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ACRONYMS

There'll also be an index of terms, I think, but it's not written yet.

NON-SCIENCE STUFF

FLOSS free/libre open source software

GPL GNU General Public License

GNU GNUs Not Unix

PLOS Public Library of Science

OS open science

SCIENCE STUFF

GPCRS G-protein coupled receptors

RA retinoic acid

5-HT 5-hydroxytryptamine

CNS central nervous system

BHLH basic helix-loop-helix protein structural motif

VMNS visceral motor neurons

SHH sonic hedgehog

ASCL1 Achaete-scute homolog 1

1 "SCIENCE STUDIES, FEMINIST THEORY, CULTURAL STUDIES"

"hook" here. My div is interesting, I promise

1.1 SCIENCE STUDIES

Both my historical time line and ideological foundation for science studies starts with Ludwik Fleck's *Genesis and Development of a Scientific Fact*, originally published in 1935 pre-WWII Germany.[15] A practicing syphilis researcher and pathologist, Fleck proposes that scientists are the creators of facts, rather than mere passive observers. He proffers an explanation that certain *styles* of thinking permeate and circumscribe scientific collectives and the people within them. Scientific knowledge is only accepted as true once the evidence been thoroughly vetted, trimmed, mediated, and judged acceptable by experts in the field. "Facts" are then not so much realities of the world but interpretations of it, made by collaboration between individual, collective, and evidence; they only take shape in a matrix of other beliefs and discoveries about the world.

Summarizing Fleck is going to take some serious work. I'm not sure how specific I should be here, w/r/t page numbers and quotes in Genesis

May include that Fleck was Jewish, working in Ukraine in 1935, and consequently subject to Nazi occupation, as a potential reason his work went hidden for so long. Also because it was radical.

His ideas re-appear in one of the most well-known historians or sociologists of science, Thomas Kuhn, famed writer of *Structures of Scientific Revolution*.[24] The publication of Kuhn's *Structure* in 1962 is considered a landmark event in philosophy and history of science. He coined the usage of "paradigm" in the incredibly-common, borderline meaningless sense it's used today.* A previous Div III expressed my feelings, with regards to at least *Structures:*

Like with Fleck, not sure how much time Kuhn deserves.

> "Thomas Kuhn's work occupies an awkward and somewhat inexplicable position in the contemporary intellectual environment. Kuhn's thinking, and here I refer specifically and exclusively to the thoughts put forth in The Structure of Scientific Revolutions (SSR), while conceptually worthwhile, erodes quickly under scrutiny. "
>
> -Campbell, *Essays on Biological Epistemology*, Div III in 2007

Fleck and Kuhn and many of their concurrent and subsequent philosophers, historians, and sociologists of science offer compelling arguments that science is, yes, evolution, but not evolution *towards* anything. Science is just another way to try to make sense of the world,.

Don't actually know enough about science studies to make these kinds of judgement, probably, but it's my general impression

[[Linking paragraph about how dissatisfying it is to deconstruct science without talking about the *implications* of a value-laden science]]

1.2 FEMINIST THEORY

At some point in the past 30-40 years (mid-1980s?), feminist science happened; not, of course, always under one name or one set of goals. New ways of knowing overlaps with technology and science studies

should read up on feminist/critical science studies chronology

*Masterman (reference not currently included) cites 21 diff uses of paradigm

overlaps with philosophy of science overlaps with a plethora of other modes of analysis. What I now call feminist science studies emerges out of activists against white supremacy, patriarchy, heteronormativity, and ecological destruction working on ways to critique science as a social institution, and find new ways of answering scientific questions.

feminist science studies more specifically tied to 1970s women's & environmental social movements: also in a specifically Western/US context

What I call feminist science studies is then at confluence of many ideas, summed up in Donna Haraway's 1994 *Cat's Cradle: Science Studies, Feminist Theory, Cultural Studies.*[19]. Per Haraway, feminist science studies is at some meeting point of:

> **"Cultural studies** . . . Not culture only as symbols and meanings, not comparative culture studies, but culture as an account of the agencies, hegemonies, counter-hegemonies, and unexpected possibilities of bodily construction. . . Relentless attention to the ties of power and embodiment. . . location and knowledge. Unconvinced by claims about insuperable natural divides between high and low culture, science and everything else, words and things, theory and practice.
>
> **Feminist, Multicultural, and Antiracist Theory/Projects**. . . situated knowledges, where the description of the situation is never self-evident, never simply "concrete," always critical; the kind of standpoint with stakes in showing how "gender," "race," or any structured inequality in each interlocking specific instance gets built into the world–i.e., not "gender" or "race" as attributes or as properties, but "racialized gender" as a practice that builds worlds and objects in some ways rather than others, that gets built into objects and practices and exists in no other way. . . gender and race are built into practice, which is the social, and have no other reality, no origin, no status as properties . . . questioning representation with a vengeance."
>
> **Science Studies:** reflexivity, constructionism. . . science in the making (not science made), actors and networks. . . science as practice and culture. . . the culture of no culture, the nature of no nature. . . All the disciplines of science studies: history, philosophy, sociology, semiology, and anthropology; but also the formation of science studies out of the histories of radical science movements, community organizing, and policy-directed work. These histories are regularly erased in the hegemonic accounts of disciplinary and interdisciplinary development in the academy and the professions."
>
> -Donna Haraway, *Cat's Cradle*, p. 66-68

So now that we know what we're dealing with (sort of, although it's a slippery web of concepts), that brings us to: so what? Sociological and historical questions are all very good, but what of the modern day?

1.3 MEANING IN PRACTICE: WHAT DOES THIS DO IN A PRACTICAL SENSE?

1.3.1 *"Asking Different Questions"*

Feminist science studies allows, and demands, a number of things of practicing scientists. It lets us ask questions of representation in our

labs, our most important journals, and our students: "Where are the women? *Who* is practicing science, and who is deciding what science is important?" This extends to questioning not just gender, but about the representation of race, physical ability, nationalities, and other sociological classifications.

Or it should *extend...*

Feminist science studies also lets – and again, demands – that we ask questions on a deeper level, about the nature of the knowledge produced. This includes (among many other things),

This section is fairly weak representationally. Mostly women (9/11), but only 3 of the 9 are women of color (African-American, Asian/American, and Indian).

- an examination the scientific *construction* of race and gender perpetuated by the perceived objectivity of the sciences,[16,14,11]
- the deep paradoxes involved in the ab/use of women's bodies in pursuit of reproductive technologies,[37,3]
- the shaping of science by gendered and racialized metaphors and languages,[22,28] and the historical complicity between scientific exploration and colonialism, misogyny, and racism? [20,34]
- challenging the artificial boundaries between "basic research" and nature/culture to explain a rapidly-growing scientific-industrial complex, and then linking basic research to community activism for women's rights and environmental movements.[39]

It asks us to look at science as a practice inseparable from culture, and what that might mean for knowledge and for scientists as the future producers of that knowledge.

1.3.2 *For Scientists*

Because feminist science asks questions that are fundamentally geared towards addressing socialized inequalities in science, it can help scientists take those inequalities into account. Scientists (in theory) care about helping people , and choose science because it seems like the best way to do so. It can't help people if it's racist, misogynistic, and not considerate of how work will be ab/used downstream. Scientists should care about where their work is coming from and where it's going, and we *need* good – read: concerned and activist – people everywhere if we want social progress. This div is (hopefully) a road map and detailed exploration into doing (good) value-laden science

I want to find a frame that really efficiently explains why this matters for given audience. The given audience being, of course, a sympathetic-but-unconvinced strict biologist (i.e. John).

1.4 THE POINT OF THE THESIS

Figure out *how* to apply all of that stuff to everything else I care about: namely, open science, open neuroscience, molecular neuroscience and then write about what did and did not work.

1.5 WHAT YOU HAVE TO LOOK FORWARD TO

Sketch of regular book introductions with what chapter is going to be about and why. Definitely *needs a lot of work*

Chapter 1 (aka what you just read) describes (in brief) the theoretical logic behind my Div III, explaining why I believe that science is just as much a cultural construct as any other knowledge project, and as a result, why scientists have a serious responsibility to consider their work in the greater context of social issues.

Chapter 2 is the background to my work – a "purely" scientific description. It describes why I think serotonin systems are important to

model and explore, why I care about them, and my attempts to create a way to explore serotonin signaling by manipulation of a stem cell line.

Chapter 3 explores the growing and heterogeneous community of open science (OS) advocates, who propose to make science more inclusive, collaborative, and useful, largely via the power of the Internet for sharing. OS is an alluring idea, especially backed with the rhetorical power of "open"; but "open" is not by itself a panacea for the hegemony of scientific establishments. I am still interested in exploring how some of the potential of OS *could* be fulfilled given a more deliberate and complex implementation.

Chapter 4 is the follow up to this – it's a description of my attempts to implement open science proposals into a biological project, and the myriad complications and barriers I've had in doing so. It offers a description of what I think the open science movement is missing in its efforts examines the open science movement with a mind to discover and analyze the values underlying those efforts. Ultimately, I'd propose how a movement hoping to democratize and equalize science desperately needs to consider and account for their values from a (feminist) different standpoint if they'd like to succeed.

Not sure where the actual content wrt "representation" should go. continuing reorganization

Chapter 5 continues, to some extent, on the same theme, considering the representation of the global scientific community in open science and science at large.

Chapter 6 is, to some extent, the capstone chapter. It is critical questions about the links between my own areas of interest – molecular signaling and psychotropic drugs – and gender, environmental concerns, indigenous rights and colonialism, and race relations. While I don't have answers to any of those questions, asking those questions has (already) helped find d a myriad of ways in which social factors are fundamental parts of my scientific process and questions.Then there will be a conclusion when I finish my div.

2 SEROTONIN, TRANSCRIPTION FACTORS, AND DIFFERENTIATION

"every biological organism is inherently individual"

But now for some "real" science.

2.1 WHY SEROTONIN?

Serotonin is 5-hydroxytryptamine (5-HT), a monoamine neurotransmitter binding 14 classes of receptors, all but one of which are G-protein coupled receptors (GPCRs). With receptors distributed across most parts of the brain, nearly every basic central nervous system (CNS) function, including mood, cognition, sleep, pain, motor function and endocrine secretion, is in some part modulated by serotonin signaling. As such, disruptions in serotonergic transmission is implicated in many psychological diseases (eg schizophrenia etc) and their corresponding pharmaceutical treatments.[30]

obviously hallucinogens are what I want to write abut but it's very far away from what I'm doing in lab, so not clear on how they'll get in yet. This section is really just a placeholder at the moment.

Model systems for serotonergic signaling are fundamental to therapeutic drug design and development, and in the case of hallucinogenic drugs, present a potential method to link molecular and sub-cellular processes to cognition and thought.

2.2 MODEL SYSTEMS

2.2.1 *What do model systems do?*

The scientific justification for model systems is the essential role they play in reducing a complex biological into simple working units. Model neuronal systems in a dish provide a carefully controlled environment, to the exclusion of external elements (rogue hormone fluctuations, mental activities of rodents/humans); the cell type can be isolated and studied as a single cell acting individually (more accurately, a single cell surrounded by thousands of identical single cells), allowing for specific genetic and environmental manipulations.

In theory, this permits the isolation and tracking of internal signaling pathways of a single cell, letting scientists construct a step-wise "map" of signaling cascades and interactions between the molecular components of the cell.

2.2.2 *current options*

Ideally, of course, one uses primary neuron cultures to study signaling – but those are expensive and hard to maintain. Differentiation of fast-growing and easy to maintain cells, that nonetheless express a relatively fully functional GPCR signaling intracellular network is an alternate model for us.

The available cell line to me is P19 stem cells, which are known to differentiate into relatively poorly-characterized neuron-like cells

when cultured with a micro-molar amount of retinoic acid (RA) in the media. The trick for us, however, is not just the production of neuronal cells, but to direct the line towards serotonergic neurons instead of *just* neurons. So how can we manipulate the P19 stem cells earlier in the process? We can (hopefully) set cell fate early on via expression of important transcription factors in serotonergic differentiation, and then allow cells to develop serotonin-receptor GPCR machinery relatively normally.

as far as cancerous, genetically manipulated, and traumatized rat cells can be "normal"

2.3 P19s

P19s are derived from rat embryonal teratocarcinoma cells, from behind the testes of XY rats. They are immortal and easy to maintain, retaining pluripotency under normal cell culture conditions. Upon application of RA and a slight modification of culture conditions, P19 differentiate into CNS cells, including glia, neurons, and fibroblast-like cells.[2] Studies of this differentiation pathway have elucidated a number of genes important for neural development,[43] and they're an established model system for exploring embryonic differentiation of neuronal cells.[13]

2.4 THE 5-HT SYSTEM

The 5-HT system is one of the most complex projection networks in the CNS. It has three descending efferents to the spinal cord, while the B5-B9 neurons project via 5 different routes to almost every region of the CNS. This large network means serotonin signaling not only transmits information, but plays a large role in *modulating* the rest of brain function.

Brain anatomy.
5-HT *actual* distribution

2.4.1 *embryonic development*

Stem cells = embryonic cells; hence, knowing and examining the embryonic precursors to 5-HT neurons and then mimicking them => 5-HT neurons in culture

During embryonic development, the different networks of 5-HT neurons are much less distinct. In mice, they're some of the earliest generated neurons, appearing between E10.5 and E12.5, starting in the rostral regions along the brainstem axis. By E12.5, almost all of the 5-HT neuron classes are present. Induction and specification of diverse neurons, and specifically 5-HT neurons, requires a set of signaling molecules, converted into a combinatorial transcriptional code.

2.5 TRANSCRIPTION FACTORS IN 5-HT DIFFERENTIATION

2.5.1 *in 5-HT progenitor cells*

more neuroanatomy! more signaling pathways!

Nkx2.2

Nkx2.2! (Nkx2.2!) is a homeodomain-containing transcription factor that specifies the ventral cell type in response tosonic hedgehog (Shh) signals

Genes	Expression	5–HT defects	KO lethality	5–HT-specific TF
Nkx2.2	ventricular zone	100% except in r1 P0	P0	lost except in r1
Mash1	ventricular zone	Almost 100%	P0	all lost
Gata2	VZ, postmitotic	100%	E10-12.5	all lost
Lmx1b	Postmitotic	100%	P0	all lost
Pet1	Postmitotic	70%	mostly viable	unknown
Gata3	Postmitotic	mostly in caudal	E11.5-13.5	unknown

Table 1: Phenotype of transcription factor KO mice (from Chen and Ding)

in the spinal cord and hind-brain. Expression of *Nkx2.2* ceases as soon as 5-HT cells become post-mitotic. Upstream of *Phox2b*, *Nkx2.2* plays a role in

1. earliest transcription factor required for 5-HT specifications
2. dispensable in r1 5-HT; Nkx2.2 KO neurons derived from r1 are unaffected
3. in the absence of Phox2b, adopts a default pathway to promote 5-HT fate

*Ascl1/Mash1 **

expression patterns & time course

Mash1 is the mouse, human, and rat basic helix-loop-helix protein structural motif (bHLH) homologue of Achaete-scute homolog 1 (Ascl1), first discovered and explored in *Drosophila* as a pro-neural gene.

It's a key fate determinant for many neuron types during fetal and adult neurogenesis. In the embryonic hind-brain, it's the only known pro-neural gene expressed in the domain of 5-HT progenitor cells, and is co-expressed with **Nkx2.2!** during vMN and 5-HT production.

Mash1 KO mice do not effectively product 5-HT neurons. visceral motor neurons (vMNs), which derive from the same set of cells, are produced normally, but without Mash1, none of the normal post-mitotic 5-HT transcription factors express. Likely, this is due to the loss of Notch signaling that ordinarily leads to 5-HT neurogenesis.

Mash1 possesses specific 5-HT characteristics; cannot be replaced by other pro-neural bHLH factors. At the same time, it is not *sufficient* to induce 5-HT differentiation; it requires cofactors, like *Nkx2.2*.

2.5.2 *in the ventricular zone & post-mitotic 5-HT neurons*

Gata2, Gata3

1. Members of the GATA family containing zinc-fingers which bind to core (A/T)GATA(A/G) sequences
2. Gata2 precedes -3;
   a) E9.0 in r4 and transiently in r2
   b) E10.5 expanded to all rhombomeres and detected in VZ progenitor cells and in post-mitotic cells
3. Gata2 KO:

   a) Leads to severe anemia and death between E10 and E11; this early lethality obviously precludes a more specific examiniation, but defects seem to appear in neurogenesis more generally. KO tissues
   b) defects in neurogenesis generally; early lethality precludes 5-HT specific examination
   c) *in vitro* KO tissues lack all 5-HT neurons, even in presence of Gata3
   d) Gata2 affects different 5-HT cluster development differently. It is necessary and sufficient in R1 neurons, and capable of inducing other 5-HT specific TFs in r1

4. Gata3 - relevant in caudal development of raphe nuclei
5. conflicting reports of Gata2 + Gata3 interactions
   a) Gata3 operates either independently or downstream of Gata2 and Lmx1b
   b) poorly understand epistatic relationships

3 OPEN SCIENCE

Defining "open"

"Open science" is a big, vague, nebulous term. First, the short and sweet version:

> "Open means **anyone** can **freely access, use, modify, and share** [content] for **any purpose**."

The "free" in that definition is, of course, free as in freedom, not as in beer. The open science movement is closely affiliated with the free/libre open source software (FLOSS) movement, and as such, there's a large overlap in terminology. Some preemptive clarification:

> "The terminology of and factions within this movement are complex, but, in short, "free software" tends to be associated with the ideology of freedom, "open source" with the openness of the development process, and "libre" with those concerned about confusion from the previous two. FLOSS are used as monikers to refer to all of these meanings." (Reagle [36])

The open science movement's unifying* principle manifests with 3 (or 4, or 6, depending on who you ask) areas of interest:

1. open access - namely, to full-text published papers and research results
2. open data - publishing raw data pre- or concurrently with paper publication
3. open research - everything else, including, but not limited to:
   a) open code distribution - code for analyses, model generation, etc. should be hosted somewhere accessible
   b) open lab notebooks - tracing the entire research process with all dead ends and kinks included

There's also a hundred other subcategories that fall under the umbrella; new systems of distributed, ongoing, or otherwise "open" peer review or community discussion of publications, like the work at PubPeer, billed as an "online journal club".More examples here: Readcube/-Mendeley, collaborative reading sofware So open science is frustratingly broad and inconsistent, just like any other community. But there are some commonalities in intent and goals, and from that some general open science values can be dissected.

3.1 VALUE(S)

I think open science is really interesting as a BIG IDEA, largely because of its ties to the free and open source software movement, and specifically

*unifying isn't actually the right word here – single shared point? overlap? lots of smaller movements all agreeing on this one

in the realm of community-driven goals. A lot more analytical work has been done on FLOSS sociological values than the narrower and newer niche of OS, so I draw largely from that.

In the FLOSS movement, there's a sharp ideological divide between the free/libre and the open licenses. Advocates of the libre licensing model list many advantages, but their main focus is libre software as a social imperative. User freedom (or their conception of it) is paramount. Open source, on the other hand, was created and remains in an explicit attempt to side-step the social values and ideological connotations of the term "free software", as laid out in the GNU General Public License (GPL). It instead has a narrow focus on access and production of source code - the 'practical' benefits of distributed production.

Bearing that distinction in mind, trivial as it initially seems, I think the usage of *open* in OS is a valuable point of entry into the ambivalent moral aspects of open science. Lots of proponents of OS either come from and/or explicitly draw from the F/LOSS movement, but the chosen movement nomenclature is "open". The same disavowal (or maybe just lack of acknowledgment) of social values seen in open source is apparent in a lot of the open science movement. It's not about science helping (or empowering) people, it's about doing "better" science – more reproducible, more reliable, more powerful (disruptive, even!). Open science is defined almost entirely by the *mechanisms*, in the same way open source is *just* focused on production. Even projects that pitch themselves as a place for citizen scientists can be construed as just a way to shift labor from cheap graduate students to even cheaper laypeople.

A lot of the following ideas draw heavily on analyses of the FLOSS movement, because that's where work has been done to some extent. "Open science" isn't nearly as widely talked about or analyzed.

UNSORTED [VALUE/D]TOPICS

3.1.1 *Lineages of open (science)*

> "The most common narrative about open science tells us that, once upon a time, science was an ethical enterprise: sharing, equality, disinterest and the common good drove the everyday work of scientists. Then evil corporations entered science and changed the rules of the game, patenting life, enclosing the commons, and eventually destroying the willingness to share data, information, and knowledge. But today, so the story goes, we have new tools that together with the old open science spirit an be used to rebel against evil, defeat it and allow scientific knowledge to flow freely again. These tools are open source and open access science, and they can be used to tear down the barriers to the access of scientific knowledge." (Delfanti, p. 5)

Open science rhetoric draws on a mystical past where information flowed free ("In the 17th century, journal publication *was* open science!"), and in so doing, constructs a seamless narrative where open science is part of every major discovery since Newton. Or whoever, pick your scientist. The construction of an illustrious history lends legitimacy to the moral appeal of the movement.

3.1.2 *Public image management*

Science has an intimate relationship with the media, and both parties use each other as a tool for various goals. The media gets a reputable scientist figure to bolster their claims; the scientist gets a public venue to couch their ideas or goals in objective-but-positive ways. Open science rhetoric is easy to use for both purposes.

Delfanti, in 2013, published "Biohackers: The Politics of Open Science".[10] It lies at the "the intersection of digital cultures, science communication and science and technology studies," a grouping that bears no little similarity to my own interests. His treatment of scientists and their public image management focuses on:

1. The J. Craig Venter Institute and J. Craig Venter himself, representing venture capitalists and open science for monetary gain and prestige
2. Ilaria Capua, a vetinarian virologist in Italy, who during the 2006 global avian influenza crisis, pushed the WHO through public shaming into changing their data policies to an open access model to better combat the disease
3. "DIYBio", a loose network of homegrown biologists.

Both Venter and Capua used publications in both prestigious journals and in more public forums (*Scientific American*, *The New York Times*) as a way to get the public involved in their work and on their side; public pressure, as created by and/or relayed by the media, was influential in both their success stories. The open science narrative was a tool in both of their toolkits used for different purposes and different effects.

citations here for when I find them

3.1.3 *Corporate uses of open science*

Open science, by intent, can be used by anybody for anything. That also means corporate entities can take advantage of the methods, tools, and data released into the public sphere.

In the free software world, corporate uses aren't bad – and here, as well, I don't think they're necessarily *bad*. But they do undercut the "open is good" in the sense that corporations are notorious for only considering the bottom line. That means any usage of open resources is for the bottom line, and not necessarily for whatever heroic potential purpose open data/science advocates had in mind.

Interestingly, there's been attempts to implement a copyright license similar to the GPL, but with a clause of "only ethical consideration"

3.1.4 *Creation and Representation*

Who gets to create?

Generally, white men. In free software communities, men outnumber women to a much greater degree than in more traditional development structures[32]; presumably, racial and ethnic minorities fare even more poorly, although there's even less data to support that.

The dismal representation in FLOSS derives in part from a flawed perception that social stratifications and classifications "don't matter" on the internet. Code is race- and gender-agnostic (except that, for somewhat obvious reasons, it's *not*). Thus, collaborative, decentralized community structures like those in FLOSS usually fail to include any

direct safeguards or rules about what kinds of behavior are acceptable. As a result, misogyny and racism run rampant and unchecked.

Whether representation is *worse* in open science than science at large is something I don't know yet, but it's probably fair to say that open science carries professional risks, and women and minorities in the sciences tend to disproportionately suffer for taking risks.

Who is it designed for?

I don't know yet! But probably I won't like it.

3.1.5 *Global Definitions of "open" and "free"*

Free software and open science are built on European/U.S. legal, moral, and social codes. Probably and definitely an issue, especially when "open science" is supposed to level the playing field but other communities, sciences, etc. aren't actually consulted in how they would like that leveling to be done in the legal sense.

Relevant citations: Christian [8], Dahdouh-Guebas et al. [9], Gorelick [18], Jolliffe [21]

3.2 EFFECT ON GLOBALIZED AND/OR INDIGENOUS SCIENCES

if indigenous sciences are local sciences, specific to the time and place and users involved, then they may not be generalizable to a mythic global community of "scientists".[†] And *if* we create a system where one of those many sciences is designated as the right one to be spreading, and making access to it the ultimate and only bridge to success, local knowledges are crowded out and erased. Indigenous sciences lose by virtue of what they are – non globalized, local knowledges, with no (monetary, legal) excuse to *not* use globalized standardized bits of (scientific) knowledge.

[†] Again, *if* science is local, there is no homogeneous global community of science/tists.

4 OPEN SCIENCE & SEROTONIN: CASE STUDY

Open notebook science has been described as the "epitome of open" and a "revolution" in scientific opportunities.

It's also (I think) the easiest for an undergraduate biologist to implement. I don't publish, yet, so I can't publish any papers open access. I don't generate a lot of data or have data sets, so publishing a data note for others to analyze is out of the question, and of course, since I'm not publishing I can't publish supplemental data.

So, starting from scratch, making all of my lab work openly accessible is the first and easiest way to implement open science. My efforts were inspired and guided by other proponents and practitioners of an Open Notebook methods.

4.1 OPEN NOTEBOOKS IN THE WILD

The first open notebook, and the originator of the term, was Jean Claude-Bradley, a chemist, in a blog post in 2006:

> "... By this [Open Notebook Science] I mean that there is a URL to a laboratory notebook (like this) that is freely available and indexed on common search engines. It does not necessarily have to look like a paper notebook but it is essential that all of the information available to the researchers to make their conclusions is equally available to the rest of the world.
>
> -Jean Claude-Bradley

He maintained, and the group has continued the effort, a project exploring synthesis and testing of anti-malarial compounds in the effort to hasten the search for an effective cure. The group has also added a similar project on HIV.

A second and more technically minded scientist is Carl Boettinger, a mathematical ecologist who's maintained an open lab notebook hosted on Github since 2010. His work and has been mentioned at least three times in Nature (once in 2013, twice in 2014).[17,29,41] His technical model for sharing his scientific progress is one that I emulated – the technicalities are detailed elsewhere, but it relies on minimal HTML, CSS, and coding knowledge to produce a reasonably clean and logical website, with lab notebook entries and any other relevant pages.

With that, I've been keeping my online notebook more or less in sync with my physical lab work since the first entry on July 15, 2014. All the entries are time stamped and track revisions, and are written in human-readable HTML Markdown.

Although the current systems may be undergoing some fairly large revisions in the next month

The bulk of this project is currently located at a Github repository (`https://github.com/kathleenleeper/workhorse`) and detailed there.

4.2 TECHNICAL DISCOVERIES

A large part of my goal with documenting my scientific process was to access its feasibility on a large scale, and for those who weren't already deeply invested in open science. What would be required for open notebooks to become common place? What would happen if they were? What do we lose when we go digital, and what do we gain?

4.2.1 *Frustrations*

1. The pure technical set up takes too much time. To mimic Carl Boettinger's Github-hosted and tracked site, it took a not-insignificant technical investment of time into exploring options and figuring out how to use the tools. There's no good guide to getting your standard wet lab "pure" biologist set up with Jekyll and Github to build a site from scratch like I did.
2. It's clear from my efforts to keep the digital version up with the paper version that any digital notebooks *need* automatic integration; they're otherwise unsustainable and always a little behind the times.
    a) Because paper notes don't translate perfectly to typed text (see 3a), it's frustrating and tiring to have to re-type and revisit a protocol run just earlier, and translate from paper to digital.
    b) Writing up negative results is *annoying* and feels *useless*. Trouble shooting procedures is incredibly tedious; having to write up and explain your attempt and subsequent failure time and again is far from encouraging, and I would venture to say increases the feeling of failure upon revisiting the entry.
3. While there are tablet and smart phone options, a basic laptop is simply not as versatile for note taking as a paper notebook. Computers can't get wet; you can't prop them against a beaker on a crowded lab bench.
    a) This also relates to the sketching and informal drawing that happens in lab notebooks – quick calculations, arrows between protocols, annotations of protocols on the fly as you mis-time, forget, or mix up steps.

Can cite this if people feel strongly

4. Studies have shown time again that physically writing notes helps students retain knowledge better than typing them. Similarly, I do more careful checking of protocols and the steps I have to follow when I'm writing them, rather than just reading and following a protocol from a typed page.
5. Some advocates claim that knowing your work flow could be examined at any time – an ever-present Potential Big Brother
    a) good to consider other people reading it, but i find it doesn't really change my choices in lab work – not my top focus
    b) dissemination is not a high priority

4.2.2 *Celebrations*

There are, of course, many benefits, although I'm not sure I'm taking full advantage of them yet. Some that have already proved immensely useful, and in fact often saved serious time for me.

1. Full text searching of entries, by date, content, and tag. This reduces the time spent flipping back and forth between physical pages, trying to figure out when exactly a sample was taken and the conditions it was processed with (Did you elute that DNA sample in TE, H_20, or elution buffer?)

2. It's very easy to share and talk about my project – because the repository and site are accessible from my smart phone, I can pull out data and explain the state of my lab work almost anywhere, quickly, efficiently, and with a minimum of fuss.*

3. Because I've already documented everything (mostly), I never have to *remember* small details that take up mental space. I'm never at a loss of which bands in a gel correspond to which samples – because I annotate my gels as soon as I get them, so that I can update the protocol with the results immediately.

4. Version control of files. It's easy to ask a computer to compare many different runs of the same protocol and show you differences in the protocols (assuming you've entered all the relevant information), which helps in comparing why an experiment may not have replicated properly.

    a) Version control of *protocols*, where if you modify a protocol, it's easy to add a note saying why. This would be very helpful for a collaborator of mine, who might wonder why a given protocol deviated from the lab standard in seemingly idiosyncratic ways.

5. Metrics on my lab entries. It's very easy to generate maps and time lines of processes; to see how many times and when my work has been done. I can run self-improvement metrics on myself

I'm not saying they're not *idiosyncratic, but at least now there's some accountability for why changes were made and when.*

Or at least prove to my committee how much work I am or am not doing

4.3 SUGGESTIONS FOR SURMOUNTING NOTEBOOK CHALLENGES

These might belong in the earlier section? Or the earlier sections analyzing OS belongs here

Some thoughts: Since being open is *not* the same as being accessible, transparent, or even useful (re: Slee, *Notes against openness*); anything that wants to accomplish those goals needs a lot more thought and planning. I think open notebooks are only a small component of what sharing procedures is; said differently, "notebooks" need redefinining. The open, accessible, etc. notebook online is identical in terms of words, graphics, etc. to my paper notebook – in many instances, it's even better. It is not, however, *complete*. No one would ever look at my paper notebook and be able to coherently trace protocols as they evolved; at least, not without my help. A direct transfer of notebook pages to web pages doesn't help the situation.

I think a more ideal situation is *not* a transfer of paper to electronic.

*This is mostly useful when John is upstairs on the 3rd floor and I forget to bring my notebook up when I ask him questions, but it's also been used when I'm traveling and unexpectedly meet someone who's interested. And then I have something to show *right then*.

Rather, multiple layers of publication - namely, including methods. Real protocols, but protocols as you might write them out for someone in your lab running an experiment for you, instead of bite-sized uber-simplified "Procedures were performed as described previously." Following an open lab notebook with nothing else is hard; using it as a reference to supplement a larger work sounds like an incredible resource.

5 REPRESENTATION & SCIENCE

ACRONYMS

OEAC Other Euro-American Countries, including Australia, NZ, and Canada

ROW "Rest of World", anything not already included

From a "purely" numbers standpoint, scientific production is unequally distributed around the world and on a variety of axes. This is basic question of representation: where are the women? Where are the colonized countries? Where are the black and brown researchers, where are the queer and trans researchers? Who gets to make science?

5.1 DEVELOPING COUNTRIES

Numbers are boring, but wow, are they depressing.

In a retrospective of 5 major medical journals, Sumathipala et al.[40] examined contributions by 4 geographic areas: the UK, USA, Other Euro-American Countries, including Australia, NZ, and Canada (OEAC), and"Rest of World", anything not already included (RoW). RoW, on average, contributed 6.5% of the research literature. The highest seen was in the Lancet (12%), and of the 151 RoW articles involved, 68.9% involved authorship from a developed county in Europe or North America. 15 original papers in the journals had data from RoW w/ no RoW coauthors.

The 10/90 problem is a clever name for enormous inequity: only 10% of the world's resources are used for 90% of health problems; in the author's previous survey of psychiatric journals, only 6% arose from regions accounting for over 90% of the population.

Science has a WEIRD problem...but like, actually. this not even accounting for gender or age

This study selected the highest impact general purpose medical journals, of all issues in one calendar year (either 2000 or 1999), and examined authorship (by institutional affiliation) and the methods, to ascertain the geographic origin of data.

Some notable variations in the regional data: 2 countries (Japan and Israel) contribute a 5th of the RoW-published literature, while China and India combined (the two most populous countries in the world) contribute a total of 13%. Only 31% of the total articles were entirely independent RoW.

5.2 GENDER DISPARITIES

> "Although there are more female than male undergraduate [especially in "softer" scientific fields" and graduate students in many countries, there are relatively few female full professors, and gender inequalities in hiring, earning, funding, satisfaction and patenting persist."

Quantitition of gender disparities in measures of scholarly output and has been few and far between – "highly localized, mono-disciplinary, and dated"; they take little account of the rise in collaborative research

etc. Larivière et al.[25] analyzed the relationship between gender and research output (authorship), collaboration extent (co-authorships) and scientific impact of publications (citation count, according to the Web of Science); The authors analyzed >5 million research papers and reviews with more than 27 million involved authors, assigning gender using data from the Social Security database.

Web of science, of course, is an extremely flawed way to do this because it barely includes anything that isn't the US or UK. See the sections on citation factors and global publishing

Some results:

1. in the most productive entries, all articles with women in dominant author positions receive fewer citations than those with men in the same position
    a) accentuated by domesticity [nationality-wise] - women benefit less from the extra citations accrued by international collaborations
2. globally, women account for <30% of fractionalized authorship, men are >70%
    a) 1:1.93 women:men first authorships
3. South America & Eastern Europe had best gender parity
    a) female authorship generally more prevalent in countries and/or states with lower output
4. **impact:** when a woman is in prominent position (sole authorship, first-author, last-author), paper attracts fewer citations; holds for national and international collaborations

There are, of course, major limitations, the biggest one being obvious – age has an enormous role to play. Many trends are likely not actually markers of overt discrimination, but rather that women aren't making it to the top ranks of science and thus are not in a position to be publishing or collaborating on the most important papers.

Basically, this is quantitative numbers to back up what women have been saying for years – there are tall, tall hurdles to jump. In 17% of countries, active scientists are equally represented: but fewer than 6% Web of Science countries come even close to gender parity in # papers published.

West et al.[44] published an extremely similar paper in PLoS one the same year, without the global analysis component but with even more papers as part of the analysis. Their source was the JSTOR corpus, "a body of academic papers...spanning five centuries". They look at similar variables – authorship order and overall percentages. This includes the humanities research as well, which is interested.

with the mention that publication counts obviously are relevant in tenure *discussions, e.g. hiring e.g. perpetuating cycle*

5.3 RESEARCH ACCESS & ASSESSMENT

5.3.1 *Global Citation Indices*

Wagner[42], in *Unseen Science: Scholarly Publication in the BRICs but not in the Web of Science*, examined representation in citation indices and found only 4% of developing countries journals were counted. Luckily, this isn't country specific – only 4% of journals in *any* country are indexed. Which is not so much an indictment of what countries get indexed, but of impact factors in general.

Also, HUGE points for their methods and reproducibility, e.g. creating the gender browser and communicating with me about making that something to apply to individual libraries in reference managers. Secret part of my div that may or may not manifest depending on the cooperation of these authors

5.3.2 *effect of open access publishing* on *access*

What is the influence of publishing OA on research attention? It's greatest impact is the development of world participation.

> Across sub-fields, the impact of commercial online availability was positive, statistically significant, and on average 40% larger than the OA effect, suggesting that most researchers rely on institutional subscriptions.
>
> The influence of OA was more than twice as strong in the developing world but was less apparent in the very poorest countries where electronic access is limited (Fig. 1D).[12]

Good/bad/always more complicated

6 CRITICAL NEUROSCIENCE

6.1 FEMINIST SEROTONIN STUDIES

6.1.1 *Stem Cells and Gender*

Problems – points of analysis – come in the form of either not enough attention to gender (seatbelts, heart attacks, stem cells) or too much attention to gender.

Stem cells: They have a "sex", in the sense that there is a chromosomal makeup, and it matters. See Ray et al. [35] and Gendered Innovations.P19s are karotypically 'male' – i.e. XY. This has consequences for how they differentiate and how their signaling pathways work downstream of differentiation.

6.1.2 *Serotonin & Gender/Race*

Questioning the use of race as a categorization without defining what is meant *by race, re feminist/womanist analyses of the use of racial categories in medicine*

- serotonin receptors are differentially distributed and have different activation levels in male vs. female rats [26,5,45]
  - especially the 5-HT2_a receptor, implicated in hallucinogen signaling
- pharmacogenetics are differential along racial and gender lines [31]
  - depression (associated with the 5-HT system, among others) shows different responses along racial and gender lines [4]
- if hallucinogens and signaling differentially affect men and women and different races/ethnicities, [27] then that has to be studied in model systems as to how it might affect plasticity and molecular effects

  > "However, the binding of serotonin-2A receptor measured with [$_3$H]ketanserin was significantly higher in females in all regions of the hippocampus." [45]

  - modulated by testosterone

6.1.3 *Serotonin Model Systems*

If serotonin systems are affected by testosterone (re: Zhang et al. [45]), how would incorporating androgens and estrogens into the cell culture dish affect the effectiveness of P19s as a model system?

6.2 CULTURAL NEUROSCIENCE

6.2.1 *Hallucinogens*

I'm a little conflicted about the relevance of this section, but I also am really *excited about it, and the possibilities for re-envisioning how I could do cultural molecular neuroscience.*

Psychotropic drugs have a rich and important history of spiritual and mental use in nearly every human culture. It seems that any and every culture has sought new insights and views with the help of native pharmacological agents. Although largely reduced now to their chemical structure* in the labs funded by the NIH, most of the compounds derive

*site of reductionism?

from different cultural traditions. Peyote (active ingredient: mescaline)[†] has historically been used by the Native American church, a right they successfully fought for in court. Ayahuasca (active ingredient: DMT combined with monooxygenase amine inhibitor) is a traditional South American drug. LSD is derived from ergot, a fungus – it's often thought that outbreaks of "witch craft" in medieval Europe are actually attributable to ergot contaminations.

Source for ergot and historical significance

On a related note – how presumptuous to take drugs from indigenous cultures and push them into the laboratory. Is plasticity and all of the signaling mechanisms relevant if the experience isn't included? Hallucinogens are notoriously sensitive to situation – or rather, individual interpretations of a situation. The quality (and thus long term effects) of a psychotropic experience is created through the *interplay* between environment and individual; like facts, it doesn't wholly reside in either, or even at the mere intersection. Trying to pull that out in a lab environment, is, as Fleck describes, not just a translation of information from one knowledge realm to another, but a full fledged transformation such that the ayahuasca in the lab is only nominally related to ayahuasca in practice.[‡]

6.3 TURTLES ALL THE WAY DOWN

"Neuroscience" as a discipline constructs a history tied to Galen and Aristotle and ancient Sumerian hieroglyphs,[1]. More realistically, "neuroscience" isn't a discipline, but rather a heterogeneous mush of an extremely broad range of nearly unrelated subfields. That said, neuroscience, the field, was deliberately named, funded, and institutionalized to lie at the intersection of complementary disciplines – interdiscplinary from the start.[1]

Disciplines aren't real, basically.

6.3.1 *Interdisciplinary studies*

Need to define scientism/find description from Crit Neuro. Also page numbers.

- In *Critical Neuroscience,*Choudhury and Slaby[7] propose "interdisciplinary" as a code word for scientism (which I recall as being a bad thing)
- Situating the brain/cognition within a culture is an expanding trend (which I should be happy about). The large problem is that when "culture" and its importance are talked about in scientific settings, culture is a fixed quantity with Right responses. Hispanic medical patients require an interpreter; cases of Vietnamese

[†] A comparison of the plant/spiritual context to the chemical structure should go here to demonstrate how we separate them out. With an analysis of the rights of traditional groups to use those drugs [re: NA church lawsuits], and also the danger of deforestation and environmental destruction to *traditional* methods of harvesting plants – making them only available with clinical approval – and chemical synthesis methods, which probably contribute to pollution and destruction.

[‡] Anne Fausto-Sterling, and many others, talk about knowledge outside the academy – communal, social, and indigenous knowledges. Hallucinogens have amazingly well-documented and supportive communities. Taking psychotropics is, for many, a spiritual and deeply-prepared for experience. Users are often hyperaware of the chemical effects, interactions with medical conditions or other drugs, how to set scenes, how to guide their mental state in meaningful ways – in short, expert and specific knowledge more typically associated with discerning scientists than hippies in the woods. But hippies in the woods may know a lot more about how to *use* those drugs than scientists who have never experienced them and treat them solely as tools in a molecular toolkit.

epilepsy require a cultural translation between spiritual/traditional Vietnamese and doctors with curative drugs.

- Epigenetics – the metaphorical and physical incorporation of social effects into the genome, is a way of explaining what culture does for human development, creating a narrative of "soma to society". But incorporating social factors as a genomic part of humans also creates new "at risk" populations, making the epigenetic traces of historical marginalization into fundamental parts of those groups that need fixing. [23,33]

6.3.2 *Molecular and genetic reductionism*

"Reductionism" is a bit of a catch all. To a large extent, the Western scientific traditions is entirely focused on reducing systems to their smallest working unit,, with the intention of finding out one "answer" and threading it into many other answers to form a kind of tapestry of knowledge. The reduction and simplification of systems roughly correlates with the notion of "pure" sciences, pure being perceived as better, "harder", and (incidentally, of course) more masculine. In the biological sciences, and in the neurosciences, reductionism is generally

- generally a trend in the biological sciences – maybe due to perception of increased objectivity/hardness (a la physics and chemistry).
- Somewhat inherent to "neuroscience", since the ultimate goal is to reduce function/cognition to a set of circuits/cells/meaningful small and completely circumscribed/understood units.
- Where does it come from?
  - What goals are there and how does reductionism accomplish them for us? What is good and not good about applications to neuro? Can and should cell studies be used to "answer" or explore questions about cognition? What do we lose when we "solve" disease in vitro? §
- Personalized medicine; or personalized neuroscience is still a way of reducing the individual to the cellular and genomic information, without accounting for personhood. "Personalized medicine" is not actually personalized; it's genomic. Relying on genetic information to give meaningful information about health care and responses is hardly specific to an individual's needs and abilities, as we'd like a feminist science t be.

§A sensible research strategy (isolationism/reducitonism) becomes a metaphysical commitment to a system, where the system is reality. For us, cell lines are indicative of some reality. It's plausible that scientists themselves know their work to be missing enormous sweeps of holistic knowledge, but any written work rarely acknowledges it. Grants and papers imply and argue, point-blank that molecular work is the answer to XYZ – and not just the answer, but the problem to be studied as well.

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