This is your brain on disk

The impact of numerical instabilities in neuroscience

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Reproducibility is measurable

Majority of studies fail to replicate

(Open Science Collaboration, 2015)

Inflated false-positive rates

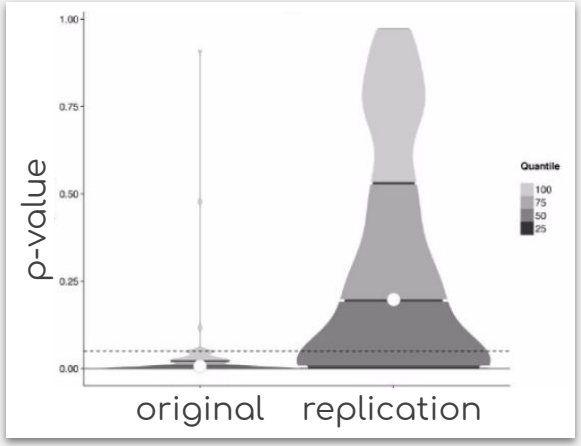
(Eklund, 2016)

Similar tools give different conclusions

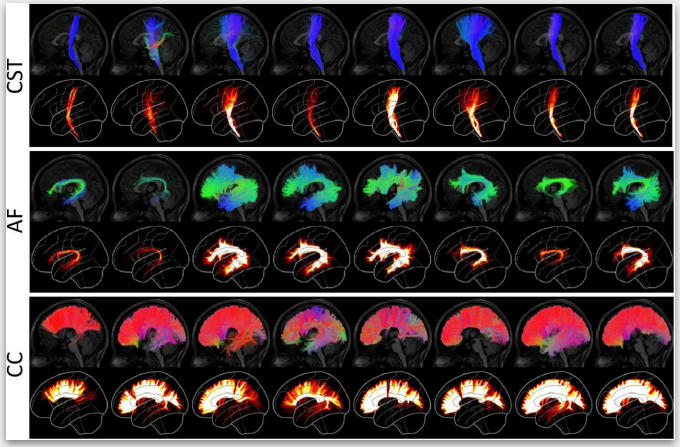
(Bowring, 2019)

Variability across analysis teams

(Botvinik-Nezer, 2020; Schilling, 2020)



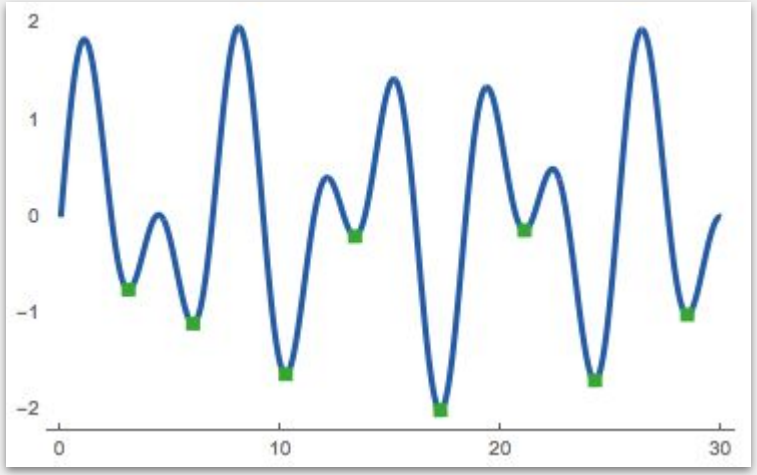
(Open Science Collaboration, 2015)



(Schilling, 2020)

Intrinsic numerical errors may play a role

```
(~) gkiar $ python3 -c "print(sum([0.001 for _ in range(1000)]))"
1.0000000000000007
```

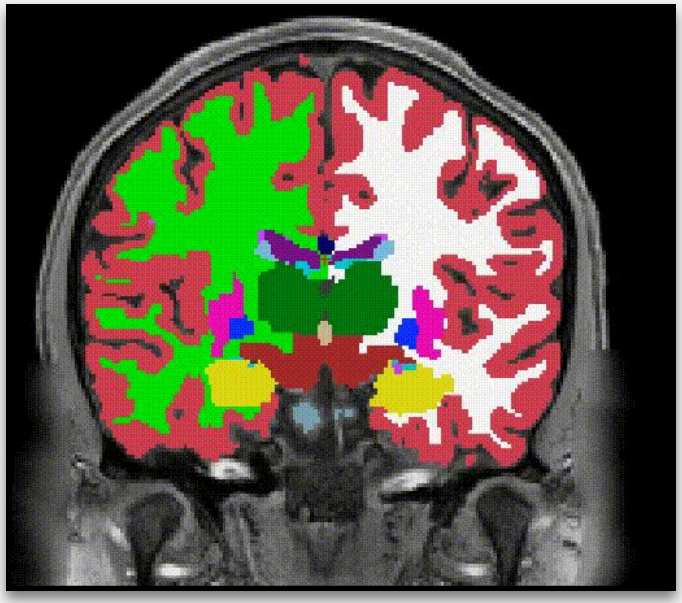


Errors may lead unstable functions towards distinct local minima

https://brilliant.org/wiki/extrema/

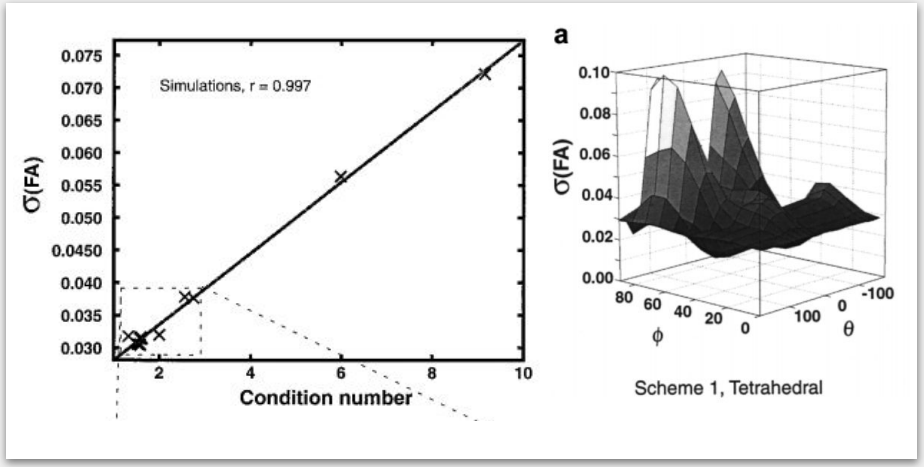
Instabilities amplify uncertainty in pipelines

Differences across OSes



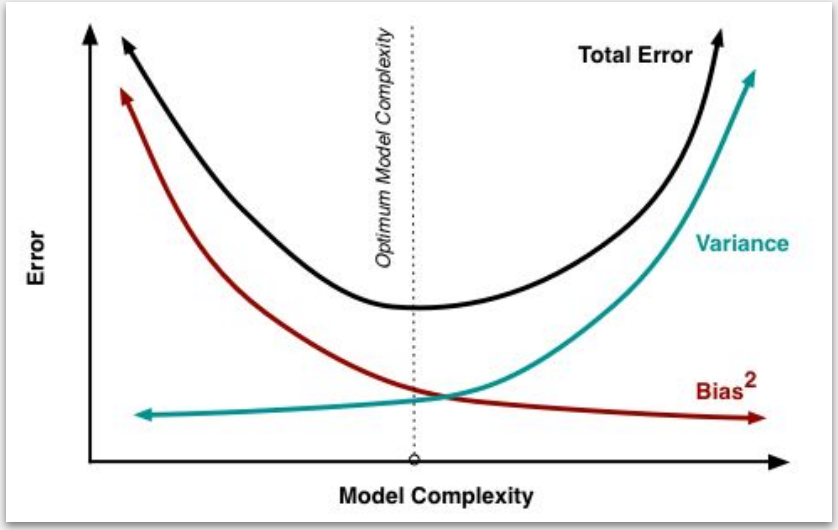
(Salari, 2020)

Tensor stability relates to variability

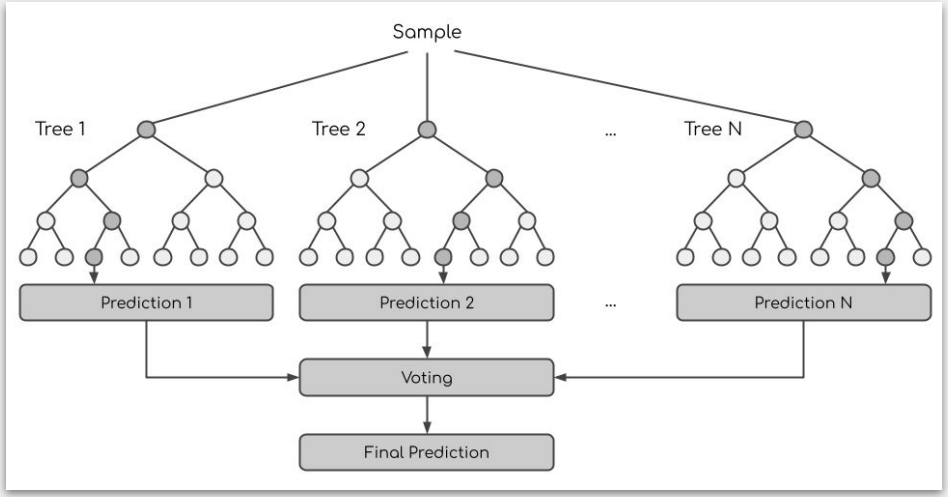


(Skare, 2000)

Variance can be useful in modelling



(Fortmann-Roe, 2012)



(Breiman, 2001)

Objective

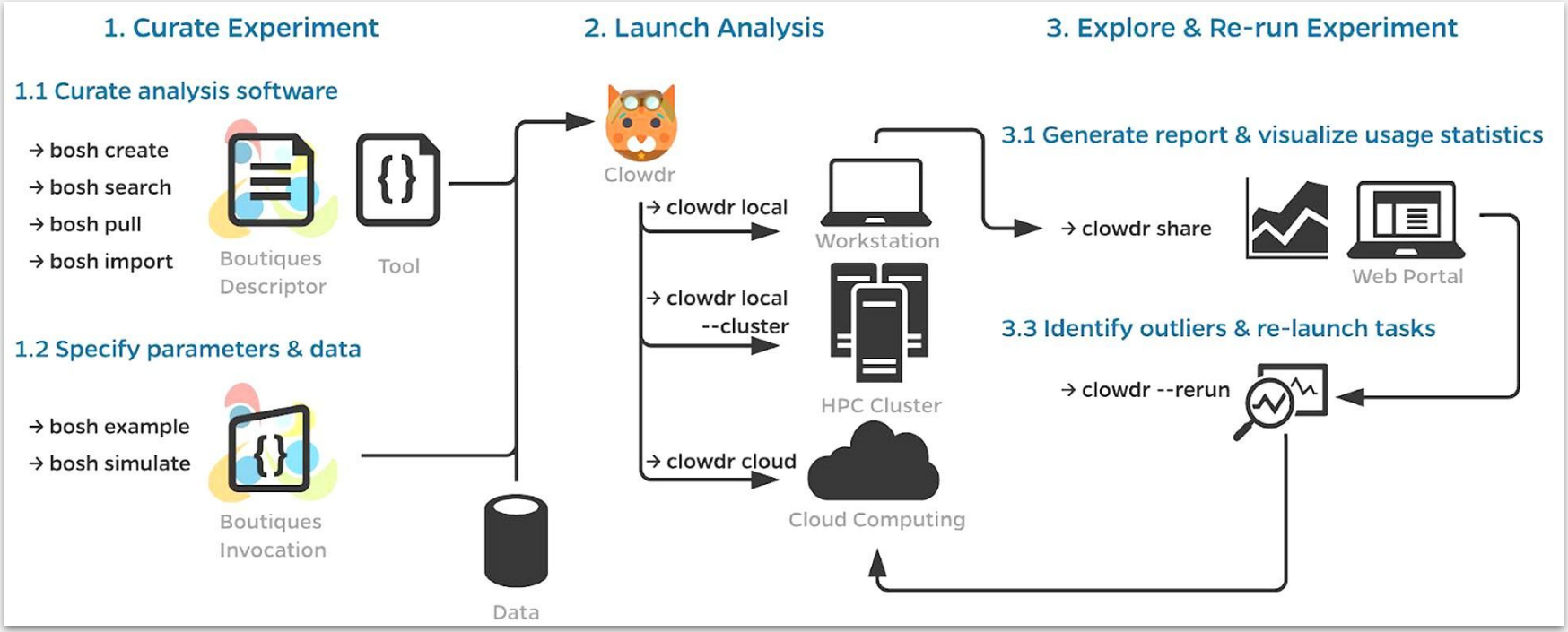
Explore,

evaluate,

and take advantage of

numerical instabilities in neuroimaging pipelines

Infrastructure for reproducible neuroimaging



(Kiar, 2019)

Estimate stability w/ Monte Carlo arithmetic (MCA)

Perturb arithmetic operations (+-x/)

Make machine error probabilistic

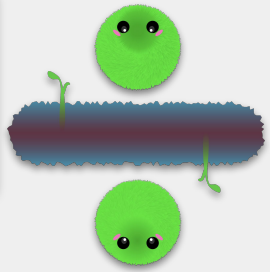
Dense or Sparse perturbations

Evaluate the stability of scientific pipelines in "Fuzzy" environments

```
   Float32   # (~ 8 digits)
>> 5/3
1.6666667
        |    # limit of machine precision
      ± 0.5  # Monte Carlo perturbation applied
             # to last digit


   Float64           # (~ 16 digits)
>> 5/3
1.666666666666667
                |    # ...
```

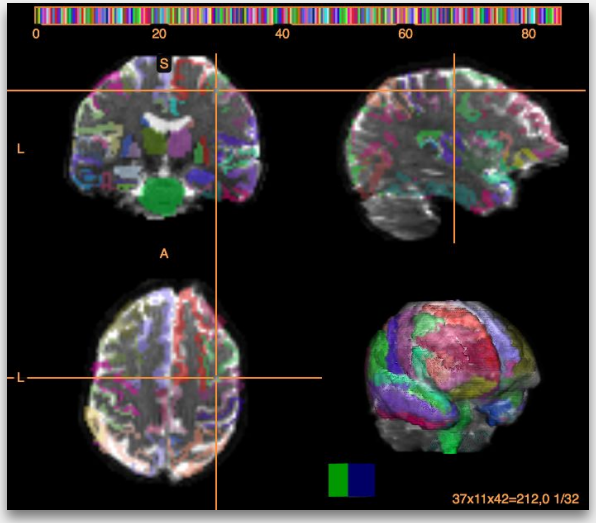
verificarlo

(Dennis, 2015)
https://github.com/verificarlo/



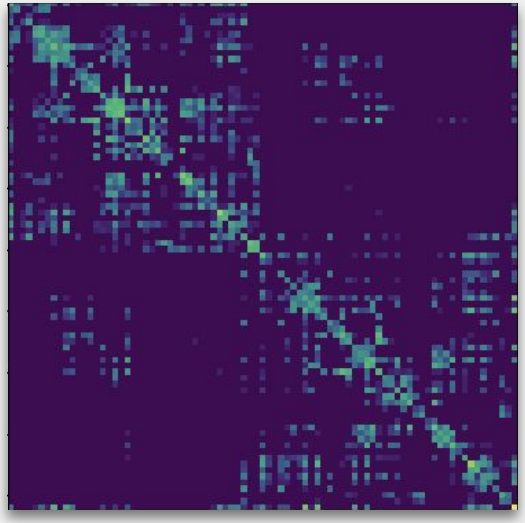
Structural connectome estimation

Diffusion MRI volumes + anatomical labels



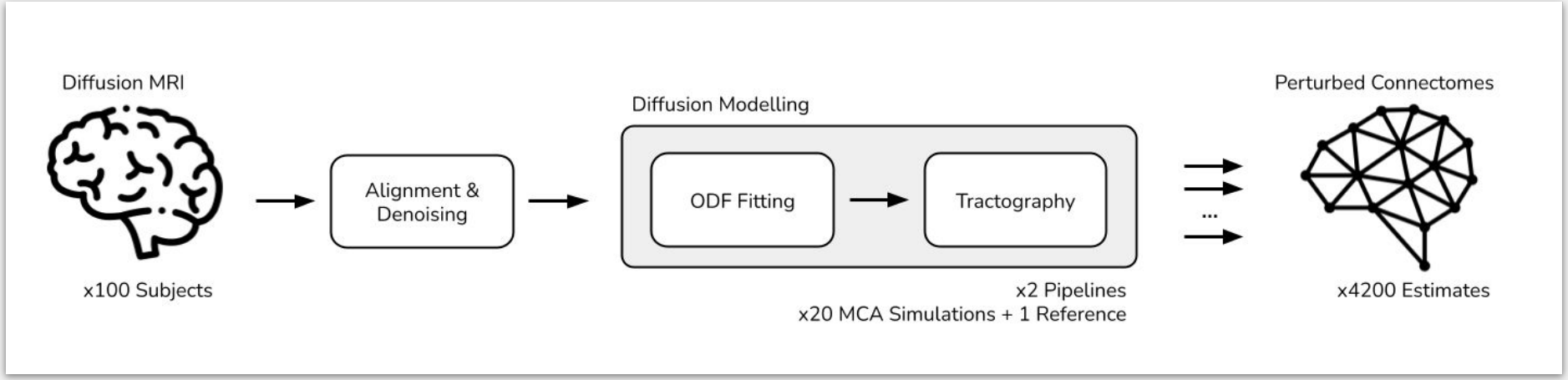
(X, Y, Z, D) ~ O(10M voxels)

Connectivity Matrix

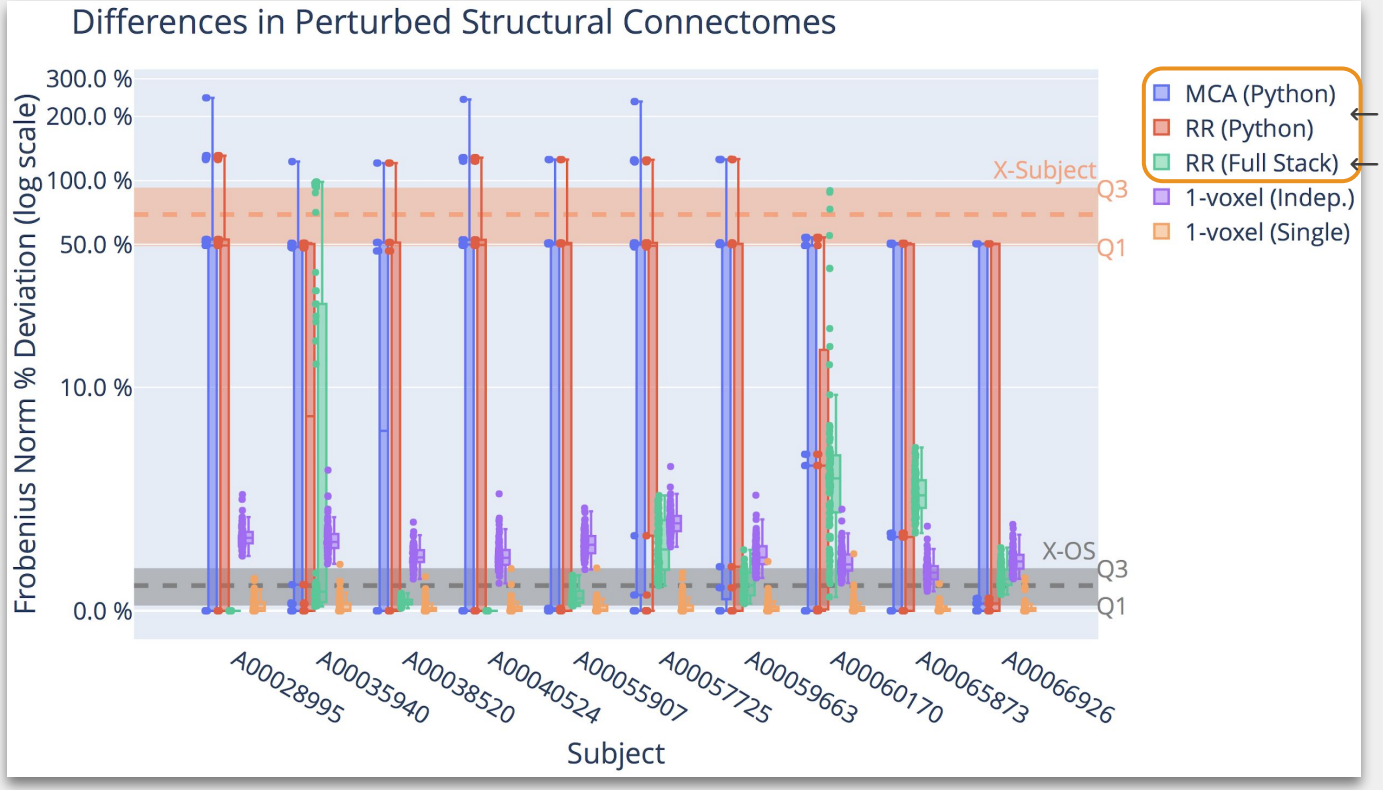


(83, 83) = 3403 edges

Outline of Perturbation Experiments

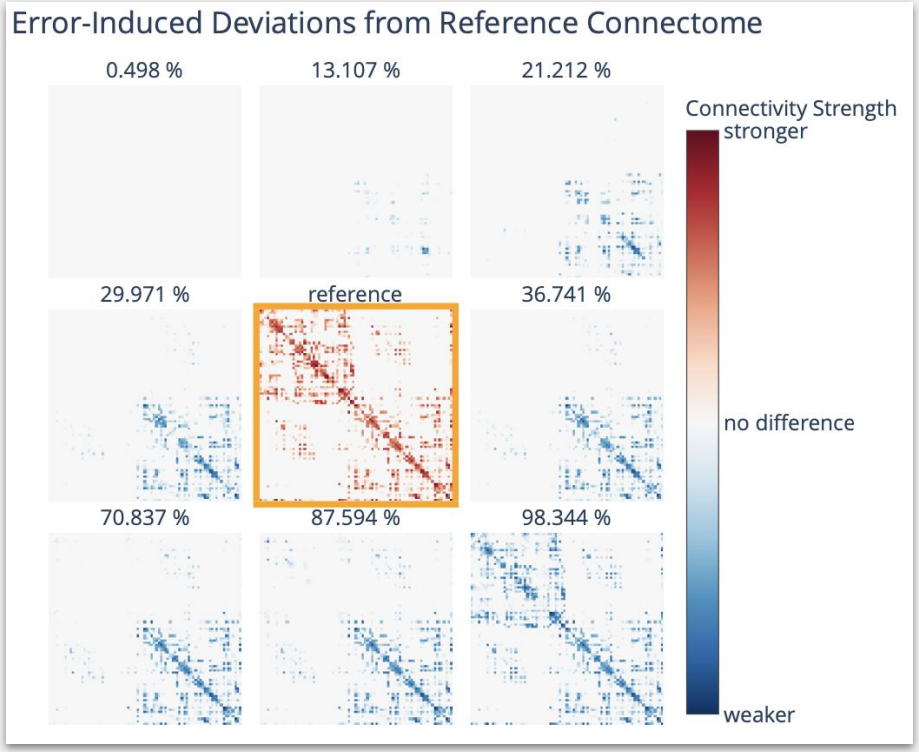


MCA induces a wide range of variability



(Kiar, 2020a)

Variability across networks is structured

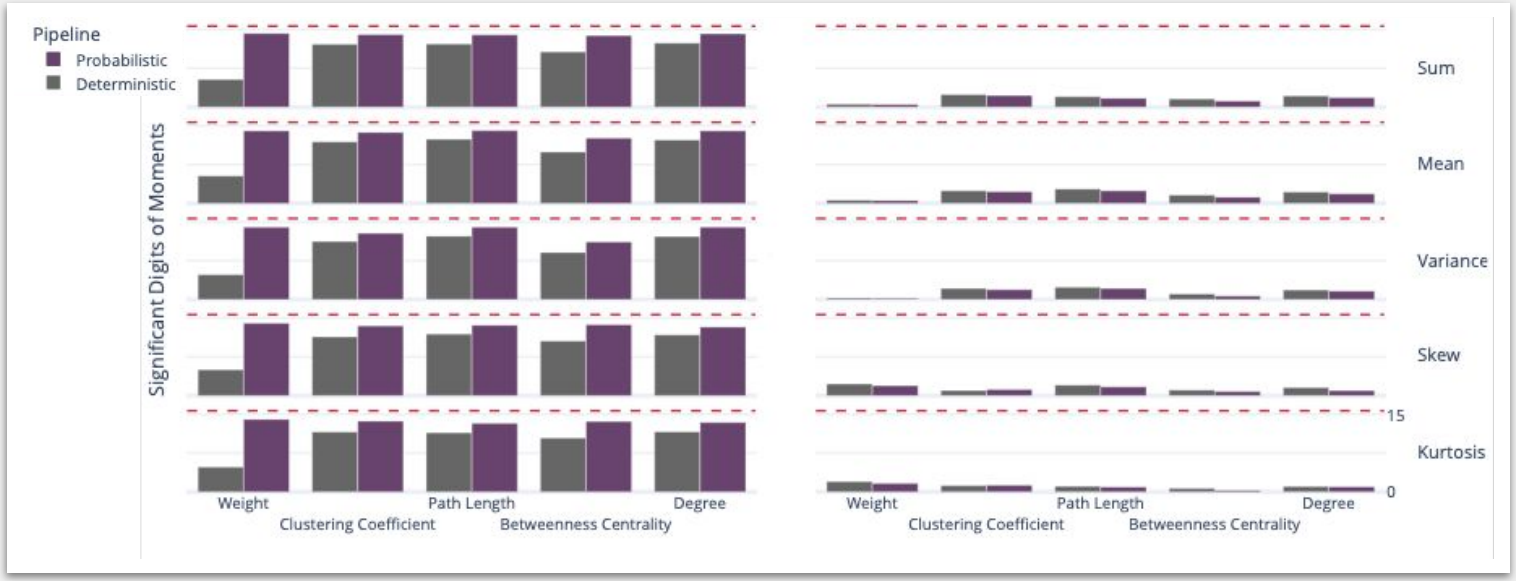


(Kiar, 2020a)

Network statistics are highly unstable...

Dense MCA Perturbations

Sparse MCA Perturbations

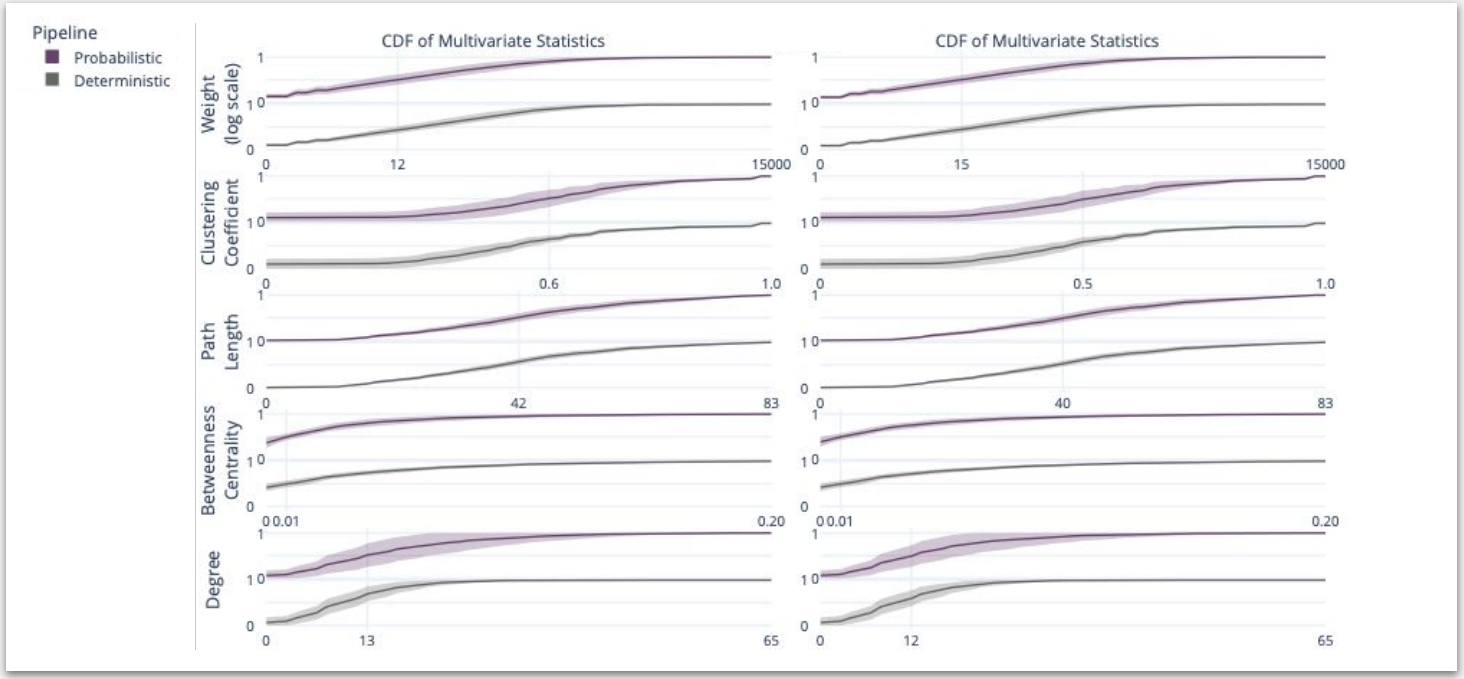


(Kiar, 2020b)

… But their distributions are stable

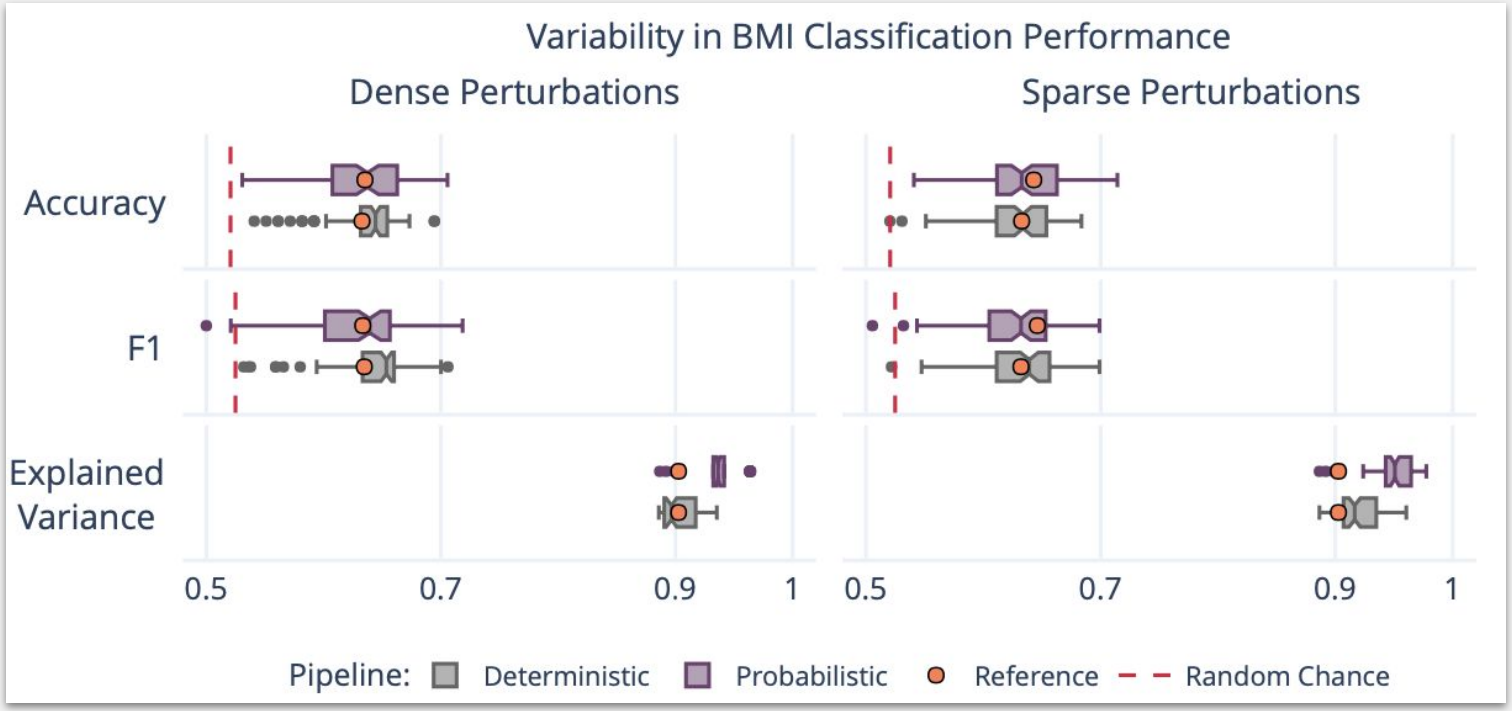
Dense MCA Perturbations

Sparse MCA Perturbations



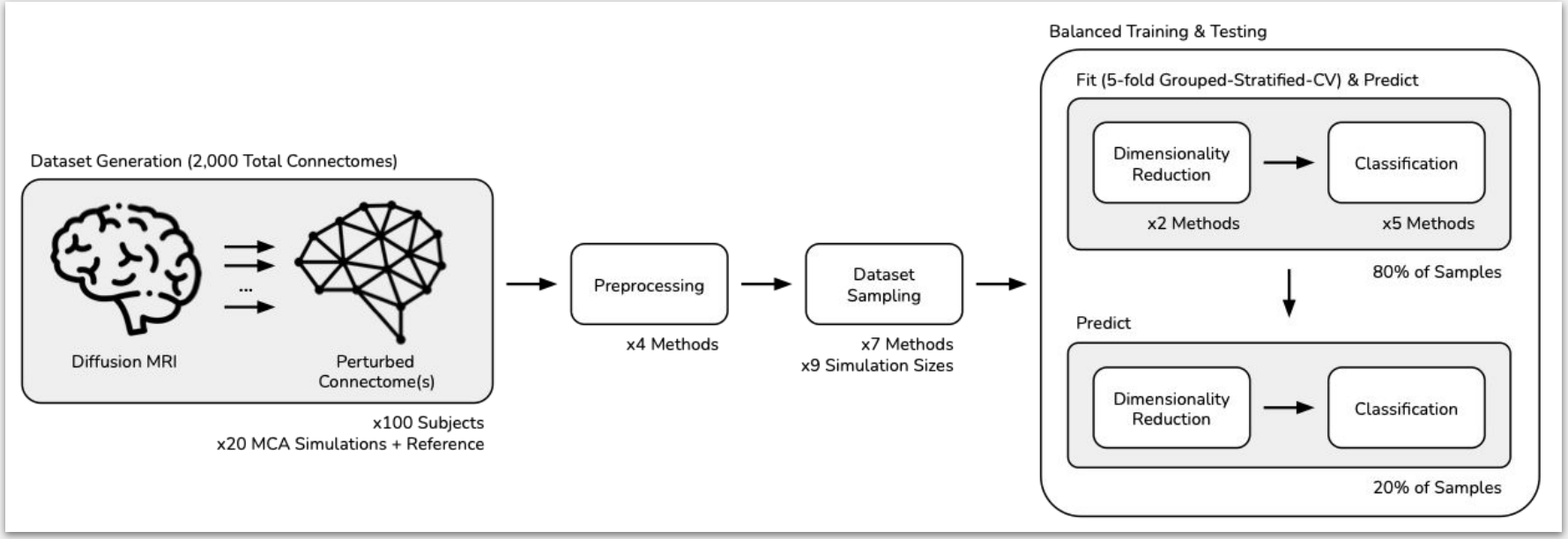
(Kiar, 2020b)

Variability in brain-phenotype relationships



(Kiar, 2020b)

Dataset augmentation via MCA perturbations



(Kiar, 2020c)

Capturing (or ignoring) variance via aggregation

Truncate: remove all variance

Jackknife: randomly sample networks

Mean, Median, Consensus: average network

Mega: include all samples of all networks

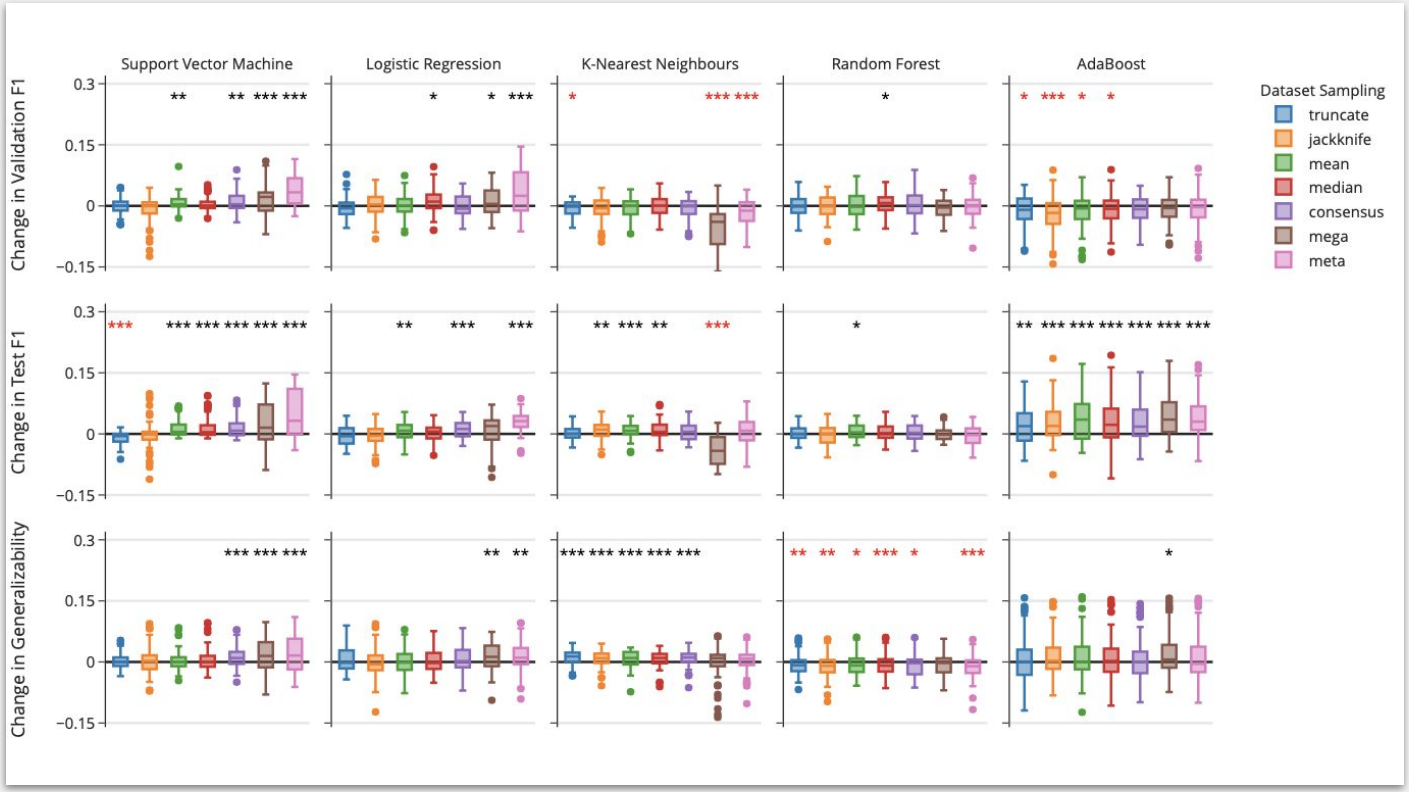
Meta: vote across jackknifed classifiers

Capturing variance improves models

Dataset Sampling	Validation	Test	Generalizability
Truncate	**		
Jackknife	**	**	
Mean		***	
Median		***	
Consensus		***	*
Mega-Analysis	*	*	***
Meta-Analysis	**	***	*

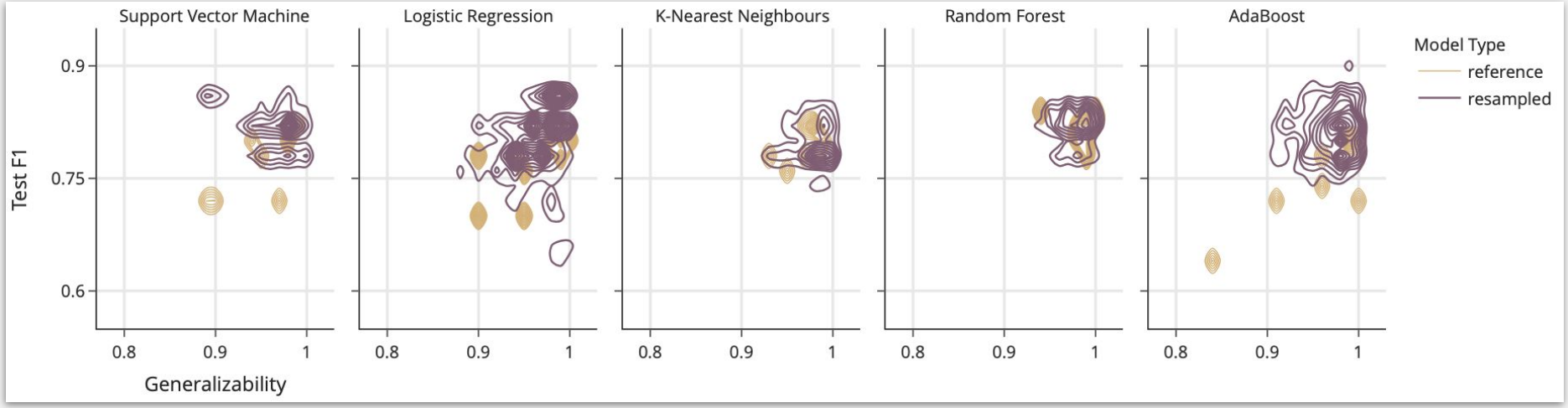
(Kiar, 2020c)

Consistent improvement across experiments



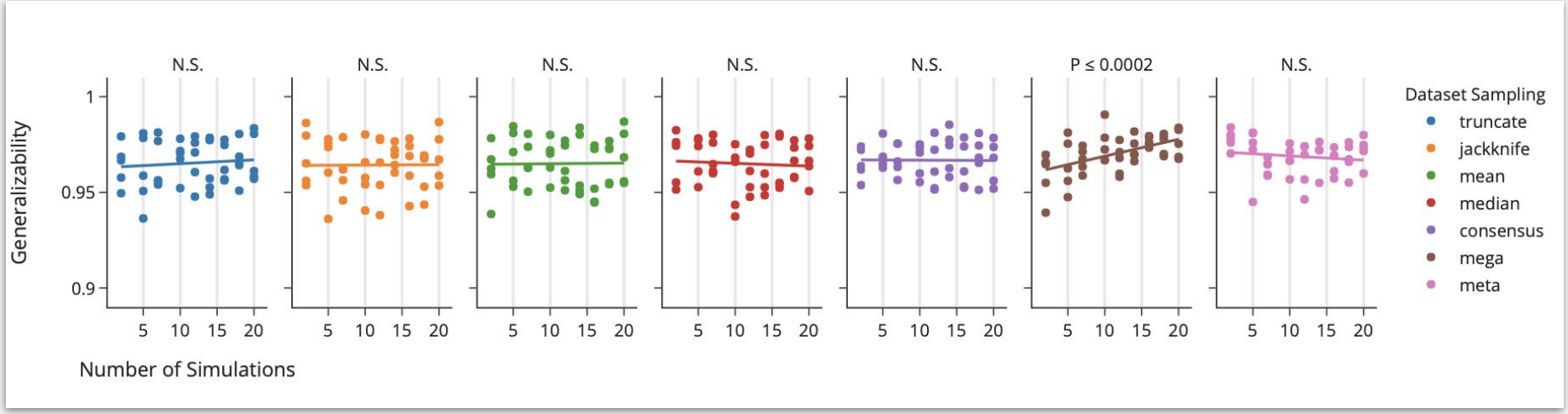
(Kiar, 2020c)

MCA improves generalizability *or* performance



(Kiar, 2020c)

The number of MCA samples is unimportant



(Kiar, 2020c)

Outcomes

Developed computational tools to explore numerical stability (Kiar, 2019)

Applied Monte Carlo arithmetic for perturbing pipelines (Kiar, 2020a)

Demonstrated the impact of numerical instabilities on results (Kiar, 2020b)

Augmented datasets to improve brain-phenotype models (Kiar, 2020c)

Applicable across the data/analysis lifecycle

... All instrumentable with Fuzzy

Acknowledgements

...

Key References

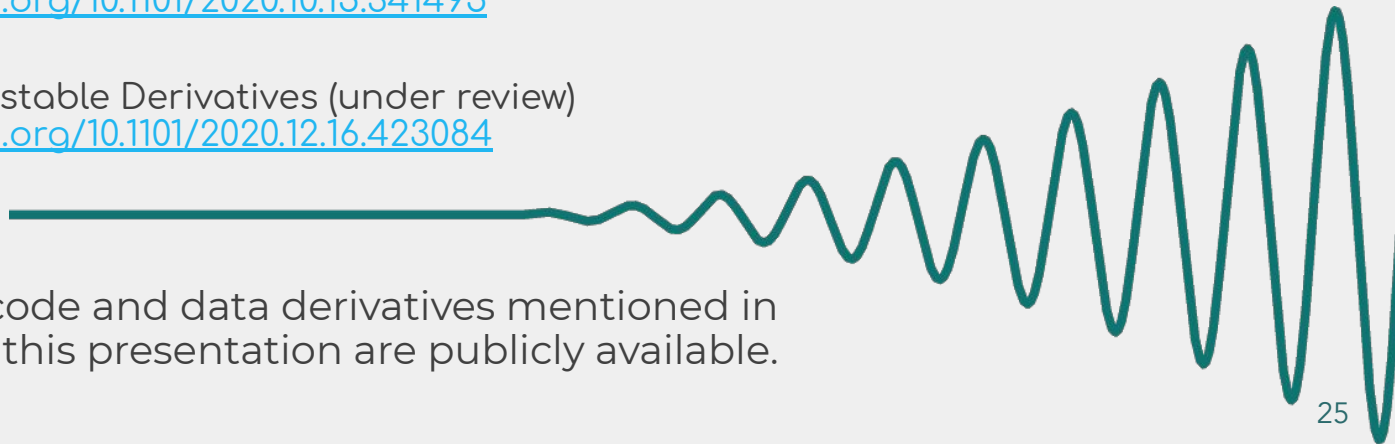
Ch. 1 Serverless Experiment Management (Front. Neuroinf.)
https://doi.org/10.3389/fninf.2019.00012

Ch. 2 Perturbing Pipelines (IJHPCA)
https://doi.org/10.1177/1094342020926237

Fuzzy (Scipy Conference)
https://github.com/verificarlo/fuzzy

Ch. 3 Impact of Instability (under review)
https://doi.org/10.1101/2020.10.15.341495

Ch. 4 Aggregating Unstable Derivatives (under review)
https://doi.org/10.1101/2020.12.16.423084



gkiar
g_kiar
https://gkiar.me

All code and data derivatives mentioned in this presentation are publicly available.

Backmatter ToC

Background

- Tool differences (fMRI)
- 1-voxel noise (sMRI)
- Pre-Freesurfer (sMRI)
- How MCA works
- Piecewise sine
- Sparse MCA
- LLN

Chapter 1

- Figure 1
- Figure 2
- Figure 3

Chapter 2

- Figure 1
- Table 1
- Figure 2
- Figure 3
- Figure 4
- Figure 5
- Figure 6

Chapter 3

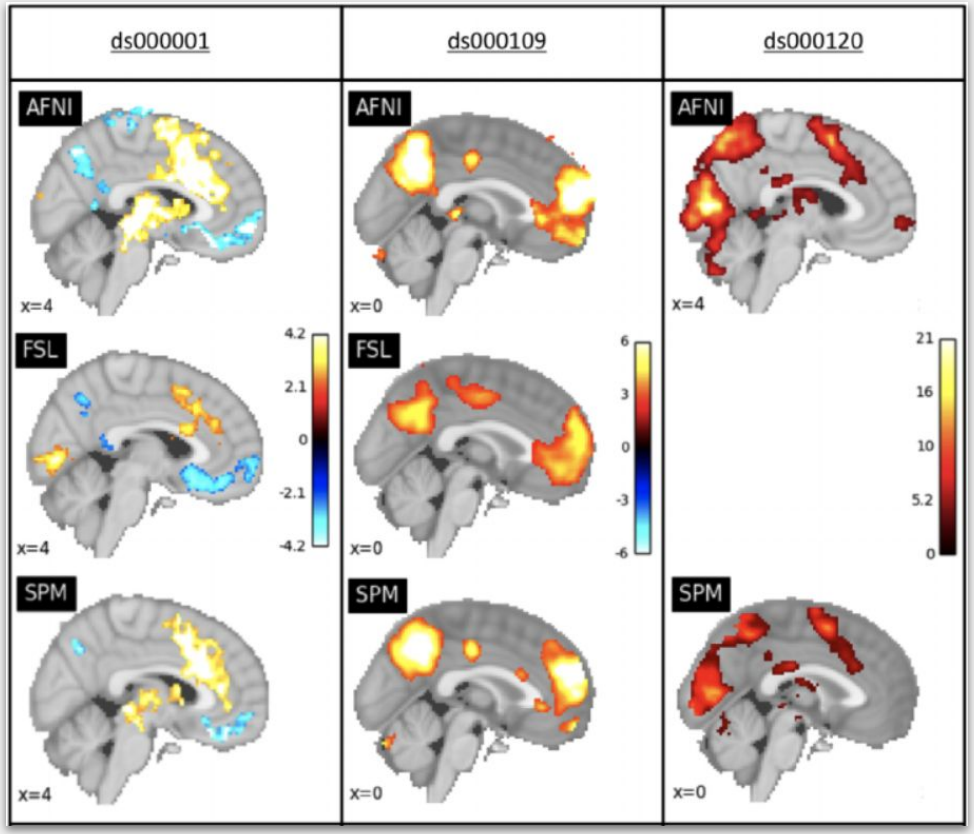
- Figure 1
- Table 1
- Figure 2
- Figure 3
- Table 1 (R)
- Figure S2

Chapter 4

- Figure 1
- Table 1
- Figure 2
- Figure 3
- Figure 4

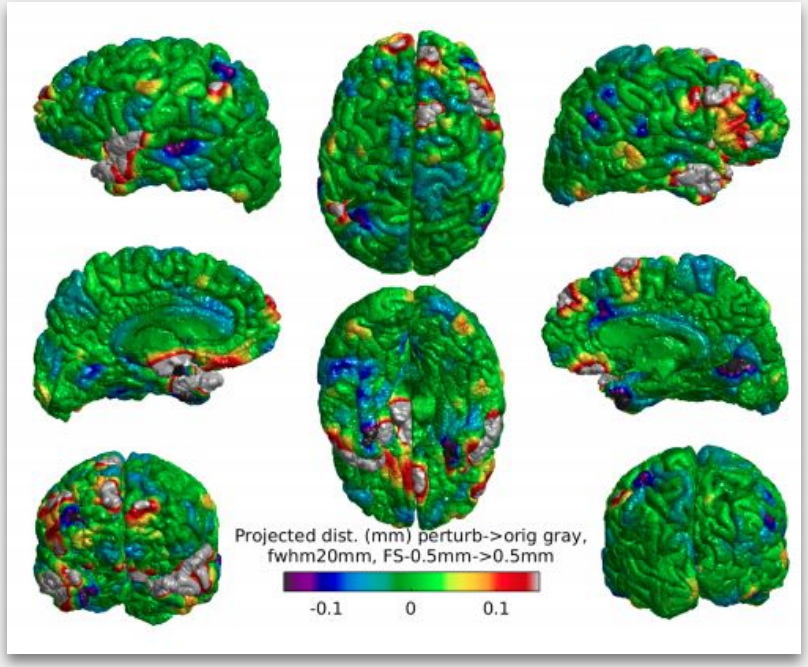
Background

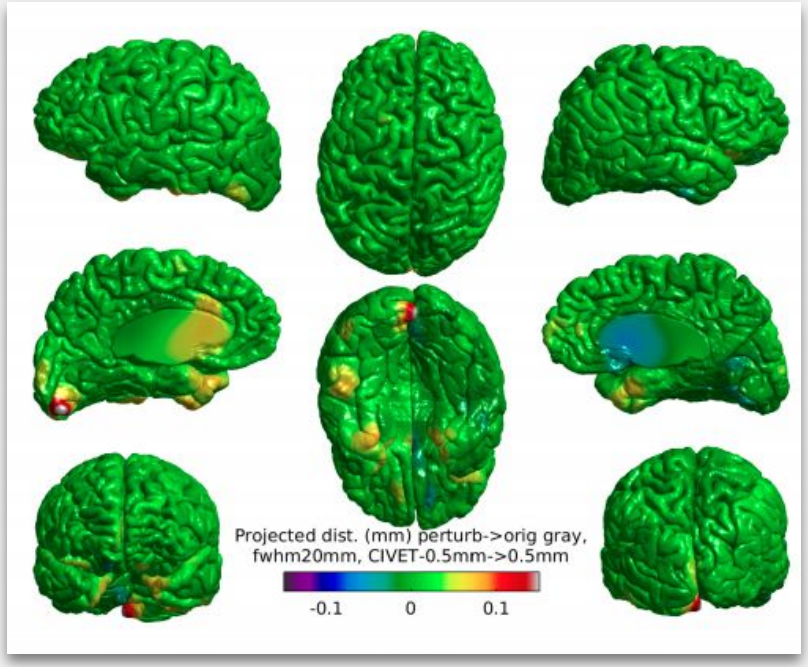
Differences across tools



(Bowring, 2019)

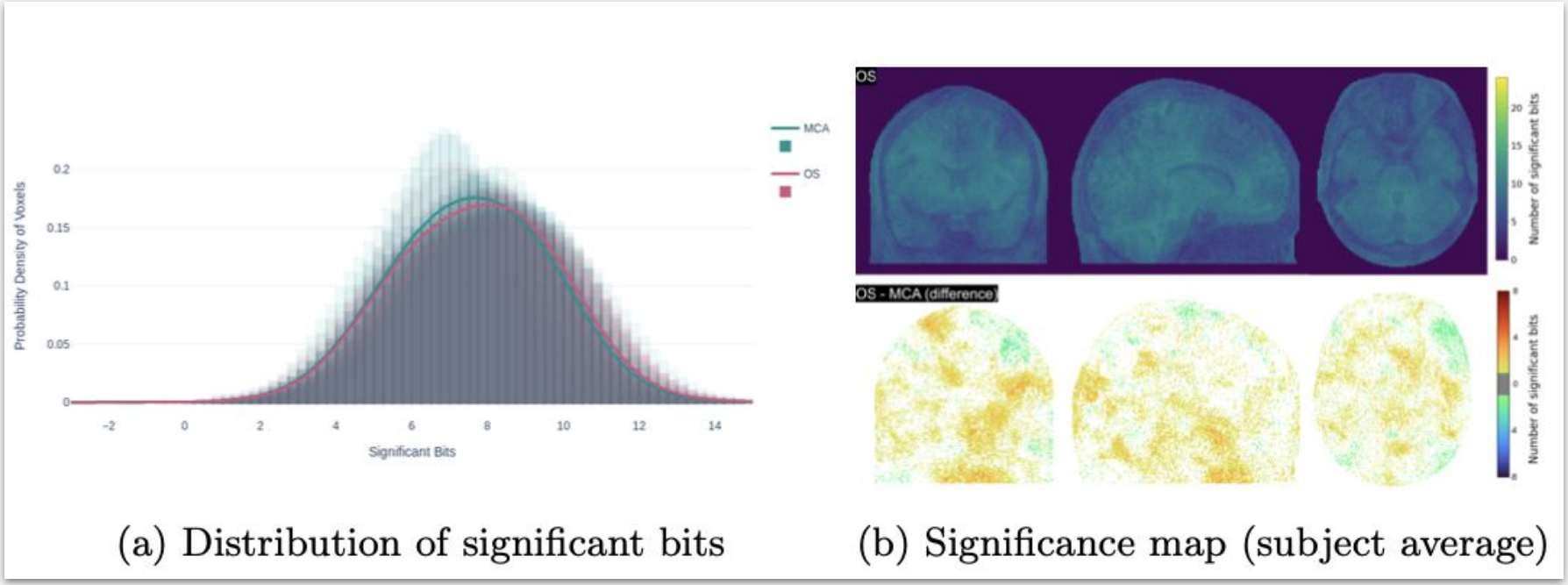
1-voxel perturbations distort cortical surfaces





(Lewis, 2017)

Pre-Freesurfer stability



(a) Distribution of significant bits

(b) Significance map (subject average)

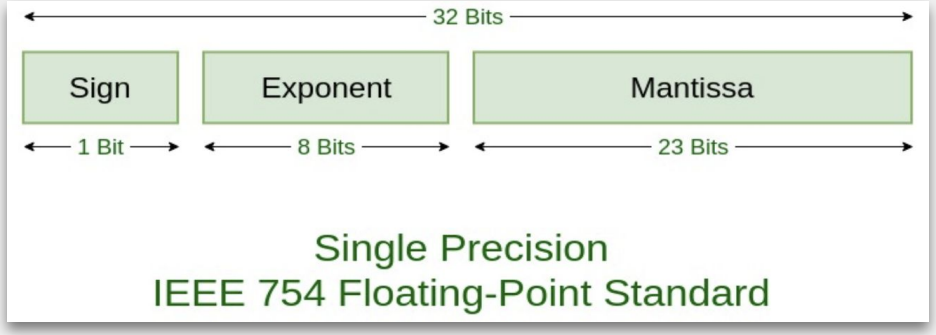
(Salari, 2021)

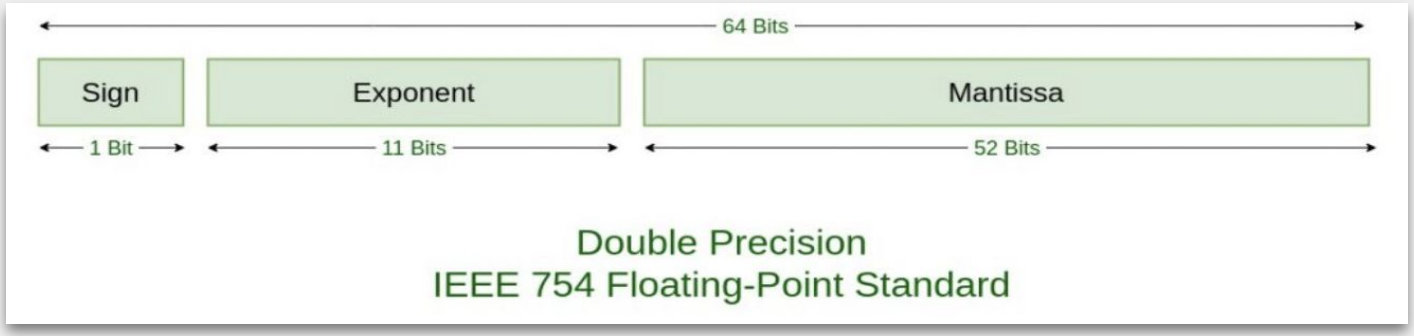
Backmatter ToC

how MCA works

(with an example)

Floating Point data are finite





Floating Point Arithmetic is Inexact

E.g. addition is non associative

Let's say we have 4 decimal digits of precision:

$$(\ 2000. \oplus -1998.\ ) \oplus 1.333 = 2.000 \oplus 1.333 = 3.333$$

$$2000. \oplus (\ -1998. \oplus 1.333\ ) = 2000. \oplus -1997. = 3.000$$

What is the right answer?

(inspired by Parker et al., 1997)

Floating Point Arithmetic is Inexact

E.g. addition is non associative

Catastrophic Cancellation

$$(\ 2000. \oplus -1998.\ ) \oplus 1.333 = 2.000 \oplus 1.333 = 3.333$$

$$2000. \oplus (\ -1998. \oplus 1.333\ ) = 2000. \oplus -1997. = 3.000$$

(inspired by Parker et al., 1997)

Floating Point Arithmetic is Inexact

E.g. addition is non associative

$$(\ 2000. \oplus -1998.\ ) \oplus 1.333 = 2.000 \oplus 1.333 = 3.333$$

$$2000. \oplus (\ -1998. \oplus 1.333\ ) = 2000. \oplus -1997. = 3.000$$

Round-off Error

(inspired by Parker et al., 1997)

Monte Carlo Arithmetic (MCA)

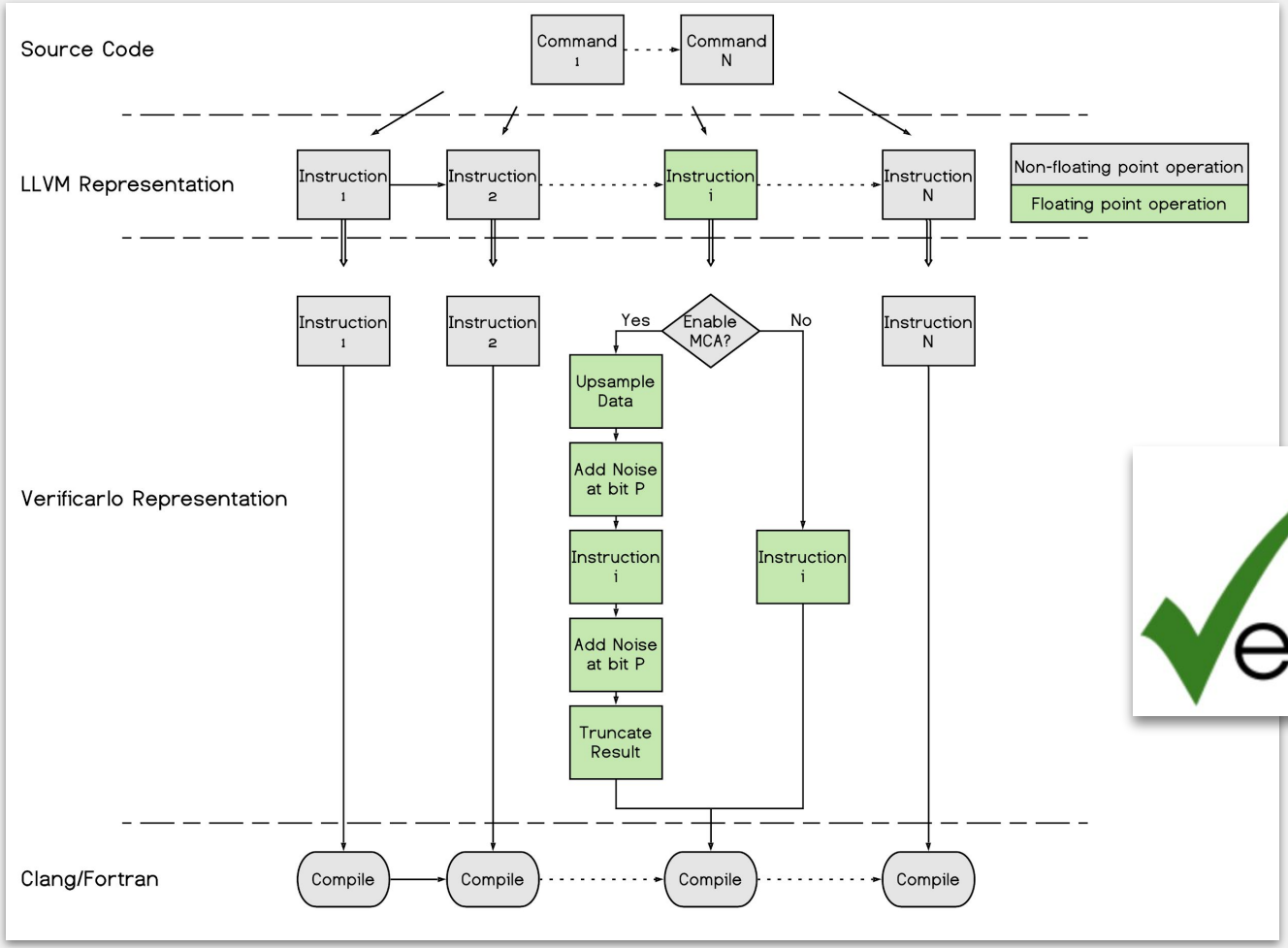
Inexact FP quantities become random variables

$$\widetilde{x} \quad = \quad \text{inexact}\,(x,\ s,\ \xi) \quad = \quad x \quad + \quad 2^{e-s}\ \xi$$

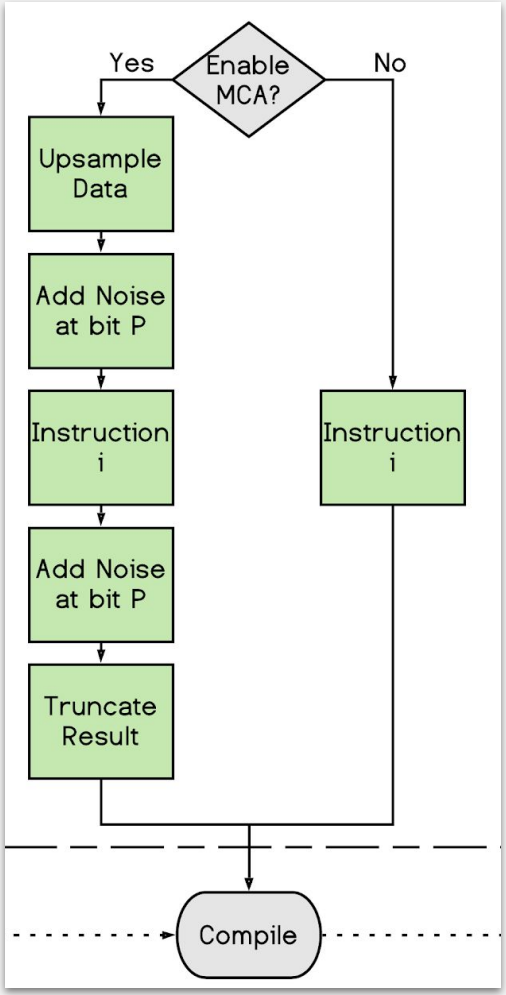
where e is the order of magnitude of x

$$t\_\text{digit\_precision}\,(x) \quad = \quad \begin{cases} x & \text{if } x \text{ can be expressed exactly with } t \text{ digits} \\ \text{inexact}\,(x,\ t,\ \xi) & \text{otherwise.} \end{cases}$$

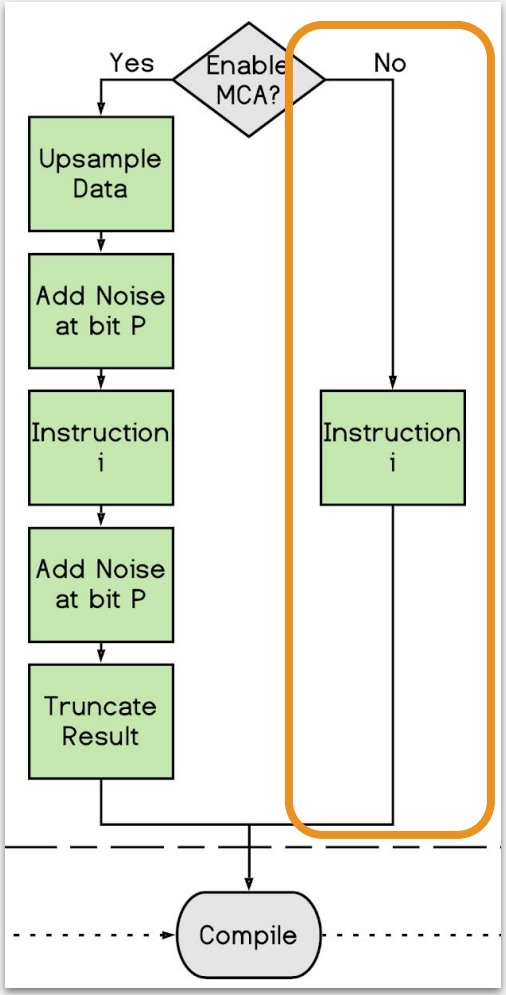
(Parker et al., 1997)



Backmatter ToC


Yes
Enable MCA?
No
Upsample Data
Add Noise at bit P
Instruction i
Add Noise at bit P
Truncate Result
Instruction i
Compile

Native

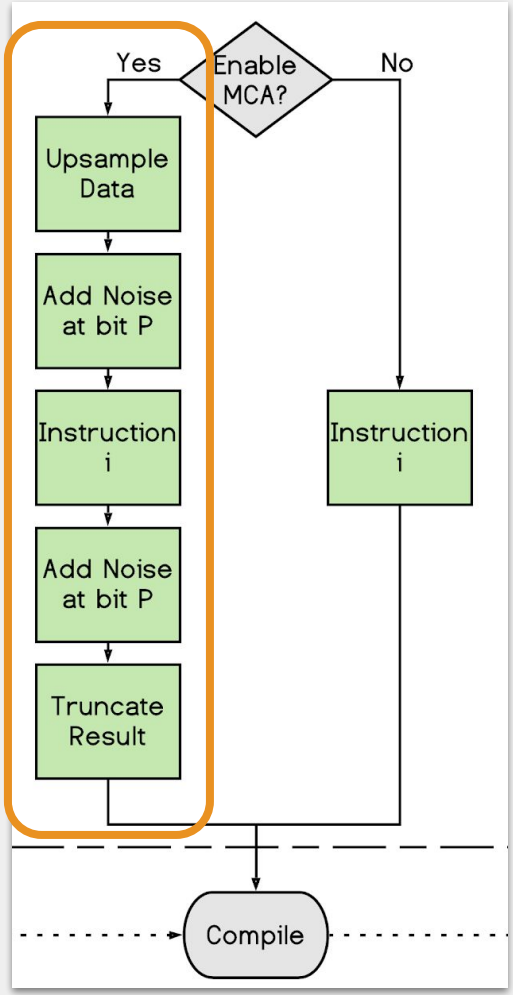


6000. + 5.452 = ...

6000. + 5.452

↳ 6005.

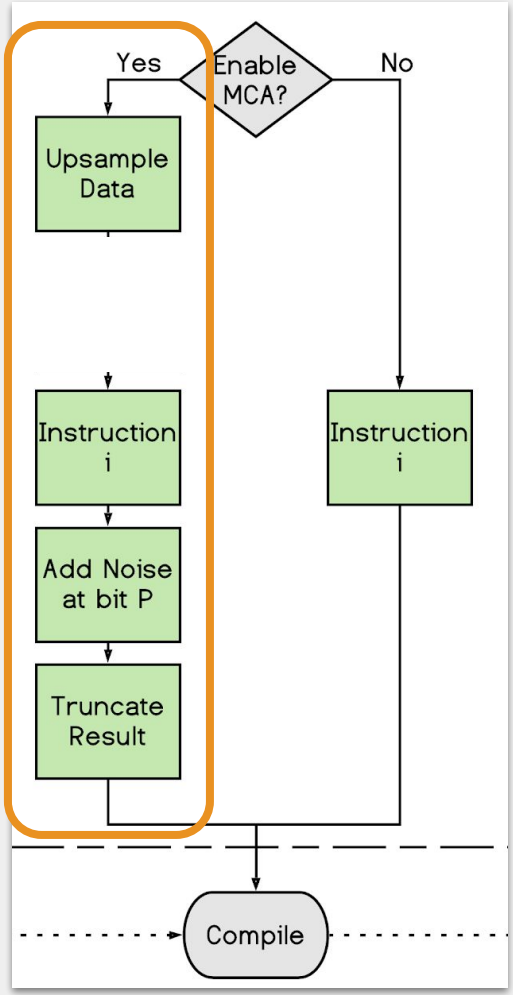
(full) MCA



6000. + 5.452 = ...

	6000.	+	5.452
Upsample:	↳ 6000.0000		↳ 5.4520000
Perturb (PB):	↳ 6000.4293		↳ 5.4519512
	6000.4293	+	5.4519512
Operate:	↳6005.8813		
Perturb (RR):	↳ 6005.4924		
Truncate:	↳ 6005.		

RR- MCA

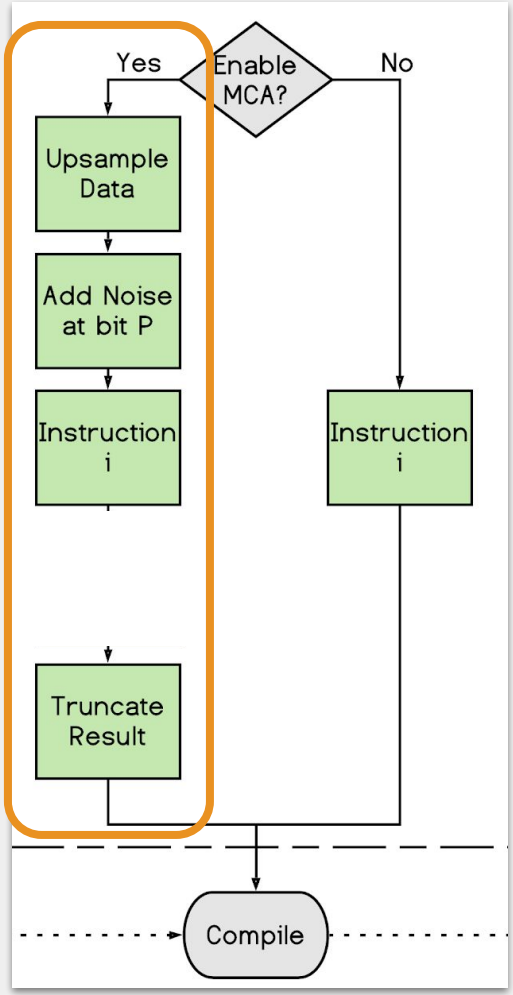


6000. + 5.452 = ...

	6000.	+	5.452
Upsample:	↳ 6000.0000		↳ 5.4520000
~~Perturb (PB):~~			
	6000.0000	+	5.4520000
Operate:	↳6005.4520		
Perturb (RR):	↳ 6005.5274		
Truncate:	↳ 6006.		

Backmatter ToC

PB- MCA



6000. + 5.452 = ...

	6000.	+	5.452
Upsample:	↳ 6000.0000		↳ 5.4520000
Perturb (PB):	↳ 6000.4293		↳ 5.4519512
	6000.4293	+	5.4519512
Operate:	↳6005.8813		

~~Perturb (RR):~~

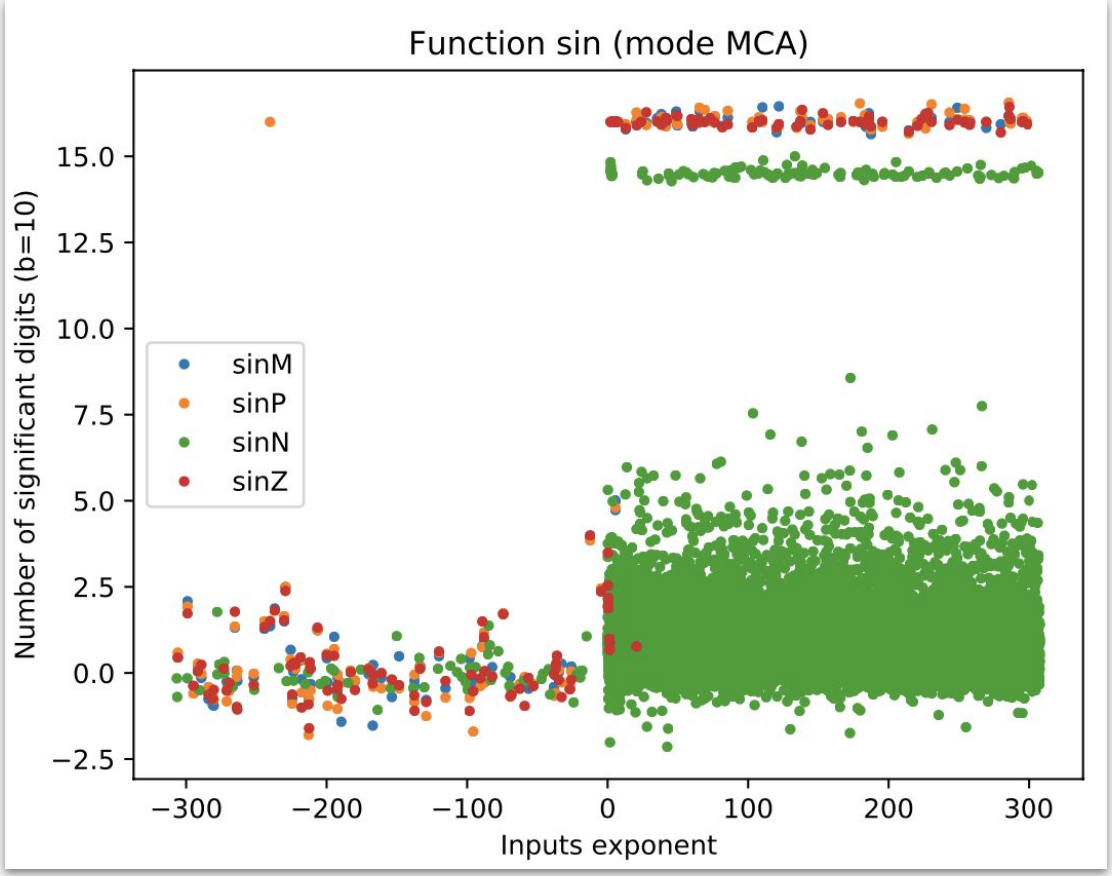
Truncate: ↳ 6006.

Backmatter ToC

Implementation of sine

```
__sin (double x)
{
/* ... a bunch of code goes here */
  if (k < 0x3e500000)           /* if x->0 =>sin(x)=x */
    { /* ...  */ }
/*-------------------------- 2^-26<|x|< 0.855469---------------------- */
  else if (k < 0x3feb6000)
    { /* ...  */ }
/*------------------------ 0.855469  <|x|<2.426265  ----------------------*/
  else if (k < 0x400368fd)
    { /* ...  */ }
/*-------------------------- 2.426265<|x|< 105414350 ----------------------*/
  else if (k < 0x419921FB)
    { /* ...  */ }
/* --------------------105414350 <|x| <2^1024------------------------------*/
  else if (k < 0x7ff00000)
    { /* ...  */ }
/*--------------------- |x| > 2^1024 ----------------------------------*/
  else
    { /* ...  */ }

  return retval;
}
```

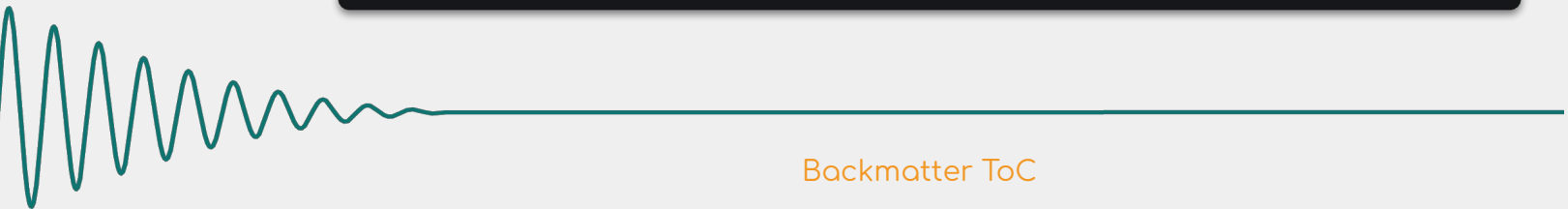
https://sourceware.org/git/?p=glibc.git;a=blob;f=sysdeps/ieee754/dbl-64/s_sin.c



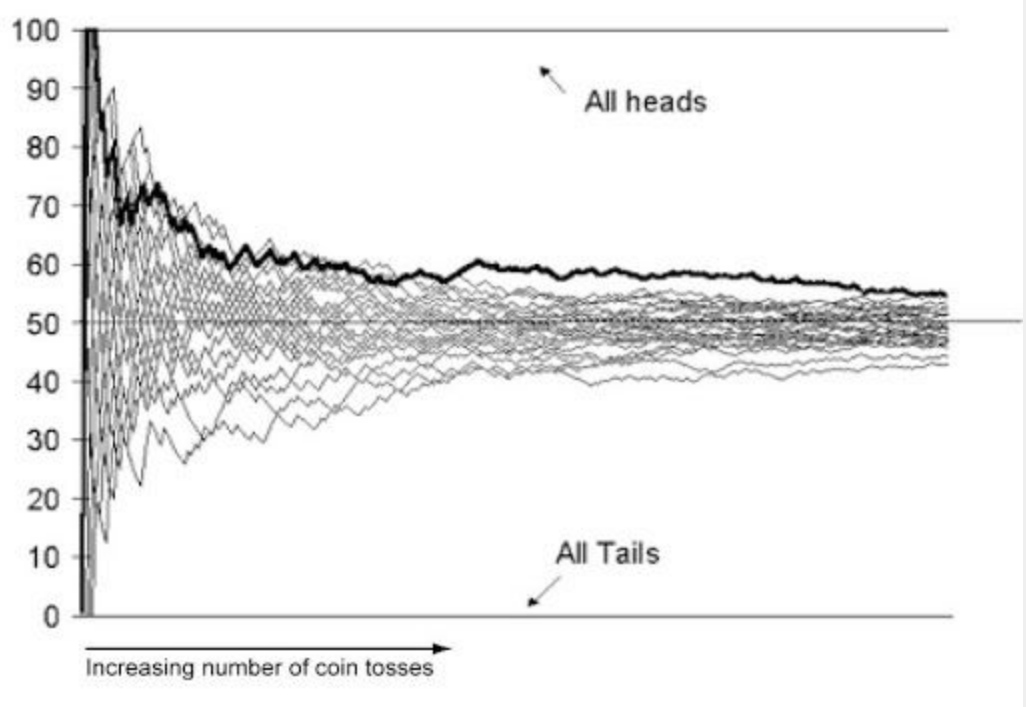
Courtesy of Yohan Chatelain

Sparse Instrumentation

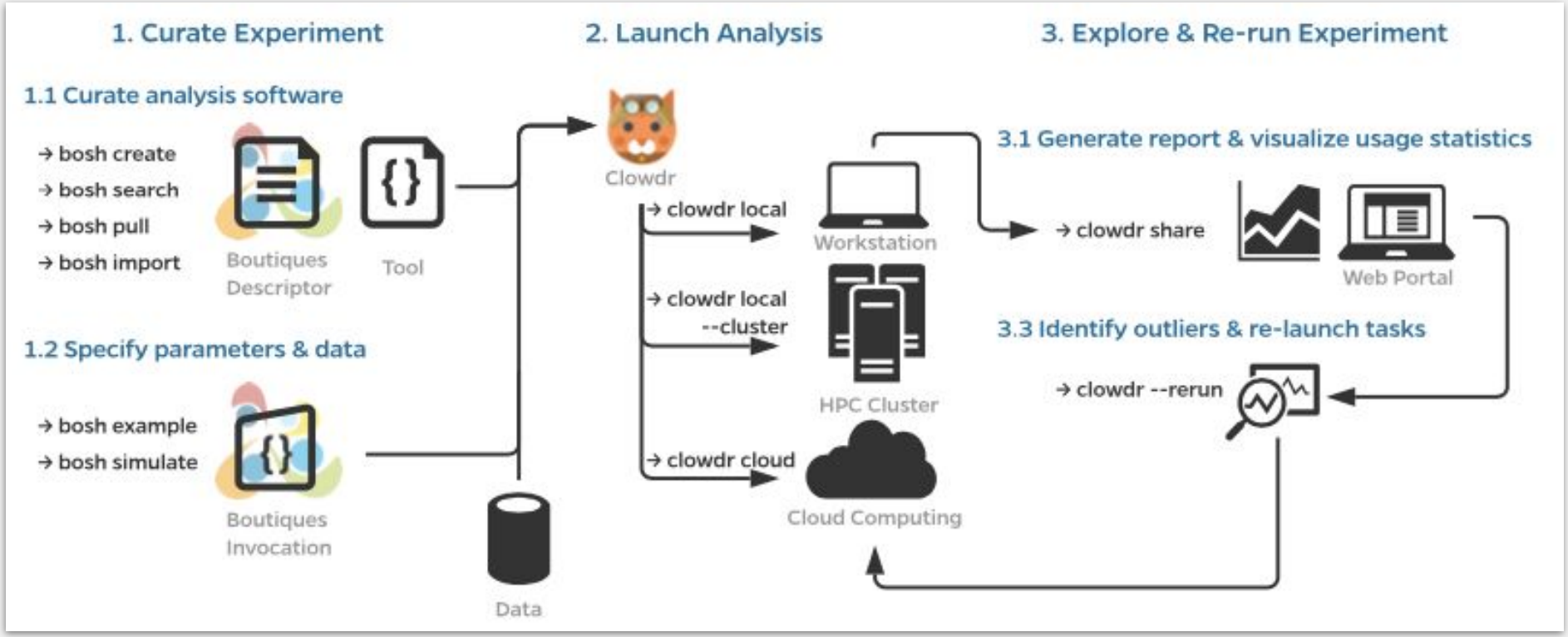
```
   Addition (+)
>>> sum([0.001]*100)
0.09999999999999998
>>> sum([0.001]*100)
0.09999999999999991

   Subtraction (-)
>>> 0.221 - 0.454
-0.23300000000000004
>>> 0.221 - 0.454
-0.23299999999999998

   Multiplication (*)
>>> 0.335 * 0.511
0.171185
>>> 0.335 * 0.511
0.17118500000000003

   Division (/)
>>> 0.335 / 0.511
0.6555772994129158
>>> 0.335 / 0.511
0.6555772994129159
```



Law of Large Numbers

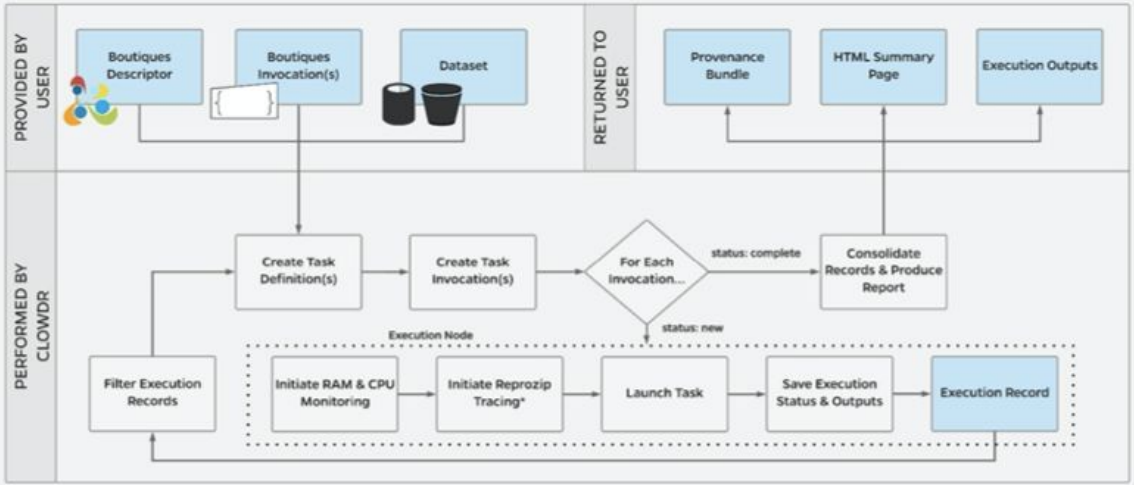


Chapter 1



Backmatter ToC

A



B

```
{
  "name": "example-command",
  "tool-version": "1.0",
  "command-line": "example-command [PARAM] > out.txt",
  "schema-version": "0.5",
  "inputs": [{
      "id": "param",
      "name": "Parameter",
      "value-key": "[PARAM]",
      "type": "Number" }],
  "output-files": [{
      "id": "output_file",
      "name": "Output file",
      "path-template": "outp.txt" }]
}
```

C

```
{
  "param": "value1"
},
{
  "param": "value2"
},
{
  "param": "value3"
}
```

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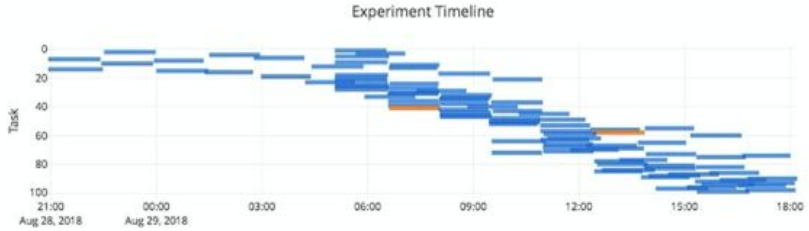
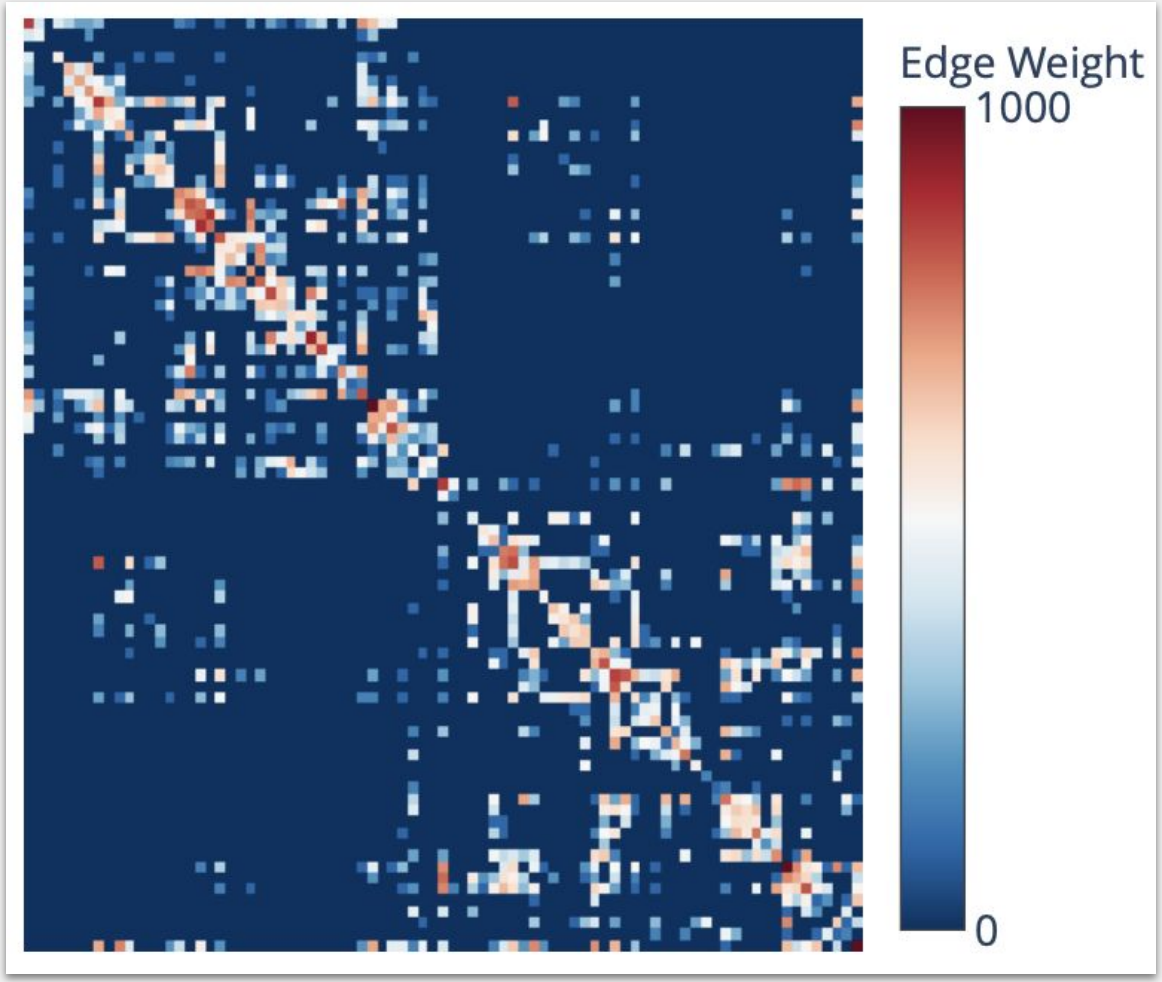
Statistics | Invocations

FILTER ROWS

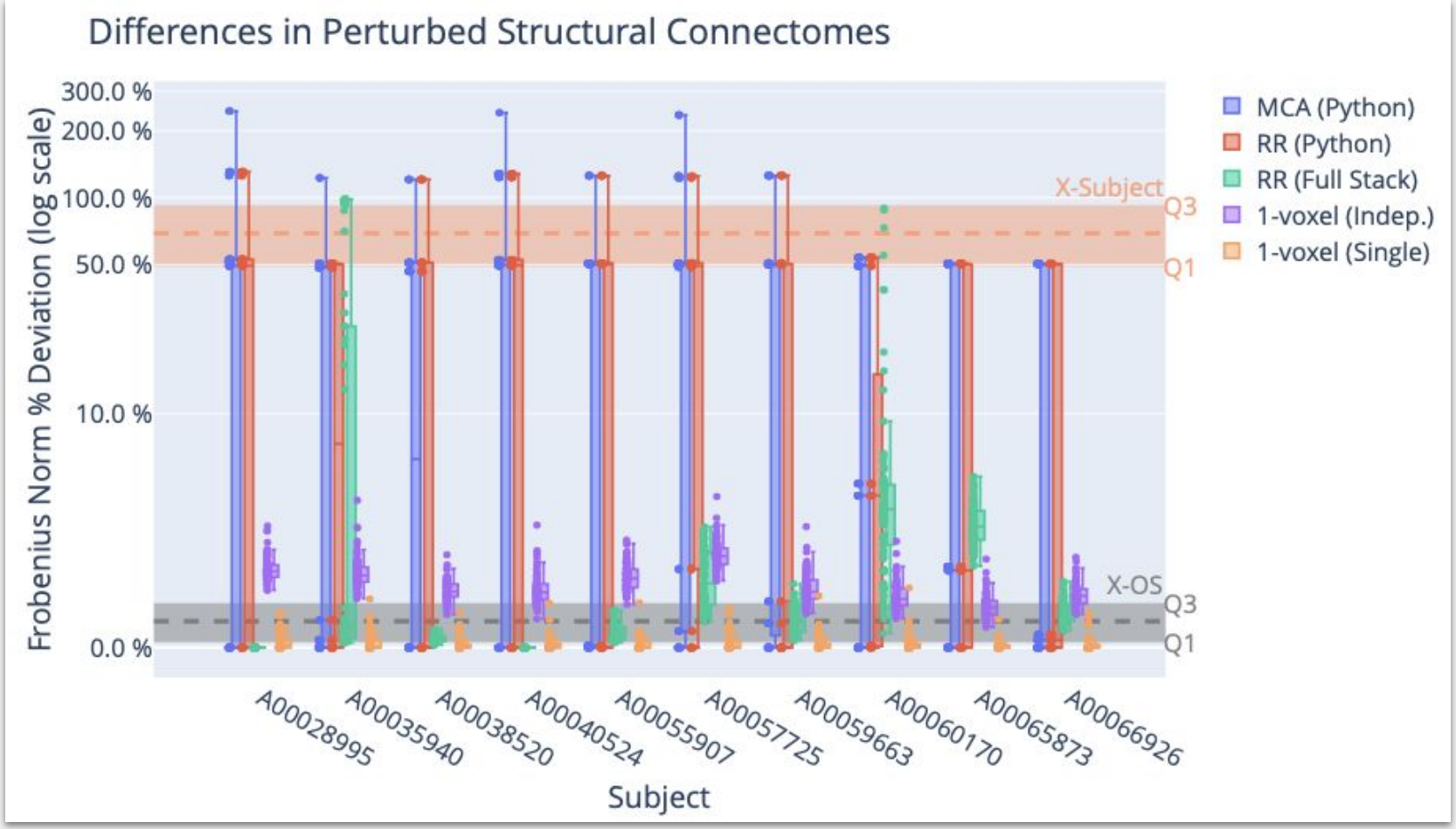
Task	Tool	Duration (s)	Max RAM (MB)	▲Max CPU (%)	Exit Code
58	ndmg				Incomplete
0	ndmg				Incomplete
80	ndmg	9.95317149162292	189.88671875	55.33	0
46	ndmg	5225.12778949737	8700.62178125	198.38	0
18	ndmg	5302.22937703132	8318.92759375	198.43	0
61	ndmg	5370.41310644149	7760.80071875	198.52	0



Chapter 2


Edge Weight
1000
0

Permutation	Description
X-Subject	Pairwise comparison of sessions based on **Subject ID**.
1-voxel	Intensity value doubled for either **Single** (one voxel in entire 4D volume) or **Independent** (one voxel per 3D sub-volume) voxels.
MCA	Simulation of all floating point operations in **Python** (Python and Cython-compiled libraries).
RR	Simulation of all rounding operations in **Python** or the **Full Stack** (BLAS, and LAPACK, Python and Cython-compiled libraries).
X-OS	One of **Ubuntu 16.04** or **Alpine 3.7.1**.



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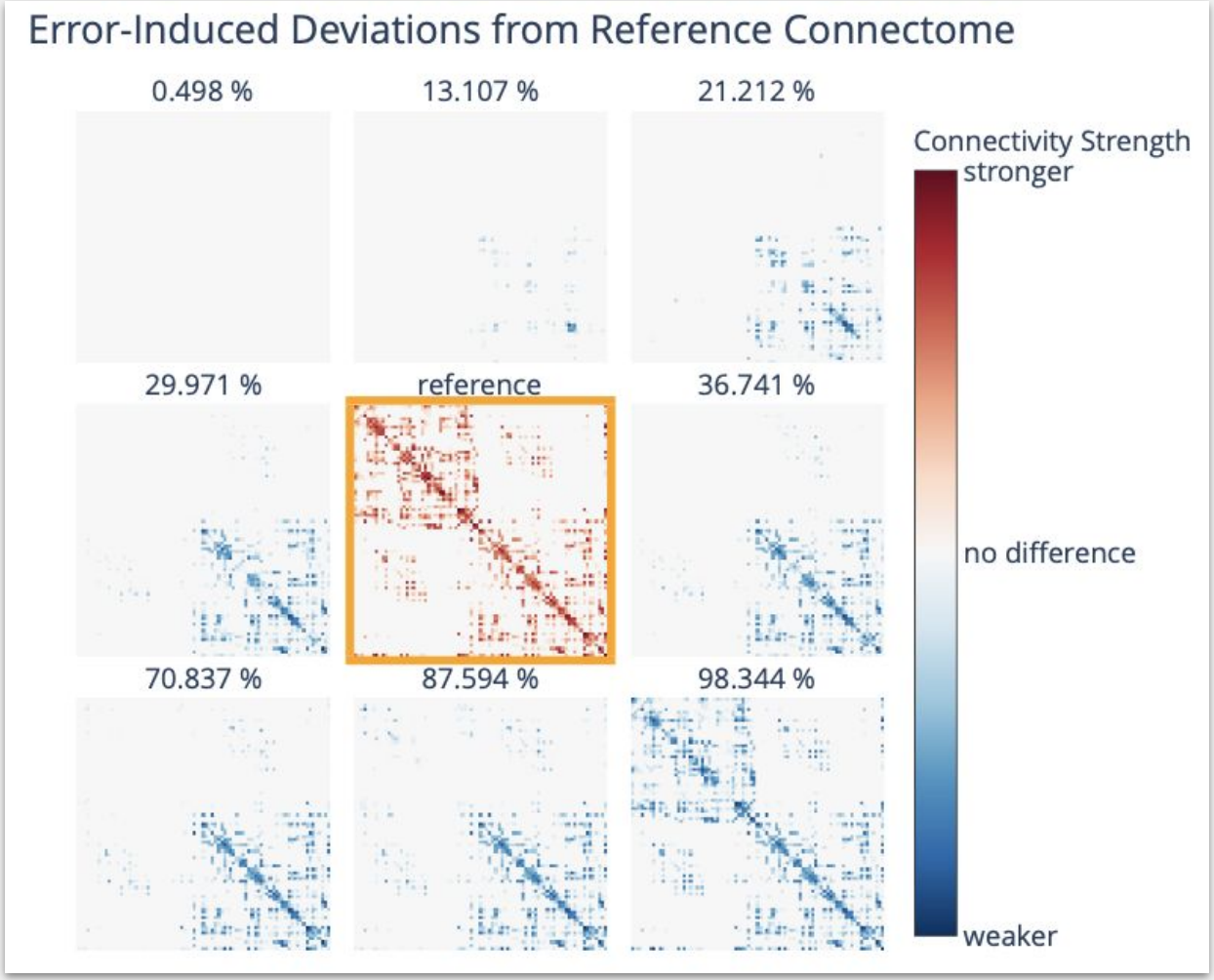

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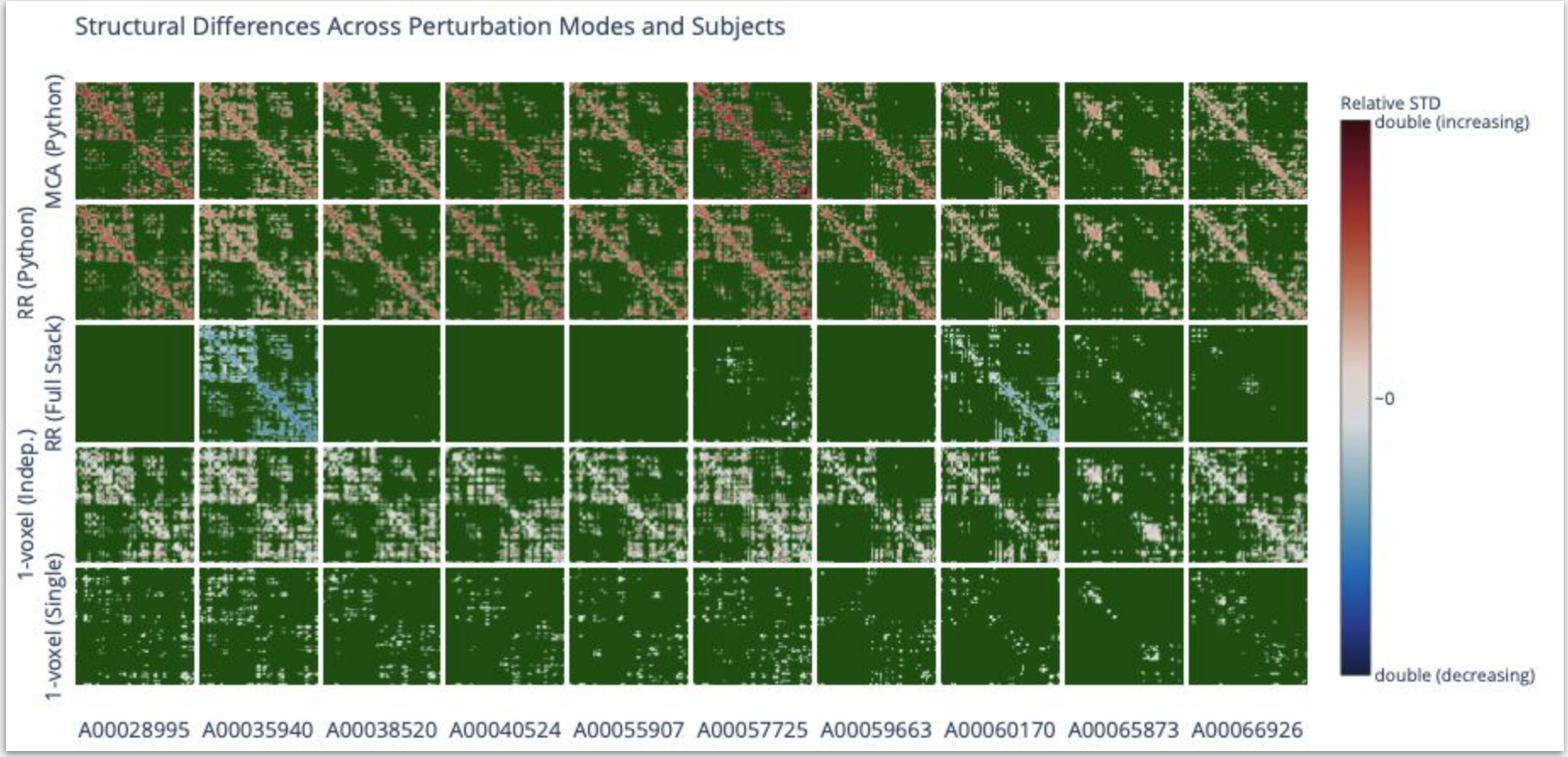

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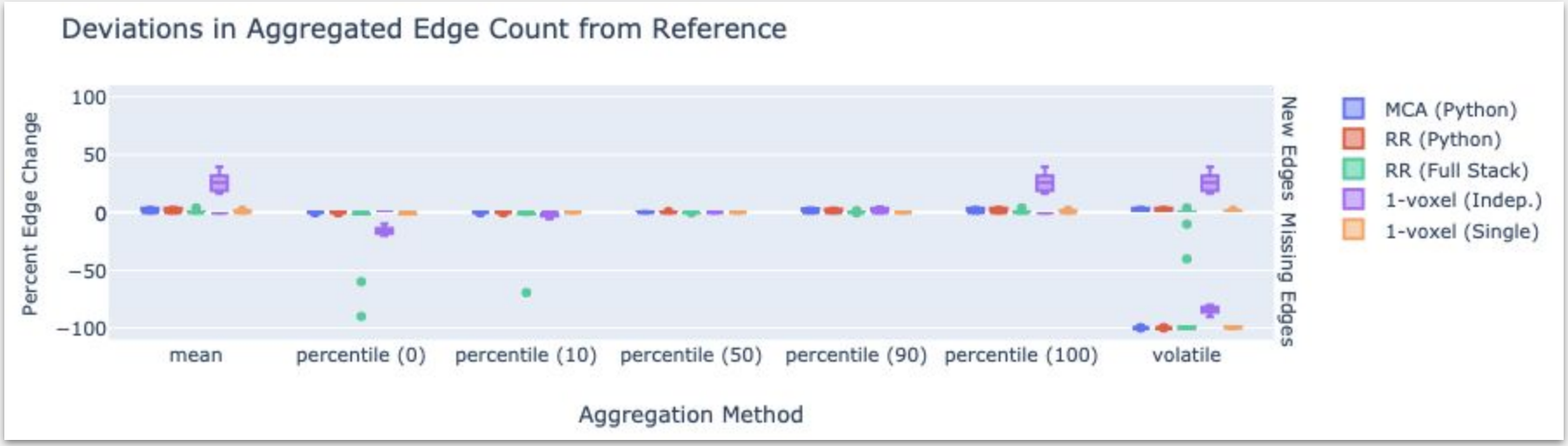

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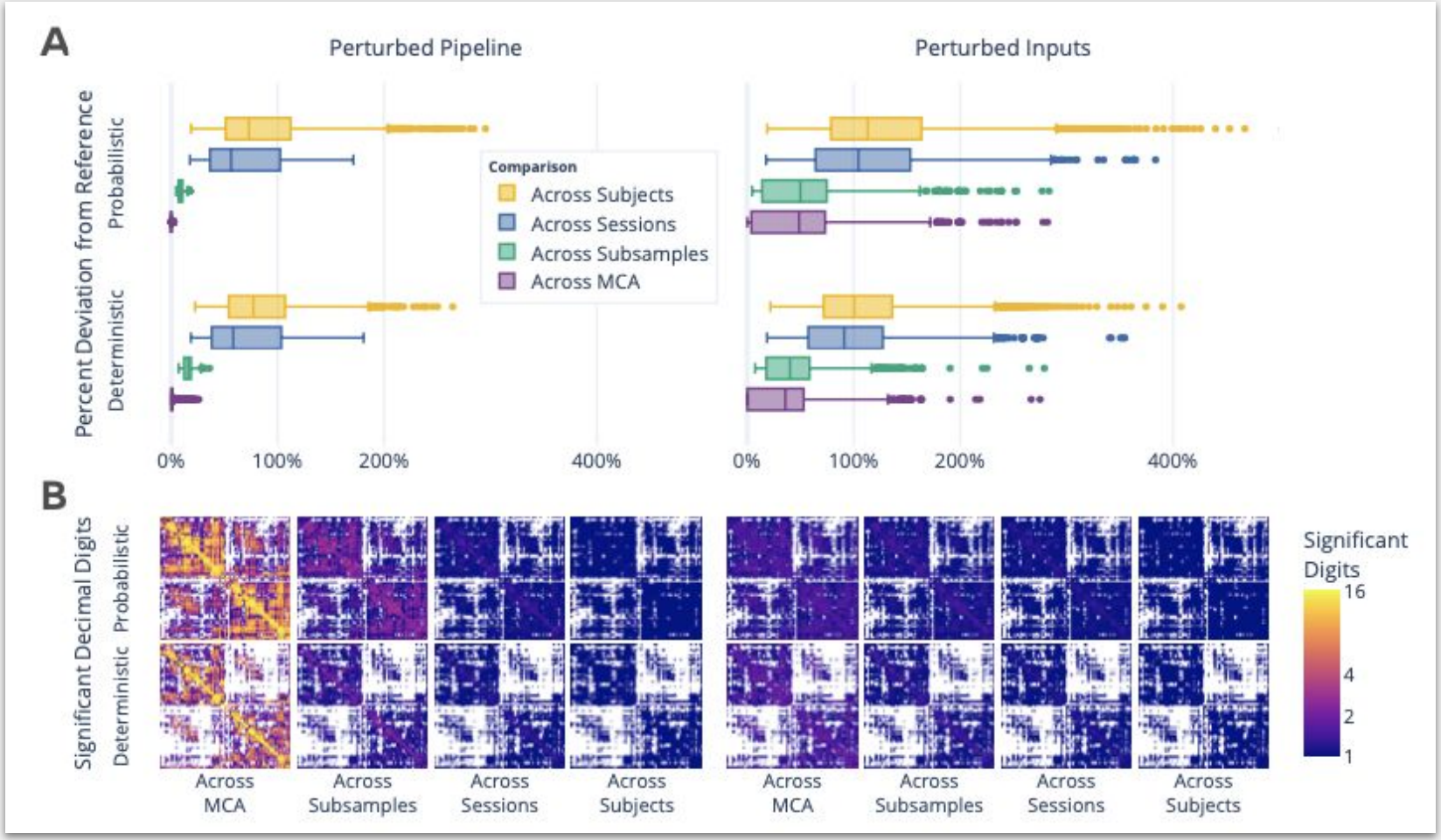
Chapter 3



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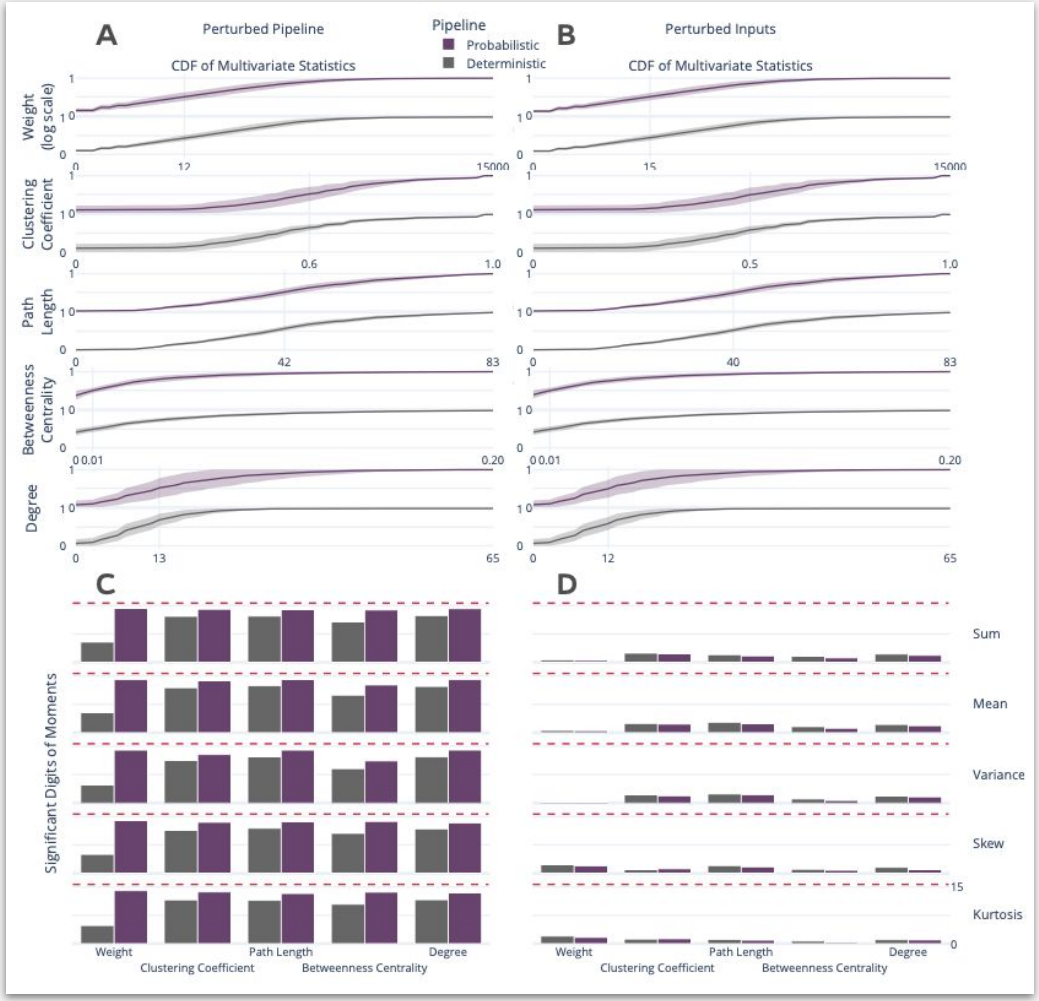
Comparison	Chance	Target	Reference Execution		Perturbed Pipeline		Perturbed Inputs	
			Det.	Prob.	Det.	Prob.	Det.	Prob.
H_1: Across Subjects	0.04	1.0	0.64	0.65	0.82	0.82	0.77	0.75
H_2: Across Sessions	0.5	0.5	1.00	1.00	1.00	1.00	0.88	0.85
H_3: Across Subsamples	0.5	0.5			0.99	1.00	0.71	0.61



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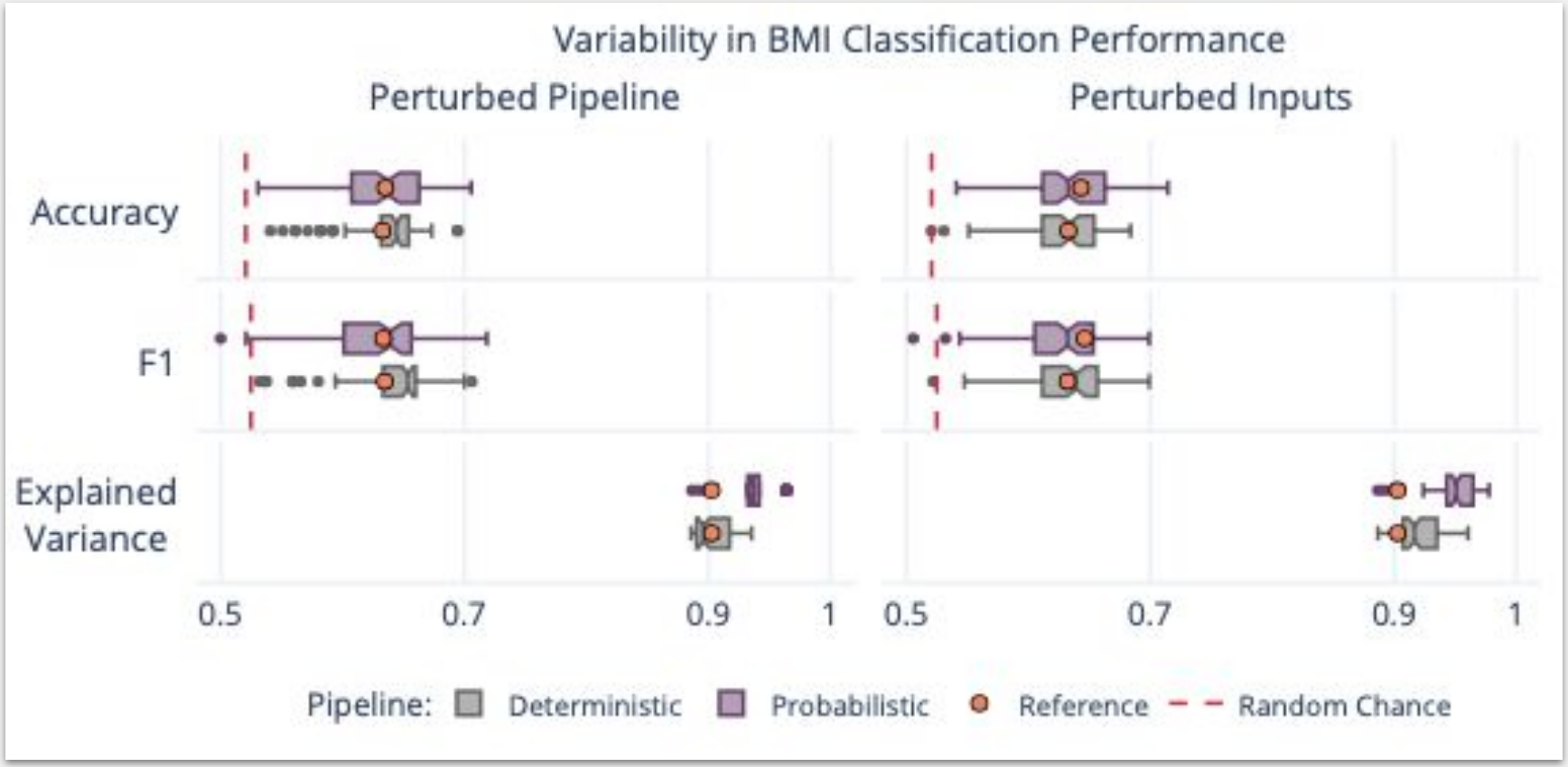

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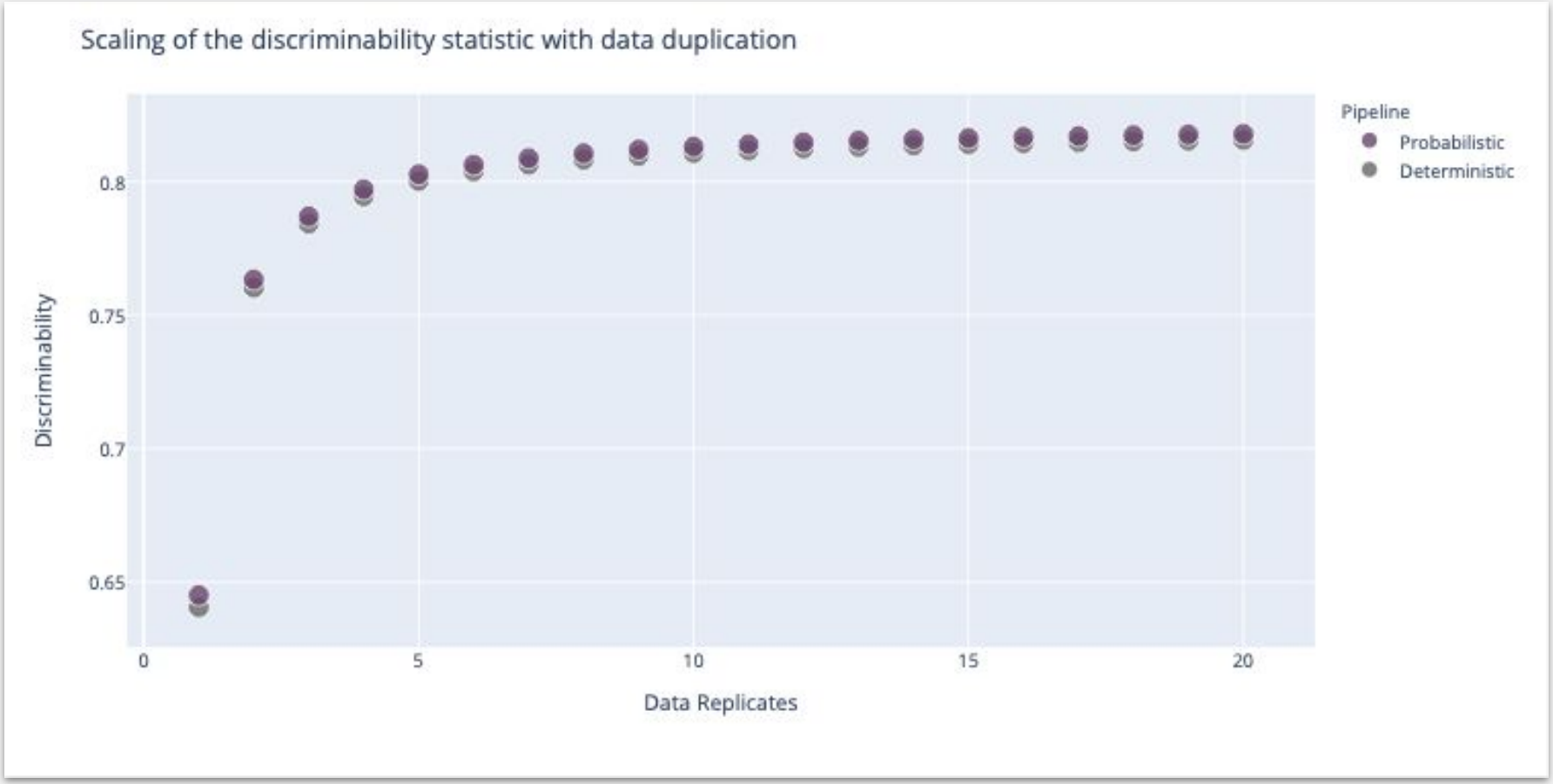
			Unscaled Ref.		Scaled Ref.		Dense MCA		Sparse MCA	
Comparison	**Chance**	**Target**	Det.	Prob.	Det.	Prob.	Det.	Prob.	Det.	Prob.
H_1: Across Subjects	0.04	1.0	0.64	0.65	0.82	0.82	0.82	0.82	0.77	0.75
H_2: Across Sessions	0.5	0.5	1.00	1.00	1.00	1.00	1.00	1.00	0.88	0.85
H_3: Across Subsamples	0.5	0.5					0.99	1.00	0.71	0.61



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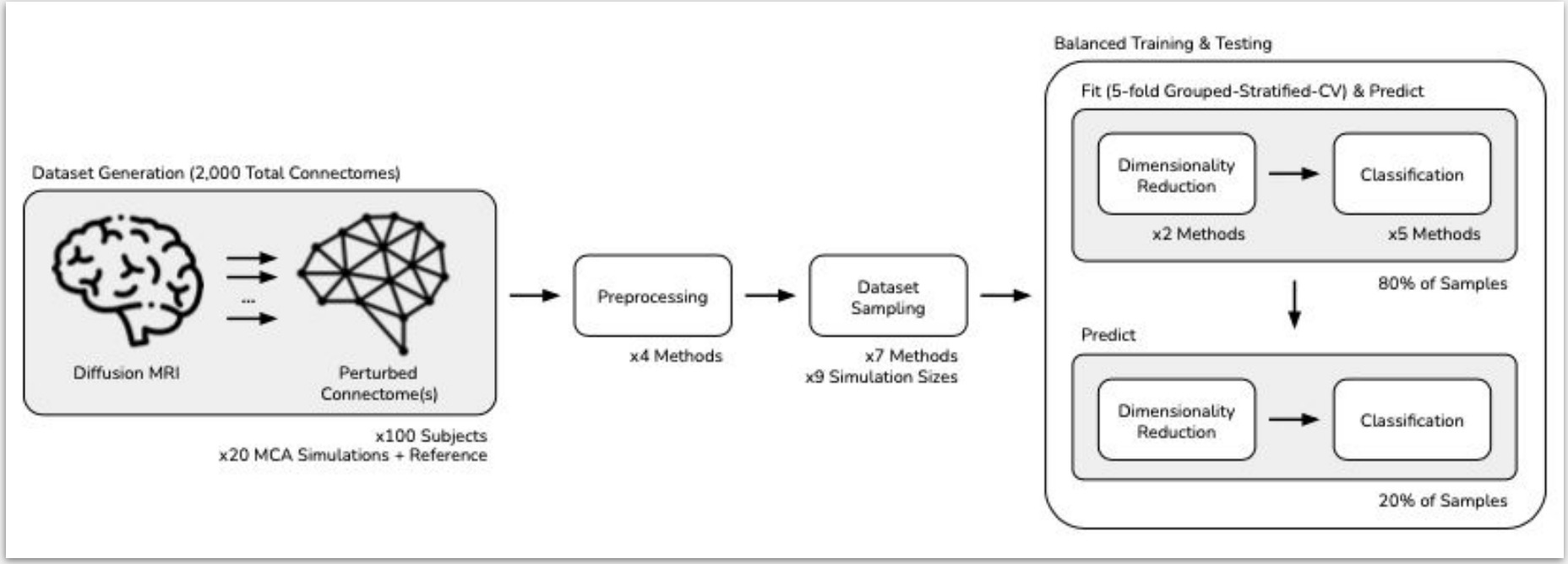
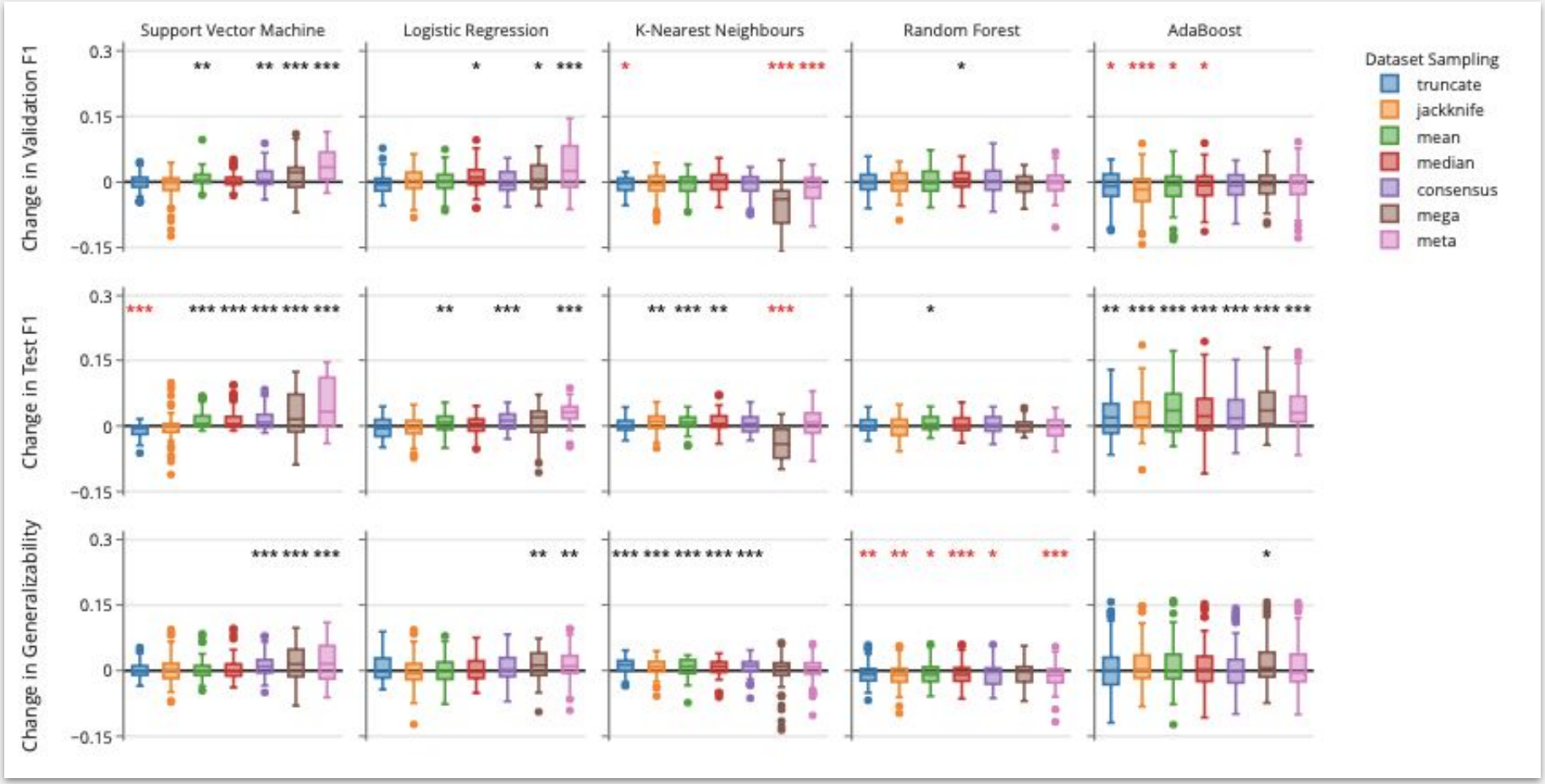
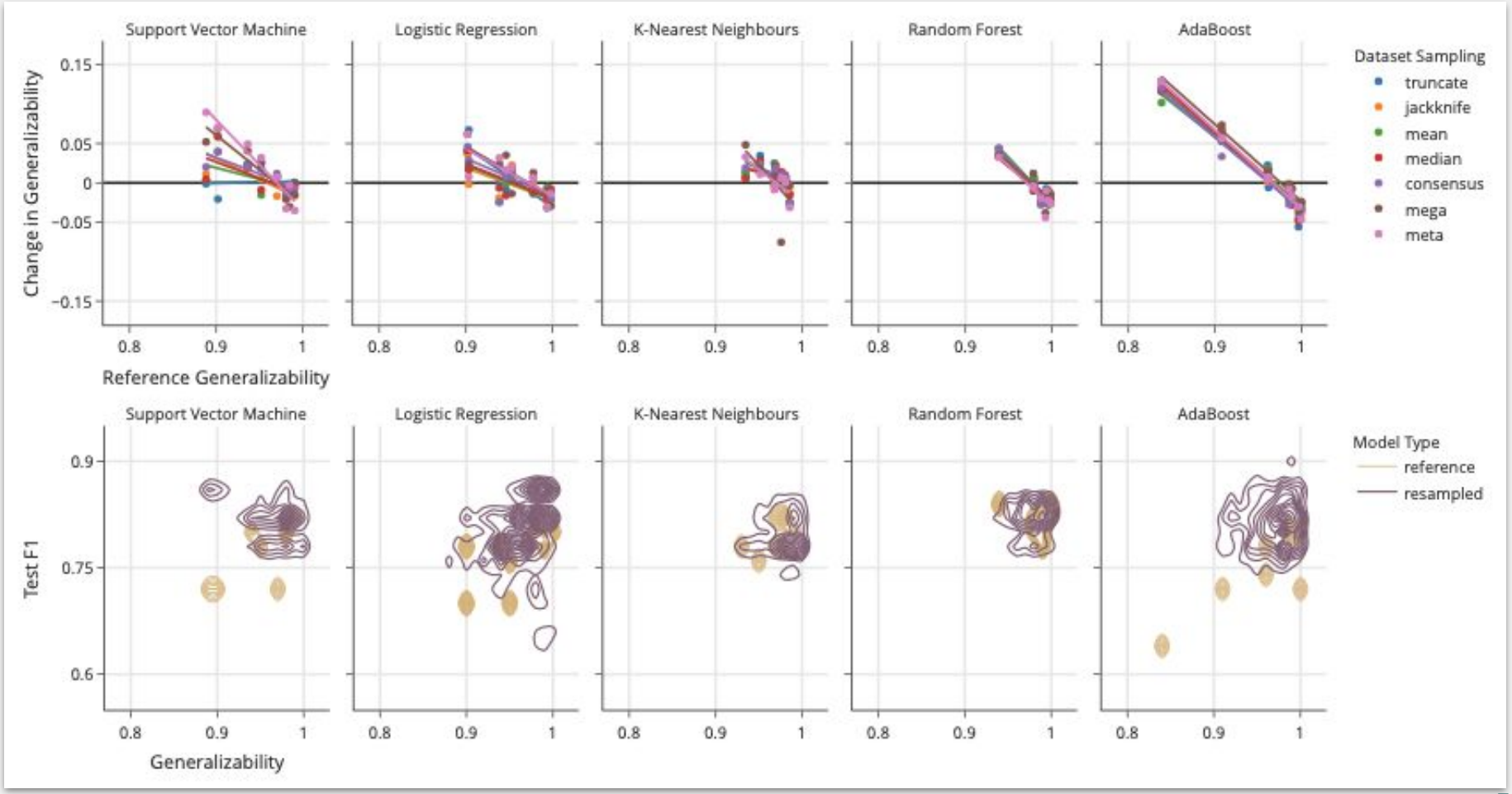
Chapter 4


Dataset Generation (2,000 Total Connectomes)
Diffusion MRI
Perturbed Connectome(s)
x100 Subjects
x20 MCA Simulations + Reference
Preprocessing
x4 Methods
Dataset Sampling
x7 Methods
x9 Simulation Sizes
Balanced Training & Testing
Fit (5-fold Grouped-Stratified-CV) & Predict
Dimensionality Reduction
x2 Methods
Classification
x5 Methods
80% of Samples
Predict
Dimensionality Reduction
Classification
20% of Samples

Dataset Sampling	Validation	Test	Generalizability
Truncate	**		
Jackknife	**	**	
Mean		***	
Median		***	
Consensus		***	*
Mega-Analysis	*	*	***
Meta-Analysis	**	***	*


Support Vector Machine
Logistic Regression
K-Nearest Neighbours
Random Forest
AdaBoost
Change in Validation F1
Change in Test F1
Change in Generalizability
0.3
0.15
0
−0.15
Dataset Sampling
truncate
jackknife
mean
median
consensus
mega
meta



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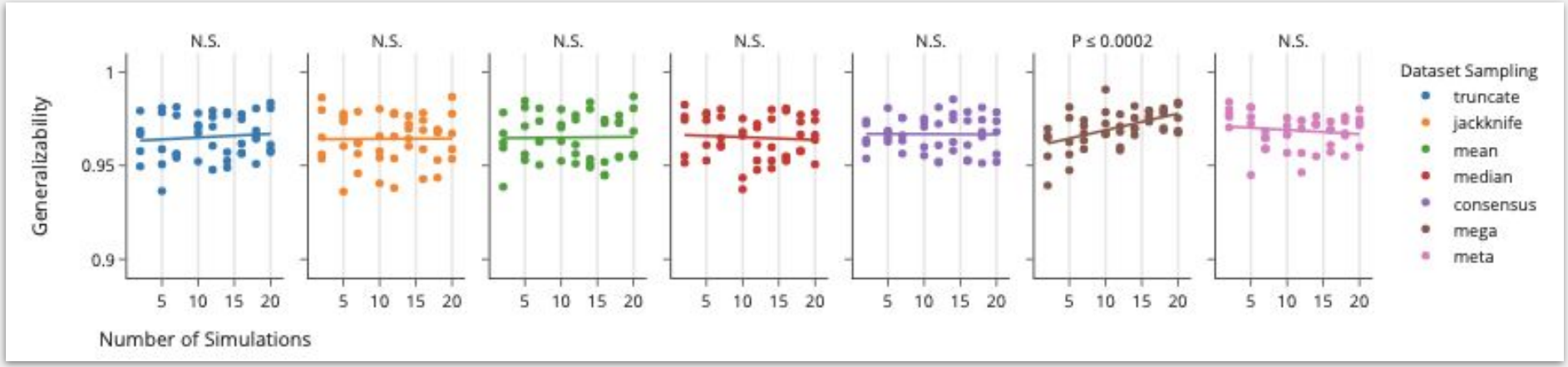

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