Introduction to Model Fitting and Calibration

Modelling for Pandemic Preparedness and Response Modular Shortcourse, 2025

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Learning Objectives

By the end of this lecture, you will be able to:

- Understand the fundamental concepts of model fitting and calibration
- Apply least squares estimation to compartmental models
- Implement maximum likelihood estimation for epidemic models
- Compare the strengths and weaknesses of different fitting methods
- Recognize when to use advanced methods like MCMC and particle filtering
- Troubleshoot common fitting problems

Introduction & Motivation

Why Model Fitting Matters

The Challenge

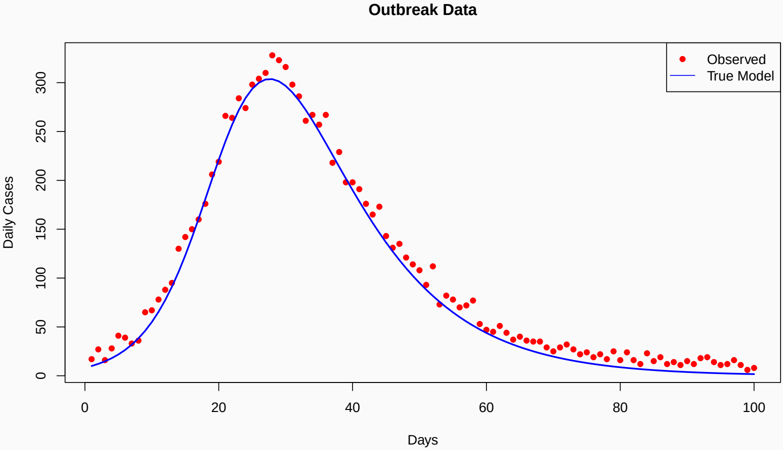
The Challenge:

- We have mathematical models (e.g., SIR, SEIR)
- We have real-world data (case counts, hospitalizations)
- **How do we connect them?**

The Goal

- Find parameter values that make our model predictions match observed data
- Quantify uncertainty in our estimates
- Make reliable predictions and policy recommendations

Example: Outbreak data



Question: How do we estimate β and γ from this noisy data?

Types of Fitting Methods

Deterministic Methods

- **Least Squares**
- **Maximum Likelihood Estimation (MLE)**

Stochastic Methods

- **Markov Chain Monte Carlo (MCMC)**
- **Sequential Monte Carlo (SMC)**
- **Particle MCMC (pMCMC)**
- **Approximate Bayesian Computation (ABC)**

Today's Focus: Least Squares and MLE as foundations

Conceptual Foundations

What is Model Fitting?

Definition: The process of finding parameter values that make a mathematical model's predictions as close as possible to observed data.

Mathematical Formulation

$$\hat{\theta} = \arg\min_{\theta} \mathcal{L}(\theta, \mathbf{y})$$

Where:

- $\theta =$ parameter vector (e.g., β, γ)
- $\mathbf{y} =$ observed data
- $\mathcal{L} =$ loss/objective function

The SIR Model as Our Example

Differential Equations:

$$\frac{dS}{dt} = -\beta S I$$

$$\frac{dI}{dt} = \beta S I - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

Parameters to Estimate

- $\beta =$ transmission rate
- $\gamma =$ recovery rate

Key Quantities

- $R_0 = \frac{\beta}{\gamma}$ (basic reproduction number)
- Infectious period $= \frac{1}{\gamma}$

Sources of Uncertainty

Model Uncertainty

- Wrong model structure
- Missing compartments or processes

Parameter Uncertainty

- True parameter values unknown
- Multiple parameter sets give similar fits

Observation Uncertainty

- Measurement error
- Reporting delays
- Underreporting

Process Uncertainty

- Stochasticity in disease transmission
- Environmental variability

The Fitting Challenge

Identifiability Problem: Multiple parameter combinations can produce similar model outputs

Example:

- High β, high γ
- Low β, low γ

Both might give similar epidemic curves!

Solution: Use additional information (e.g., known infectious period)

Least Squares Estimation

Least Squares: The Intuitive Approach

Core Idea: Minimize the sum of squared differences between model predictions and observations

Mathematical Formulation:

$$\mathsf{SSE} = \sum_{i=1}^{n} (y_i - f(t_i, \theta))^2$$

Where:

- y_i = observed value at time t_i
- $f(t_i, \theta)$ = model prediction at time t_i
- θ = parameter vector

Why Squared Errors?

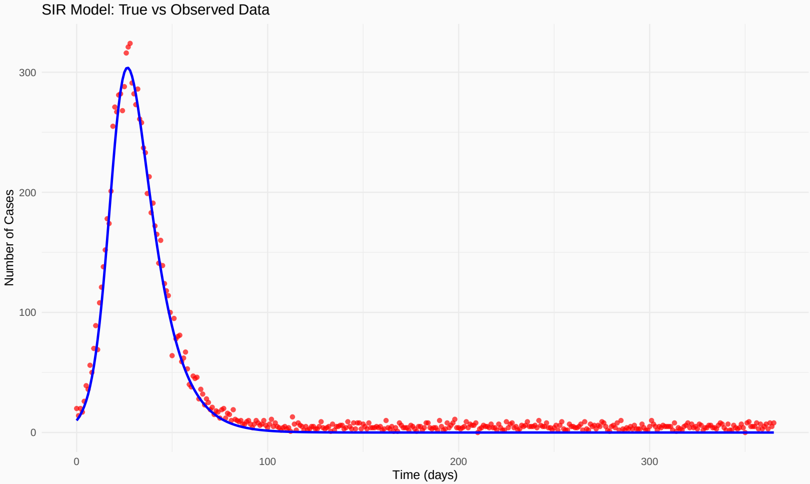
Advantages:

- Penalizes large errors more heavily
- Differentiable (smooth optimization)
- Mathematically tractable
- Gives maximum likelihood estimates when errors are normal distributed

Disadvantages

- Sensitive to outliers
- Assumes constant variance
- No probabilistic interpretation

Least Squares Example: SIR Model



Implementing Least Squares

```
# Define objective function
sse_function <- function(params, data) {
  beta <- params[1]
  gamma <- params[2]

  # Simulate model
  out <- ode(
    y = init_conds,
    times = data$time,
    func = sir_model,
    parms = c(beta = beta, gamma = gamma)
  )

  # Calculate sum of squared errors
  predicted <- out[, "I"] * 1000
```

Strengths of Least Squares

Computational Advantages:

- Fast and efficient
- Well-established algorithms
- Easy to implement
- Good for initial parameter estimates

Statistical Properties

- Unbiased estimates (under certain conditions)
- Minimum variance among linear unbiased estimators
- Maximum likelihood when errors are normal

Practical Benefits

- Intuitive interpretation
- Widely understood
- Good starting point for more complex methods

Limitations of Least Squares

Statistical Limitations:

- Limited uncertainty quantification
- Assumes constant variance
- Sensitive to outliers
- No probabilistic framework

Practical Limitations

Practical Limitations:

- Parameter identifiability issues
- No confidence intervals
- Difficult to compare models
- Assumes measurement error only

Example Problem

```
# Show how different parameter combinations can give simila
param_combos <- data.frame(
  beta = c(0.25, 0.35, 0.30),
  gamma = c(0.08, 0.12, 0.10),
  label = c("Low  , Low  ", "High  , High  ", "True")
)

# Plot different fits
ggplot(plot_data, aes(x = time)) +
  geom_point(aes(y = observed), color = "red", alpha = 0.7)
  geom_line(aes(y = true_model), color = "blue", linetype =
  labs(x = "Time (days)", y = "Number of Cases",
       title = "Multiple Parameter Sets Can Give Similar Fi
  theme_minimal()
```

Multiple Parameter Sets Can Give Similar Fits

R implementation practicals

- Let's turn to the tutorials

Maximum Likelihood Estimation

Maximum Likelihood: The Probabilistic Approach

Core Idea: Find parameter values that make the observed data most probable

Mathematical Formulation:

$$\hat{\theta} = \arg\max_{\theta} L(\theta) = \arg\max_{\theta} \prod_{i=1}^{n} f(y_i|\theta)$$

Where: - $L(\theta)$ = likelihood function - $f(y_i|\theta)$ = probability density of observation i

In Practice: Maximize log-likelihood

$$\widehat{\theta} = \arg\max_{\theta} \ell(\theta) = \arg\max_{\theta} \sum_{i=1}^{n} \log f(y_i|\theta)$$

Why Maximum Likelihood?

Theoretical Advantages:

- Principled statistical framework
- Provides uncertainty quantification
- Enables model comparison (AIC, BIC)
- Asymptotically optimal properties

Practical Benefits:

- Confidence intervals
- Hypothesis testing
- Model selection
- Incorporates different error structures

Choosing a Probability Distribution

For Count Data (Cases):

- **Poisson**: $Y_i \sim \text{Poisson}(\lambda_i)$
- **Negative Binomial**: $Y_i \sim \text{NB}(\mu_i, \phi)$

Choosing a Probability Distribution

For Continuous Data:

- **Normal**: $Y_i \sim N(\mu_i, \sigma^2)$
- **Log-normal**: $\log Y_i \sim N(\log \mu_i, \sigma^2)$

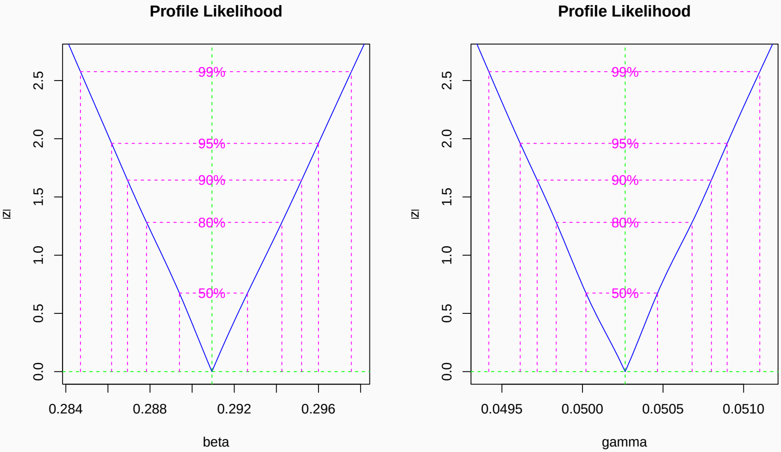
For Our SIR Example: We'll use Poisson since we're modeling case counts

MLE Implementation: Poisson Likelihood

```r
# Define negative log-likelihood function
nll_function <- function(beta, gamma, data) {
  # Simulate model
  out <- ode(y = init_conds, times = data$time,
             func = sir_model, parms = c(beta = beta, gamma

  # Model predictions (scaled to cases)
  predicted <- out[,"I"] * 1000

  # Poisson negative log-likelihood
  nll <- -sum(dpois(data$observed, lambda = predicted, log

  return(nll)
}

# Use optimization to find MLE
```

Uncertainty Quantification with MLE

```
# Profile likelihood for uncertainty
prof <- profile(fit_mle)
plot(prof, absVal = TRUE, main = "Profile Likelihood")
```



Model Comparison with MLE

```
# Fit different models and compare
# Model 1: SIR with Poisson
# Model 2: SIR with Negative Binomial

# Negative Binomial likelihood
nll_nb <- function(beta, gamma, phi, data) {
  out <- ode(y = init_conds, times = data$time,
             func = sir_model, parms = c(beta = beta, gamma

  predicted <- out[,"I"] * 1000

  # Negative Binomial negative log-likelihood
  nll <- -sum(dnbinom(data$observed, mu = predicted, size =

  return(nll)
}
```

Strengths of Maximum Likelihood

Statistical Rigor:

- Principled probabilistic framework
- Asymptotic optimality properties
- Natural uncertainty quantification
- Enables formal hypothesis testing

Practical Benefits

- Confidence intervals and standard errors
- Model comparison via AIC/BIC
- Handles different error structures
- Extensible to complex models

Limitations of Maximum Likelihood

Computational Challenges:

- More complex than least squares
- Requires optimization algorithms
- Can get stuck in local minima
- Sensitive to starting values

Statistical Assumptions

- Requires specification of error distribution
- Assumes model structure is correct
- Asymptotic properties may not hold
- Can be sensitive to outliers

Identifiability Issues

- Still suffers from parameter identifiability
- Profile likelihood can be computationally expensive
- May not converge for complex models

R implementation practicals

- Let's turn to the tutorials

Comparison of Methods

When to Use Each Method

Use Least Squares When:

- Quick exploratory analysis needed
- Getting initial parameter estimates
- Computational speed is critical
- Simple error structure assumed

Use Maximum Likelihood When:

- Uncertainty quantification needed
- Comparing different models
- Formal statistical inference required
- Complex error structures present
- Publication-quality results needed

Advanced Methods

Beyond Least Squares and MLE

Why We Need Advanced Methods:

- Parameter identifiability issues
- Complex error structures
- Model uncertainty
- Computational challenges
- Real-time fitting requirements

Advanced Approaches

1. **Bayesian Methods** (MCMC)
2. **Particle Filtering**
3. **Approximate Bayesian Computation (ABC)**
4. **Ensemble Methods**

Bayesian Methods: MCMC

Core Idea: Treat parameters as random variables with prior distributions

Bayes' Theorem:

$$P(\theta|\mathbf{y}) = \frac{P(\mathbf{y}|\theta)P(\theta)}{P(\mathbf{y})}$$

Advantages

- Natural uncertainty quantification
- Incorporates prior knowledge
- Handles parameter identifiability
- Model comparison via Bayes factors

Example with Stan

```
# Stan model for SIR fitting
"
// SIR model in Stan (walkthrough)
// Functions block: derivative of [S, I, R]
functions {
  vector SIR(real t, vector y, array[] real theta) {
    real S = y[1]; real I = y[2]; real R = y[3];
    real beta = theta[1]; real gamma = theta[2];
    vector[3] dydt;
    dydt[1] = -beta * S * I;
    dydt[2] =  beta * S * I - gamma * I;
    dydt[3] =  gamma * I;
    return dydt;
  }
}
```

Particle Filtering

Core Idea: Sequential Monte Carlo method for state-space models

When to Use:

- Real-time parameter estimation
- State estimation in stochastic models
- Handling of missing data
- Time-varying parameters

Advantages

- Handles stochasticity naturally
- Real-time updates
- No assumption of constant parameters
- Robust to model misspecification

Example Application

```r
# Particle filter for SIR model
library(pomp)

# Define SIR model with stochasticity
sir_pomp <- pomp(
  data = data.frame(time = covid_times, cases = covid_obser
  times = "time",
  t0 = 0,
  rprocess = euler.sim(
    step.fun = "sir_step",
    delta.t = 0.1
  ),
  rmeasure = "cases_measure",
  dmeasure = "cases_dmeasure",
  initializer = "sir_init",
```

Approximate Bayesian Computation (ABC)

Core Idea: Approximate posterior without likelihood evaluation

When to Use:

- Complex likelihoods
- Intractable models
- High-dimensional parameter spaces
- Model comparison

Algorithm:

1. Sample parameters from prior
2. Simulate data from model
3. Compare simulated to observed data
4. Accept if distance $<$ threshold

Advantages:

- No likelihood required
- Handles complex models
- Model comparison
- Intuitive approach

Ensemble Methods

Core Idea: Combine multiple models or methods

Types:

- **Model Ensembles**: Average predictions from different models
- **Method Ensembles**: Combine LS, MLE, MCMC results
- **Bootstrap Ensembles**: Multiple fits with resampled data

Advantages:

- Reduces overfitting
- Quantifies model uncertainty
- More robust predictions
- Handles model selection uncertainty

Practical Considerations

Common Fitting Problems

Convergence Issues:

- Poor starting values
- Flat likelihood surfaces
- Numerical instabilities
- Parameter bounds

Identifiability Problems:

- Multiple solutions
- Correlated parameters
- Insufficient data
- Model overparameterization

Solutions:

- Multiple starting points
- Profile likelihood
- Data augmentation

Troubleshooting Guide

If Optimization Fails:

1. Check starting values
2. Verify parameter bounds
3. Examine objective function
4. Try different algorithms
5. Simplify the model

If Parameters Are Unidentifiable:

1. Fix some parameters
2. Use additional data
3. Add regularization
4. Consider model reduction
5. Use prior information

If Results Are Unrealistic:

1. Check model assumptions
2. Verify data quality
3. Examine residuals
4. Test sensitivity
5. Consider alternative models

Best Practices

Before Fitting:

- Understand your data
- Check model assumptions
- Set realistic parameter bounds
- Prepare multiple starting values

During Fitting:

- Monitor convergence
- Check for local minima
- Validate results
- Document everything

After Fitting:

- Assess goodness of fit
- Quantify uncertainty
- Test sensitivity
- Validate predictions

Software Recommendations

R Packages:

- `bbmle`: Maximum likelihood
- `rstan`: Bayesian inference
- `pomp`: Particle filtering

Specialized Software:

- `Stan`: Probabilistic programming
- `JAGS`: Bayesian analysis
- `PyMC`: Bayesian inference

Conclusions

Key Takeaways

Least Squares:

- Fast and intuitive
- Good for exploration
- Limited uncertainty quantification
- Sensitive to assumptions

Maximum Likelihood:

- Principled statistical framework
- Natural uncertainty quantification
- Enables model comparison
- More computationally intensive

Advanced Methods:

- Handle complex scenarios
- Provide robust uncertainty
- Require more expertise
- Often computationally expensive

Choosing the Right Method

For Quick Exploration: Least Squares

For Publication: Maximum Likelihood

For Complex Models: Bayesian Methods

For Real-time: Particle Filtering

For Model Comparison: ABC or MCMC

General Principle: Start simple, add complexity as needed

Final Thoughts

Model fitting is both art and science:

- Requires domain expertise
- Demands statistical rigor
- Benefits from computational tools
- Needs careful validation

The goal is not just to fit models, but to:

- Understand disease dynamics
- Make reliable predictions
- Inform policy decisions
- Advance scientific knowledge

Any Questions?

Resources

Full courses (free)

- Model fitting and inference for infectious disease dynamics by Sebastian Funk, Anton Camacho, Helen Johnson, Amanda Minter, Kathleen O'Reilly and Nicholas Davies. Link

Core concepts

- Introduction to the Concept of Likelihood and Its Applications
- *Key considerations for model fitting and calibration*: Choices and trade-offs in inference with infectious disease models
- *A compilation of model fitting tutorials*: Tooling-up for infectious disease transmission modelling

Least squares

- *Key tutorial on the least squares method*: Fitting dynamic models to epidemic outbreaks with quantified uncertainty: A primer for parameter uncertainty, identifiability, and forecasts
- Fitting Epidemic Models to Data by James Holland Jones

MLE

- Fitting Epidemic Models to Data by James Holland Jones
- *R tutorial on MLE*: Estimating model parameters by maximum likelihood

MCMC

- Markov Chain Monte Carlo: an introduction for epidemiologists
- A simple introduction to Markov Chain Monte–Carlo sampling

pMCMC

- Introduction to particle Markov-chain Monte Carlo for disease dynamics modellers

ABC

- Approximate Bayesian Computation for infectious disease modelling

Others

- Bayesian workflow for disease transmission modeling in Stan
- POMP
- Odin and Monty

References

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- Bolker, B. (2008). *Ecological Models and Data in R*. Princeton University Press.
- King, A.A. et al. (2016). "Statistical inference for partially observed Markov processes via the R package pomp." *Journal of Statistical Software*.
- Carpenter, B. et al. (2017). "Stan: A probabilistic programming language." *Journal of Statistical Software*.