Introduction to Reproducible Research

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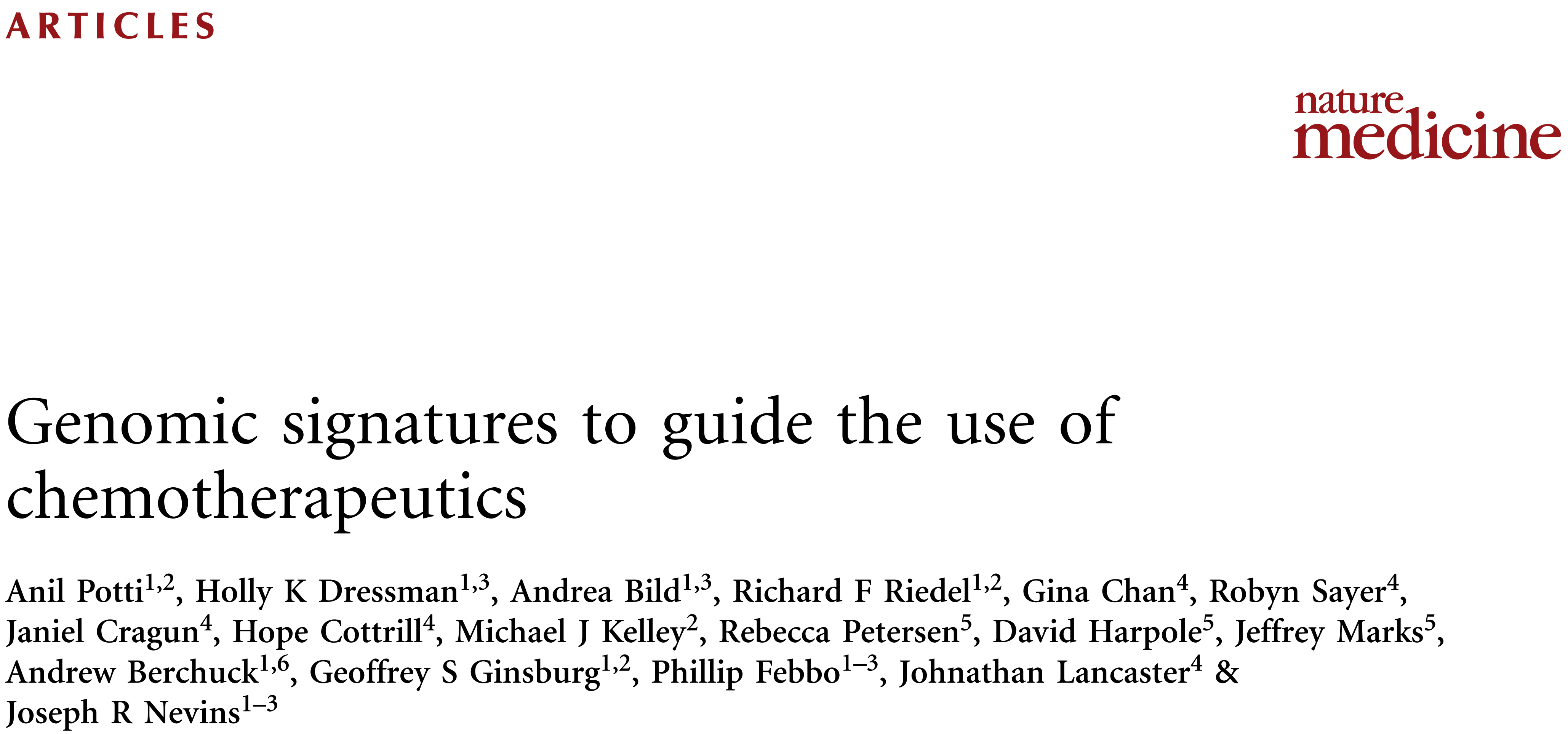
UW SISBID

July 2015

Parable



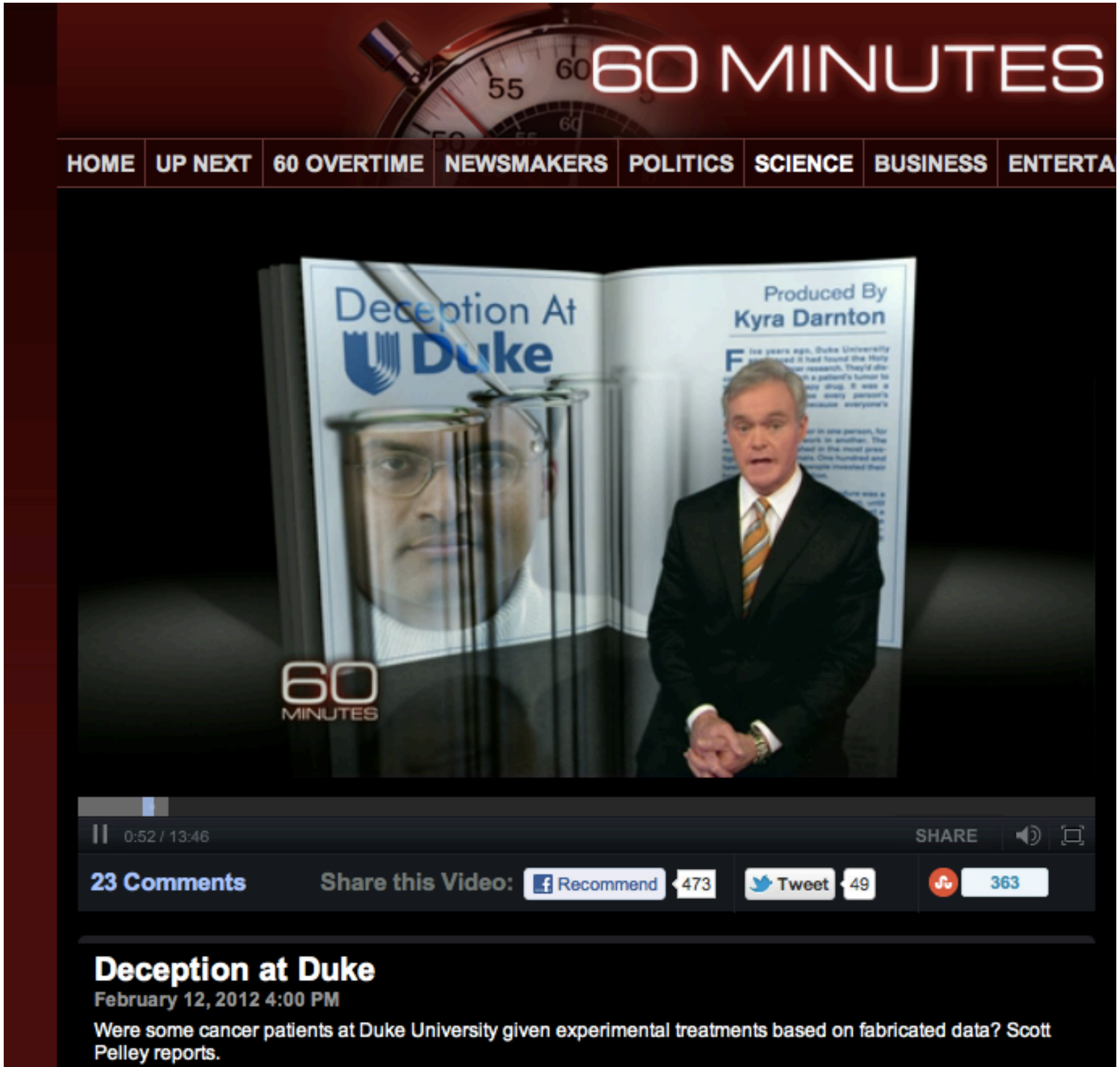
ARTICLES

nature medicine

Genomic signatures to guide the use of chemotherapeutics

Anil Potti[1,2], Holly K Dressman[1,3], Andrea Bild[1,3], Richard F Riedel[1,2], Gina Chan[4], Robyn Sayer[4], Janiel Cragun[4], Hope Cottrill[4], Michael J Kelley[2], Rebecca Petersen[5], David Harpole[5], Jeffrey Marks[5], Andrew Berchuck[1,6], Geoffrey S Ginsburg[1,2], Phillip Febbo[1–3], Johnathan Lancaster[4] & Joseph R Nevins[1–3]

Deception at Duke



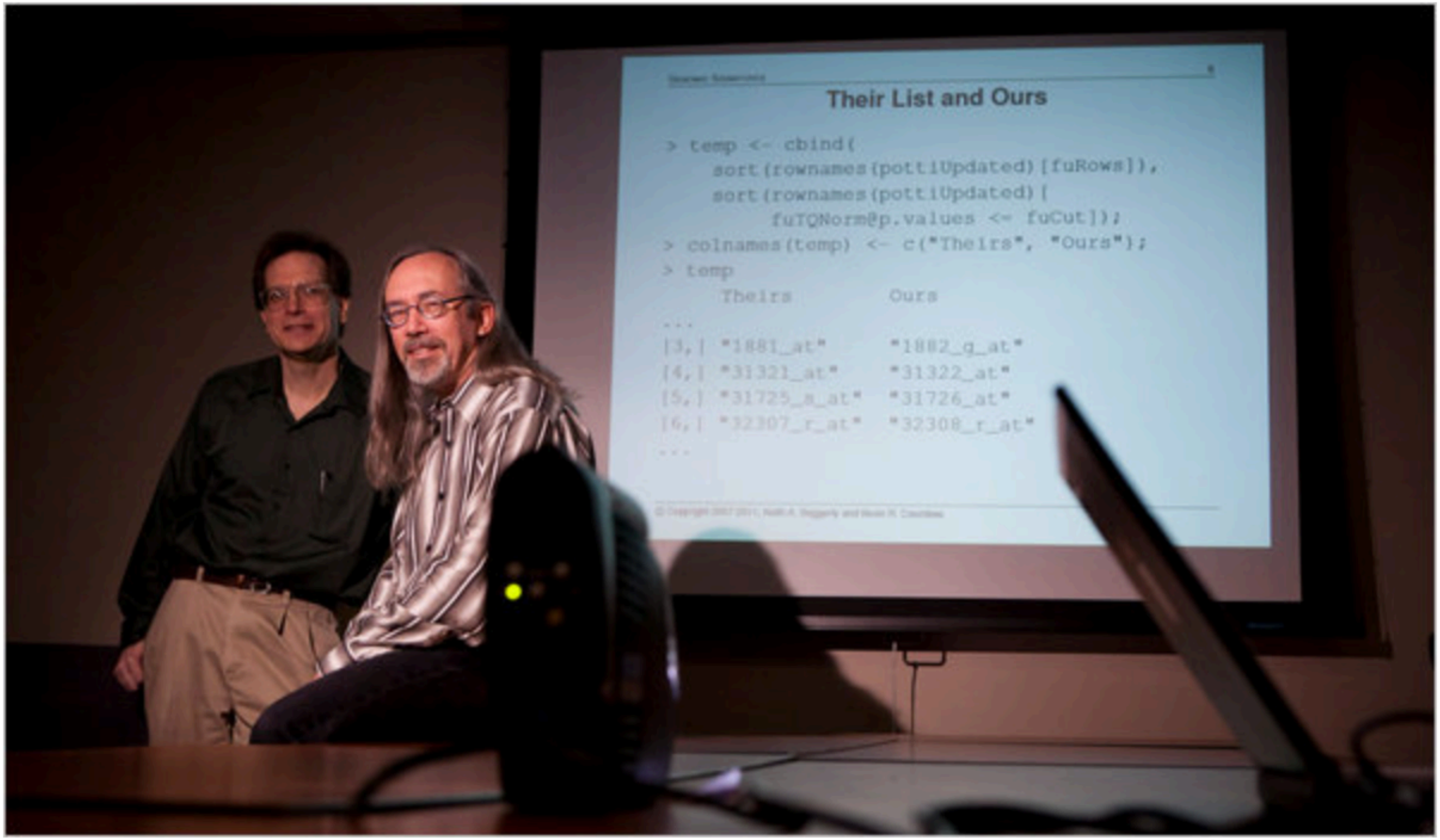
Deception at Duke

February 12, 2012 4:00 PM

Were some cancer patients at Duke University given experimental treatments based on fabricated data? Scott Pelley reports.

“Rock Star” Statisticians

How Bright Promise in Cancer Testing Fell Apart



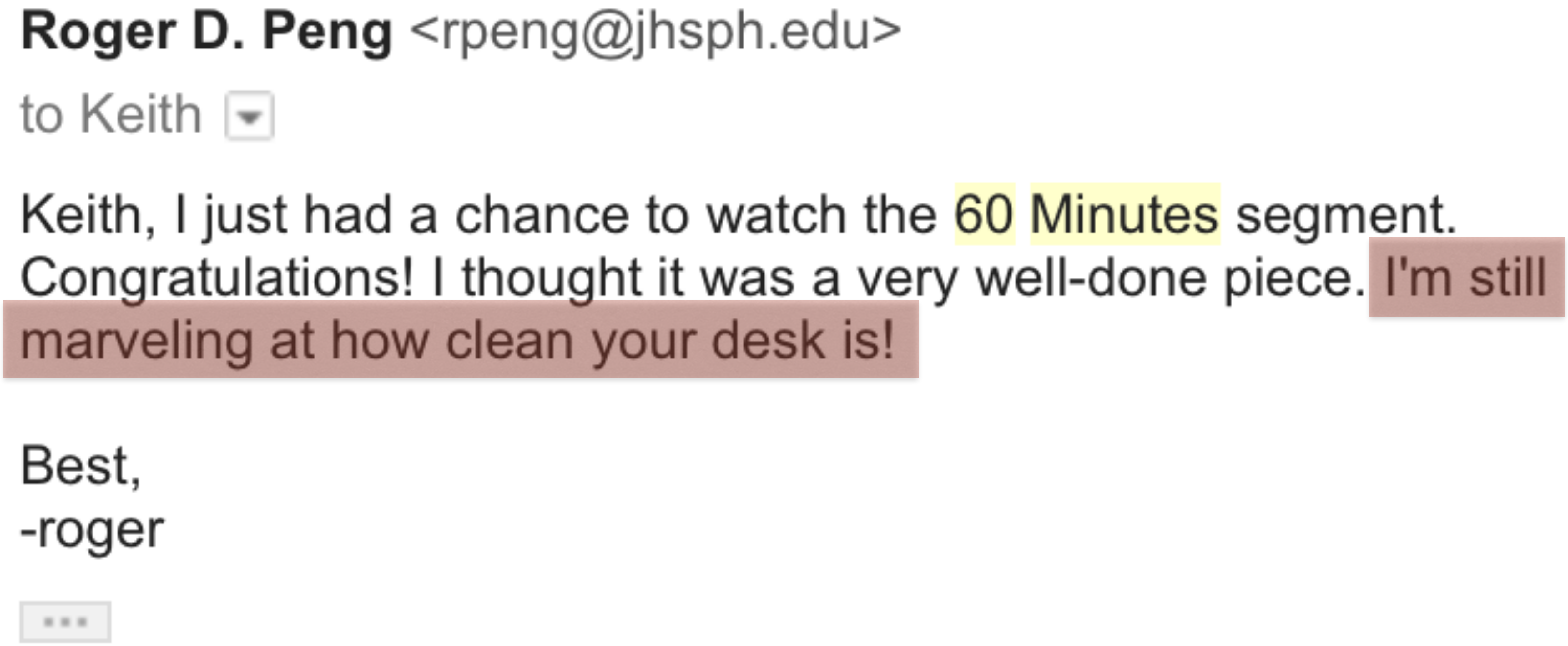
Their List and Ours

```
> temp <- cbind(
    sort(rownames(pottiUpdated)[fuRows]),
    sort(rownames(pottiUpdated)[
        fuTQNorm@p.values <= fuCut]));
> colnames(temp) <- c("Theirs", "Ours");
> temp
     Theirs          Ours
...
[3,] "1881_at"       "1882_g_at"
[4,] "31321_at"      "31322_at"
[5,] "31725_s_at"    "31726_at"
[6,] "32307_r_at"    "32308_r_at"
...
```

Michael Stravato for The New York Times

New York Times

“Deception” at MDACC



Roger D. Peng <rpeng@jhsph.edu>

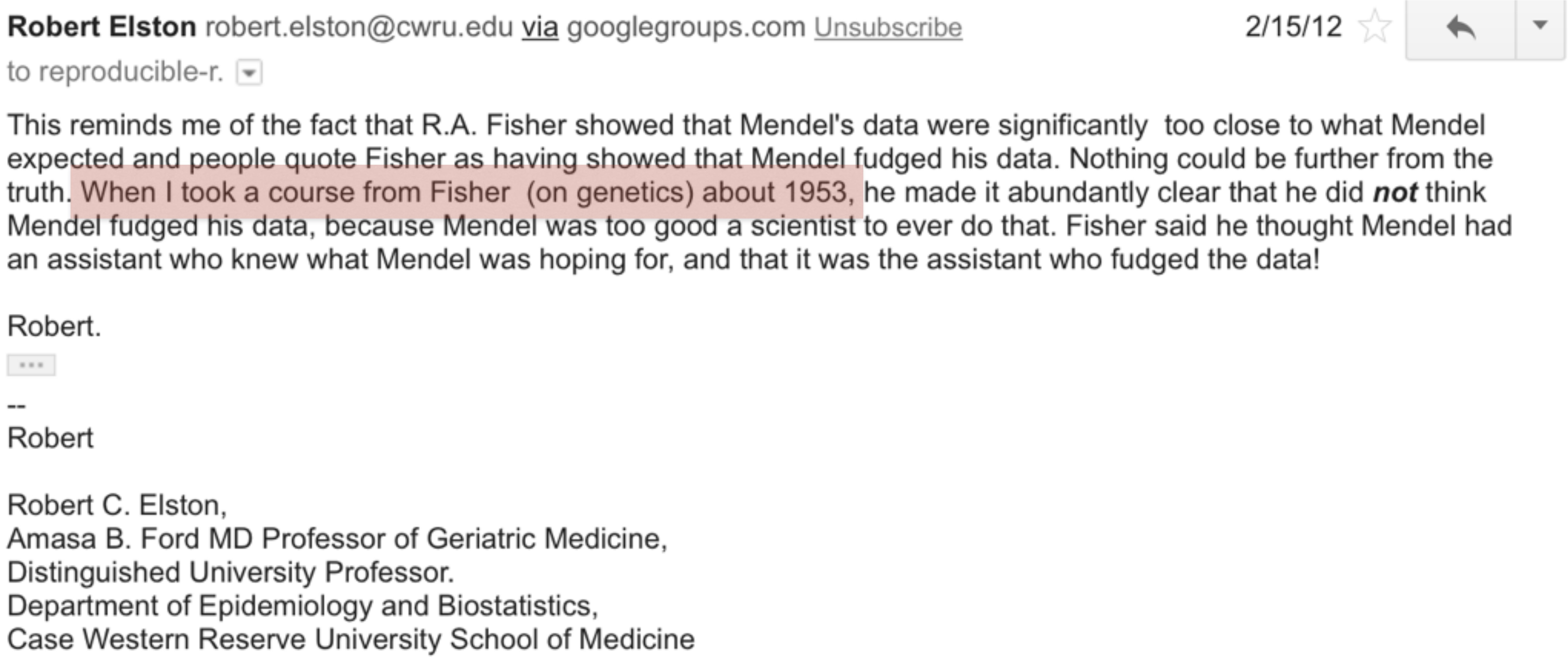
to Keith

Keith, I just had a chance to watch the 60 Minutes segment. Congratulations! I thought it was a very well-done piece. I'm still marveling at how clean your desk is!

Best,
-roger

February 2012

Follow-up Discussion



Robert Elston robert.elston@cwru.edu via googlegroups.com Unsubscribe 2/15/12

to reproducible-r.

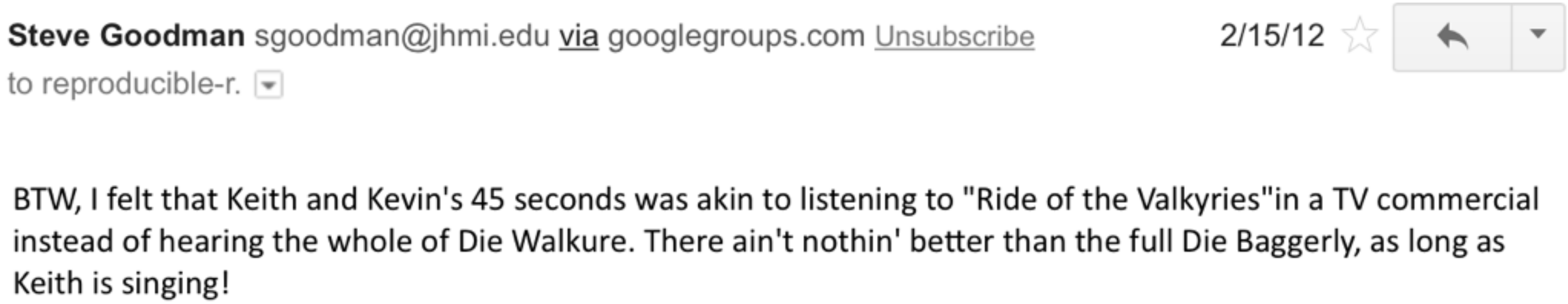
This reminds me of the fact that R.A. Fisher showed that Mendel's data were significantly too close to what Mendel expected and people quote Fisher as having showed that Mendel fudged his data. Nothing could be further from the truth. When I took a course from Fisher (on genetics) about 1953, he made it abundantly clear that he did ***not*** think Mendel fudged his data, because Mendel was too good a scientist to ever do that. Fisher said he thought Mendel had an assistant who knew what Mendel was hoping for, and that it was the assistant who fudged the data!

Robert.

--
Robert

Robert C. Elston,
Amasa B. Ford MD Professor of Geriatric Medicine,
Distinguished University Professor.
Department of Epidemiology and Biostatistics,
Case Western Reserve University School of Medicine

Follow-up Discussion



Steve Goodman sgoodman@jhmi.edu via googlegroups.com Unsubscribe 2/15/12

to reproducible-r.

BTW, I felt that Keith and Kevin's 45 seconds was akin to listening to "Ride of the Valkyries"in a TV commercial instead of hearing the whole of Die Walkure. There ain't nothin' better than the full Die Baggerly, as long as Keith is singing!

Lessons?

Clinical medicine (tightly controlled) + Genomics (wild west) = Wild West

Institute of Medicine Committee

REPORT BRIEF MARCH 2012

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES

Advising the nation • Improving health

For more information visit www.iom.edu/translationalomics

Evolution of Translational Omics
Lessons Learned and the Path Forward

EVOLUTION OF TRANSLATIONAL
OMICS
Lessons Learned and the Path Forward

The IOM Report

- **Data/metadata** used to develop test should be made publicly available
- The **computer code** and fully specified computational procedures used or development of the omics-based test should be made available
- Ideally, the computer code that is released will **encompass all of the steps** of computational analysis, including all data preprocessing steps

Replication and Reproducibility

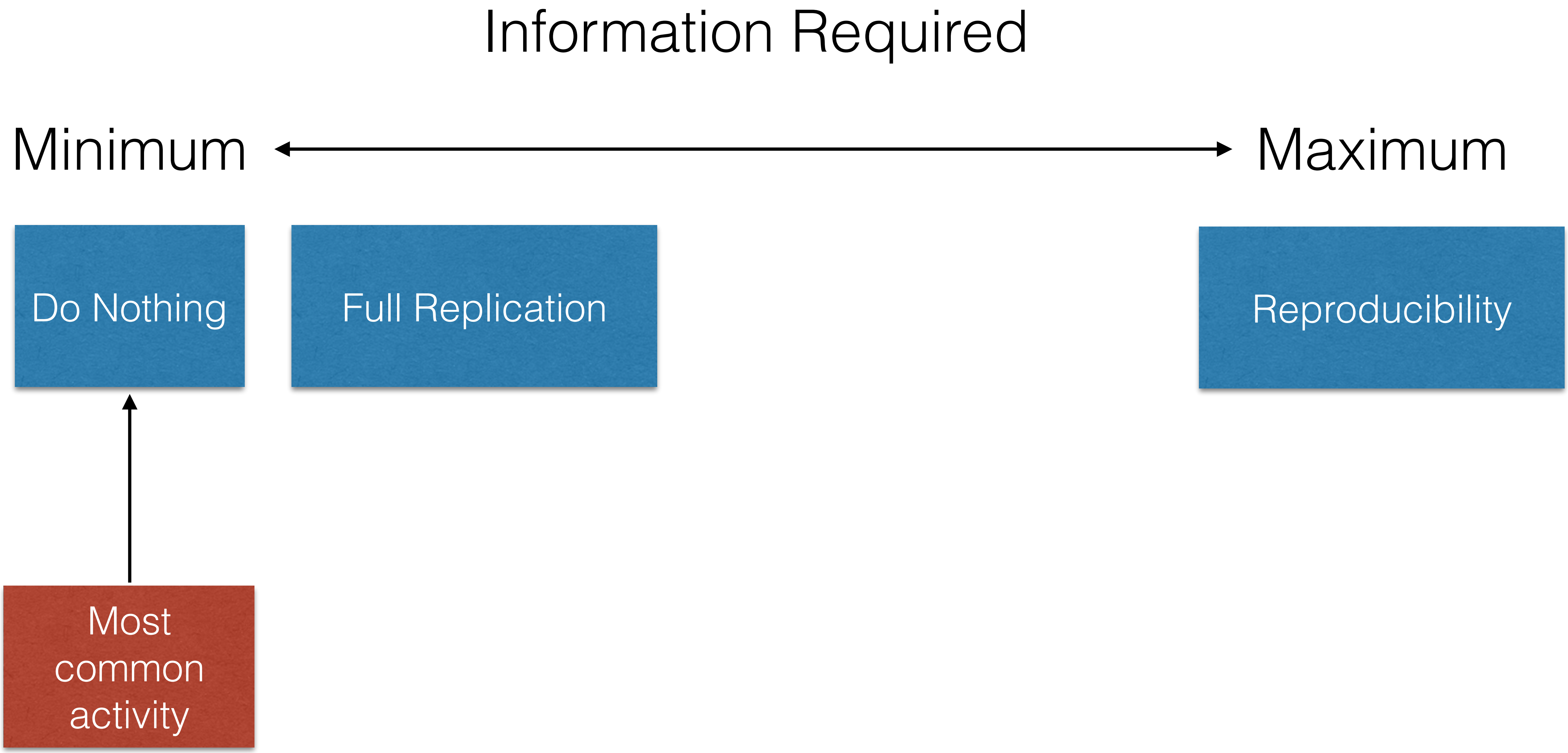
- **Replication**
  - Focuses on the validity of the *scientific claim*
  - "Is this claim true?"
  - Ultimate standard for scientific evidence
  - New investigators, data, analytic methods, labs, instruments, etc.
  - Important in studies that can impact policy or regulation

- **Reproducibility**
  - Focuses on the validity of the *data analysis*
  - "Can we trust this analysis?"
  - A minimum standard
  - New investigators, same data, same methods
  - Important when replication is impossible

What's Wrong with Replication?

- Nothing, but…
- Some studies cannot be replicated
    - No time, opportunistic
    - No money
    - Unique
- **Reproducible Research**: Make analytic data and code available so that others may reproduce findings

Upon Seeing Your Work…



Information Required

Minimum

Maximum

Do Nothing

Full Replication

Reproducibility

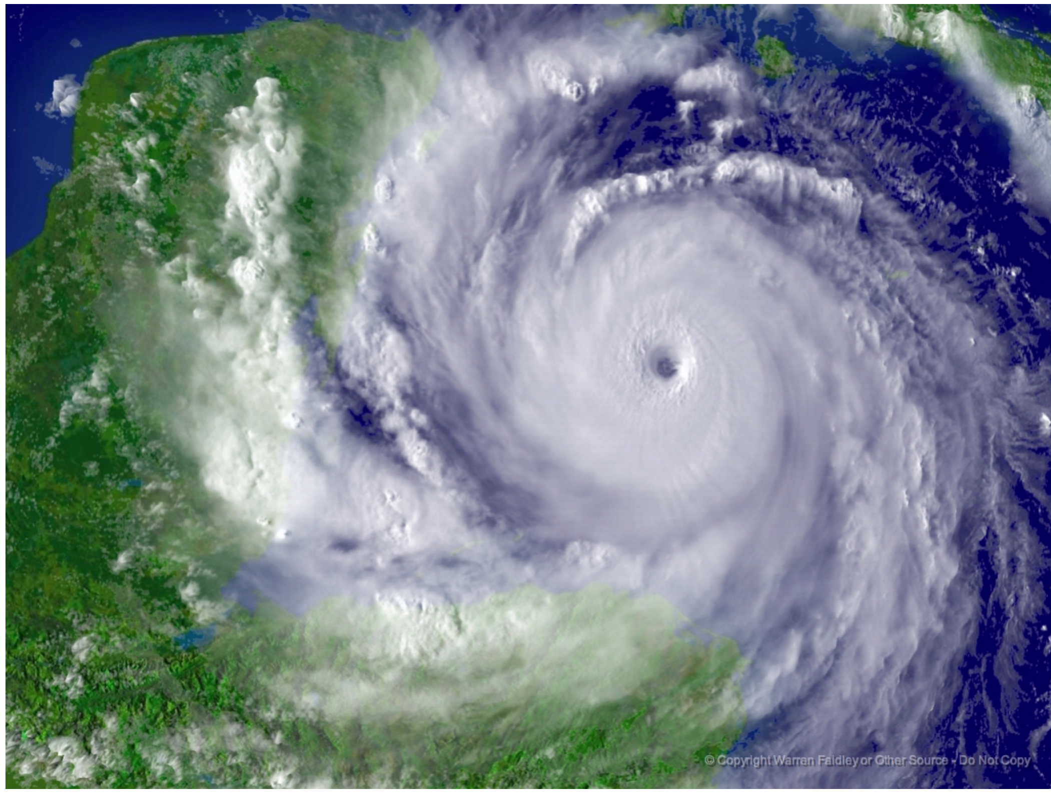
Most common activity

Why Do We Need Reproducible Research?

- New technologies increasing data collection throughput
- Data are more complex and high dimensional
- Existing databases can be merged into new and bigger databases
- Computing power is greatly increased, allowing more sophisticated/complicated analyses
- For every field “X” there is a field “Computational X”

Air Pollution and Health: A Perfect Storm?

- Estimating small health effects in the presence of much stronger signals
- Results inform substantial policy decisions and affect many stakeholders
- EPA regulations can cost billions of dollars
- Complex statistical methods are needed and subjected to intense scrutiny



What Problem Does Reproducible Research Address?

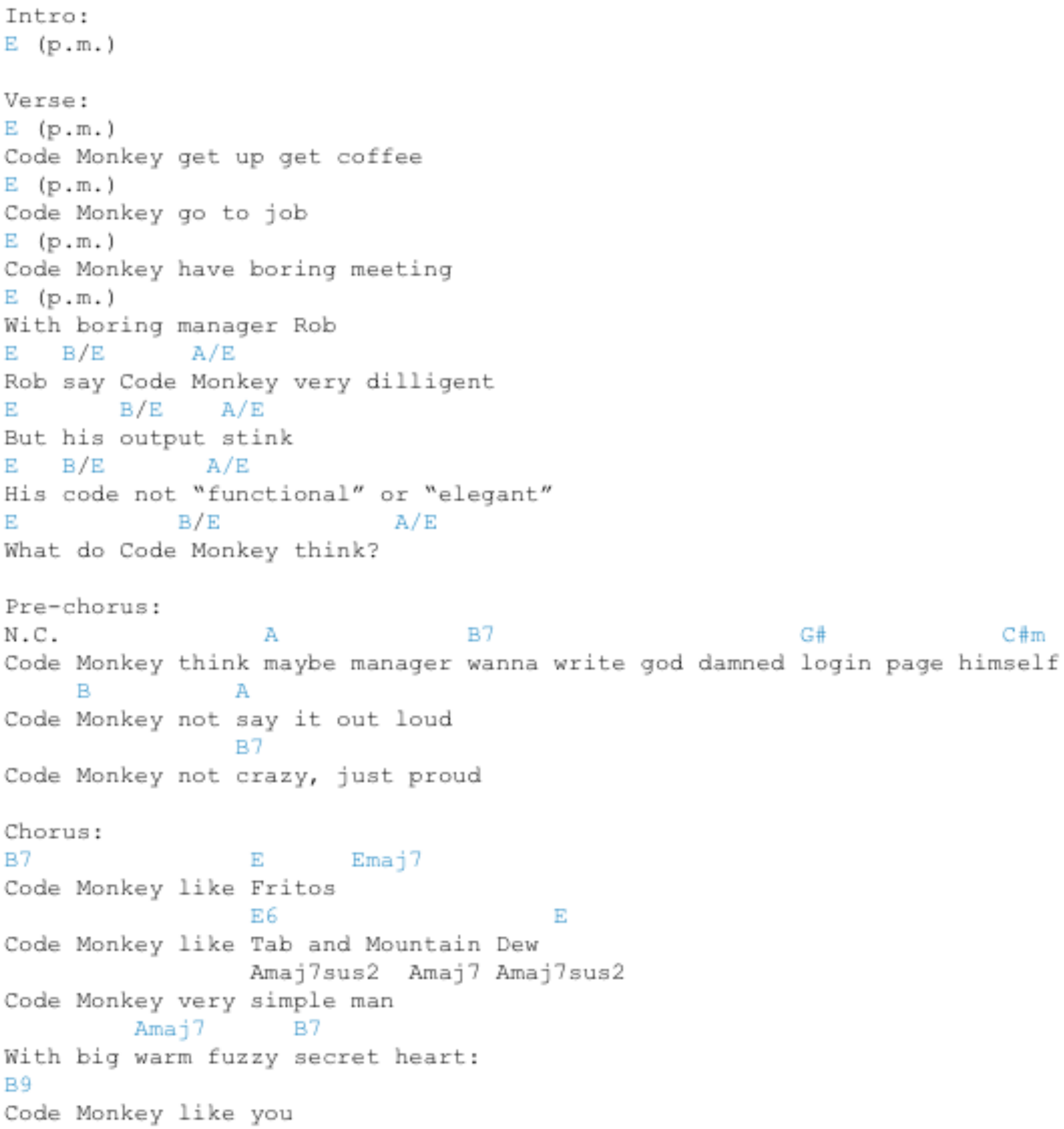
Data Analysis Then…

Data Analysis Then…

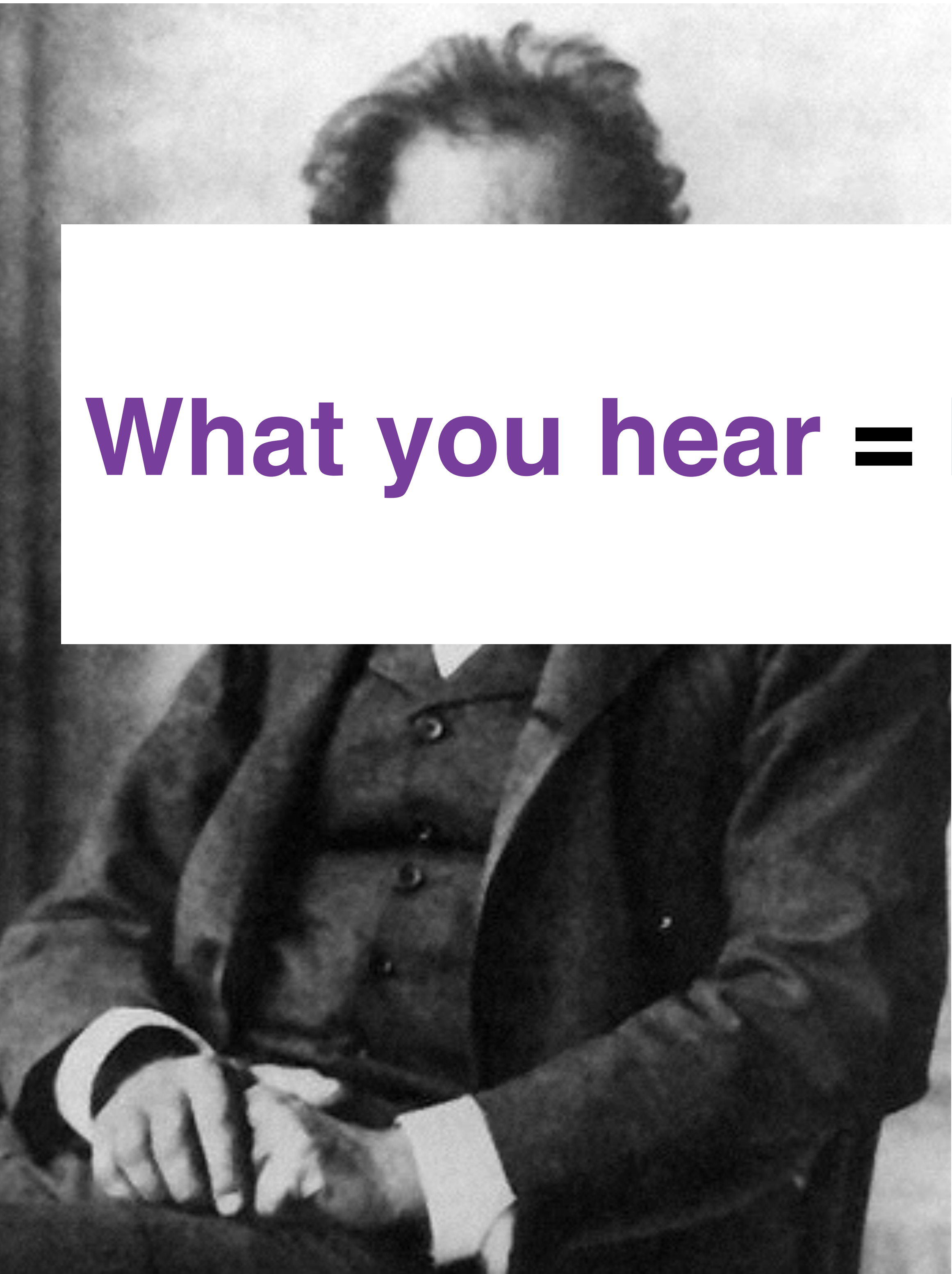
…And Now

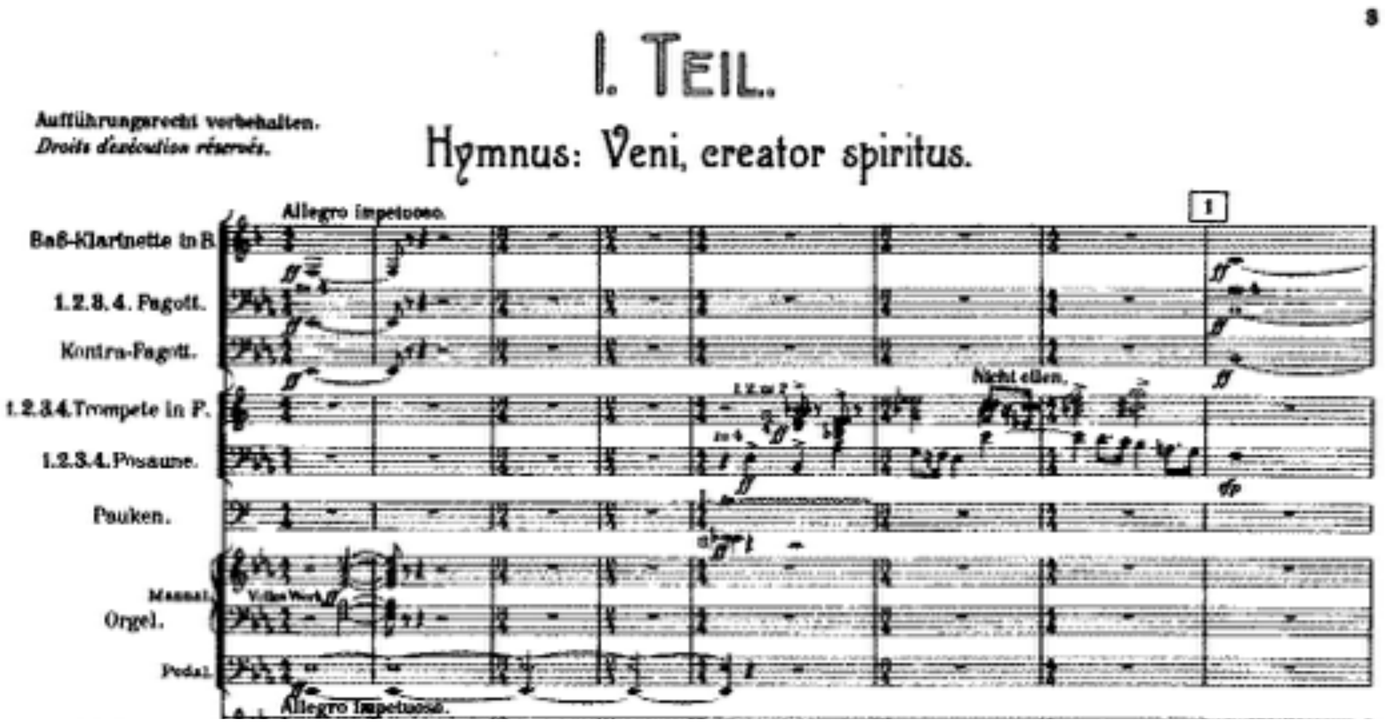
…And Now

The Central Problem

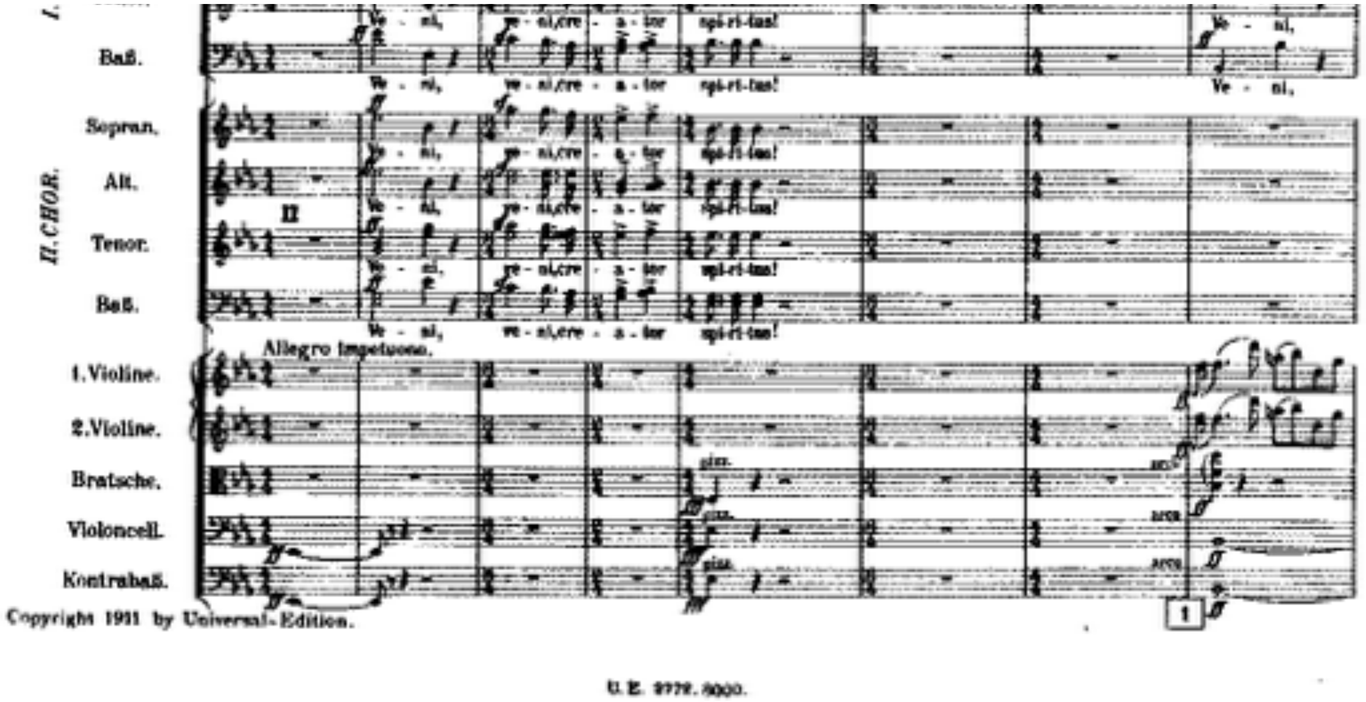

```
Intro:
E (p.m.)

Verse:
E (p.m.)
Code Monkey get up get coffee
E (p.m.)
Code Monkey go to job
E (p.m.)
Code Monkey have boring meeting
E (p.m.)
With boring manager Rob
E   B/E      A/E
Rob say Code Monkey very dilligent
E       B/E    A/E
But his output stink
E   B/E       A/E
His code not "functional" or "elegant"
E           B/E            A/E
What do Code Monkey think?

Pre-chorus:
N.C.              A             B7                     G#            C#m
Code Monkey think maybe manager wanna write god damned login page himself
     B          A
Code Monkey not say it out loud
                B7
Code Monkey not crazy, just proud

Chorus:
B7               E      Emaj7
Code Monkey like Fritos
                 E6                   E
Code Monkey like Tab and Mountain Dew
                 Amaj7sus2  Amaj7 Amaj7sus2
Code Monkey very simple man
         Amaj7      B7
With big warm fuzzy secret heart:
B9
Code Monkey like you
```

The Central Problem





What you hear = Notation + Performance



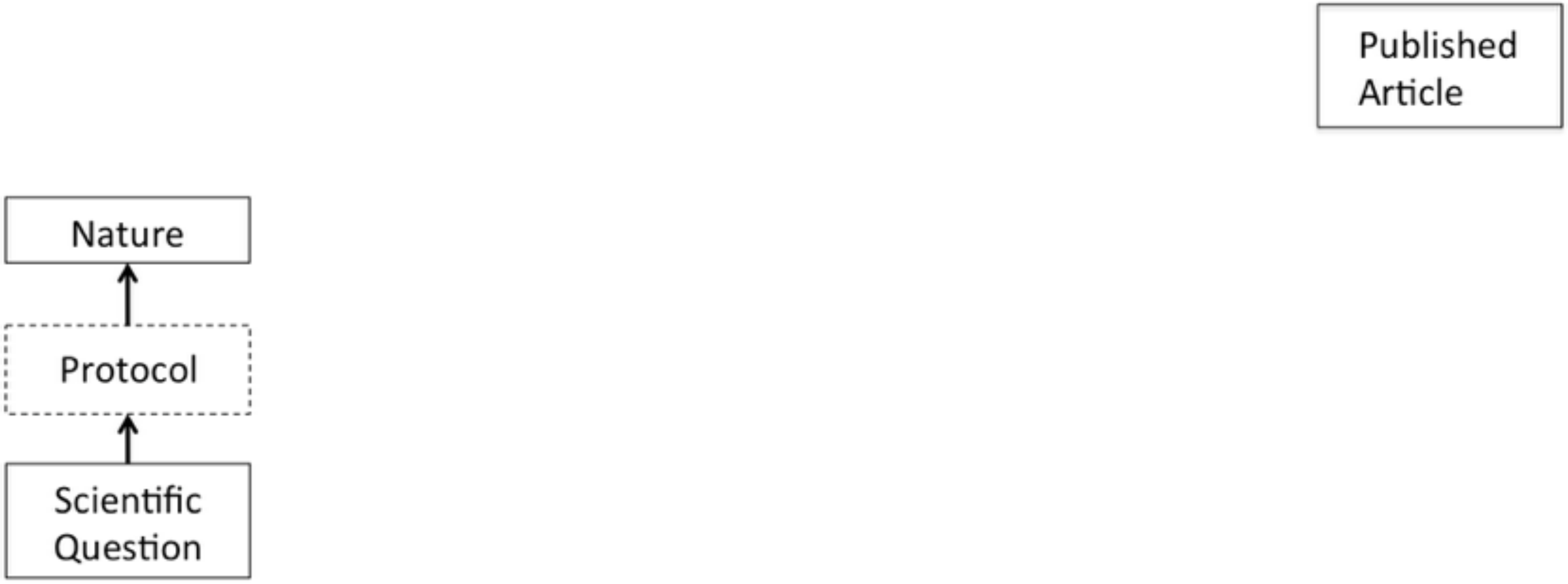
The Central Problem

Data Analysis = ???

The End Result

- Basic analyses can be difficult to describe
- Heavy computational requirements are thrust upon people without adequate training in statistics and computing
- Errors are more easily introduced into long and complex analysis pipelines
- Knowledge transfer is limited
- Complicated analyses cannot be trusted

What is Reproducible Research?



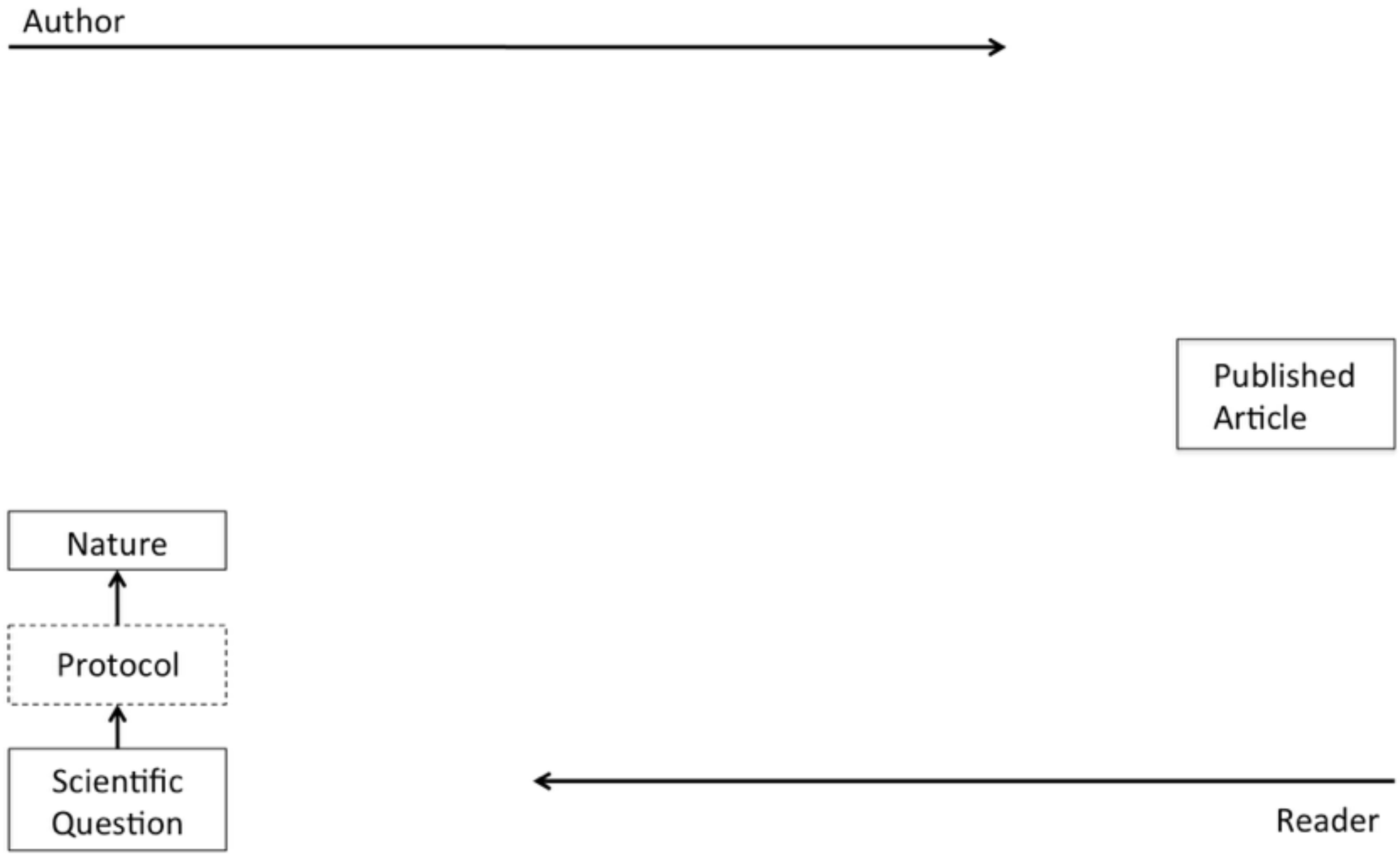
Published Article

Nature

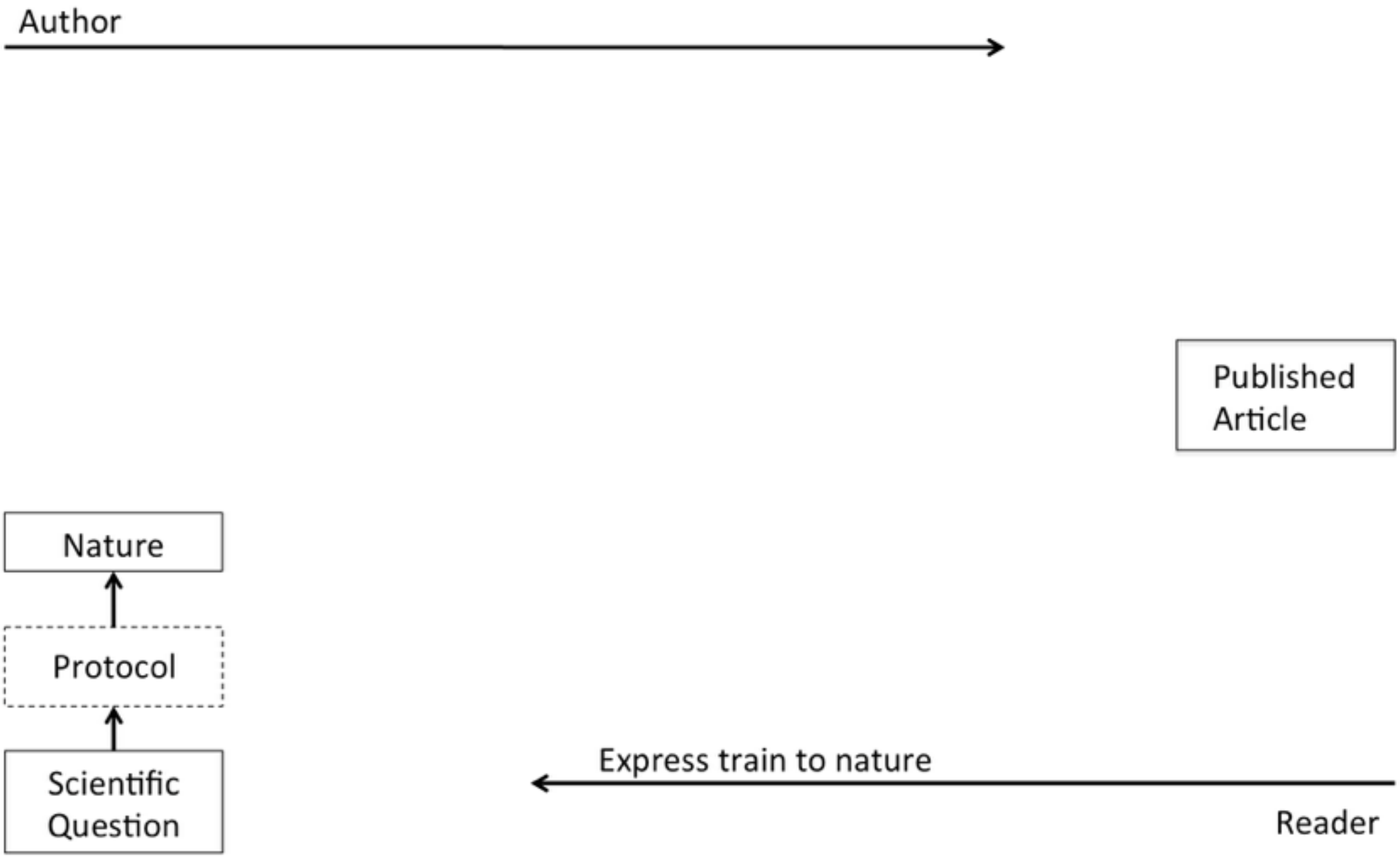
Protocol

Scientific Question

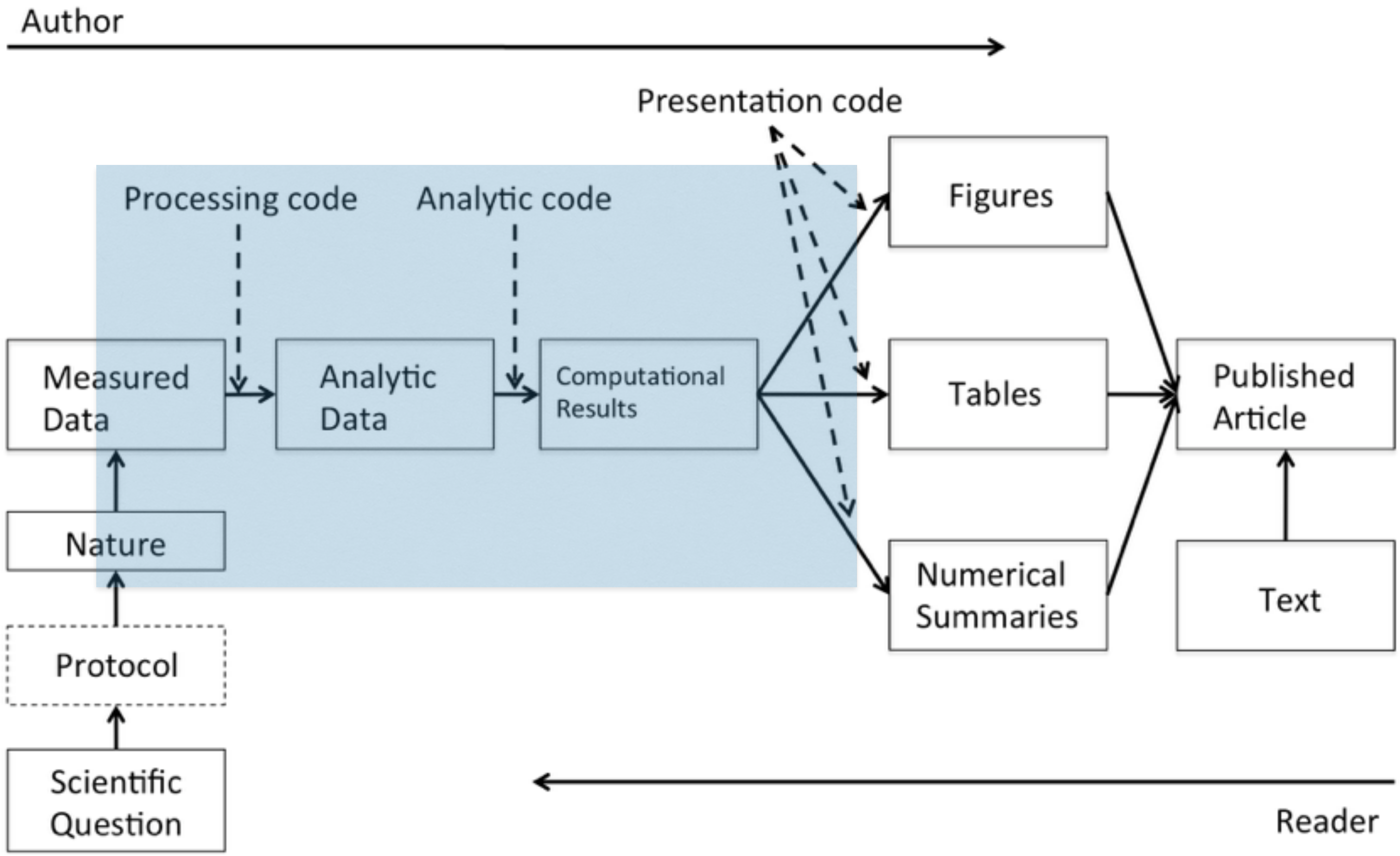
What is Reproducible Research?



What is Reproducible Research?



What is Reproducible Research?



What is Reproducible Research?

- Analytic data are available
- Analytic (and preprocessing) code are available
- Documentation of code and data
- Standard means of distribution

What is Reproducible Research?

- Authors
  - Want to make their research reproducible
  - Want tools for RR to make their lives easier (or at least not much harder)
- Readers
  - Want to reproduce (and perhaps expand upon) interesting findings
  - Want tools for RR to make their lives easier

Challenges

- Authors must undertake considerable effort to put data and results on the web (may not have resources like a web server)

- Readers must download data/results individually and piece together which data go with which code sections, etc.

- Readers may not have the same resources as authors

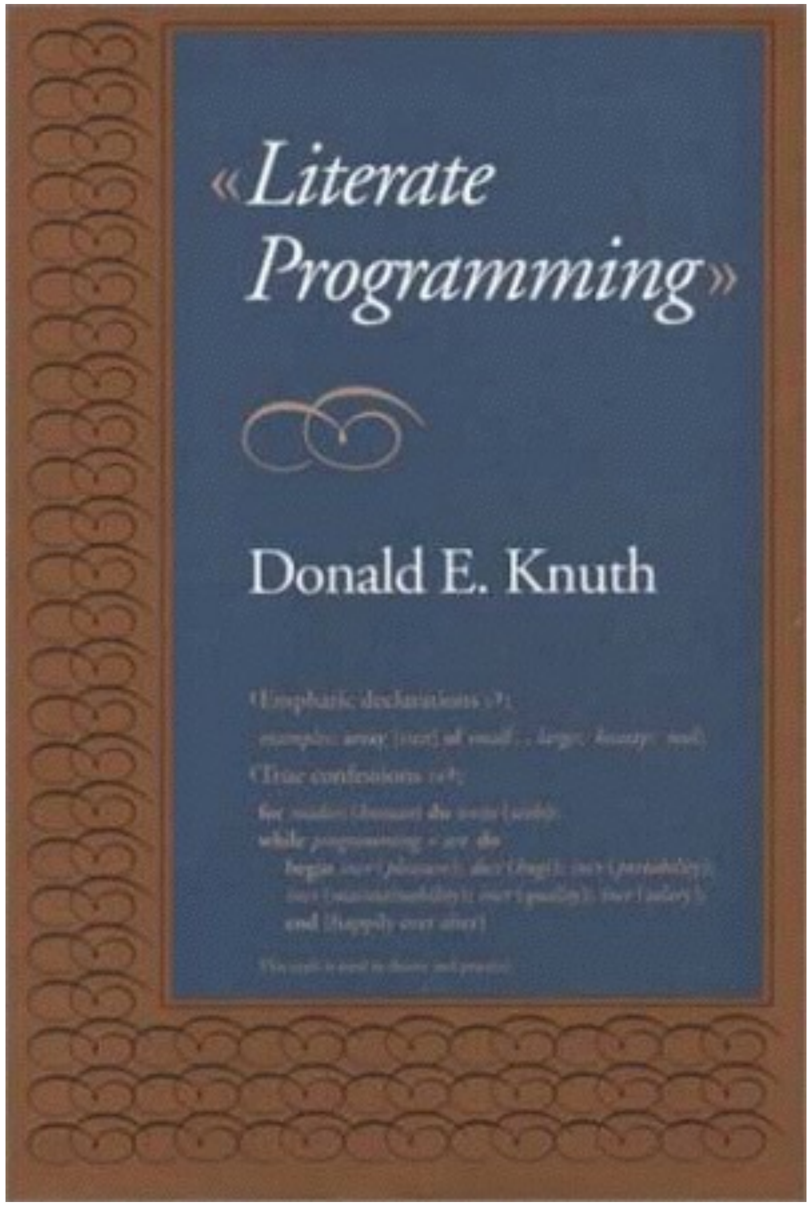
- Few tools to help authors/readers (although toolbox is growing!)

Recent Developments

- **Software**: iPython Notebooks, knitr, markdown, LONI, Galaxy
- **Repositories**: GitHub, NCBI, ICPSR, Dataverse
- **Policy**: *Science*, *Nature*, *PLOS ONE*, OSTP, NIH

Literate Statistical Programming

- An article/report is a stream of text and code
- Analysis code is divided into text and code “chunks”
- Each code chunk loads data and computes results
- Presentation code formats results (tables, figures, etc.)
- Article text explains what is going on
- Literate programs can be **weaved** to produce human-readable documents and **tangled** to produce machine-readable documents
- See *Literate Programming* by Donald Knuth

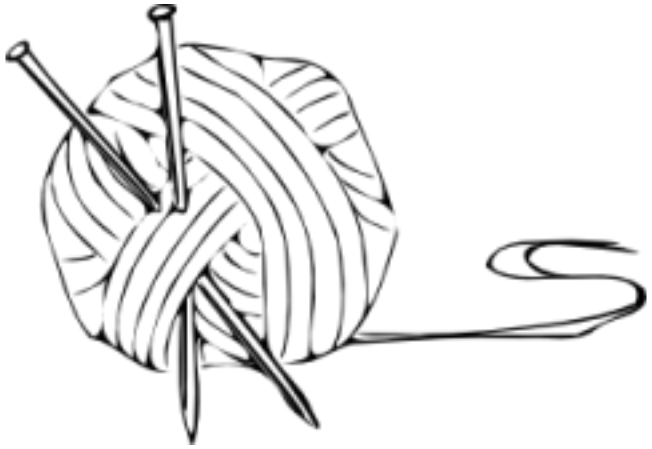


Literate Statistical Programming

- Literate programming is a general concept that requires
  - A documentation language (human readable)
  - A programming language (machine readable)
- Sweave uses LaTeX and R as the documentation and programming languages
- Sweave was developed by Friedrich Leisch (member of the R Core) and is maintained by R core
- Main web site: http://www.statistik.lmu.de/~leisch/Sweave

Literate Statistical Programming

- knitr is package that brings together many features added on to Sweave to address limitations
- knitr uses R as the programming language knitr was developed by Yihui Xie (while a graduate student in statistics at Iowa State, now at RStudio)
- knitr uses the R programming language (although others are allowed) and variety of documentation languages
  - LaTeX, Markdown, HTML
- Built into RStudio pipeline
- See http://yihui.name/knitr/



What Problem Does Reproducibility Solve?

- What we get
  - Transparency / Improved knowledge transfer
  - Data availability
  - Software / Methods
- What we do NOT get
  - Validity / Correctness of the analysis

What’s Next?

- Reproducibility is critical for *communicating* a data analysis

- One cannot sufficiently describe an analysis in words

- General consensus about its importance

- Infrastructure for making all research reproducible is not there yet, but things are ever improving

“There ain’t nothin’ better than the full Die Baggerly, as long as Keith is singing!”

–Steve Goodman