# Importance of Open Access to Research Data: A Case in Point

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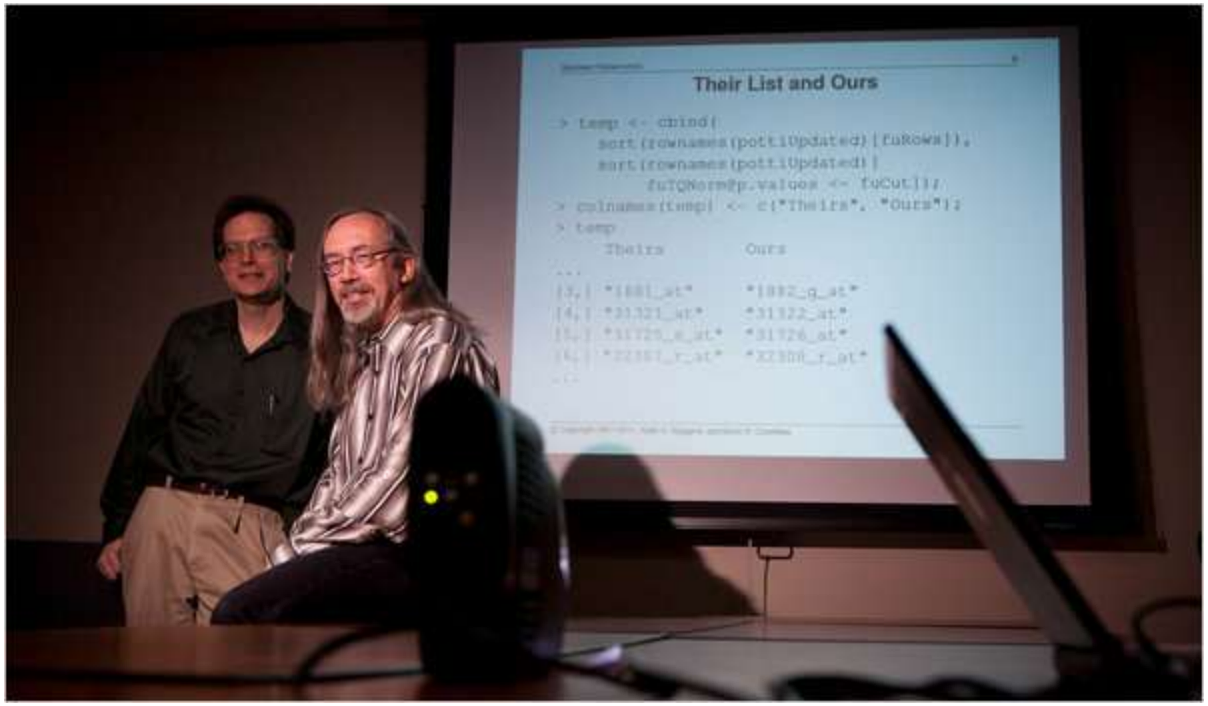
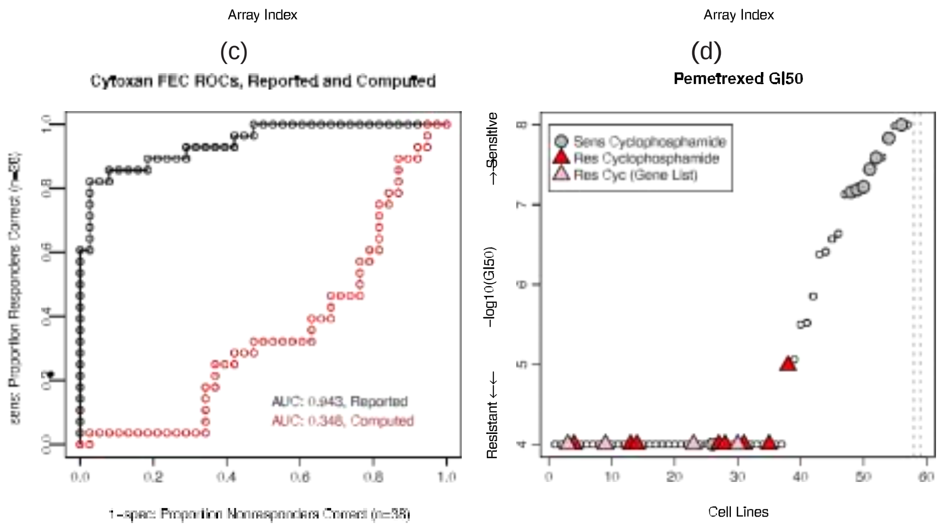
## How Bright Promise in Cancer Testing Fell Apart




Keith Baggerly, left, and Kevin Coombes, statisticians at M. D. Anderson Cancer Center, found flaws in research on tumors.

NY Times 7/7/11




( c) ROC curves for the single best set of drug predictions: cyclophosphamide for FEC. The reported curve has an AUC of 0.943, indicating extremely good prediction. Our best approximation has an AUC of 0.348, indicating if anything performance worse than chance.

**Retraction Watch**

Tracking retractions as a window into the scientific process

**Anesthesiologist Fabricates 172 Papers**

**A researcher in Japan faked patient data on nearly 200 studies over the past 2 decades, according to an investigating committee.**

**Parkinson's Researcher Fabricated Data**

**Neuroscientist Mona Thiruchelvam agrees to retract two studies linking neurodegeneration to pesticides.**

**By Hayley Dunning | June 29, 2012**

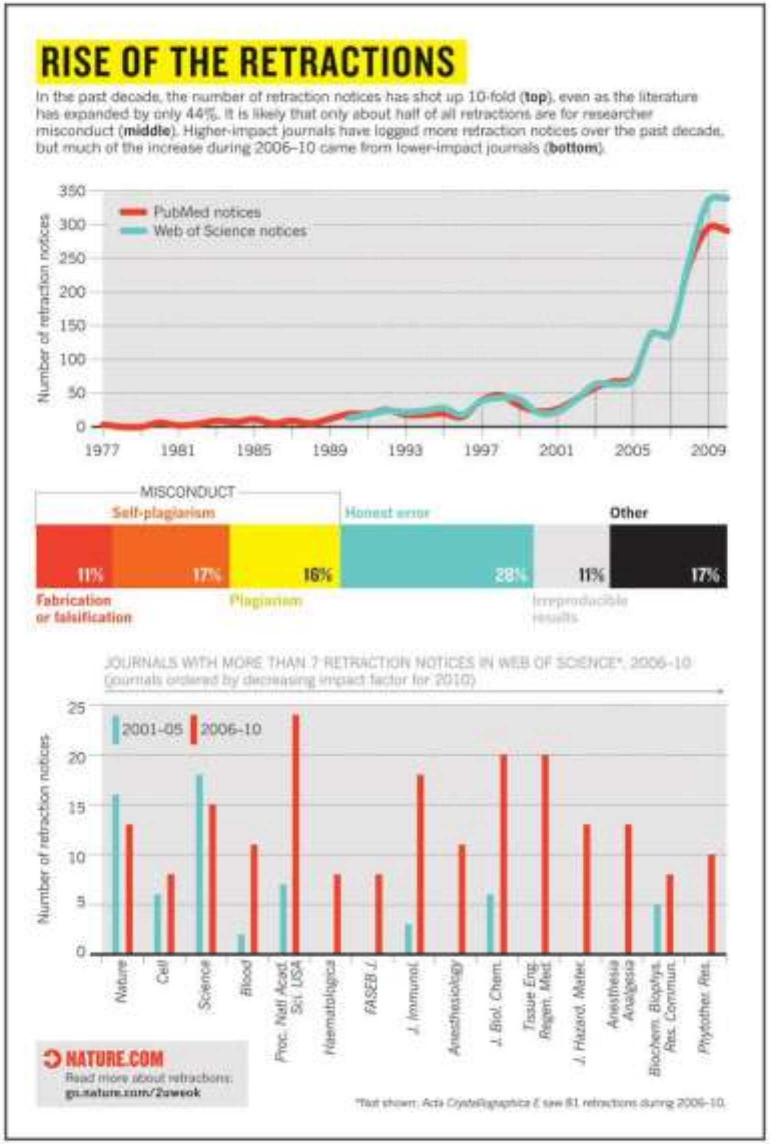
**University of Michigan psychologist resigns following concerns by statistical sleuth Simonsohn: Nature**

*J Med Ethics doi:10.1136/jme.2010.040923*

•Research ethics

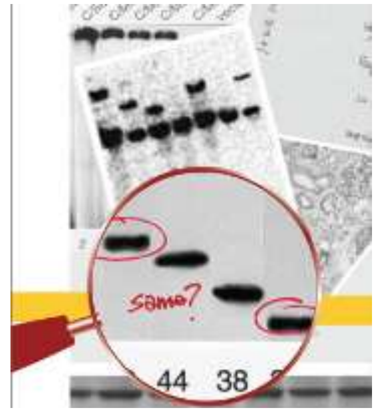
**Retractions in the scientific literature: is the incidence of research fraud increasing?**

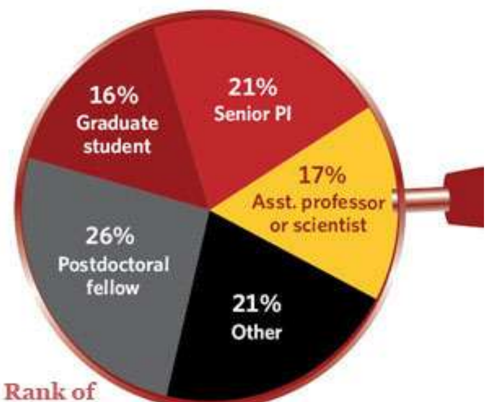
1. R Grant Steen


RISE OF THE RETRACTIONS
In the past decade, the number of retraction notices has shot up 10-fold (top), even as the literature has expanded by only 44%. It is likely that only about half of all retractions are for researcher misconduct (middle). Higher-impact journals have logged more retraction notices over the past decade, but much of the increase during 2006–10 came from lower-impact journals (bottom).
Number of retraction notices
PubMed notices
Web of Science notices
350
300
250
200
150
100
50
0
1977
1981
1985
1989
1993
1997
2001
2005
2009
MISCONDUCT
Self-plagiarism
Honest error
Other
11%
17%
16%
28%
11%
17%
Fabrication or falsification
Plagiarism
Irreproducible results
JOURNALS WITH MORE THAN 7 RETRACTION NOTICES IN WEB OF SCIENCE*, 2006–10
(journals ordered by decreasing impact factor for 2010)
2001–05
2006–10
25
20
15
10
5
0
Nature
Cell
Science
Blood
Proc. Natl Acad. Sci. USA
Haematologica
FASEB J.
J. Immunol.
Anesthesiology
J. Biol. Chem.
Tissue Eng. Regen. Med.
J. Hazard. Mater.
Anesthesia Analgesia
Biochem. Biophys. Res. Commun.
Phytother. Res.
NATURE.COM
Read more about retractions: go.nature.com/2uweok
*Not shown: Acta Crystallographica E saw 81 retractions during 2006–10.

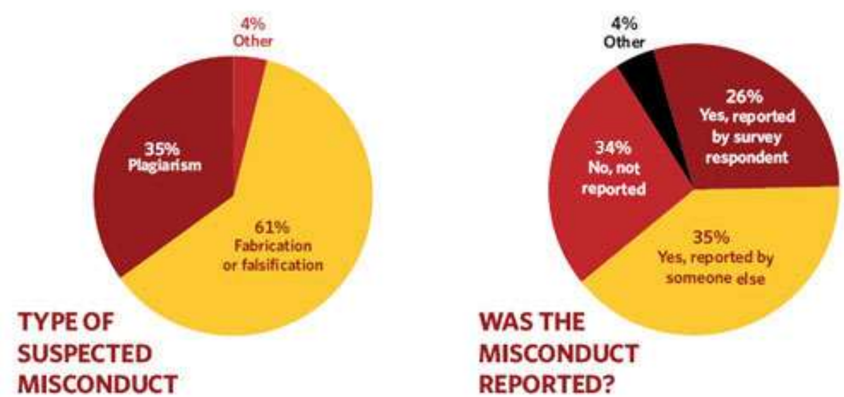
# A Gawrylewski Fixing Fraud *The Scientist* **23: 67** (2009)

Images are the easiest to spot




Rank of researcher suspected of fraud




*According to a 2008 Gallup poll sent to 2,296 researchers receiving NIH grants

Fanelli D (2009) How Many Scientists Fabricate and Falsify Research? A Systematic Review and Meta-Analysis of Survey Data. **PLoS ONE 4(5):** e5738. doi:10.1371/journal.pone.0005738

“A pooled weighted average of 1.97% (N = 7, 95%CI: 0.86–4.45) of scientists admitted to have fabricated, falsified or modified data or results at least once –a serious form of misconduct by any standard– and up to 33.7% admitted other questionable research practices. In surveys asking about the behaviour of colleagues, admission rates were 14.12% (N = 12, 95% CI: 9.91–19.72) for falsification, and up to 72% for other questionable research practices. “

“…misconduct was reported more frequently by medical/pharmacological researchers than others.”

# Source of the Data

- *Qui tam* is a suit filed by a private individual – relator – on behalf of the federal government charging violation of the False Claims Act
- An NCI grant application and its renewal (9 years of funding, $2.5 million) were at stake
- Discovery is the period during which documents are exchanged: PDF files of scans of the laboratory notebooks from 1995 – 2003 were provided by the defense
- The Court ruled in favor of the defendants. The ruling was sustained on appeal
- The Courts decisions had nothing to do with the science, only with the timing of the alleged fraud

# Importance of the Studies We Analyzed

in the PI's own words

"The outcome of this research is expected to have a major impact on understanding and predicting biological response of tumor and normal tissue to nonuniform distributions of radioactivity."

The studies are "of importance to risk estimation in diagnostic nuclear medicine and radiation protection (radon, radiological terrorism), as well as clinical outcome in therapeutic nuclear medicine"

"In….diagnosis, the risk of radiation insult can …be drastically underestimated and … lead to increased risk of inducing cancer. In contrast, patients can be over or under treated in radionuclide therapy of cancer"

# Data We Analyzed

- Numbers recorded by hand taken from the screen of a Coulter ZM Counter
  - In triplicate: 3 independent samples from an original cell suspension were counted
- Stained colonies on 60mm tissue culture dishes were counted by marking each on the underside of the dish
  - In triplicate: 3 independent samples from the same original suspension diluted appropriately were counted
- There were 5155 Coulter counts in 171 experiments and 3501 colony counts in 114 experiments performed by post-doctoral fellow AB
- There were 2759 Coulter counts in 99 experiments and 1556 colony counts in 59 experiments performed by 7 other individuals in the laboratory
- There were 674 Coulter ZM counts in 27 experiments provided by 2 outside laboratories

# Coulter ZM

# Chinese hamster lung V79 colonies

(A)

# Terminal Digit Analysis

Accountability in Research, 9: 75–92, 2002

0898-9621/02 $12.00 + .00
DOI: 10.1080/08989620290009530

***Terminal Digits and the Examination of Questioned Data***

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*Accountability in Research*, Vol. 4, pp. 31–55
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## Data Fabrication: Can People Generate Random Digits?

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# Our Working Hypotheses

- Terminal digits of Coulter counts should be uniformly distributed (equal probability for each of the 10 digits 0, 1, 2, etc)
- Terminal digits of colony counts should likewise be uniformly distributed
- In Coulter counts, the second rightmost digit should be equal to the rightmost digit 10% of the time

## Examples of Triplicate Coulter Counts

These were reported in an experiment by laboratory investigator AB and in an experiment by another laboratory investigator (OI). **The terminal digits are shown in bold**.

| Sample # | AB Triplicate Counts | | | OI Triplicate Counts | | |
|---|---|---|---|---|---|---|
| **1** | 57**7** | 59**2** | 56**3** | 8**9** | 9**7** | 8**6** |
| **2** | 61**1** | 60**7** | 65**3** | 33**1** | 31**6** | 32**9** |
| **3** | 58**1** | 59**3** | 61**7** | 37**8** | 33**0** | 37**5** |
| **4** | 63**3** | 64**5** | 61**9** | 33**3** | 40**4** | 36**7** |
| **5** | 51**1** | 53**7** | 54**9** | 39**6** | 38**2** | 40**8** |
| **6** | 54**4** | 56**2** | 57**3** | 34**2** | 33**1** | 34**4** |
| **7** | 66**6** | 67**2** | 69**3** | 34**0** | 34**9** | 34**4** |
| **8** | 60**1** | 57**2** | 63**3** | 32**5** | 34**7** | 30**4** |
| **9** | 51**1** | 52**9** | 54**1** | 31**5** | 29**1** | 28**3** |
| **10** | 53**2** | 55**5** | 56**2** | 30**7** | 33**9** | 32**3** |
| **11** | 51**3** | 54**9** | 56**2** | 28**5** | 31**4** | 32**3** |
| **12** | 56**2** | 53**9** | 54**7** | 26**0** | 26**2** | 28**4** |
| **13** | 56**0** | 54**2** | 52**2** | 36**1** | 31**5** | 29**8** |
| **14** | 68**0** | 66**9** | 67**1** | 35**5** | 32**4** | 35**6** |

**The Terminal Digit Counts from Above Table and The Chi-Squared Probability of Uniform Distribution**

The chi-squared goodness of fit was determined in Microsoft Excel (9 degrees of freedom) for the digit frequencies of AB and OI compared with the control uniform distribution.

| Digit | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | Total | Chi Sq | Chi sq p for uniform |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **AB Freq** | 2 | 7 | 9 | 8 | 1 | 2 | 2 | 5 | 0 | 6 | **42** | **21.8** | **0.0095** |
| **OI Freq** | 3 | 4 | 3 | 4 | 7 | 6 | 4 | 4 | 3 | 4 | **42** | **3.7** | **0.93** |
| **Ctrl Freq** | 4.2 | 4.2 | 4.2 | 4.2 | 4.2 | 4.2 | 4.2 | 4.2 | 4.2 | 4.2 | **42** | | |

## Examples of Triplicate Coulter Counts

These were reported in an experiment by laboratory investigator AB and in an experiment by another laboratory investigator (OI). The terminal digits are shown in **bold**. The terminal duplicates are shown in red. There are 10 doubles in AB's samples (23.8%) and 4 in the other investigator's samples (9.5%).

| Sample # | AB Triplicate Counts | | | OI Triplicate Counts | | |
|---|---|---|---|---|---|---|
| 1 | 577 | 592 | 563 | 89 | 97 | 86 |
| 2 | 611 | 607 | 653 | 331 | 316 | 329 |
| 3 | 581 | 593 | 617 | 378 | 330 | 375 |
| 4 | 633 | 645 | 619 | 333 | 404 | 367 |
| 5 | 511 | 537 | 549 | 396 | 382 | 408 |
| 6 | 544 | 562 | 573 | 342 | 331 | 344 |
| 7 | 666 | 672 | 693 | 340 | 349 | 344 |
| 8 | 601 | 572 | 633 | 325 | 347 | 304 |
| 9 | 511 | 529 | 541 | 315 | 291 | 283 |
| 10 | 532 | 555 | 562 | 307 | 339 | 323 |
| 11 | 513 | 549 | 562 | 285 | 314 | 323 |
| 12 | 562 | 539 | 547 | 260 | 262 | 284 |
| 13 | 560 | 542 | 522 | 361 | 315 | 298 |
| 14 | 680 | 669 | 671 | 355 | 324 | 356 |

**The Terminal Digit Counts from Above Table and The Chi-Squared Probability of Uniform Distribution**

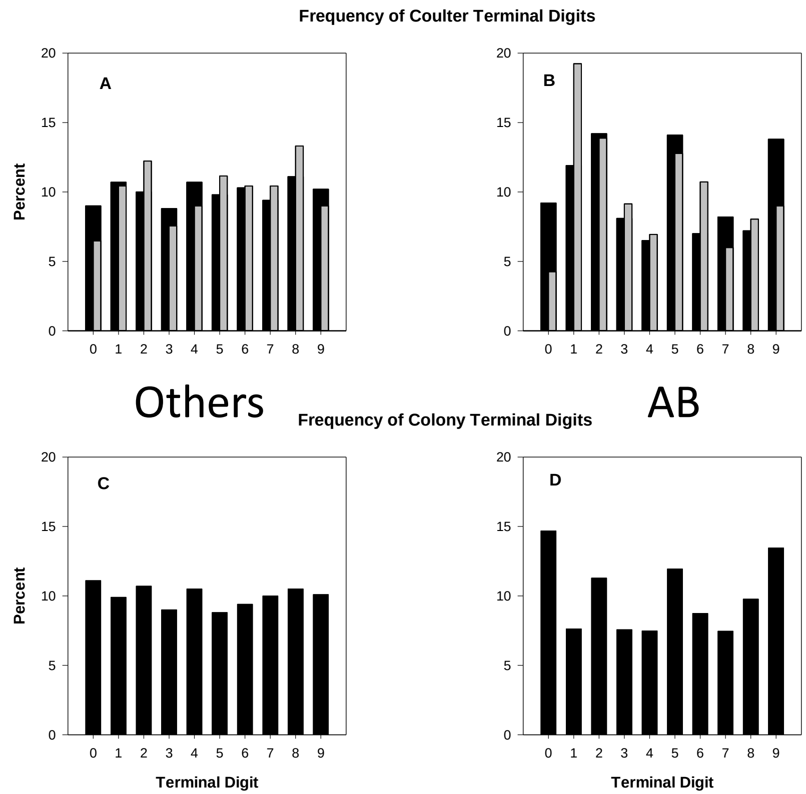
The chi-squared goodness of fit was determined in Microsoft Excel (9 degrees of freedom) for the digit frequencies of AB and OI compared with the control uniform distribution.

| Digit | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | Total | Chi Sq | Chi sq p for uniform |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| AB Freq | 2 | 7 | 9 | 8 | 1 | 2 | 2 | 5 | 0 | 6 | **42** | **21.8** | **0.0095** |
| OI Freq | 3 | 4 | 3 | 4 | 7 | 6 | 4 | 4 | 3 | 4 | **42** | **3.7** | **0.93** |
| Ctrl Freq | 4.2 | 4.2 | 4.2 | 4.2 | 4.2 | 4.2 | 4.2 | 4.2 | 4.2 | 4.2 | **42** | | |

# Terminal Digit Analysis

In Figure A, black bars, the distribution of terminal digits of 2759 Coulter counts recorded by 7 members of the laboratory are shown. The grey bars show the distribution of terminal doubles in this set. Figure B shows similar results for 5155 Coulter counts recorded by post-doc AB.

Figure C shows the distribution of the terminal digits of 1556 colony counts recorded by 7 members of the lab. Figure D shows the 3501 colony terminal digit distribution for post-doc AB. Note the similarity of the patterns in B and D.



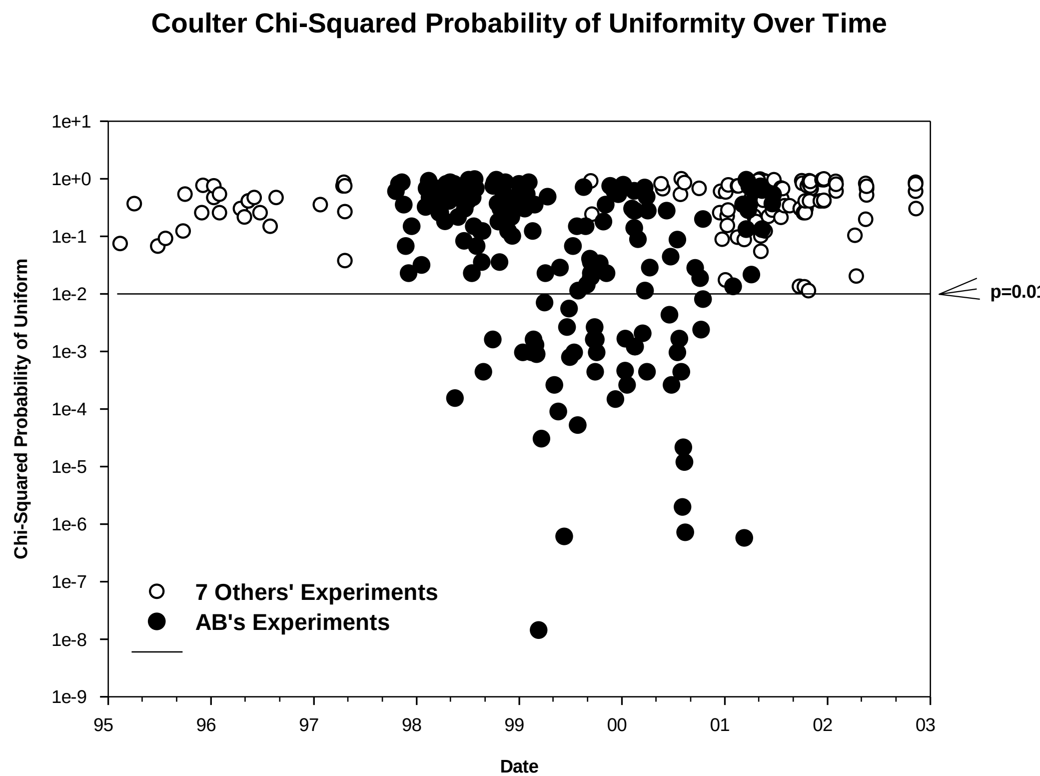
## Terminal Digit Analysis of Coulter and Colony Counts

Chi Squared p-values were calculated using the program available in Excel by comparing the actual digit counts to the uniform distribution. The Coulter and colony distributions by others in the lab and from outside are quite likely due to chance. AB's distributions are extremely unlikely to be due to chance.

| | | Digit | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Type** | **Investigator** | **0** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **Total** | **Chi-sq** | **P-value** |
| **Coulter** | **AB: 171 experiments** | 472 | 612 | 730 | 416 | 335 | 725 | 362 | 422 | 370 | 711 | 5155 | 456.4 | **$1.22 \times 10^{-92}$** |
| **Coulter** | **AB: terminal doubles** | 27 | 124 | 88 | 58 | 43 | 81 | 68 | 38 | 52 | 57 | 636 | 113.1 | **$3.40 \times 10^{-20}$** |
| **Coulter** | **7 Others: 99 experiments** | 249 | 294 | 276 | 244 | 296 | 270 | 284 | 258 | 306 | 282 | 2759 | 13.9 | **0.13** |
| **Coulter** | **7 Others: terminal doubles** | 18 | 29 | 34 | 21 | 25 | 31 | 29 | 29 | 37 | 25 | 278 | 10.6 | **0.30** |
| **Coulter** | **Outside lab 1: 11 experiments** | 28 | 34 | 29 | 24 | 27 | 36 | 44 | 33 | 26 | 33 | 314 | 9.9 | **0.36** |
| **Coulter** | **Outside lab 2: 17 experiments** | 34 | 38 | 45 | 35 | 32 | 42 | 31 | 35 | 35 | 33 | 360 | 4.9 | **0.84** |
| **Colonies** | **AB 114 experiments** | 514 | 267 | 395 | 265 | 262 | 418 | 306 | 261 | 342 | 471 | 3501 | 228.4 | **$3.56 \times 10^{-44}$** |
| **Colonies** | **7 Others: 59 experiments** | 173 | 154 | 166 | 140 | 163 | 137 | 147 | 156 | 163 | 157 | 1556 | 7.6 | **0.57** |

# Coulter Chi-Squared p-Values Over Time

AB joined the lab in October, 1997 and left in July, 2001. For 45 experiments the hypothesis of uniformity would be rejected at the 0.01 level, a stringent testing condition. All of the improbable results were seen in experiments performed by AB.



# Colony Counts ~ PDF Copy from AB's Notebook

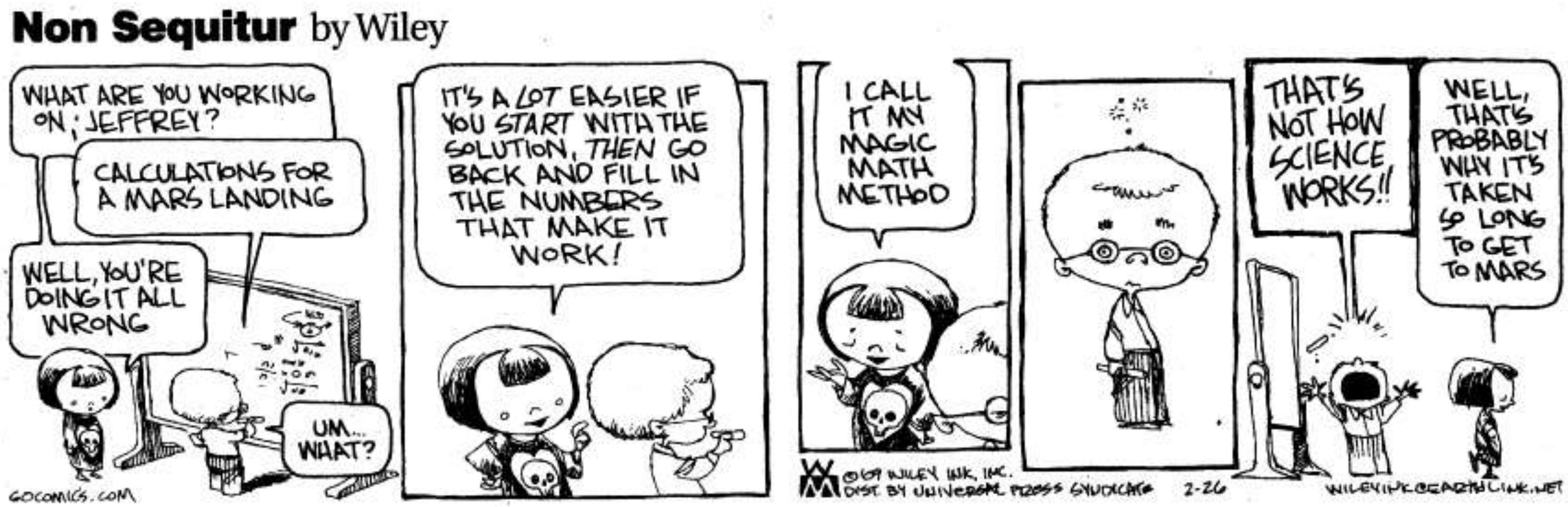
- We noticed that the **rounded** average of the 3 counts appeared unusually often as one of the triplicate counts in AB's colony records. In this example , it appears in 9 of the 10 samples (high-lighted in aquamarine). SF stands for Surviving Fraction, assumed to be 1.00 in Sample 1.2

Expt #: 2 Date: 02/22/99

**Colony Counts and Survival Fraction**

| Tube.dilution | Colony 1 | Colony 2 | Colony 3 | Avg Colony | SF | |
|---|---|---|---|---|---|---|
| 1.2 | 130 | 149 | 142 | 140.33 | — | |
| 2.2 | 131 | 137 | 143 | 137.0 | 0.9762 | |
| 3.2 | 123 | 131 | 138 | 130.66 | 0.9311 | |
| 4.2 | 128 | 134 | 140 | 134 | 0.9548 | |
| 5.2 | 125 | 130 | 136 | 130.33 | 0.9287 | µM |
| 6.3 | 115 | 126 | 137 | 12.6 | 0.089 | 0 |
| 7.2 | 17 | 20 | 24 | 20.33 | 0.1484 | 20 |
| 8.2 | 29 | 35 | 41 | 35 | 0.2678 | 40 |
| 9.2 | 62 | 70 | 54 | 62 | 0.4626 | 80 |
| 10.2 | 70 | 79 | 62 | 70.33 | 0.5396 | 100 |

# The Mid-Ratio



# The Mid-Ratio

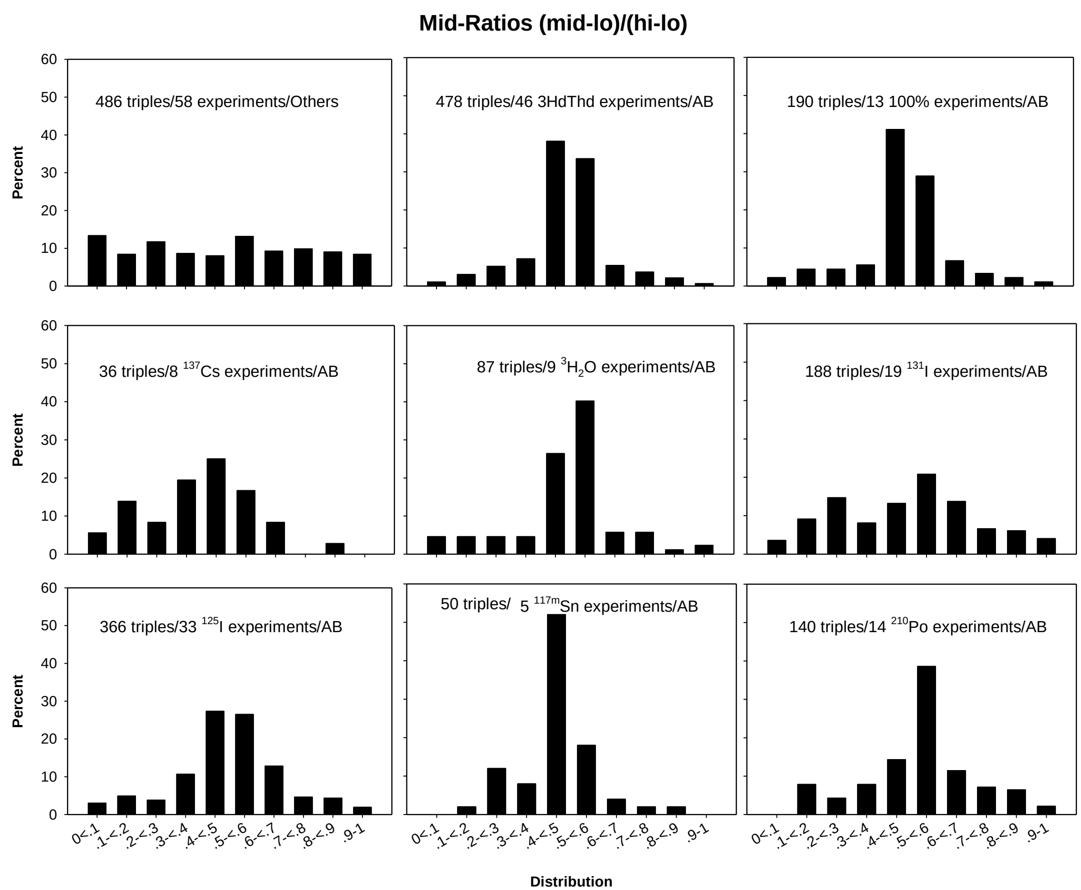
- The Mid-Ratio is the difference between the middle colony count and the lowest colony count divided by the highest count minus the lowest (for colony counts in rank order, (b-a)/(c-a)). When one of the counts in the triple is close to the triple average, its mid-ratio will be close to 0.5
- E.g. for the triple 17, 27, 35: MR = (27-17)/(35-17) = 0.55

## The Mid-Ratio and the Appearance of the Rounded Average in Some of the Triple Colony Counts

Two experiments, one performed by AB, the other by another investigator (OI) in the lab. The rounded average, shown in aquamarine, appears in 9 of AB's 10 samples, but does not appear at all in the OI's samples. AB's mid-ratios are all close to 0.5. OI's are much more spread out.

| Sample # | AB Triplicate Counts | | | Average | Mid-ratio (b-a)/(c-a) | OI Triplicate Counts | | | Average | Mid-ratio (b-a)/(c-a) |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 130 | 149 | 142 | 140.33 | 0.63 | 92 | 111 | 119 | 107.33 | 0.70 |
| 2 | 131 | **137** | 143 | 137 | 0.5 | 78 | 85 | 74 | 79 | 0.36 |
| 3 | 123 | **131** | 138 | 130.66 | 0.53 | 142 | 126 | 120 | 129.33 | 0.27 |
| 4 | 128 | **134** | 140 | 134 | 0.5 | 120 | 129 | 121 | 123.33 | 0.11 |
| 5 | 125 | **130** | 136 | 130.33 | 0.45 | 64 | 68 | 79 | 70.33 | 0.27 |
| 6 | 115 | **126** | 137 | 126 | 0.5 | 92 | 101 | 78 | 90.33 | 0.61 |
| 7 | 17 | **20** | 24 | 20.33 | 0.43 | 74 | 62 | 94 | 76.67 | 0.38 |
| 8 | 29 | **35** | 41 | 35 | 0.5 | 89 | 69 | 67 | 75 | 0.091 |
| 9 | **62** | 70 | 54 | 62 | 0.5 | 85 | 87 | 97 | 89.67 | 0.17 |
| 10 | **70** | 79 | 62 | 70.33 | 0.47 | 71 | 58 | 55 | 61.33 | 0.19 |

# Mid Ratios in AB's Experiments with Different Isotopes



# Statistical Analysis Of The Number Of Triples That Contain Their Rounded Mean: Calculating the Probability That One of the Triples Will be Equal to the Rounded Mean of that Triple

- The gap between the highest and lowest of the colony counts is variable, so the probability that one of the triples will equal the mean varies with the size of the gap. For example
  - The triple 8,x,10 has a gap of only 2 and the probability that the middle number will equal the rounded mean is 0.33
    - for x=8, the mean is 8.7 (rounds to 9)
    - for x=9, the mean is 9
    - for x=10, the mean is 9.3 (rounds to 9))
  - The triple 21,x,49 has a gap of 18. The middle is 35 and the probability that x=35 is 1/36 (about 0.28)
- Worse than that, the probability also depends on whether the gap is odd or even

# The Probability of Hitting the Rounded Mean Depends on Whether the Gap is Odd or Even

- For triple colony counts 10,x,20, the gap is 10 (even) and there is 1 middle value, 15
  - For x=14 (triple is 10,14,20), the mean is 14.7 (rounds up to 15)
  - For x=<u>15</u> (triple is 10,<u>15</u>,20), the mean is <u>15</u>
  - For x=16 (triple is 10,16,20), the mean is 15.3 (rounds down to 15)

Only for x=15 is the rounded mean contained in the triple and the probability that the rounded mean is in the triple is 1/11

- For triple colony counts, 10,x,21, the gap is 11 (odd) and there are 2 middle values, 15 and 16
  - For x=<u>15</u> (triple is 10,<u>15</u>,21), the mean is 15.3 (rounds down to <u>15</u>)
  - For x=<u>16</u> (triple is 10,<u>16</u>,21), the mean is 15.7 (rounds up to <u>16</u>) and the probability that the rounded mean is in the triple 2/12

# Statistical Analysis Of The Number Of Triples That Contain Their Rounded Mean

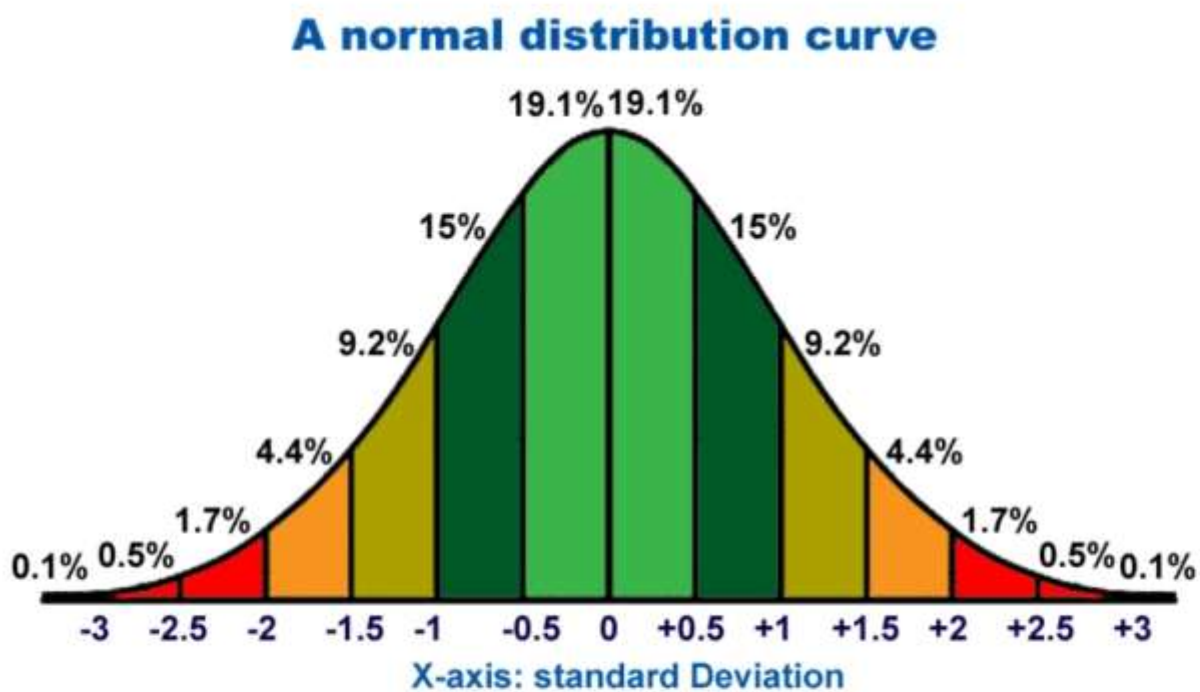
We can now calculate the probability of hitting the mean by chance for any given gap

- For even gap: probability of hitting the mean is 1/(1 + c – a) or 1/(1+gap)
- For odd gap: probability of hitting the mean is 2/(1+c-a) or 2/(1+gap)

# Demonstration of Z-Scores

## Z-Score

“a standard score [that] indicates how many standard deviations an observation or datum is above or below the mean.” *Wikipedia*




ycanaustralia.com

## Calculating the Z-score and its probability

The values in column 4 were calculated for even gaps using the expression 1/(1+gap) and for odd gaps 2/(1+gap). The variances in column 5 were calculated from the values in column 4: variance = (col 4 value)*(1-col 4 value).

The Z-score is the actual number minus the expected number divided by the expected standard deviation.

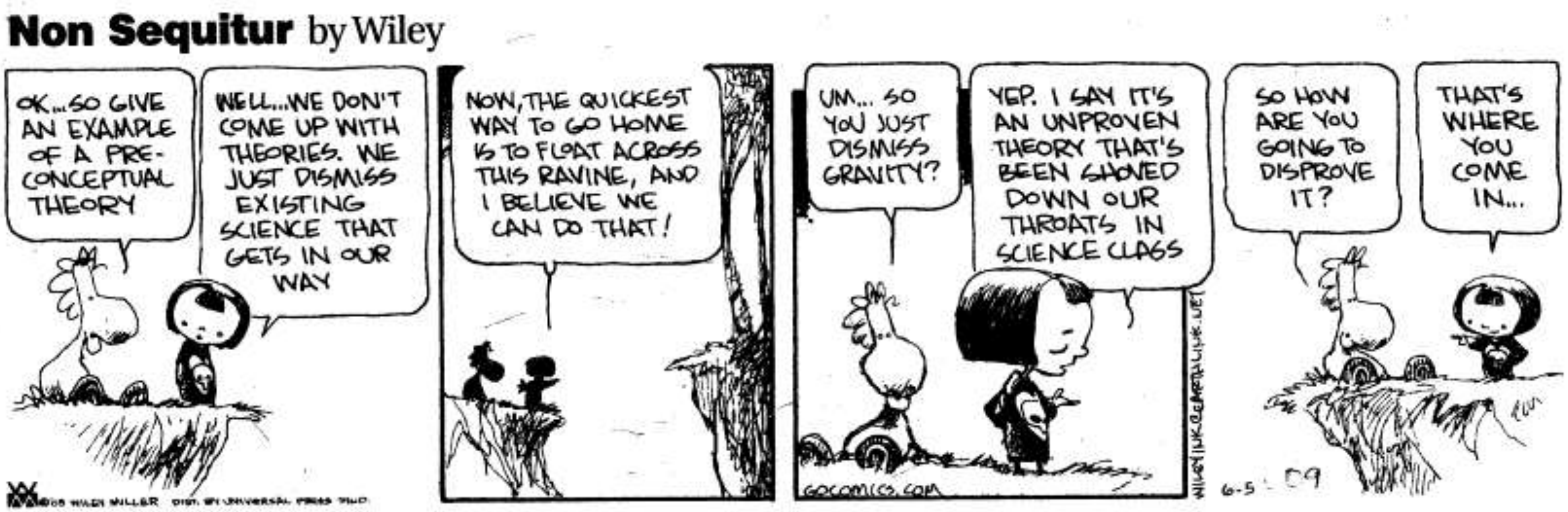
| | Sample # | Gap (c-a) | Column 4 Expected Number Rounded Means in Triples | Variances of Expected | Standard Deviation | Actual Number of Rounded Means in Triples | Z-Score for Actual Number | Probability of Z-Score |
|---|---|---|---|---|---|---|---|---|
| **AB** | **1** | 19 | 0.100 | 0.090 | | | | |
| | **2** | 12 | 0.077 | 0.071 | | | | |
| | **3** | 15 | 0.125 | 0.109 | | | | |
| | **4** | 12 | 0.077 | 0.071 | | | | |
| | **5** | 11 | 0.167 | 0.139 | | | | |
| | **6** | 22 | 0.043 | 0.042 | | | | |
| | **7** | 7 | 0.250 | 0.188 | | | | |
| | **8** | 12 | 0.077 | 0.071 | | | | |
| | **9** | 16 | 0.059 | 0.055 | | | | |
| | **10** | 17 | 0.111 | 0.099 | | | | |
| | **Sum** | | **1.086** | **0.934** | **0.967** | **9** | **8.19** | **$<1x10^{-9}$** |
| **OI** | **1** | 27 | 0.071 | 0.066 | | | | |
| | **2** | 11 | 0.167 | 0.139 | | | | |
| | **3** | 22 | 0.043 | 0.042 | | | | |
| | **4** | 9 | 0.200 | 0.160 | | | | |
| | **5** | 15 | 0.125 | 0.109 | | | | |
| | **6** | 23 | 0.083 | 0.076 | | | | |
| | **7** | 20 | 0.048 | 0.045 | | | | |
| | **8** | 22 | 0.043 | 0.042 | | | | |
| | **9** | 12 | 0.077 | 0.071 | | | | |
| | **10** | 16 | 0.059 | 0.055 | | | | |
| | **Sum** | | **0.917** | **0.806** | **0.898** | **0** | **-1.02** | **0.154** |

# Z-Scores and Probabilities That Triples Contain Their Rounded Means Grouped by Isotope Experiments

| Investigator | Isotope | # Experiments | # Triples | Expect # Triples Containing Rounded Means | Actual # Triples Containing Rounded Means | Z-Score for Actual Number | Probability of Z-Score or Higher |
|---|---|---|---|---|---|---|---|
| AB | $^{117m}Sn$ | 5 | 50 | 6.1 | 28 | 9.7 | << $1 \times 10^{-9}$ |
| AB | $^{210}Po$ | 14 | 140 | 19.7 | 67 | 12.0 | << $1 \times 10^{-9}$ |
| AB | $^{3}H_2O$ | 9 | 90 | 13.2 | 28 | 4.8 | $1 \times 10^{-6}$ |
| AB | $^{137}Cs$ External Beam | 4 | 36 | 4.8 | 14 | 4.8 | $1 \times 10^{-6}$ |
| AB | $^{125}I$ | 33 | 375 | 67.9 | 174 | 18.4 | <<< $1 \times 10^{-9}$ |
| AB | $^{131}I$ | 20 | 198 | 33.6 | 61 | 5.6 | $1 \times 10^{-8}$ |
| AB | $^{3}$HdThd | 44 | 478 | 65.0 | 301 | 35.1 | <<<< $1 \times 10^{-9}$ |
| OI | Various | 59 | 534 | 86.4 | 95 | 1.2 | 0.123 |

Many of the survival experiments we examined involved compounds that contained different isotopes. In AB's hands, the actual number of triples that contain their rounded means far exceeds expectations based on expectations of randomness and independence. For other investigators (OI) using the same methods as AB, the frequency of rounded means is within the predicted expectation

# RadioBiology



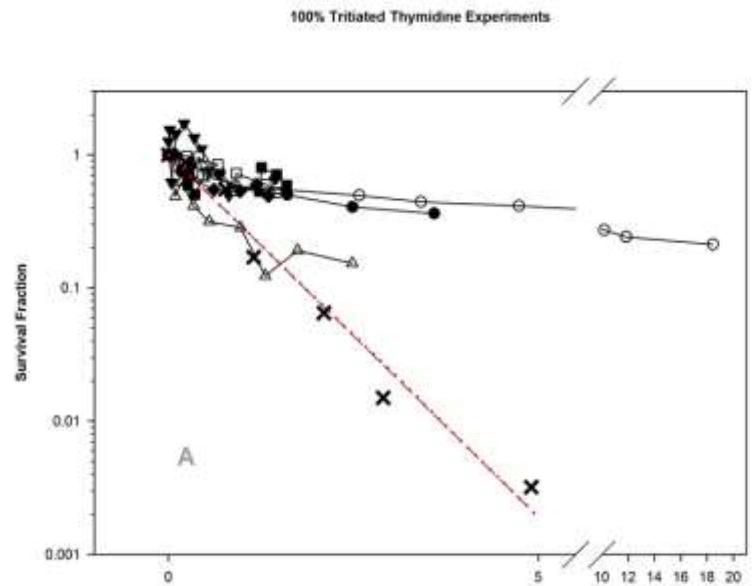
# AB's $^3$HdThd Survival Results Could Not be Replicated

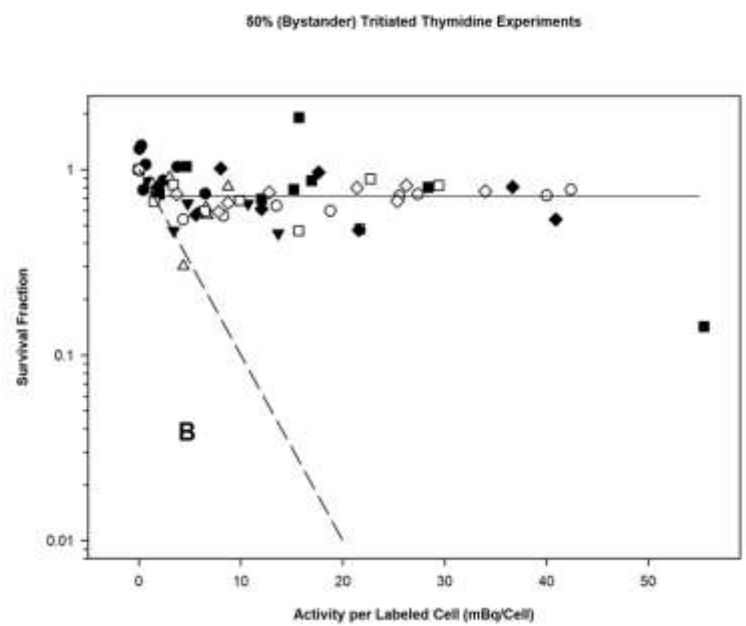
The exponential survival s of V79 cells incubated with $^3$HdThd reported in 2 publications could not be reproduced in 22 attempts to do so. In A, 100% of the cells were incubated with $^3$HdThd. The dashed line and X's represents results published in the two papers based on experiments performed by AB. The red line is the theoretical survival based on radiobiological principles. Ten attempts (symbols) to repeat AB's results were made by the PI and a second post-doctoral fellow.

Graph B shows 12 experimental attempts to repeat the bystander (50% experiments) results of AB (dashed line from the two papers). In these experiments, radioactive cells were incubated with non-radioactive cells.

AB's results would argue for a bystander effect, the 12 experiments by the PI and a second post-doc (symbols) would argue against such an effect, at least under these conditions.

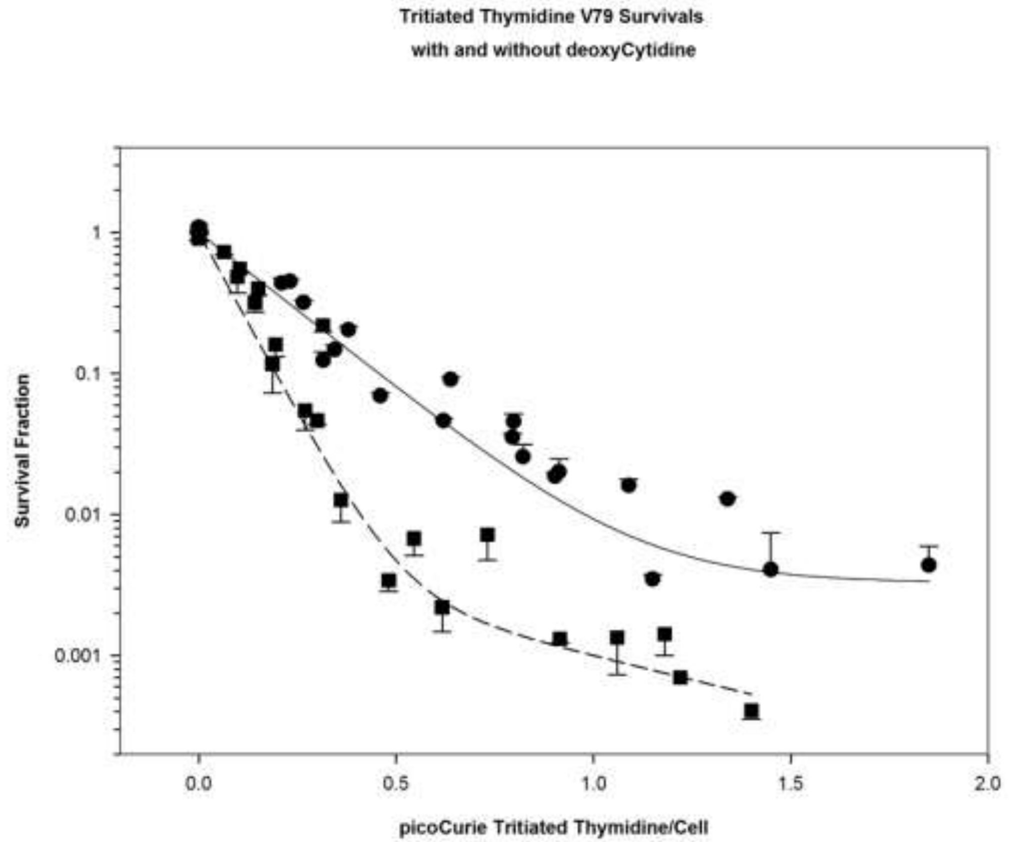
The results of these attempts to replicate are consistent with radiobiological literature that demonstrates $^3$HdThd blocks the cell cycle unless deoxycytidine is present, which it was not in any of these experiments.



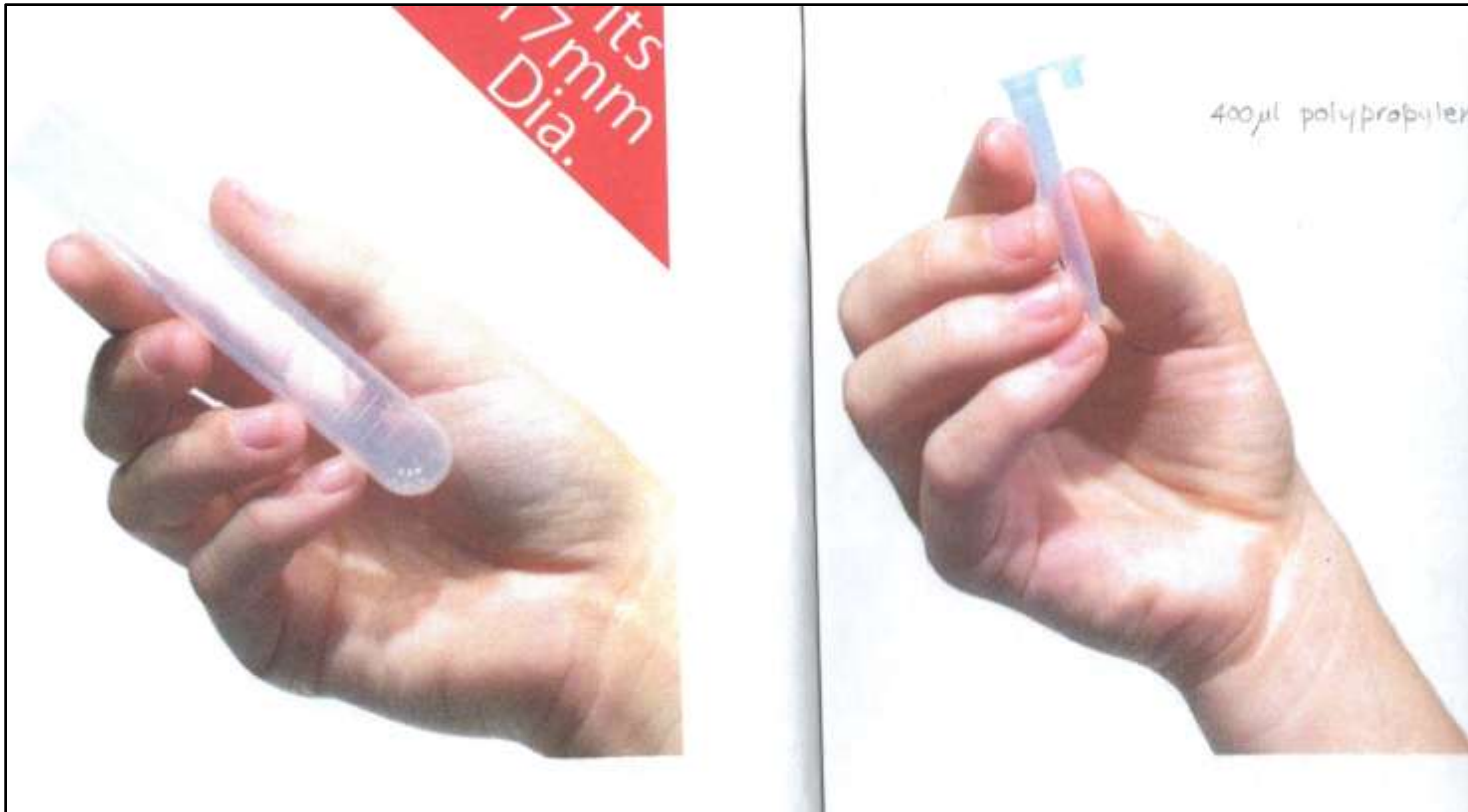



# Deoxycytidine Reverses the Cell Cycle Blocking Effect of $^3$HdThd: No deoxycytidine was present in the experiments described in the preceding posters

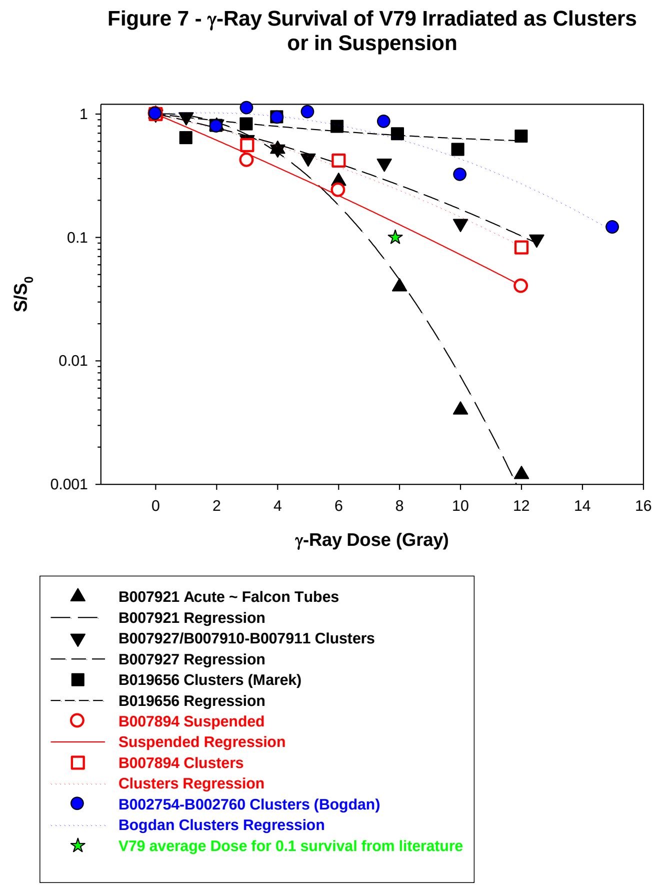
These are 6 experiments performed by another investigator in the lab – 3 with deoxycytidine (squares) and 3 without (circles) that demonstrate the reversal by deoxycytidine of the cell cycle blocking effect of $^3$HdThd. No deoxycytidine was present in any of the other experiments described in these posters so AB's survival results are expected to be biphasic – but they are not.



# Culture Tubes



# The Helena Tubes Are Hypoxic



# Summary

- The analysis reported here was only made possible because all the notebooks in the laboratory in question were made available through *subpoena*. Ordinarily, the raw data that underlies experiments are opaque to all but a few. We believe this was a rare and unique opportunity.
- We were fortunate to be able to compare data produced by several other individuals using the same instrument and techniques to that of a single individual, whose results alone could not be explained based on assumptions of randomness, uniformity or chance.
- We used the following tests, all of which are simple and could be put to use in any laboratory
  - Terminal digits of Coulter counts: AB's digit distributions diverged markedly from uniform, while others distributions were consistent with the assumption of uniformity*
  - Terminal digits of colony counts: AB's distributions were highly unlikely to be uniform or random, whereas others' colony terminal digit distributions are likely to have come about by chance*
  - Double terminal digits in the Coulter counts: AB's doubles are not likely to be due to chance, others' doubles are close to the expected 10%
  - Presence of the average as one of the triples in colony counts: AB's results had an inordinately high frequency of the rounded average occurring as one of the triplicate counts, results of others were consistent with the predicted frequency based on gap size
- The statistical analyses are bolstered by the inability to replicate AB's radiobiological results. The differentials in survivals are astounding – about 1000 fold in the 100% experiments, about 100 fold in the 50% (bystander) experiments

* Terminal digit analysis is recommended as a forensic tool on the USPHS Office of Research Integrity WebSite.

# Conclusions

- The results of the statistical analyses reported here argue strongly for making raw data used in the production of scientific papers, research reports and grant applications available to all researchers, reviewers and granting agencies
- Our analyses also argue for sharing such raw data with other researchers in the field in order for them to understand their own, possibly unexpected, experimental results and/or allowing them to avoid performing unnecessary experiments
- The experiments involved in these studies were designed to alleviate a vexing problem in Nuclear Medicine – that of the non-uniform distribution of radio-isotopes in the human body. These results were planned to be used in setting standards for allowable exposures for healthcare workers and to determine isotope doses to be used for diagnostic and therapeutic procedures
- Miscalculations based on these results could have serious consequences for patients and workers in nuclear medicine: over-estimating doses could lead to tissue and organ damage and even to cancer; under-estimating doses could lead to misdiagnoses and lack of therapeutic efficacy

# Thanks

- Mike Falvo, PhD for listening to my story
- George J Hill, MD, DLitt for his constant support and encouragement
- Joel Pitt, PhD My expert Statistician
- Mike Robbins, PhD My expert Radiobiologist
- Drummond Rennie, MD
- Harold Sox, MD
- Miriam Wahl, PhD

# My Website
# www.helenezhill.com

Have Comments?

Email Me

Helene Z. Hill, Ph.D.

*Truth even unto its innermost parts*

Home | My Family | My Career | Committees | Qui Tam | Publications | Raw Data | Travel | Blog

**This Website Exposes a Scientific and Medical Cover Up**

Welcome to my WebPage. Please understand that it is still under construction and many of the links are yet to be completed.

In October of 2003, I filed a case for *qui tam* in the Federal District Court of Newark charging my university and two scientists with whom I had been working with violation of the False Claims Act. I lost the case. There are a number of posts on the web regarding that case, all of which present one side of the story: that of the defendants. This webpage is my answer to those posts, and it shares a story themed around medical cover up. On it, I tell all who visit it something about me, my family, my scientific career, but most of all, I will present the information that I acquired during the case in order for others to decide whether I was right or wrong.

Most important, it will become apparent that the whistleblower has no right to appeal unfavorable decisions at the university level – although the defendant can appeal. Secondly, I would have had no access to the original data that I eventually analyzed had it not been for the filing of the *qui tam* case, so I argue strongly that raw data on which papers, reports and grant applications are based must be freely available for scrutiny by both readers and referees; a practice that would greatly promote **scientific accountability**.

Helene Z Hill, PhD

The data here analyzed were involved in the following publications:

Bishayee, A., H. Z. Hill, et al. (2001). "Free radical-initiated and gap junction-mediated bystander effect due to nonuniform distribution of incorporated radioactivity in a three-dimensional tissue culture model." Radiat Res **155**(2): 335-344.

Bishayee, A., D. V. Rao, et al. (2000). "Protection by DMSO against cell death caused by intracellularly localized iodine-125, iodine-131 and polonium-210." Radiat Res **153**(4): 416-427.

Bishayee, A., D. V. Rao, et al. (1999). "Evidence for pronounced bystander effects caused by nonuniform distributions of radioactivity using a novel three-dimensional tissue culture model." Radiat Res **152**(1): 88-97.

Bishayee, A., D. V. Rao, et al. (2000). "Radiation protection by cysteamine against the lethal effects of intracellularly localized Auger electron, alpha- and beta-particle emitting radionuclides." Acta Oncol **39**(6): 713-720.

Bishayee, A., D. V. Rao, et al. (2000). "Marrow-sparing effects of 117mSn(4+)diethylenetriaminepentaacetic acid for radionuclide therapy of bone cancer." J Nucl Med **41**(12): 2043-2050.

Goddu, S. M., A. Bishayee, et al. (2000). "Marrow toxicity of 33P-versus 32P-orthophosphate: implications for therapy of bone pain and bone metastases." J Nucl Med **41**(5): 941-951.

Howell, R. W. and A. Bishayee (2002). "Bystander effects caused by nonuniform distributions of DNA-incorporated (125)I." Micron **33**(2): 127-132.

Howell, R. W., S. M. Goddu, et al. (1998). "Radioprotection against lethal damage caused by chronic irradiation with radionuclides in vitro." Radiat Res **150**(4): 391-399.

Howell, R. W. (2000-2006). 1R01CA083838-01A1 Effects of Nonuniform Distributions of Radioactivity.

Howell, R. W. (2006-2011). "1R01CA083838-06A1 Effects of Nonuniform Distributions of Radioactivity ".