

BIOE 498 / BIOE 599: Computational Systems Biology for Medical Applications

CSE 599V: Advancing Biomedical Models

Lecture 11: Modeling Workflow

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**BioEngineering

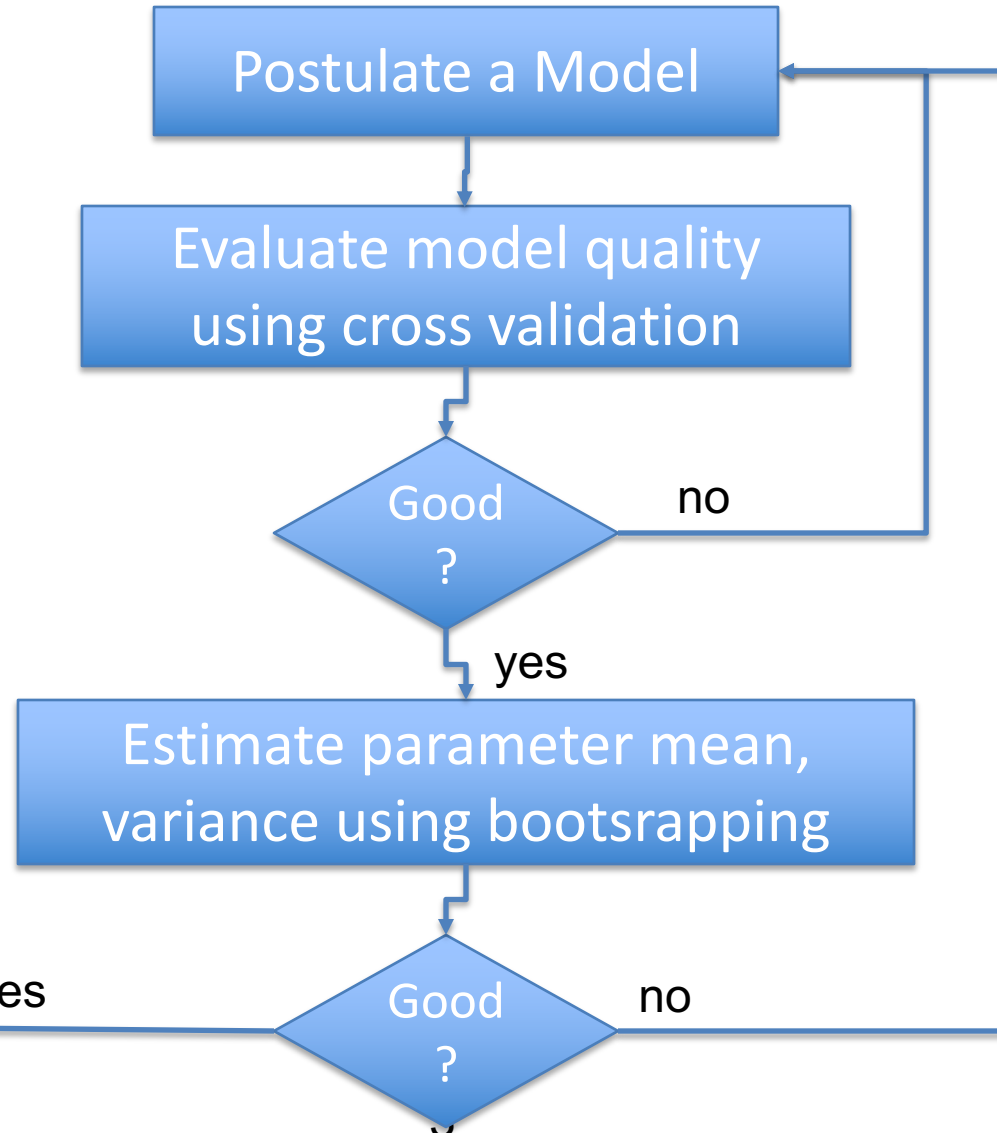


Learning Objectives

- Can do the following in combination
 - Fit parameters to a model
 - Evaluate a model using cross validation
 - Estimate parameter variances using bootstrapping
- Diagnose deficiencies in a model and propose an improved model
- Software Engineering basics



Computational Workflow



Software Engineering Basics

Reproducible Modeling

- Create reusable functions
- Comment function interfaces
- Use meaningful names for variables
- Write unit tests



Review of Fitting

```
import lmfit
import numpy

# Synthetic data
x = np.linspace(0, 10, 100)
AMP = 3.0
FREQ = 1.0
PHASE = 0.0
DECAY = 0.1
data = AMP*sin(x*FREQ + PHASE)*exp(-x*x*DECAY)
```



Review of Fitting

```
# Calculation
def calculate(x, amp, phase, freq, decay):
    return amp*sin(x*freq + phase)*exp(-x*x*decay)

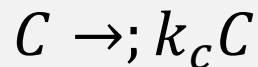
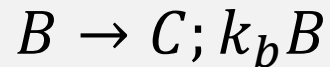
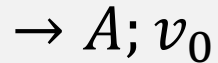
# Fitting
params = lmfit.Parameters()
params.add('amp', value=10)
params.add('freq', value=3)
params.add('phase', value=.2)
params.add('decay', value = 1.0)

model = lmfit.Model(calculate)
fitter = model.fit(data, params, x=x)
fitter.params
```



Exercise: Fitting a Simulation Model: Part 1

Model



$$v_0 = 10; k_a = 0.4;$$

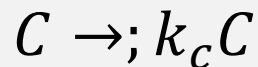
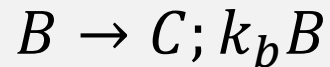
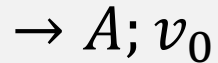
$$k_b = 0.32; k_c = k_a$$

1. Use the simulation of the Model as “observations” by adding a normally distributed error term $N(0,1)$ to the concentration B.
2. Now try to estimate the constants in the model by fitting to the observations of B.



Exercise: Fitting a Simulation Model: Part 2

Model

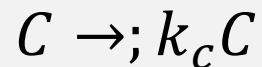
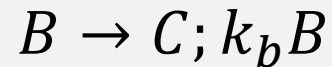
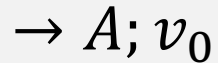


1. Use the simulation of the Model 1 as “observations” by adding a normally distributed error term $N(0,1)$ to the concentrations of A, B, C.
2. Now try to estimate the constants in the model by fitting to the observations of A, B, C.



Exercise: Fitting a Simulation Model: Part 3

Model

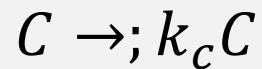
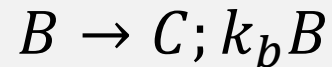
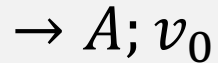


Extend Part 2 by using cross validation to evaluate the model quality.



Exercise: Fitting a Simulation Model: Part 4

Model



Extend Part 3 by using bootstrapping to estimate the variability of the model parameters.



Discussion Question

- Suppose that all you know is that there are 3 floating species (A, B, C), an input boundary species, and an output boundary species.
- How would you figure out the structure of the pathway?
- How would you determine the kinetics (e.g., Hill equation parameters)?

