Pharmacokinetic Modeling Using Parametric, Non-Parametric, and Machine Learning Models

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How can we best model how a drug is broken down by the human body?

Purpose

Mathematical models are used by pharmaceutical companies, clinicians, and researchers to predict how a patient might respond to a drug. We investigate the effectiveness of three different kinds of models.

Model

Nonlinear Mixed-Effect Model

This model depends on a formal representation of the human body called a one-compartment model. This is a pharmacokinetic model that represents the body as a single “blood compartment”, along with parameters representing the different stages of the pharmacokinetic process, which can be modeled by differential equations as a function of time.

Nonparametric Adaptive Grid

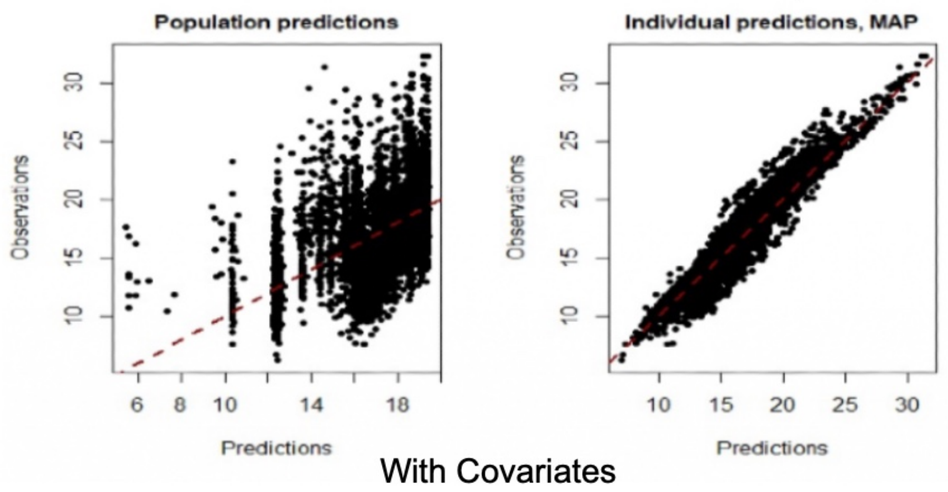
This model uses a Nonparametric Expectation Maximization (NPEM) algorithm to create an adaptive grid. NPEM is another form of Nonparametric Likelihood Method, which is suited to deal with the latent variables present in our data.

Machine Learning

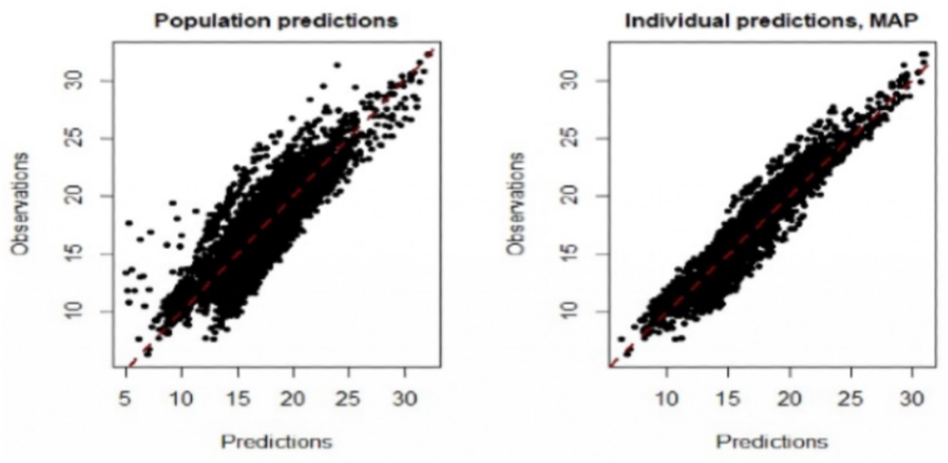
Neural networks are effective when massive amounts of training data are available. They don’t rely on a previously defined compartment model, and can be effective in spite of messy or incomplete data.

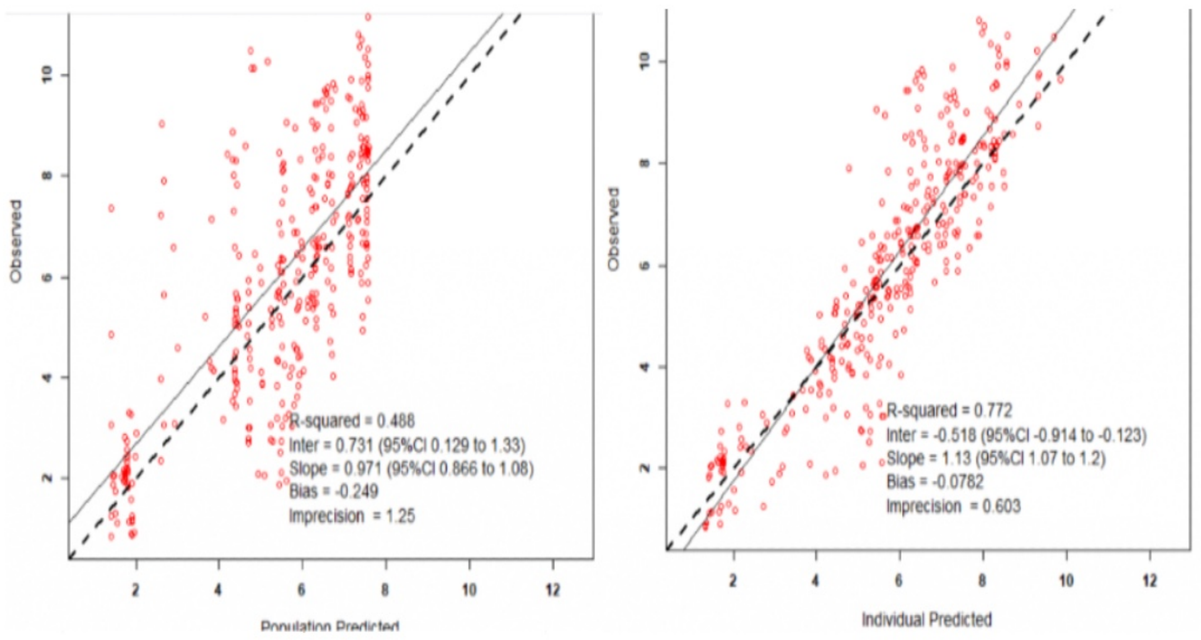
Results

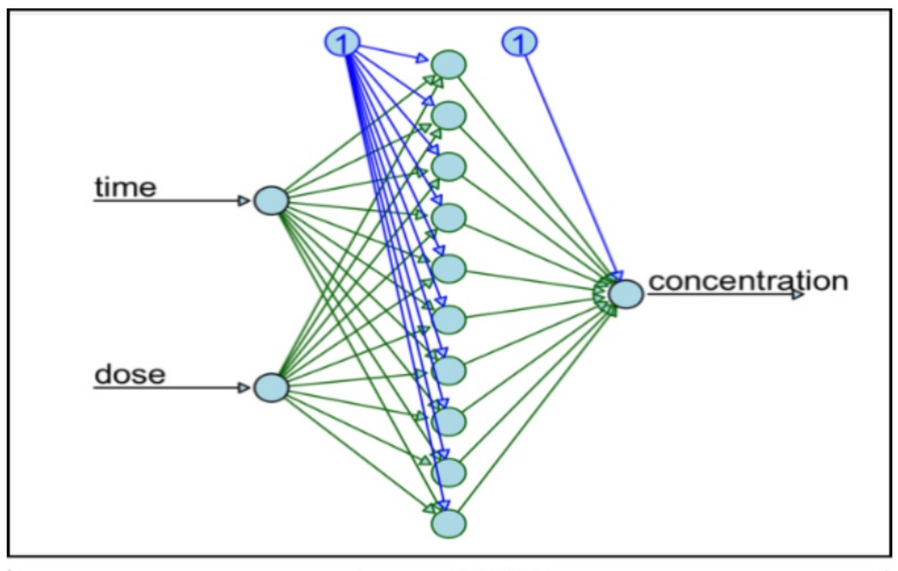
No Covariates



With Covariates







Loss: 0.0311

Conclusion

The one compartment model is doing exactly what we wanted, population predictions improved as covariates were added in. Further research would include expanding the model to take multiple compartments in to account.Single compartment program is doing exactly what we wanted, population predictions improved as covariates were added in. Further research would include expanding the model to take multiple compartments in to account.

We used a nonparametric adaptive grid algorithm called pmetrics. Using a smaller portion of the dataset, we found that individual predictions were better than, population predictions. In the future we hope to add more compartments and use a bigger data set.

We implemented a simple feedforward neural network as both a baseline, and a starting point for exploring the use of these methods with our data. The simple network only has two input variables: the initial dose and the time of measurement. It’s single output is the predicted concentration measurement for that given time. With a loss of approximately 0.0311, even a rudimentary network like this shows respectable results.

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