Yesterday: Maximum Likelihood ⟹ Negative Log Likelihood (NLL)

Introduction to Numerical Methods for Identifiability

MSRI Algebraic Geometry Summer School 2022

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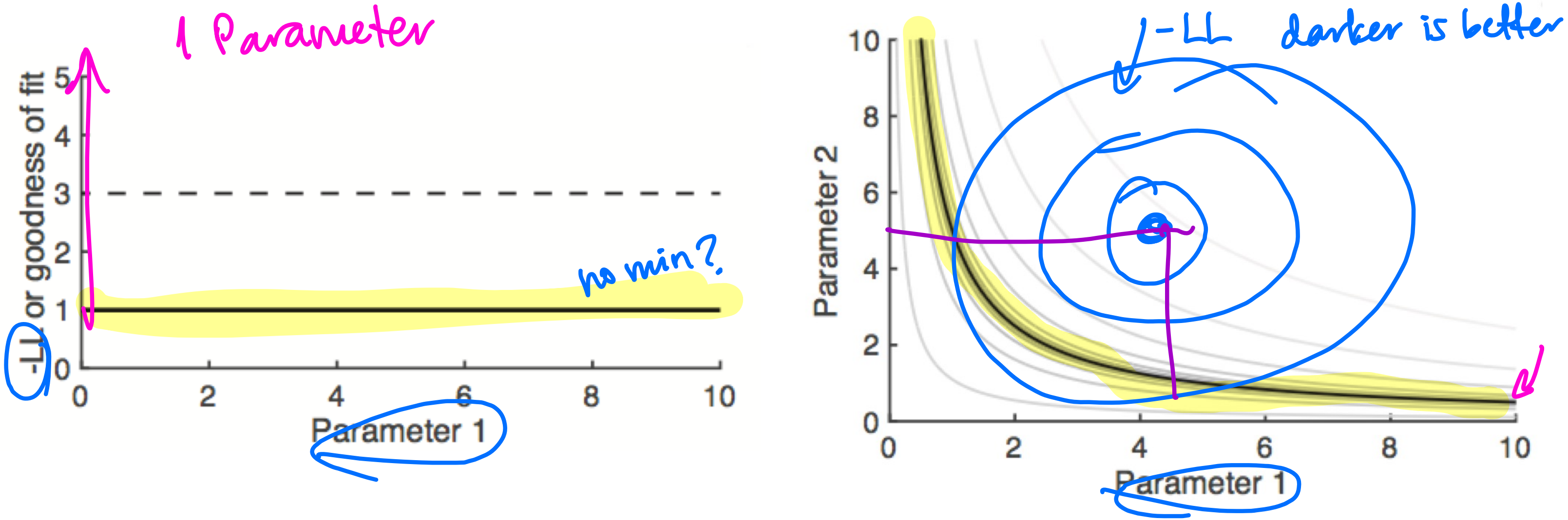
Consider the following approach:

- Assume your model is structurally identifiable and choose a set of "true" parameters
  - Generate simulated output data from these "true" parameters

- Attempt to fit your simulated data using a range of parameter values and solve for the "best" parameter set to reproduce the simulated data

- IF your original parameter set is returned, your model may be identifiable
  - What does it mean if the simulated data is without noise?
  - With noise?

2-parameter relationship



What can we expect to see?

Many other numerical methods exist! (Ex: Bayesian)

Next we will look at the Fisher Information Matrix

Think of this as a numerical snapshot of potential dependencies between parameters—all wrapped up in a matrix!

Ok but what if visualization isn't your thing?

Then what is the Fisher Information Matrix?

- FIM represents the amount of information that the output y contains about parameter p
- It relates to the sensitivity matrix via the score: $\frac{\partial}{\partial p} \ln L(z,p)$
  - This is the sensitivity of the log likelihood
  - How does our likelihood change wrt p?
- The variance of the score is the Fisher Information Matrix:

$$I(p)_{ij} = \mathrm{E}\left[\left(\frac{\partial}{\partial p_i} \log L(z,p)\right)\left(\frac{\partial}{\partial p_j} \log L(z,p)\right) \mid p\right]$$

- Under certain conditions, we can write the FIM as the Hessian matrix
  - Interpret FIM as the curvature of the likelihood

- When the error is normally distributed, we can write:

$$F = X^T W X$$

  - If just checking structural identifiability, we only need to find $\hat{F} = X^T X$

FIM and Cramer-Rao Bound

- Cramer-Rao Bound: $FIM^{-1} \leq Cov(p)$
  - The diagonal of the covariance matrix gives variances for the parameters (used for defining confidence intervals)
  - Large CI indicate practical un-identifiability

- Rank(FIM) = number of identifiable parameter combinations
  - Use FIM to find blocks of related parameters

Caution!

- FIM is local and asymptotic
- Just a local approximation of the curvature of the likelihood

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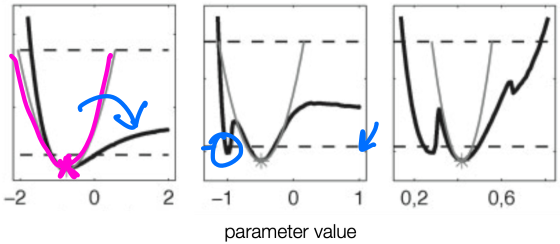

Raue et al. 2010

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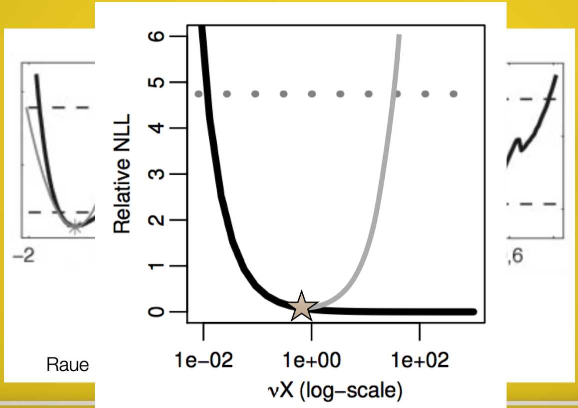

Brouwer, Meza, Eisenberg 2017

5 Minute Break!

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Time to Code!...

Don’t Panic. Again.