Writing in the Sciences

Module 7.1: Plagiarism

Plagiarism of others' work

- Passing off other people's writing (or tables and figures) as your own.
  - Includes:
    - cutting and pasting sentences or even phrases from another source
    - slightly rewriting or re-arranging others' words
    - "borrowing" material from sites like Wikipedia

Example

- **Original Version (Wikipedia):** Ernest Miller Hemingway (July 21, 1899– July 2, 1961) was an American author and journalist. His economical and understated style had a strong influence on 20th-century fiction, while his life of adventure and his public image influenced later generations. (Source: Wikipedia)

- **Plagiarized Version:** Ernest Hemingway's thrifty and understated style strongly influenced 20th-century fiction. His audacious lifestyle and public image also influenced later generations.

When writing about others' ideas/work:

- You must understand the material well enough to put it in your own words!
- Work from memory
- Draw your own conclusions
- Do not mimic the original author's sentence structure or just re-arrange the original author's words.

Self-plagiarism and duplication

- Recycling your own writing or data, including:
  - Copying or only slightly rewriting text from your own previously published papers.
  - Adding new data to already published data and presenting it as new results.
  - Submitting identical or overlapping data to multiple journals.

Prevalence of plagiarism?

- In pilot studies, publishers that used CrossCheck to look for plagiarism had to reject 6% to 23% of submitted papers (due to plagiarism or self-plagiarism/duplication).

Reference:
Journals step up plagiarism policing. *Nature* **466**, 167 (2010).

Prevalence of plagiarism?

- 2-year study of plagiarism in the *Croatian Medical Journal* (automatic detection software followed by manual confirmation):
  - 8% of papers plagiarized others' work
  - 3% of papers were self-plagiarized

Reference:

Baždarić K, et al. Prevalence of plagiarism in recent submissions to the *Croatian Medical Journal*. *Sci Eng Ethics*. 2012 Jun;18(2):223-39.

Prevalence of plagiarism?

- Study of plagiarism in residency applications:
  - Using plagiarism detection software, researchers analyzed about 5000 personal statements in applications to five residency programs at Brigham and Women's Hospital.
  - 5% of essays had clear evidence of plagiarism (confirmed on manual review).

Segal S, et al. Plagiarism in Residency Application Essays. *Ann Intern Med*. 20 July 2010;153(2):112-120.

Plagiarism example

Original passage (Klibanski et al. 1995):

> “One possibility is that the dose of estrogen effective in treating postmenopausal women is inadequate in a younger population. Second, whether continued improvement in bone mass can be seen in patients treated for a duration of time longer than the current study is unknown. A third possibility is that patients were not compliant with hormone therapy....A fourth and likely explanation is that estrogen therapy alone cannot correct the multiple factors contributing to bone loss in women with anorexia nervosa. In addition to profound estrogen deficiency, nutritional and other hormonal variables have been implicated in the pathogenesis of bone loss. These factors, including IGF-1 deficiency cortisol excess and decreased androgen production are unaffected by estrogen administration and may have a continuing deleterious effect on bone mass.”

Plagiarism example

Plagiarized passage (Munoz et al. 2002):

"One possibility is that the ~~dose of estrogen~~ estrogen dose which is effective in treating postmenopausal women is inadequate in a younger population. Second, whether continued improvement in bone mass ~~can~~ may be seen in patients treated for ~~a duration of time longe~~r longer period of time than the current study is unknown~~. A third possibility is that patients were not compliant with hormone therapy~~....A ~~fourth~~ third and more likely explanation is that estrogen therapy alone cannot correct the multiple factors contributing to bone loss in women with ~~anorexia nervosa~~ AN. In addition to profound ~~estrogen deficiency~~ hypoestrogenism, nutritional and other hormonal variables have been implicated in the pathogenesis of bone loss. These factors, including IGF-1 deficiency cortisol excess and decreased androgen production are unaffected by estrogen administration and may have a continuing deleterious effect on bone mass."

Plagiarism example, same paper

Original passage (Klibanski et al. 1995):

"Our data demonstrate that, despite its usefulness in perimenopausal women, estrogen and progestin administration does not reverse the profound osteopenia seen in all young women with anorexia nervosa. Trabecular bone loss is severe and may progress despite estrogen therapy."

Plagiarized passage (Munoz et al. 2002):

"In conclusion, our data demonstrate that, despite its usefulness in perimenopausal women, estrogen and progestin administration does not reverse the profound osteopenia seen in all young women with AN. Trabecular bone loss is severe and may progress despite estrogen therapy."

Plagiarism example, same paper

Original passage (Klibanski et al. 1995):

"There are no prospective studies of trabecular BD in adult women with anorexia nervosa, and it is unknown whether there is a progressive and permanent decline in bone mass. Although the role of estrogen replacement therapy in preventing bone loss in premenopausal women is clearly established, no studies have addressed whether is is beneficial in young women with premenopausal osteopenia."

Plagiarized passage (Munoz et al. 2002):

"There are some published data on trabecular bone mineral density (BMD) in adult women with AN. but it is still unknown whether there is a progressive or permanent decline in bone mass. Although the role of estrogen replacement therapy in preventing bone loss in menopausal women has been clearly established, no studies have been carried out to determine whether it is beneficial in young women with premenopausal osteopenia"

Another example:

- Original paper (2004): “Although earlier registry-based analyses of second neoplasms after breast cancer (BC) did not detect an increased risk of cutaneous melanoma (CM),[1][2] several more recent registry-based[3][4] and hospital-based[5] studies have documented a statistically significant increased risk of CM after BC with standardized incidence ratios (SIRs) ranging from 1.4 to 2.7.”
- Second paper (2009): “Recent registry-based [1,2] and hospital-based [3,4] studies have documented a statistically significant increased risk of CM after BC with standardized incidence ratios (SIRs) ranging from 1.4 to 2.7.”
- References 1,2,3,4 are identical!

Writing in the Sciences

Module 7.2: Ghostwriting and Guest Authorship

Ghost authors and guest authors

- Ghost authors: Writers-for-hire who draft manuscripts (usually for companies), but are not listed as authors.

- Guest or “honorary” authors: Academic researchers who are minimally involved in a paper, but “lend” their name as an author (often first author!) to bolster the paper’s credibility.

Prevalence of guest/ghost authorship?

- Anonymous survey of corresponding authors of articles from top medical journals:
  - *Annals of Internal Medicine*, J*AMA*, *Lancet*, *Nature Medicine*, *New England Journal of Medicine*, and *PLoS Medicine*.
- Results: 17.6% reported honorary/guest authors; 7.6% reported ghost authors

BMJ 2011;343:d6128

Case study: Merck and Vioxx

- Researchers systematically reviewed 250 court documents obtained through the Vioxx litigation (against Merck).
- Included internal company emails and documents related to publishing clinical trials papers or review papers.

Ross JS, Hill KP, Egilman DS, Krumholz HM. Guest Authorship and Ghostwriting in Publications Related to Rofecoxib: A Case Study of Industry Documents From Rofecoxib Litigation *JAMA*.2008;299(15):1800-1812.

Results

- For clinical trials papers (n=24): “Documents were found describing Merck employees working either independently or in collaboration with medical publishing companies to prepare manuscripts and subsequently recruiting external, academically affiliated investigators to be authors. Recruited authors were frequently placed in the first and second positions of the authorship list.”

Ross JS, Hill KP, Egilman DS, Krumholz HM. Guest Authorship and Ghostwriting in Publications Related to Rofecoxib: A Case Study of Industry Documents From Rofecoxib Litigation *JAMA*.2008;299(15):1800-1812.

From an internal company email to a potential guest author:

- “ I would like to invite you to be an author on the abstract and manuscript for this study. We are currently preparing both for submission before the end of this year. Could you please let me know if you would be interested in authorship on both the abstract and manuscript, 1 of the 2 planned publications, or none? In making your decision, you may want to take into consideration that the results of this study were negative at first glance.”

Ross JS, Hill KP, Egilman DS, Krumholz HM. Guest Authorship and Ghostwriting in Publications Related to Rofecoxib: A Case Study of Industry Documents From Rofecoxib Litigation *JAMA*.2008;299(15):1800-1812.

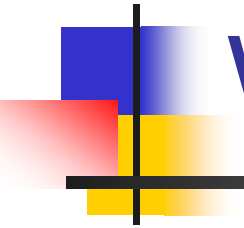
Results

- For review papers (n=72): “Documents were found describing Merck marketing employees developing plans for manuscripts, contracting with medical publishing companies to ghostwrite manuscripts, and recruiting external, academically affiliated investigators to be authors. Recruited authors were commonly the sole author on the manuscript and offered honoraria for their participation.”
- Only half of the review articles disclosed Merck sponsorship!

Ross JS, Hill KP, Egilman DS, Krumholz HM. Guest Authorship and Ghostwriting in Publications Related to Rofecoxib: A Case Study of Industry Documents From Rofecoxib Litigation *JAMA*.2008;299(15):1800-1812.

More in the NY Times

- Medical Papers by Ghostwriters Pushed Therapy
  - “The court documents provide a detailed paper trail showing how Wyeth contracted with a medical communications company to outline articles, draft them and then solicit top physicians to sign their names, even though many of the doctors contributed little or no writing. The documents suggest the practice went well beyond the case of Wyeth and hormone therapy, involving numerous drugs from other pharmaceutical companies.”—Natasha Singer, NY Times, 2009
- Ghostwriting Is Called Rife in Medical Journals
- Medical Editors Push for Ghostwriting Crackdown



Writing in the Sciences

Module 7.3: Conflicts of Interest/Disclosure

Conflicts of interest

- Any financial or personal relationship that might influence (bias) an author, reviewer, or editor's judgments. (International Committee of Medical Journal Editors)

Conflicts of interest:

- Should be disclosed (most biomedical journals require this).
- May influence an editor's (or reviewer's) decision to reject or accept a paper.
- Are often printed in the published paper.

Case Study: CT screening for lung cancer

- Researchers screened >30,000 smokers (and others at high-risk) yearly with CT scans to identify early-stage lung cancers.

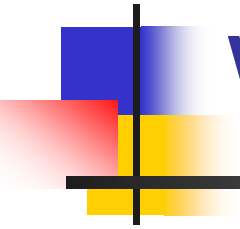
- Survival of patients with stage I lung cancer detected on CT screening. *N Engl J Med.* 2006;355(17):1763-71.

Case Study

- They identified 484 lung cancers (411 stage I); and these patients had high survival rates.
- Conclusion: “In a population at risk for lung cancer, such screening could prevent some 80% of deaths from lung cancer.”
- Study was highly criticized for methodological flaws and unwarranted conclusions.

The authors failed to disclose a key conflict of interest:

- One of the studies disclosed funding sources ($3.6 million) was the Foundation for Lung Cancer: Early Detection, Prevention and Treatment.
- *NEJM* editors later learned that this foundation was:
  - Run by the principal investigator of the 2006 study
  - Housed at her institution
  - Funded almost solely by the Vector Group, the parent company of Liggett, a major tobacco company.
- *NEJM* editors in a 2008 editorial "We and our readers were surprised to learn that the source of the funding of the charitable foundation was, in fact, a large corporation that could have an interest in the study results."



Writing in the Sciences

Module 7.4: Reproducible research and the changing publication landscape

The push for “reproducible research”

- In a “reproducible” paper:
  - The data are available.
  - The code that was used to analyze the data is available (and can be run on standard software)
  - An independent investigator can run the code on the data and generate figures and tables that match those published in the original paper

Reproducing a paper's results is surprisingly hard!

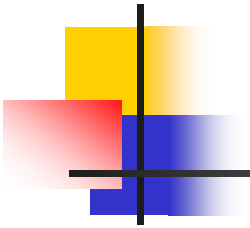
- Researchers attempted to reproduce just one table or figure from 18 microarray-based gene expression profiling papers published in *Nature Genetics* (which requires authors to make data publicly available) in 2005–2006.
- Results:
  - Two studies (11%) were reproduced "in principle"
  - Six studies (33%) were partially reproduced (some discrepancies)
  - Ten (56%) could not be reproduced at all. These studies aren't necessarily wrong—but they're uncheckable.

Ioannidis JP, et al. Repeatability of published microarray gene expression analyses. *Nat Genet*. 2009;41:149-55.

Case Study: Duke Scandal

- Researchers at Duke published a series of papers on a new method for predicting patient response to cancer drugs. (named one of the "Top 6 Genetics Stories of 2006" by *Discover* magazine)
  - Used publicly available data (complex data!).
- Biostatisticians (Keith Baggerly and Kevin Coombes) at MD Anderson Cancer Center tried to replicate their results, so others at their institution could use the approach.

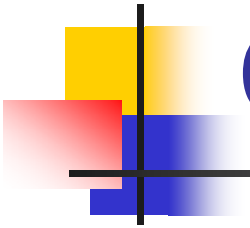
Case Study: irreproducible research



- Baggerly and Coombes uncovered multiple troubling “bookkeeping errors,” such as:
  - Off-by-one errors in Excel
  - Reversal of the labeling of drug-sensitive and drug-resistant cells
- Once these errors were corrected, the method no longer worked.
- Despite these criticisms, Duke researchers started using the approach to treat cancer patients.
- Eventually, officials took heed and shut down trials; Duke researcher resigned; he has retracted 10 papers (and corrected 8 others) in the medical literature.

Reproducibility Editor, *Biostatistics*

- Authors may request a “reproducibility review”:
  - The editor re-runs the code on the data to make sure the paper’s tables and figures are completely reproducible.
  - Paper gets an “R” for reproducible; “D” for data available; and “C” for code available.

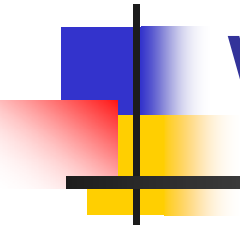


Challenges

- How will journals host all this?
- Who (if anyone) will be charged with running reproducibility checks?
- What about proprietary data and software?
- What about issues of privacy for data from human subjects?

Reproducible research:

- Improves transparency
- Uncovers mistakes
- Prevents fraud and “cherry-picking”
- Makes replication easier
- Makes collaboration easier
- Makes science progress faster!



Writing in the Sciences

Module 7.5: Demo edit #1

Immortality is an alluring concept. Some scientists believe that it will be possible to "upload" one's mind by recreating the circuitry of the brain *in silico*. Before we can upload brains, we first must reverse-engineer neural circuitry and begin by creating a circuit map.

Electron microscopy provides the only possible method through which we're able to clearly visualize synapses and follow neural processes. Volumetric reconstruction of neural tissue using electron microscopic resolution is necessary to map neural circuitry. Focused ion-beam scanning electron microscopy (Knott et al. 2008) gives excellent quality images, but fails to process tissue pieces larger than 40 microns in diameter. Thin sections imaged with transmission electron microscopy succumb to the damaging effects of manual handling and section distortion. Thus, it's most prudent to use a method that images the block-face directly and is capable of imaging large block-faces. Serial block-face scanning electron microscopy (SBEM; Denk and Horstmann 2004) provides both necessary components.

Using SBEM, Dr. Kevin Briggman and associates (Briggman, Helmstaedter, and Denk 2011) recently mapped the connections between starburst amacrine cells and bipolar ganglion cells in the mouse retina to better understand the wiring specificity, elucidating the cellular circuit between starburst amacrine cells and direction-selective bipolar retinal ganglion cells.

By staining a 200-micron piece of retina, which contained the entire arborization field of a starburst amacrine cell with an extracellular stain that could outline cells and neural processes in SBEM, Briggman was then able to reconstruct neural processes. Based on morphology, he assessed the locations and sizes of putative synapses on these processes.

Unfortunately, synapses were invisible within the data because the tissue was only stained with an extracellular, electron-dense stain and some synaptic features are intracellular. In an effort to address this ambiguity, Briggman then stained a second piece of tissue where synapse-associated features were stained and visible. He then correlated the extracellular morphology found at synapses between the first and second pieces of tissue.

This is the first example of relatively large neural circuit reconstruction and it solved controversy about exactly how starburst amacrine cells are wired to be directionally-selective. The next steps in whole-brain circuit reconstruction will be large sample preparation (Mikula, Binding, and Denk 2012) and imaging on a whole-brain SBEM for mapping the whole mouse brain as a first mammalian complete connectome (Seung 2011).

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References

- Knott, Graham,et al. “Serial Section Scanning Electron Microscopy of Adult Brain Tissue Using Focused Ion Beam Milling.” The Journal of Neuroscience 28, no. 12 (March 19, 2008): 2959–2964.
- Denk, Winfried, and Heinz Horstmann. “Serial Block-Face Scanning Electron Microscopy to Reconstruct Three-Dimensional Tissue Nanostructure.” PLoS Biology 2, no. 11 (November 2004).
- Briggman, Kevin L., Moritz Helmstaedter, and Winfried Denk. “Wiring Specificity in the Direction-selectivity Circuit of the Retina.” Nature 471, no. 7337 (March 10, 2011): 183–188.
- Mikula, Shawn, Jonas Binding, and Winfried Denk. “Staining and Embedding the Whole Mouse Brain for Electron Microscopy.” Nature Methods In press (2012).
- Seung, H. Sebastian. “Neuroscience: Towards Functional Connectomics.” Nature 471, no. 7337 (March 10, 2011): 170–172

Immortality is an alluring concept. Some scientists believe that it will be possible to "upload" one's mind by recreating the circuitry of the brain *in silico*. Before we can upload brains, we first must reverse-engineer neural circuitry and begin by creating a circuit map.¶

In the first example of a relatively large neural circuit reconstruction, Dr. Kevin Briggman and colleagues (Briggman, Helmstaedter, and Denk 2011) recently mapped the connections between key neurons—starburst amacrine cells and bipolar ganglion cells—in the mouse retina. The work solves a long-standing controversy about exactly how starburst amacrine cells are wired to be directionally-selective.¶

Briggman's team used serial block-face scanning electron microscopy (SBEM; Denk and Horstmann 2004) to visualize synapses and follow neural processes. Electron microscopic resolution is necessary to map neural circuitry. Focused ion-beam scanning electron microscopy (Knott et al. 2008) fails to process tissue pieces larger than 40 microns in diameter; and transmission electron microscopy requires thin samples that often succumb to the damaging effects of manual handling and section distortion. Thus, it's most prudent to use a method that images the block-face directly and is capable of imaging large block-faces. SBEM provides both necessary components.¶

Briggman's team treated a 200-micron piece of retina, including the entire arborization field of a starburst amacrine cell, with an extracellular stain that could outline cells and neural processes in SBEM. Due to their many intracellular features, Briggman's team could not directly visualize synapses (neural connections). But, based on morphology, they inferred the locations and sizes of putative synapses. They also stained a second piece of tissue with an intracellular stain that revealed synapse-associated features; and they correlated the synapse maps between the first and second pieces of tissue.¶

ADD: PARAGRAPH ABOUT THE CONTROVERSY THEY SOLVED!¶

The next steps in whole-brain circuit reconstruction will be to prepare, image, and map the whole mouse brain using SBEM (Mikula, Binding, and Denk 2012). This would represent the first mammalian complete connectome (Seung 2011) and would be the closest anyone has ever come to immortalizing a mammalian brain.¶

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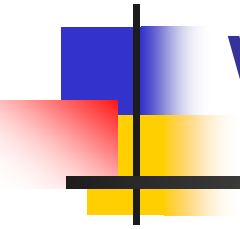

Writing in the Sciences

Module 7.6: Demo edit #2

Scientists are still looking for small size smart robots that can navigate in dynamic and unknown environments. This challenge inspired Tahmid Latif and Alper Bozkurt from North Carolina State University to use cockroaches as biobots (biological robots). They developed a wireless biological interface that uses an electronic interface to remotely steer cockroaches. This concept helps to create a mobile web of sensors that uses cockroaches to collect and transmit data, such as locating survivors in hard areas during earthquakes.

Cockroaches have antennas -called cerci- to sense: tactile, temperature and humidity. Researchers used these antennas to drive the cockroach by sending a series of electrical pulses to it. The system consists of: a microprocessor with Zigbee interface [1], electrodes and a battery. The user controls the microprocessor wirelessly using a Zigbee transceiver; the microprocessor sends electrical pulses to the cockroach's antennas using electrodes and then the cockroach moves.

Tahmid Latif and Alper Bozkurt used Madagascar Hissing cockroach during their analysis because of: its larger size (~50-75mm), slow speed (~3cm/s), long life span (~2 years) and robustness. Before the experiment starts, they anesthetized the cockroach by cold-treatment (4C) for 45-60 minutes. They attached one side of the electrodes (5cm long stainless steel coated with 250um thick Teflon) to the antennas to serve as electronic reins, injecting small charges into the roach's neural tissue. The charges trick the roach into thinking that the antennas are in contact with a physical barrier, which effectively steers them in the opposite direction. The researchers evaluated two microprocessors that control the electrodes: Microchip's PIC16F630 [2] and Texas Instrument's CC2530 [3]. CC2530 was better because of its low weight (500mg), Zigbee module connectivity and the availability of 21 general purpose I/O. CC2530 gets its power from the 90mAh Li-Po battery.

Cockroaches followed an S-shaped trajectory drawn on the laboratory floor and spent 81 sec. with 10% success rate to complete the route. This finding opens the door to scientists to start using insects in biobots world but the system's overall weight is still a concern in this new field and needs more studies to reduce its size..

References

- [1] ZigBee Technology, http://www.zigbee.org/About/AboutTechnology/ZigBeeTechnology.aspx
- [1] Microchip, "14-Pin, Flash-Based 8-Bit CMOS Microcontrollers," PIC16F630/676 datasheet, Jan. 2010 [Revised May 2010].
- [2] Texas Instruments, "A True System-on-Chip Solution for 2.4-GHz IEEE 802.15.4 and ZigBee Applications," CC2530 datasheet, Apr.2009 [Revised Feb. 2011].
- [3] http://ibionics.ece.ncsu.edu/EMBC_12.wmv

Scientists are looking for small, smart robots that can navigate in dynamic and unknown environments, such as the aftermath of an earthquake. This challenge inspired Tahmid Latif and Alper Bozkurt from North Carolina State University to turn cockroaches into biobots (biological robots). Their remotely-controlled cockroaches could someday serve as a mobile web of sensors that collect and transmit data from hard-to-reach places. ¶

Cockroaches have antennas (called cerci) that can sense tactile input, temperature, and humidity. Latif and Bozkurt created a wireless device that attaches to these antennas and can deliver small electrical pulses that drive the cockroach. The electric charges trick the insect into thinking that the antennas are in contact with a physical barrier, which effectively steers them in the opposite direction. ¶

The device consists of a microprocessor with Zigbee interface [1], electrodes and a battery; the user controls the microprocessor using a Zigbee transceiver. The researchers tested two microprocessors: Microchip's PIC16F630 [2] and Texas Instrument's CC2530 [3]. They incorporated the CC2530 in their final device due to its low weight (500mg), Zigbee module connectivity, and greater number of I/O ports. ¶

Latif and Bozkurt used the Madagascar Hissing cockroach because of its large size (~50-75mm), slow speed (~3cm/s), long life span (~2 years), and robustness. After anesthetizing the cockroaches with cold-treatment (4C) for 45-60 minutes, they attached one side of each electrode (5cm long stainless steel coated with 250um thick Teflon) to the antennas. ¶

In tests of the system, cockroaches followed an S-shaped trajectory drawn on the laboratory floor and spent 81 sec. with 10% success rate to complete the route. NEED MORE DETAILS HERE! ¶

The system is still too large because….. But this finding opens the door for scientists to start using insects as biobots. Someday, armies of cockroaches may be the best hope for rescue for natural disaster survivors. ¶

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