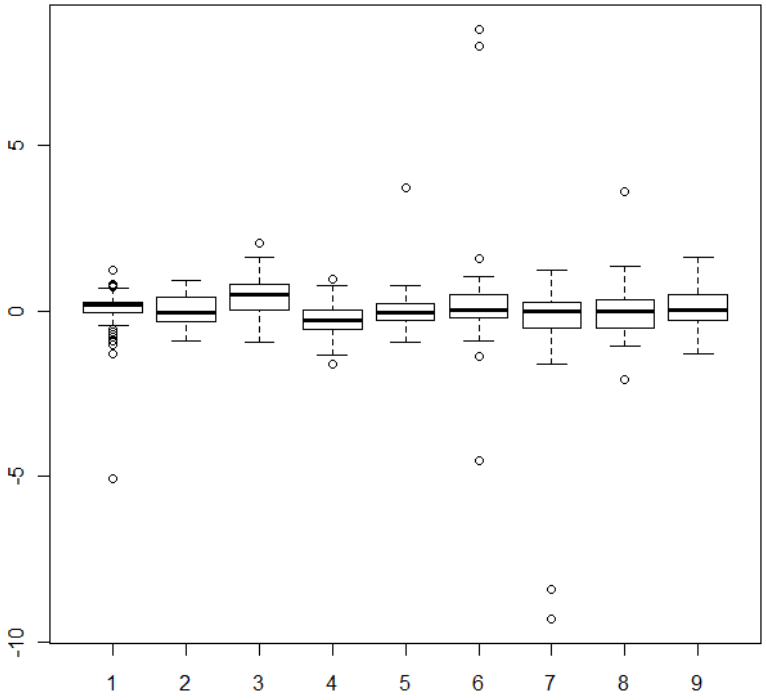


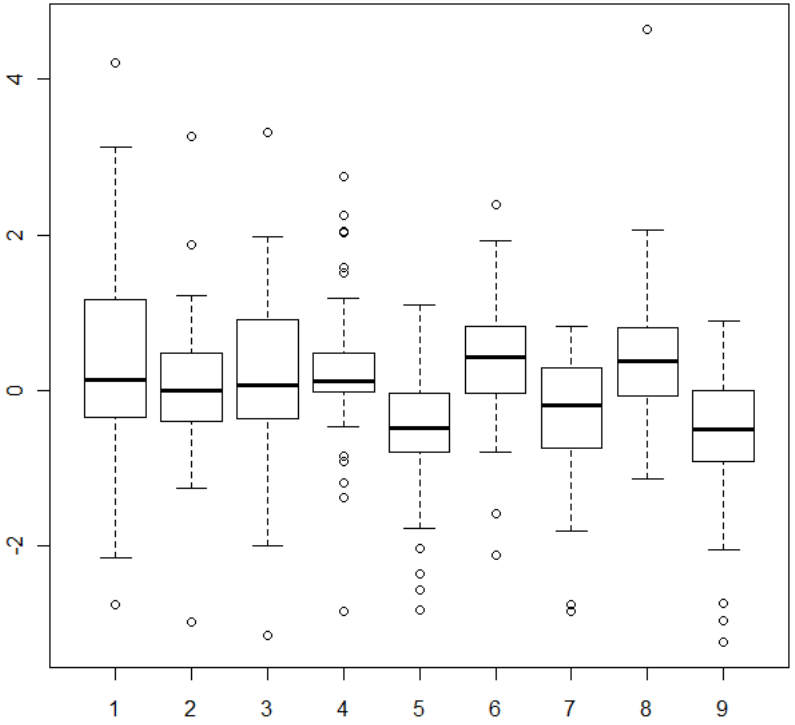
# Residuals by Location



# Assumptions/Residuals

- Regression assumes variance of the error term is constant across observations (homoscedasticity)



# Problems with Data-Blind spots

- Every human has a blind spot, causing a value of 0 in the dataset.

- This misrepresents the disease level in that part of the eye, causing error in our prediction

- Possible solution: Treat the blind spot the same as a boundary point

# Problems: Ongoing Treatment

- For ethical reasons, patients were being treated for their disease, so some areas did show improvement.

- It was not possible to know which improvement was caused by measurement error and which was caused by medical intervention.

# Conclusions and Future Work

- Model is promising because our regression assumptions to do not appear to be violated.

- More accurate model will be possible when controlling for blind spots.

- Future work will include finding β for all patients, diseased and normal, in order to find the distribution of β.

# Future Work

- We must compare this model to a model for non-diseased patients.

- We need to find a way to incorporate the effects of treatment into the model.

- We may need to account for the lower bound of possible measurement values.

# Acknowledgements

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