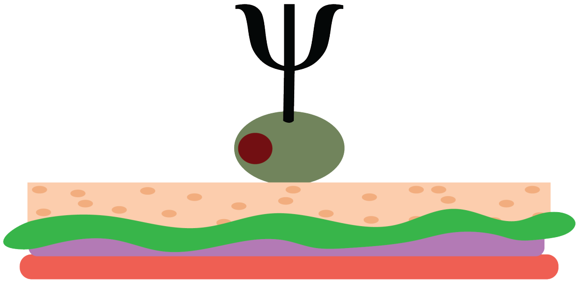
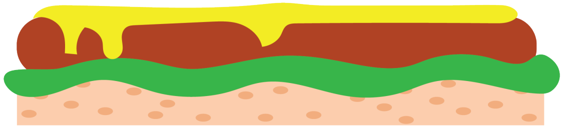


ABC's of M-estimation



Paul Zivich,[1] Rachael Ross,[2] Bonnie Shook-Sa[1]

[1]University of North Carolina, [2]Columbia University

Acknowledgements

Supported by NIH K01-AI177102 (PNZ), R01-DA056407 (RKR), R01-AI157758 (BES).

pzivich@unc.edu pzivich

Run Code

`github.com/pzivich/ABCs_of_M-estimation`

- Open your preferred statistical software
- Open corresponding `mean.*` script
- Run the full script

```
Closed-form:  8.0
Root-finder:  8.0
95% CI: [ 0.8, 15.2]
```

Overview

Why M-estimation?

Learning M-estimation during my postdoc fundamentally changed how I think about and do epidemiology

- I approach estimation problems from a very different perspective

This has made my work easier by

- Making it easier to construct novel estimators
- Simplifying variance estimation[1]
- Being better equipped to read more theoretical papers
- Giving me a tool set to prove statistical properties

[1] I almost never use the bootstrap anymore!

Why M-estimation?

Metrika
https://doi.org/10.1007/s00184-024-00962-4

Variance estimation for average treatment effects estimated by g-computation

Stefan Nygaard Hansen[1] · **Morten Overgaard**[1]

Received: 3 February 2023 / Accepted: 8 March 2024

Why M-estimation?

Assume now that an estimator $\hat{\dot{\boldsymbol{\beta}}}_n(\mathbf{z})$ of $\dot{\boldsymbol{\beta}}(\mathbf{z})$ exists for all $\mathbf{z}$. The asymptotic covariance matrix of Theorem 2 may then be estimated by the following plug-in estimator

$$\hat{\boldsymbol{\Gamma}}_n^{\mathbf{a}} = \frac{1}{n}\sum_{i=1}^{n}\left\{\boldsymbol{\mu}(\hat{\boldsymbol{\beta}}_n;\mathbf{X}_i^{\mathbf{a}}) - \hat{\boldsymbol{\theta}}_n^{\mathbf{a}} + \left(\frac{1}{n}\sum_{j=1}^{n}\frac{\partial}{\partial\boldsymbol{\beta}}\boldsymbol{\mu}(\hat{\boldsymbol{\beta}}_n;\mathbf{X}_j^{\mathbf{a}})\right)\hat{\dot{\boldsymbol{\beta}}}_n(\mathbf{Z}_i)\right\}^{\otimes 2} \tag{8}$$

where $\mathbf{x}^{\otimes 2} = \mathbf{x}\mathbf{x}^T$ for a column vector $\mathbf{x}$.

Under some mild regularity conditions on the estimator $\hat{\dot{\boldsymbol{\beta}}}_n$, this plug-in estimator will be consistent for the asymptotic covariance matrix as the following result shows.

Theorem 3 *Make the assumptions of Theorem 2 and assume furthermore that* $\hat{\dot{\boldsymbol{\beta}}}_n$ *satisfies*

$$\|\hat{\dot{\boldsymbol{\beta}}}_n(\mathbf{z}) - \dot{\boldsymbol{\beta}}(\mathbf{z})\| \leq g_n \cdot f(\mathbf{z}) \tag{9}$$

for a sequence of random variables $g_n \xrightarrow{\mathrm{P}} 0$ *and a measurable function* f *with* $\mathrm{E}(f(\mathbf{Z})^2) < \infty$. *Then* $\hat{\boldsymbol{\Gamma}}_n^{\mathbf{a}} \xrightarrow{\mathrm{P}} \boldsymbol{\Gamma}^{\mathbf{a}}$.

Proof See the Appendix. □

Why M-estimation?

As an alternative to the two-step approach of this paper, one could consider formulating the two steps as two estimating equations and use (stacked) M-estimation. The sandwich variance estimator from the stacked M-estimation approach corresponds to the variance estimator of this paper. This M-estimation approach has been implemented in the Python library `delicatessen` as pointed out by a reviewer.

M-estimation Use-cases

Causal inference

- Reifeis et al. (2020) 'Assessing exposure effects on gene expression' *Genetic Epidemiology*
- Tchetgen Tchetgen et al. (2024) 'Universal difference-in-differences for causal inference in epidemiology' *Epidemiology*
- Zivich et al. (2023) 'Introducing proximal causal inference for epidemiologists' *American Journal of Epidemiology*
- Zivich et al. (2023) 'Empirical sandwich variance estimator for iterated conditional expectation g-computation' *arXiv:2306.10976*

Sensitivity analysis

- Cole et al. (2023) 'Higher-order evidence' *European Journal of Epidemiology*
- Cole et al. (2023) 'Sensitivity analyses for means or proportions with missing outcome data' *Epidemiology*

Measurement error

- Boe et al. (2024) 'Practical Considerations for Sandwich Variance Estimation in 2-Stage Regression Settings' *American Journal of Epidemiology*
- Ross et al. (2024)'Leveraging External Validation Data: The Challenges of Transporting Measurement Error Parameters' *Epidemiology*

M-estimation Use-cases

Target trial emulation

- DeMonte et al. (2024) 'Assessing COVID-19 Vaccine Effectiveness in Observational Studies via Nested Trial Emulation' *arXiv:2403.18115*

Generalizability / transportability

- Dahabreh, et al. (2020) 'Extending inferences from a randomized trial to a new target population' *Statistics in Medicine*
- Dahabreh, et al. (2023) 'Sensitivity analysis using bias functions for studies extending inferences from a randomized trial to a target population' *Statistics in Medicine*
- Robertson et al (2024) 'Estimating subgroup effects in generalizability and transportability analyses' *American Journal of Epidemiology*

Data fusion

- Cole et al. (2023) 'Illustration of 2 fusion designs and estimators' *American Journal of Epidemiology*
- Shook-Sa et al. (2024) 'Fusing trial data for treatment comparisons: single versus multi-span bridging' *Statistics in Medicine*

Overview

Section 1: introduction

Break (15min)

Section 2: applied examples

Break (15min)

Section 3: in context

Overview

Section 1: introduction

Break (15min)

Section 2: applied examples

Break (15min)

Section 3: in context

Overview: Section 1

Review notation / definitions

M-estimator by-hand

M-estimator with computer

Some statistical properties

Notation

Review notation and mathematical operations used

- If unfamiliar with something, don't worry!
- Operations will be
  - Contextualized in following sections
  - Mainly done by the computer
- Definitions can be returned to later

Notation – Basics

O_i: observed data for unit i

- $O_i = (X_i, Y_i)$

$\sum_{i=1}^{n} i \; = \; 1 + 2 + ... + n$: cumulative sum

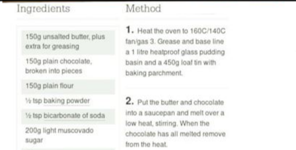
$\prod_{i=1}^{n} i \; = \; 1 \times 2 \times ... \times n$: cumulative product

expit$(a) = 1/(1 + \exp(-a))$

Notation – Basics

estimand θ
(parameter of interest)

estimator $\hat{\theta}$



Ingredients

150g unsalted butter, plus extra for greasing
150g plain chocolate, broken into pieces
150g plain flour
½ tsp baking powder
½ tsp bicarbonate of soda
200g light muscovado sugar

Method

1. Heat the oven to 160C/140C fan/gas 3. Grease and base line a 1 litre heatproof glass pudding basin and a 450g loaf tin with baking parchment.

2. Put the butter and chocolate into a saucepan and melt over a low heat, stirring. When the chocolate has all melted remove from the heat.

estimate 0.5

[2]

[2] Estimand also denoted by θ_0 or θ^*

Notation – Matrix Algebra

Transpose

$$\mathbf{A} = \begin{bmatrix} a & b \\ c & d \\ e & f \end{bmatrix} \quad \mathbf{A}^T = \begin{bmatrix} a & c & e \\ b & d & f \end{bmatrix}$$

Notation – Matrix Algebra

Dot product (matrix multiplication)

$$\mathbf{A}\ \mathbf{B} = \mathbf{C}$$

$$\begin{bmatrix} a_{11} & a_{12} & \dots & a_{1p} \\ a_{21} & a_{22} & \dots & a_{2p} \\ \vdots & \vdots & \ddots & \vdots \\ a_{m1} & a_{m2} & \dots & a_{mp} \end{bmatrix} \begin{bmatrix} b_{11} & b_{12} & \dots & b_{1n} \\ b_{21} & b_{22} & \dots & b_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ b_{p1} & b_{p2} & \dots & b_{pn} \end{bmatrix} = \begin{bmatrix} c_{11} & c_{12} & \dots & c_{1n} \\ c_{21} & c_{22} & \dots & c_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ c_{m1} & c_{m2} & \dots & c_{mn} \end{bmatrix}$$

$$a_{11}b_{11} + a_{12}b_{21} + \dots + a_{1p}b_{p1}$$

- Number of rows in first matrix must match columns in the second matrix

Notation – Matrix Algebra

Dot product (matrix multiplication)

$$\mathbf{A}\;\mathbf{B} = \mathbf{C}$$

$$\begin{bmatrix} a_{11} & a_{12} & \dots & a_{1p} \\ a_{21} & a_{22} & \dots & a_{2p} \\ \vdots & \vdots & \ddots & \vdots \\ a_{m1} & a_{m2} & \dots & a_{mp} \end{bmatrix} \begin{bmatrix} b_{11} & b_{12} & \dots & b_{1n} \\ b_{21} & b_{22} & \dots & b_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ b_{p1} & b_{p2} & \dots & b_{pn} \end{bmatrix} = \begin{bmatrix} c_{11} & c_{12} & \dots & c_{1n} \\ c_{21} & c_{22} & \dots & c_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ c_{m1} & c_{m2} & \dots & c_{mn} \end{bmatrix}$$

$$a_{21}b_{21} + a_{22}b_{21} + \dots + a_{2p}b_{p1}$$

- Number of rows in first matrix must match columns in the second matrix

Notation – Matrix Algebra

Inverse of 2×2 matrix

$$\mathbf{D} = \begin{bmatrix} w & x \\ y & z \end{bmatrix} \quad \mathbf{D}^{-1} = \frac{1}{w\ z - x\ y} \begin{bmatrix} z & -\ y \\ -\ x & w \end{bmatrix}$$

- Only applies to matrices with same number of rows and columns

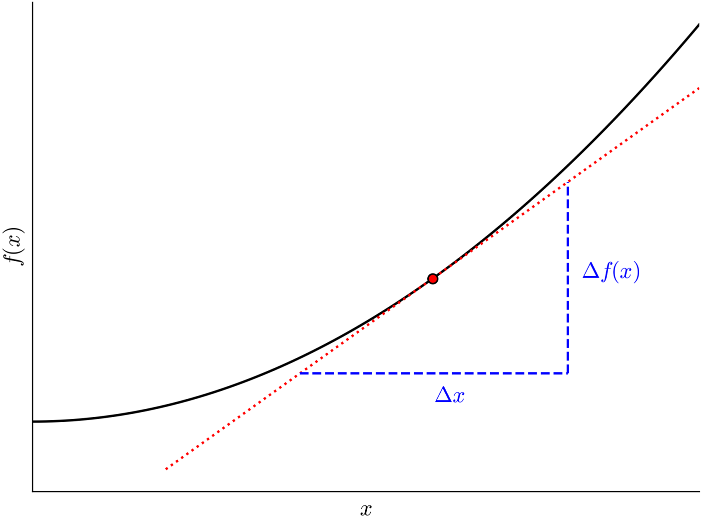
Derivatives – Basics

$$f'(x) = \frac{d}{dx} f(x)$$

Helpful to think of derivative as slope of tangent line at a point

$$f'(x) = \lim_{h \to 0} \frac{f(x+h) - f(x)}{h}$$

Derivatives – Basics



Derivatives – Generalizations

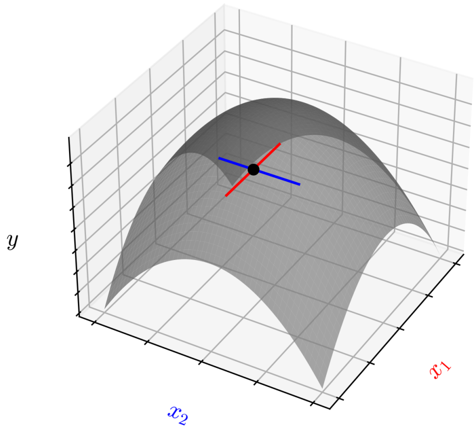
If $\boldsymbol{x} = (x_1, x_2, ..., x_m)$ and $f(\boldsymbol{x}) = y$, then the partial derivative is

$$\frac{\partial}{\partial x_1} f(\boldsymbol{x})$$

The gradient is

$$\nabla f(\boldsymbol{x}) = \begin{bmatrix} \frac{\partial}{\partial x_1} f(\boldsymbol{x}) \\ \frac{\partial}{\partial x_2} f(\boldsymbol{x}) \\ \vdots \\ \frac{\partial}{\partial x_m} f(\boldsymbol{x}) \end{bmatrix}$$

Derivatives – Generalizations



Derivatives – Generalizations

The Hessian is

$$\Delta H_f(\boldsymbol{x}) = \begin{bmatrix} \frac{\partial^2}{\partial x_1 \partial x_1} f(\boldsymbol{x}) & \dots & \frac{\partial^2}{\partial x_1 \partial x_m} f(\boldsymbol{x}) \\ \vdots & \ddots & \vdots \\ \frac{\partial^2}{\partial x_m \partial x_1} f(\boldsymbol{x}) & \dots & \frac{\partial^2}{\partial x_m \partial x_m} f(\boldsymbol{x}) \end{bmatrix}$$

- Jacobian (transpose gradient, ∇^T) of the gradient

Derivatives – Generalization

Function

$$f(x_1, x_2) = y$$

Gradient

$$\nabla f(x_1, x_2) = \begin{bmatrix} \frac{\partial}{\partial x_1} f(x_1, x_2) \\ \frac{\partial}{\partial x_2} f(x_1, x_2) \end{bmatrix}$$

Hessian

$$\Delta H_f(\boldsymbol{x}) = \begin{bmatrix} \frac{\partial^2}{\partial x_1 \partial x_1} f(x_1, x_2) & \frac{\partial^2}{\partial x_1 \partial x_2} f(x_1, x_2) \\ \frac{\partial^2}{\partial x_2 \partial x_1} f(x_1, x_2) & \frac{\partial^2}{\partial x_2 \partial x_2} f(x_1, x_2) \end{bmatrix}$$

Notation – M-estimation

Estimating *function*

$$\psi(O_i; \theta)$$

Estimating *equation*

$$\sum_{i=1}^{n} \psi(O_i; \theta)$$

Definition: M-estimator

An M-estimator, $\hat{\theta}$, is the solution to

$$\sum_{i=1}^{n} \overbrace{\psi}^{k\text{-dimensional estimating function}} \left(\underbrace{O_i}_{\text{Observation } i} , \overbrace{\hat{\theta}}^{k\text{-dimensional parameter}} \right) = \underbrace{0}_{\text{root: where } f(x) = 0}$$

- Don't worry if any of the above isn't clear yet

M-estimator for the mean

Problem: Learn the Mean

Want to learn the population mean

- Estimand: $\mu = E[Y]$

Suppose we have the following observations to estimate μ

$$7, 1, 5, 3, 24$$

Usual method

Estimator for mean Observed value for unit i

$$\hat{\mu} = \frac{1}{n} \sum_{i=1}^{n} Y_i$$

Total number of units

Applying to data in example (estimate)

$$\frac{7+1+5+3+24}{5} = \frac{40}{5} = 8$$

Then you might look up a formula for the variance from a book

but let's use M-estimation instead

M-estimator steps

1. Determine estimating function
2. Find the roots of the estimating equations
3. Estimate variance via the sandwich

Goal: rewrite mean as a function that is equal to zero

$$\hat{\mu} = \frac{1}{n} \sum_{i=1}^{n} Y_i$$ definition

$$\hat{\mu} \; n = \sum_{i=1}^{n} Y_i$$ multiply by n

$$0 = \left(\sum_{i=1}^{n} Y_i \right) - \hat{\mu} \; n$$ subtract $\hat{\mu} n$

$$0 = \left(\sum_{i=1}^{n} Y_i \right) - \left(\sum_{i=1}^{n} \hat{\mu} \right)$$

$$0 = \sum_{i=1}^{n} (Y_i - \hat{\mu})$$

1. Determine Estimating Function

This formula is our M-estimator for the mean

$$\sum_{i=1}^{n} \underbrace{\overbrace{\psi}^{\text{Estimating function}} (\underbrace{O_i}_{\text{Observation } i} , \overbrace{\hat{\theta}}^{\text{Parameter}})} = \sum_{i=1}^{n} (\underbrace{Y_i}_{\text{Observation } i} - \overbrace{\hat{\mu}}^{\text{Parameter}}) = 0$$

2. Root-finding

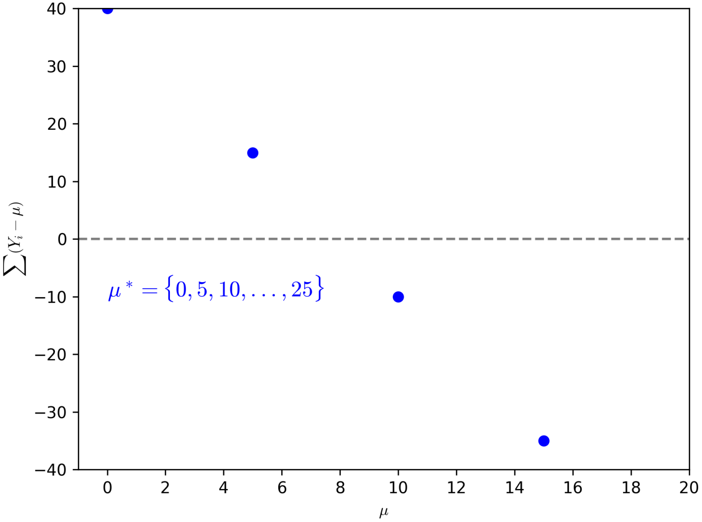
How can we find $\hat{\mu}$?

- Ignore the closed-form solution for the time

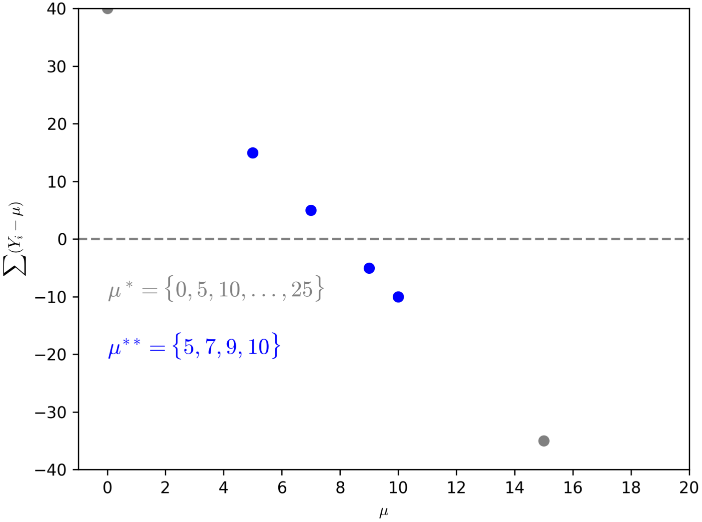
Broadly

- Take some guesses at $\hat{\mu}$, denoted as $\hat{\mu}^*$
- Compute $\sum_{i=1}^{n} \psi(O_i;\ \hat{\mu}^*\ )$
- Find the guesses that are close to zero
- Generate some new guesses, $\hat{\mu}^{**}$
- Repeat process until we find $\hat{\mu}$

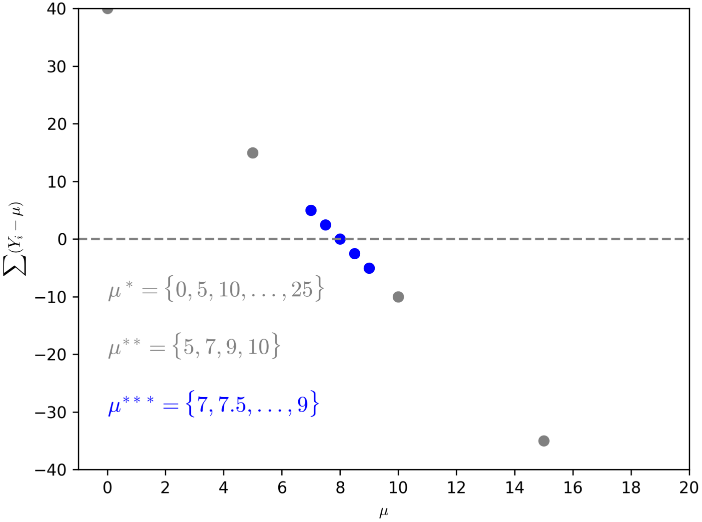
2. Root-finding



2. Root-finding



2. Root-finding



3. Variance

Closed-form estimator[3]

$$\widehat{Var}(\hat{\mu}) = \frac{1}{n} \sum_{i=1}^{n} (Y_i - \hat{\mu})^2$$

but let's use M-estimation instead

[3]Note: n is often replaced by $n-1$ in practice, which can lead to differences for small sample sizes

3. Sandwich Variance Estimator

Sandwich variance

Filling (meat) matrix

$$V(\hat{\theta}) = B(\hat{\theta})^{-1} \; F(\hat{\theta}) \left(B(\hat{\theta})^{-1} \right)^{T}$$

(inverse of) Bread matrix

3. Sandwich Variance Estimator

Bread matrix

$$\boxed{B(\hat{\theta})} = \frac{1}{n} \sum_{i=1}^{n} \left[- \boxed{\psi'(O_i, \hat{\theta})} \right]$$

Partial derivatives (Jacobian)

Filling matrix

$$\boxed{F(\hat{\theta})} = \frac{1}{n} \sum_{i=1}^{n} \left[\boxed{\psi(O_i, \hat{\theta})} \; \boxed{\psi(O_i, \hat{\theta})^T} \right]$$

Dot product of estimating functions

Baking the Bread: By-Hand

Need the derivative of $\psi(O_i; \mu)$

$$\begin{aligned}
\psi'(O_i; \hat{\mu}) =& \frac{\partial}{\partial \hat{\mu}} \psi(O_i; \hat{\mu}) && \text{definition of derivative} \\
=& \frac{\partial}{\partial \hat{\mu}} (Y_i - \hat{\mu}) && \text{definition of estimating function} \\
=& -1
\end{aligned}$$

Therefore

$$\boxed{\frac{1}{n} \sum_{i=1}^{n} \left[-\psi'(O_i, \hat{\theta}) \right]} = \frac{1}{n} \sum_{i=1}^{n} \left[- \boxed{-1} \right] = 1$$

From derivative above

Definition of Bread

Cooking the Filling: By-Hand

Definition of Filling

$$\boxed{\frac{1}{n}\sum_{i=1}^{n}\left[\psi(O_i,\hat{\theta})\psi(O_i,\hat{\theta})^T\right]} = \frac{1}{n}\sum_{i=1}^{n}\left[\boxed{(Y_i - \hat{\mu})(Y_i - \hat{\mu})}\right]$$

Plugging in estimating function

Therefore

$$\frac{1}{5}\sum_{i=1}^{5}\left[(Y_i - 8)^2\right] = 68$$

Assembling the Sandwich: By-Hand

Sandwich variance

Filling

$$V(\hat{\mu}) = 1^{-1} \; 68 \left(1^{-1} \right)^{T} = 68$$

Bread

Wald-type confidence intervals

$$\hat{\mu} \pm z_{\alpha} \sqrt{\frac{V(\hat{\mu})}{n}} = 8 \pm 1.96 \sqrt{\frac{68}{5}} = (0.8, 15.2)$$

Computation for M-estimators

Computation for M-estimators

Solved for M-estimator of mean by-hand

- By-hand is not needed

Consider how M-estimators can be implemented algorithmically

- Root-finding
- Approximation of derivatives
- Matrix algebra

Follow along in `mean.R`, `mean.sas`, or `mean.py`

- Start of code inputs data and sets up estimating equations

Root-Finding – Algorithms

Performed a by-hand search for $\hat{\mu}$

- Similar to the *bisection method*

Variety of multidimensional root-finding algorithms exist

- Secant method (quasi-Newton)
- Levenberg-Marquardt
- Powell hybrid method

Root-Finding – Code

Under `Root-finding` see implementation

- SAS – `nlplm`
- R – `rootSolve::multiroot`
- Python – `scipy.optimize.root`

Derivatives – Back to the Definition

Derivative of function

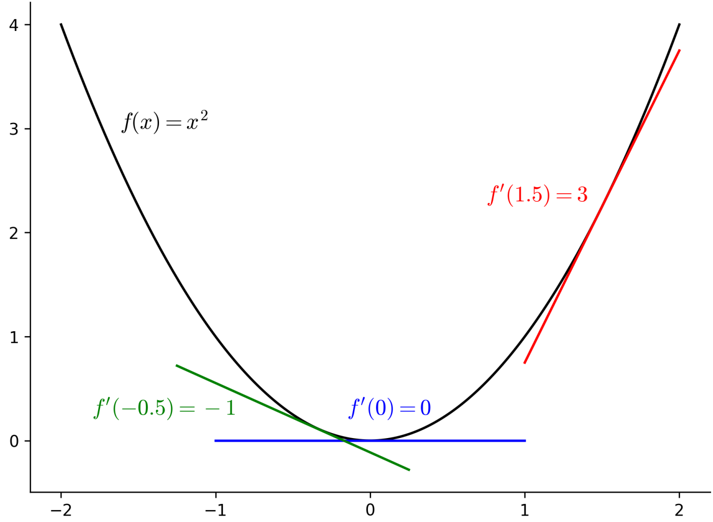
Change in output (rise)

$$f'(x) = \lim_{h \to 0} \frac{f(x+h) - f(x)}{h}$$

Behavior as h becomes small

Divided change in input (run)

Derivatives – Intuition



Derivatives – Numerical Approximation

Central Difference Method[4]

$$\underbrace{\tilde{f}'(x)}_{\text{Approximation}} = \frac{f(\overbrace{x+a}^{\text{Slightly above } x}) - f(\overbrace{x-a}^{\text{Slightly below } x})}{2\,a}$$

Here a is a small value (e.g., 1×10^{-9})

[4] Automatic differentiation, which computes the derivatives exactly via the chain rule, could be used instead

Baking the Bread – Code

Under `Baking the bread` see implementation

- SAS – `nlpfdd`
- R – `numDeriv::jacobian`
- Python – `scipy.optimize.approx_fprime`

Cooking the Filling – Code

Under `Cooking the filling` see implementation

- Transpose
  - SAS – `'`
  - R – `base::t`
  - Python – `numpy.transpose`
- Dot product
  - SAS – `*`
  - R – `%*%`
  - Python – `numpy.dot`

Assembling the Sandwich – Code

Under `Assembling the sandwich` see implementation

- Inverse
  - SAS – `inv`
  - R – `base::solve`
  - Python – `numpy.linalg.inv`

Implications

To implement an M-estimator, we only need to provide

- Valid estimating functions
- Data

Everything else can be done by the computer

- Potential to simplify complex analyses
- Open-source libraries
  - R: `geex`[5]
  - Python: `delicatessen`[6]

[5] Saul & Hudgens (2020) *Journal of Statistical Software*
[6] Zivich et al. (2022) *arXiv:2203.11300*

Extensions

But Why M-estimation?

So far, all we've done is calculate the mean in a complicated way

So why bother with M-estimation?

- Flexibility of the framework
  - Extensions of these basics
  - Simplified proofs for properties of estimators

How M-estimators are extended

As will be seen in applied examples

1. Stacking estimating functions
2. Automation of delta method

Stacking estimating functions

Often want to estimate more than 1 parameter

- Regression models
- Effect measure modification
- Inverse probability weighting requires estimating propensity scores

Stacking Estimating Functions

M-estimators extend by stacking estimating functions

$$\sum_{i=1}^{n} \begin{bmatrix} \psi_{\theta_1}(O_i; \hat{\theta}) \\ \psi_{\theta_2}(O_i; \hat{\theta}) \\ \vdots \\ \psi_{\theta_k}(O_i; \hat{\theta}) \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ \vdots \\ 0 \end{bmatrix} = \mathbf{0}$$

- Easy to stack estimating functions together
- Unlike maximizing a likelihood
  - Likelihood has a single value for individual contribution
  - More difficult to combine likelihood functions

Stacking Estimating Functions

Example

$$\sum_{i=1}^{n} \begin{bmatrix} \psi_{\theta_1}(O_i;\theta) \\ \psi_{\theta_2}(O_i;\theta) \end{bmatrix} = \sum_{i=1}^{n} \begin{bmatrix} Y_i - \theta_1 \\ (Y_i - \theta_1)^2 - \theta_2 \end{bmatrix} = \mathbf{0}$$

- Stacking important when parameter depends on other parameters
- Concept explored further in applications

Delta Method

Theorem: smooth function of an asymptotically normal estimator is also asymptotically normal[7]

Application:

$$Var\left\{ \overbrace{\boxed{g(\alpha)}}^{\text{Transformation of } \alpha} \right\} \approx \underbrace{g'(\alpha)}_{\text{Derivative of transformation}} \; \overbrace{\Sigma_\alpha}^{\text{Covariance of } \alpha} \; \underbrace{g'(\alpha)}_{\text{Derivative of transformation}}$$

[7] Boos & Stefanski *Essential Statistical Inference* pg. 237-240

Delta Method

Many variance formulas you know are Delta method results

- $Var(RD)$, $Var(\log(RR))$, $Var(\log(OR))$
- Formulas follow from Delta method argument
- Don't need to manually solve due to known formulas
    - Not always the case

Delta Method with M-estimation

The estimating function for the transformed parameter, θ_t is

$$\psi_{g(\theta)}(O_i; \theta, \theta_t) = g(\theta) - \theta_t$$

- Estimating function does not depend on data

Therefore, the stacked estimating equations are

$$\sum_{i=1}^{n} \begin{bmatrix} \psi^*(O_i; \theta) \\ \psi_{g(\theta)}(O_i; \theta, \theta_t) \end{bmatrix} = 0$$

Delta Method with M-estimation

Following some derivatives and matrix algebra

$$V(\theta, \theta_t) = \begin{bmatrix} V^*(\theta) & g'(\theta)V^*(\theta) \\ V^*(\theta)g'(\theta)^T & g'(\theta)V^*(\theta)g'(\theta) \end{bmatrix}$$

where

Sandwich covariance for θ

$$V(\theta_t) = g'(\theta) \; V^*(\theta) \; g'(\theta)$$

Derivative of transformation

- which is the same result from the delta method!

M-estimators automate the Delta method

Robust Variance

To close this section, let's discuss the robust variance

- The sandwich variance is also known as the 'robust' variance
- 'Robust' designates that the variance estimator is not sensitive to violations of *certain* assumptions[8]
  - Variance estimator is consistent when parametric model is wrong
  - However this has some difficulties
- Relates back to Maximum Likelihood Estimation
  - The variance can be estimated two ways

[8]See Mansournia et al. (2021) *International Journal of Epidemiology* for further details

Robust Variance

Variance estimators

1. Inverse Hessian of the log-likelihood
   - Equivalent to $B(\theta)^{-1}$
2. Residuals of the score function
   - Equivalent to $F(\theta)^{-1}$

- When the model is correctly specified
  - These variance estimators asymptotically equivalent
  - $B(\theta) = F(\theta)$

Robust Variance

When the model is not correctly specified

- $B(\theta) \neq F(\theta)$
- By combining, sandwich is robust to assumptions
  - Variance estimator is consistent even if model is wrong

- Example: log-Poisson model to estimate the risk ratio
  - Here, estimated variance is too large

Warning[9]

- Does not correct for bias in parameter estimates

[9] See Freedman DA *Am Stat* 2006 for details

Overview

Section 1: introduction

Break (15min)

Section 2: applied examples

Break (15min)

Section 3: in context