MAPPING PSYCHEDELIC SCIENCE
Signaling Pathways and Cultural Spaces

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ACRONYMS

NON-SCIENCE STUFF

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

IP Intellectual Property

FLOSS free/libre open source software

GPL GNU General Public License

GNU GNUs Not Unix

OS open science

FLOSS free/libre open source software

GPL GNU General Public License, the founding document of the Free Software Movement

OS open science

OA Open Access

APC Article Processing Charge

IF Journal Impact Factor

STEM Science, Technology, Engineering, and Math

DIY Do It Yourself

HGP Human Genome Project

Tools

WOK *Web of Knowledge*

BLAST Basic Local Alignment Search Tool

SDSS Sloan Digital Sky Survey

Organizations

FSF Free Software Foundation

CIA Central Intelligence Agency

NCBI National Center for Biotechnology Information

HEW Department of Health, Education, and Welfare

USPHS U.S. Public Health Service

PLOS Public Library of Science

OKF Open Knowledge Foundation

OECD Organisation for Economic Co-operation and Development

Places

FDA Food and Drug Administration

MIT the Massachusetts Instituite of Technology

NIH National Institute of Health

NYU New York University

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

ROW "Rest of World", for what that's worth

BRICS Brazil, Russia, India, China, South Africa, considered the rising economic and scientific powerhouse countries

ROW "Rest of World", for what that's worth

SCI Science Citation Index

WOS Web of Science

SCIENCE

fMRI functional MRI

FACS Fluorescence Activated Cell Sorting

5-HT 5-hydroxytryptamine

LSD lysergic acid diethylamide

MESCALINE 3,4,5-trimethoxyphenethylamine

OCD obsessive-compulsive disorder

DMT *N*,*N*-Dimethyltryptamine

DOI 2,5-Dimethoxy-4-iodoamphetamine

DOB 2,5-Dimethoxy-4-bromoamphetamine

DOM 2,5-Dimethoxy-4-methylamphetamine

STP Serenity, Tranquility, Peace

MDMA 3,4-methylenedioxy-methamphetamine

PET positron emission tomography

DEA Drug Enforcement Administration

MAOI monoamine oxidase inhibitor

CHO Chinese Hamster Ovary

HEKS human embryonic kidney 293 cells

SIRNA small interfering RNA

PTSD PostTraumatic Stress Disorder

PPV Positive Predictive Value

Signalling Pathways

GPCR G-protein coupled receptor

G-PROTEIN guanine nucleotide-binding proteins

GRK G-protein coupled receptor kinase

GDP guanosine diphosphate

GTP guanosine triphosphate

PLC phospholipase C

IP_3 inositol triphosphate

DAG diacylglycerol

PKC protein kinase C

PKB protein kinase B

CAMP cyclic adenosine monophosphate

PLA$_2$ phospholipase A2

AA arachidonic acid

IEG immediate early genes

RSK2 ribosomal s6 kinase 2

PI3K phosphoinositide 3-kinase

C-SRC tyrosine-protein kinase Src

PTX pertussis toxin

MAPK Mitogen-activated protein kinase

Part I

INTRODUCTIONS

1 INTRODUCTION

Division III is a year long undergraduate thesis project. For me, it's both articulating and creating a way to "feel okay" about studying psychedelic drugs when I also see my self/scientific work as enmeshed and entangled in socio-political power struggles.

Three years ago I came to study neuroscience at Hampshire, with a naive and relatively simplistic fascination with "basic research" into cellular aspects of cognition and perception. After hitting my first academic pay wall, I discovered the free/*libre* software movement and its scientific sibling, open science. Both movements acknowledge more than just the functionality of science and technology; they include society in their calculations of technology and science. While open science is not explicitly political, it has extremely strong undercurrents of an idealistic moral spirit focused on something greater than just science.

I have since learned or come to believe that my interests, and what I do with those interests, has an impact on the world. This is both self-interest, for otherwise what's the point? and self-recrimination; my impact on the world is my responsibility, and I need to understand the consequences.

The thread between all of the questions/answers I explore here is: Who should control the flow of knowledge?

Cultural Contexts

Chapter 2 describes the theoretical underpinnings 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.

Troubling Scientific Systems

Chapter 3 starts where more general criticisms of science stem from: the scientific ecosystem, and the ways in which the current system of reward, funding, and prestige distorts the pursuit of truth and knowledge in science.

Chapter 4 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.

Chapter 5 continues on a similar theme of scientific production, considering the question of representation within the global scientific community.

Chapter 6 is the my own scientific system, and the part that qualifies me as a Natural Science student at Hampshire. It is a quasi-comprehensive review of the evidence that psychedelic effects are mediated

Flows of Knowledge

The next three chapters turn to more personal and complex situations, the "heart" of my project.

Chapter 7 is personal, code- and computer-based results. It's a description of my attempts to implement open science proposals into a biological project, and the myriad complications and barriers I've surmounted – or not – in doing so. It offers a description of what I think the open science movement is missing on a practical implementation level. It also offers a small bibliometric analysis, examining gender representation in my work in an attempt to trace how individual researchers perpetuate gendered systems.

In Chapter 8, I explore the possible implications of "fixing" science through greater sharing and dissemination of information. This hegemony is not merely theoretical. The proposed 'solutions' to the scientific systems's failures have serious implications, from a science studies and a feminist point of view, on the production and kind of knowledge production.

Chapter 9 is the capstone chapter of sorts. 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, and how control of the flow knowledge continues to shape all kinds of knowledge production.

1.1 TERMINOLOGY NOTE: GLOBAL DIVIDES

There is a widely-acknowledged economic, and corresponding scientific, gap between areas of the world. During the Soviet era, this was a West-East or First/Second/Third world split. In 1949, Harry Truman used the term "areas needing development," and for many years, the divide was between developed and developing countries.

While the "divide" itself is as porous as any binary, and subject to uncountable caveats, we need some term to reference the different research capacities.

"Global South" is the currently used term, without many of the hierarchical connotations of "developing world" or "Third world." It divides the globe along the equator into the economically wealthy (The U.S & Canada, western Europe, plus Australia and New Zealand) and poor (South). As a term, it eliminates the global poor north of the equator, ignores the immense diversity among countries, and continues to define the scope of the world largely around the the G8 nations of the North.

G8 - France, Germany, Italy, the United Kingdom, Japan, the United States, Canada, and Russia

"Majority world" is an alternative coined by Bengali writer and photographer Shahidul Alam.[?] It highlights that the G8 countries making world-shaping decisions actually represent a tiny fraction of humankind, and the rest of the world has a working and loud voice.

I use minority world, the counterpart, somewhat interchangeably with "the West" and the "North".

2 MAPPING SCIENCE

Scientific work leads to technology that empowers; science provides a sense of systematic inquiry that satisfies some deep drive to understand and explain the world around us. Science is part of a long and storied heritage of bold exploration, innovation, and human ingenuity.

Science is, simultaneously and harmoniously, a handmaiden to social-technical progress and a crucial strut in the reinforcement of systematic societal inequities. It is both a compelling and evidence-driven narrative about biological and physical realities, and a knowledge necessarily developed in and shaped by a social context. The question that opens most scientific philosophy classes is "what is science?" The point is not to answer it, but to teach students to question how our concepts have been structured and bounded. I am more interested in understanding what science *does* rather than in the concept, how it moves into the world, shaping and being shaped in the process; in many ways, the science is in the doing. "Science" is not any one grand enterprise. For our purposes, it is roughly sketched as

Science, a technological and systematic enterprise building and organizing knowledge in the form of testable explanations and predictions about nature and the universe; *progress*

***Science*,** an international weekly science journal, published by the American Association for the Advancement of Science

Science, an individual way of exploring the world from a specific cultural/philosophical/technical viewpoint; a practice and culture and a "culture of no culture"; knowledge wrapped up in consequences; technoscience, where the knowing of science is inseparable from the doing of technology

Science, the enterprise, is enabled by *Science* and its kin, scientific journals that publish and codify communication. Science, the way of exploring the world, underlies the enterprise and the journal; and science, whatever else it may be, is *made by scientists.* If science has an effect on the world, we, the producers of scientific knowledge, have the responsibility of taking care for what we make.

2.1 ETHICS VS. VALUE: SCIENTIFIC RESPONSIBILITIES

This is not a discussion of bioethics, that part of the duties and responsibilities of an academic scientist managed locally by Institutional Review Boards and systematically by the Republican Party. Ethics are part of the limited frame of experimental design and execution. The notions of informed consent, "do no harm", and the humanity of people are what I would call ethical responsibilities, and are critical and basic scientific practices. But that's not exactly what I mean. I instead am thinking of the underlying value-assumptions guiding research assumptions and effects.

Take, for example, a well known case of biomedical ethical failure: Tuskegee Syphilis experiments. In 1932 Tuskegee, Alabama, the U.S.

and they were testing with the Wasserman reaction!

Public Health Service (USPHS) enrolled 400 syphilis-positive black men to observe the "natural" course of untreated, latent syphilis. The study heads began by enticing their participants with explicit promises of free health care and treatment; they tested them for syphilis and concealed the information from their subjects. This led, of course, to the spread of the disease through the local community. To ensure the disease stayed "natural", the USPHS researchers took steps to prevent their subjects from being seen or treated by local physicians. When the draft came through in 1941 and tested for syphilis, the study leaders supplied the draft board with a list of names to be excluded from treatment; the U.S. Army complied. In 1932, no effective syphilis treatment existed, although it was believed that certain mercury ointments could slow its course. Twenty years into the study, when penicillin *had* become established as an effective syphilis treatment, researchers increased their efforts to prevent interference by the outside world. Halfway through the study, more than 30% of the test group had died *directly* from advanced syphilitic lesions, with many more suffering from secondary complications.[?] The "study" finally ceased forty years after it started, in 1972, after a whistle-blower publication in the *New York Times* and Congressional hearings.

In 1973, a year after the cessation of the study, the Department of Health, Education, and Welfare (HEW) released a damning report of the ethical failures over the course of the study. The report focused on the (1) lack of treatment, arguing that once penicillin had been discovered, it should have been used and (2) the "informed consent issue", wherein the report argued men had submitted to *an* experiment, merely without being told what the experiment entailed. This remains the dominant interpretation:

> "...controversial for reasons related to ethical standards, primarily because researchers knowingly failed to treat patients appropriately after the 1940s validation of penicillin as an effective cure for the disease they were studying."
>
> Wikipedia on the Tuskegee Syphilis experiments[?]

To our modern sensibilities, this was a complete ethical failure on the part of the scientists involved, their funding body, and the hospital. The criticism are founded in notions of what a *good* doctor would have done differently; clearly, the involved doctors made a relatively isolated mistake by not practicing rules of informed consent. These are largely ethical considerations, without regard to the unique cultural context of the experiment.

The HEW report and our current understanding elide the deep social structures that *allowed* the Tuskegee experiments to be conceptualized as a valid course of research. Doctors and researchers discounted the socioeconomics of black America, arguing that better medical care could not alter the "evolutionary scheme" of things. The discovery of penicillin had no bearing on their decision to watch the natural course of death proceed. If it had, the men would have been given the (believed to be effective) mercury treatments. Researchers never *intended* to treat these men, because in their (white) eyes, black men were a subhuman species – animalistic, promiscuous, and a fascinating object of research.[?]

The most critical part of this, for us, is that these researchers genuinely believed in what they were doing, and they were implicitly backed by the scientific community. After the initiation of the study in 1932, *JAMA* (formerly the *Archives of Internal Medicine*) The details of the study were available for the medical community starting in 1936**?** , with 10 more publications 1964.**?** hidden to the scientific community, yet it took a whistle blower and a Congressional Hearing to get stopped.

JAMA: The Journal of the American Medical Association

2.2 SCIENCE STUDIES

In 1935, Ludwik **?** published a small monograph in Germany. Although it anticipated the conclusions of one of the most cited books in post-WWII history, Thomas Kuhn's *Structure of Scientific Revolutions,* it remained relatively obscure until the**?** *The Genesis and Development of a Scientific Fact* proposes that scientists are the creators of facts, rather than mere observers; or rather, that the very act of scientific observation also creates facts. Fleck likens scientific thought collectives to a group of people who together produce an idea; facts held in a common tension, without a distinct origin. "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.

Pertinent here is the discussion of different kinds of knowledge, and the necessarily simplified translational nature of communication. The most evocative narrative is the interactions between a doctor, a bacteriologist, and the mother of a sick child. The doctor, passing on the throat culture to the bacteriologist from the child, asks for a diagnosis. The response to the doctor would be "... the microscropic specimens correspond to diptheria," ignoring most of the technical information. However, the *same finding* conveyed to another bacteriologist would include morphological, staining, and arrangement notes; and "... based on the origin of the examined material... the diagnosis [of diptheria] seems well established." And the *same finding* conveyed again to the mother of the child would only be "your child has diptheria." None of these are wrong, but the fact of needing to *communicate* requires simplifications for communication between individuals.

Fleck, p 114-118

Those same simplifications and transformations of knowledge-concepts are in journal science, the fragmented and idiosyncratic 'cutting-edge' of science. As journal science is incorporated into *vademecum* science, , built from a mosaic of journal science and communication and personal experience, the collective of researchers shapes which facts are included. By the end of it, the "true creator of a fact is not an individual but the thought collective."**?**

Fleck, p. 123

vademecum *"handbook", the collected working knowledge of a field or discipline*

Fleck, Kuhn and their many philosophical heirs and contempories offer compelling arguments that science is, yes, evolution, but not evolution *towards* anything in particular. Fleck's culturally-conditioned science is a stepping stone onto a bigger question of not just what science *is,* but what it *does,* what values are built in.

2.3 CONTEMPORARY SCIENCE

The modern scientific system began in an era of European colonialism, in 1665, with the major powers sending 'civilizing' missions to the Sino-Japanese coasts, the Indian subcontinent, vast swathes of Africa, South

America, North America, Australia and the Indonesian islands. The beginnings of biological classifications and the Scientific Revolution, coincided with the gentlemen scientists of Darwin's era, rooted in exploratory voyages and specimen collection by Europeans. The Scientific Revolution was enabled by and allowed the continuing expansion of European powers into the rest of the world.

Take, for example, malaria. For much of early European missions, malaria proved an insurmountable hurdle to the troops of colonial powers. The interior of Africa and the swampy Chinese coast were rife with mosquitos and their disease; troops died due to disease and infection at a rate many times higher than actual warfare. The same colonial missions of research, proselytizing, and conquering were accompanied by botanical missions and collections. Eventually, Europeans, via the acquired medical knowledge of Jesuit missionaries in South America, came into contact with the Peruvian bark of the cinchona tree. The bark contains quinine, one of the earliest effective treatments for malaria. The discovery, classification, and medically-useful malarial treatment allowed the penetration of European troops into hitherto inaccessible areas.[?]

Closer to temporal and spatial home, racism – the peculiar brand of American racism, derived from slave-owners desperate to justify their brutality of human bondage – was created through the collusion of science and society, specifically a science that carefully cataloged and characterized the way black men and women differed, and were therefore lesser, than White slaveholders. Darwin's great proposal of evolution let scientists justify the status quo (White men, White Women, Black men, Black women, in that order) as a mere consequence of natural selection.[?]

That was the 40's and 50's – today, we have genetic surveillance. Genetic information is increasingly part of publicly accessible medical records. Police in the some areas of the United States and in the United Kingdom have the legal right to collect blood samples without warrant or permission, not only after a conviction, but after merely an arrest, or in some cases, from the family members of suspected criminals. The disproportionate arrest and imprisonment of black men means the genetic information of 77% of black men aged fifteen to thirty-five, compared with only 6% of white men, is captured in the U.K's database. An unequal form of racialized biomedical surveillance that, with the increasing power of biological analysis, will inevitably be used to perpetrate new injustices.[?]

A science of homosexuality focused on homosexual men, not women, not bisexuals, and not trans folks

We have the sciences of homosexuality. If being gay is a genetic inheritance, then we should be careful to screen our prenatal children and not allow gay men to donate sperm.. If it's cultural, we should be more careful to police the kind of culture we give our children, carefully isolating them in heterosexual spaces. We could cure the queers, if only we knew *why* they were homosexual.[?]

This is the scientific heritage, the accumulated knowledge upon which we build our futures, and it is not exempt from criticism more commonly leveled at explicitly political institutions. At the same time, the undeniable power of science and technology to do "good" – hormone therapy for medical gender transitions, Internet communities for otherwise isolated activists, the reclamation of environmental sciences by Native communities, technologies that re-enable disabled bodies, pharmaceuticals that prolong lifespans, raise quality of life, and allow

people to take control of their reproductive health* – means we need science to keep pushing. Not to mention the insatiable curiously to understand and the delightful appeal of "basic" research, of discovering something new.

Science is not going away, and nor should it. But to ignore our scientific inheritance, the long-term complicity between science and power, and the role of individual scientists in perpetuating and creating power dynamics is to be neutral in the face of injustice.

2.4 FEMINIST THEORY

"...Questioning representation with a vengeance."

What I now call feminist science studies emerges out of academic feminist and activists against white supremacy, patriarchy, heteronormativity, and ecological destruction working on ways to critique science as a social institution, and using that critique to forge new ways of asking and answering scientific questions. Feminist science studies is then, like most fields, at confluence of many networks.

For a solid history, see **?**

Donna Haraway's *Cat's Cradle: Science Studies, Feminist Theory, Cultural Studies* drew a picture of a field at the intersection 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...gender and race are built into practice 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."

*Given access and governments that don't insist on fucking bullshit, lookin' @ you, United States.

-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? Why bother? Why shouldn't we, as one professor urged me, "cut the sociology, focus on the science"?

2.5 IN PRACTICE: "ASKING DIFFERENT QUESTIONS"

Feminist science studies both allows and demands practicing scientists engagement with more than "just" science. It lets us ask questions of representation in our labs, our literature, 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 race, physical ability, nationalities, and other sociological classifications.

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

- an examination of the scientific *construction* of race and gender perpetuated by the perceived objectivity of the sciences???
- the deep paradoxes involved in the ab/use of women's bodies in pursuit of reproductive technologies??
- the shaping of science by gendered and racialized metaphors and languages,?? and the historical complicity between scientific exploration and colonialism, misogyny, and racism (all at once, not as isolated variables)???
- challenging the artificial boundaries between "basic research" and nature/culture to explain a rapidly-growing scientific-industrial complex; linking basic research to community activism for women's rights and environmental movements.?
- re-examining the "global" nature of research findings?
- re-conceptualizing what kind of knowledges are considered valid and legitimate ways of knowing??

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.

2.6 WHY CARE?

Because feminist science asks questions that are fundamentally geared towards addressing socialized inequalities in science, it can (and has) help scientists take those inequalities into account. Scientists (in theory) care about the effect their work has, to cure cancer or send someone to space. If they are in fact interested in those effects, it's a fundamental part of scientific work to consider the values that are part of scientific work.

For this thesis, my feminist questions are largely about control of information. If knowledge is power, how can we better distribute both?

Who has the right to control information? Who can control it, and what are ways to circumvent systems of power?

My questions are focused on the value systems of scientific knowledge control and flow in scientific ecosystems as a whole, and on the "revival" of psychedelic science. From an original interest in increasing access to knowledge and understanding the molecular pathways of psychedelics, I've come up with a whole host of new understandings around communication and participation.

Both open science and psychedelic research are tied to local knowledges and global science systems. Who has the right to control them?

Part II

SCIENTIFIC ECOSYSTEMS

3

SCIENTIFIC STRUCTURES

Science, an international weekly science journal, published by the American Association for the Advancement of Science;

In the history and sociology and feminism of science, we talk about science as a commons of knowledge. The scientific project "builds on the shoulders of giants"; the intense, methodological, and highly-specific technoscientific answers we seek in scientific inquiry are building blocks to theories. To stand on those shoulders, we need communication – we collaborate within buildings and between labs, we maintain social ties that influence gifts of stem cell lines and antibodies, we go out to bars at conferences, we track the ever-cresting wave of published academic research. Science is yes, the experiment, but the experiment and information gathered by others goes hand in hand.

Moreover, scientific progress is essentially meaningless unless it's communicated ("success in conveying one's ideas or in evoking understanding in others.") In the philosophical tradition of Ludwik **?**'s work, facts only emerge from a community process of discussion and assessment.**?** In a more practical sense, there's no benefit in synthesizing the mythological cure for cancer unless you (a) get community credit for your and/or (b) cancer patients actually receive the magic drug.

Science has always been tied to the communication networks of researchers and amateurs. The 1665 establishment of the first journal, the *Philosophical Transactions of the Royal Society of London*, "aimed at creating a public record of original contributions to knowledge."**?** This "original" journal was a bi-annual periodical of "letter-excerpts, reviews and summaries of recently-published books, and accounts of observations and experiments from European natural philosophers", and remained a money-losing endeavor until the middle of the 20th century.**?**

Today, the structures of scientific communication number over 25,000 journals, along with an ever-expanding and specializing network of conferences, blogs, and tweets, to name a few. The rate at which scientific information moves within communities and between scientists and the "public" has increased dramatically, in both speed and scope. Like most other institutions no longer limited to the mail system and the printing press, the advent of Internet and the increasing role of digital technologies has a transformative effect on communication, and thus science itself.

There are, however, crises brewing in scientific communication, even for those within the ranks of those firmly ensconced in the scientific establishment. Scientific communication has always been limited, in both the scope and application, and underwritten by concerns about prestige rather than progress. Academic scientific work his constrained by funding issues, an increasingly competitive academic environment where only 1 in 10 PhD recipients will find a stable (i.e. tenured) job in their academic field,**?** outside pressures that lead to data fudging, an increasing amount scientific spin on what an experiment has actually accomplished, worst of all, and a decreasing amount of "purely exploratory" research.

what kind *of progress?*

SCIENTIFIC ACTIVITY	COMMUNICATION REQUIREMENTS
idea discovery hypothesis generation	awareness lit. review informal discussion
funding/approval	lit review
conduct research	awareness
disseminate results	formal publication informal dissemination

Table 1: communication requirements in research cycle (**?**)

The criticism of production of knowledge is reaching a fever pitch of excitement about fraud, funding, reproducibility, access, and a flock of other issues. The scientific ecosystem has been metaphorically thrust into the punishing light of the democratizing Internet, and it turns out science isn't the foolproof method our 7th grade biology teachers said it was, to everyone's disappointment.

3.1 COMMUNICATION CYCLES

At every step of even the canonical research cycle, communication with and from other researchers plays a role. It is impossible to participate in any academic-scientific discourse without both intellectual and financial access to the communication. The "scientific process", suffused with cross links and interpolations, but communication is crucial to all of them (summarized in Table 1).The concerns around a scientific transformation persist along all steps of the research cycle, starting with publishing and literature access.

3.2 ACCESS TO KNOWLEDGE

Bernice Dahn is the chief medical officer of Liberia's Ministry of Health, where Vera Mussah is the director of county health services. Cameron Nutt is the Ebola response adviser to Dr. Paul Farmer at the nonprofit group Partners in Health.

> "The conventional wisdom among public health authorities is that the Ebola virus, which killed at least 10,000 people in Liberia, Sierra Leone and Guinea, was a new phenomenon, not seen in West Africa before 2013.
>
> The conventional wisdom is wrong. We were stunned recently when we stumbled across an article by European researchers in *Annals of Virology*: "The results seem to indicate that Liberia has to be included in the Ebola virus endemic zone." The paper was published in 1982.
>
> There is an adage in public health: "The road to inaction is paved with research papers."
>
> . . . Part of the problem is that none of these articles were co-written by a Liberian scientist. The investigators collected their samples, returned home and published the startling results in European medical journals. Few Liberians were then trained in laboratory or epidemiological methods. Even today, downloading one of the papers would cost a physician here $45, about half a week's salary."
>
> Bernice Dahn, Vera Mussah, and Cameron Nutt[?]

"Yes, We Were Warned About Ebola", *The New York Times*

Papers are crucial for scientists keeping up to date with new techniques, with writing backgrounds to grants and formulating new research questions. Literature access for academic scientists is typically mediated through institutional, library-based journal subscriptions. Surveys of academic researchers, largely those at high-profile and wealthy minority world institutions, report their access to the literature is "generally good and improving."[?] However, 84% of librarians, responsible for overseeing fiscal access to scholarly resources, disagreed with "There is no access problem to scientific publications in Europe."[?] For the non-affiliated researcher or member of the public with Internet access, just 35% of the peer-reviewed literature is freely available, with this figure falling to less than 30% for recently published work.[?]

And by available, it's the PDF version, the article is likely in English, and is almost digitally data-heavy

3.2.1 *The rights to knowledge*

At it's most moral, access to knowledge – often defined as synonymous with literature – is a human right. Scientific research is conducted for and funded by the public interest.[?] Developments in ecology can immediately effect ecosystem management and conservation policies;[?] materials science has implications for building and design. Advances in medical knowledge can be literally life-saving; if it were for any reason other than profit, denying information about health interventions to nurses and doctors would have already been condemned as a human rights violation. Specifically, in the case of healthcare workers, barriers to accessing scientific literature[?]:

1. Prevent healthcare workers from accessing information,
2. Prevent policy makers from accessing info on building better systems,
3. Impede research capacity and sustainable country-specific scientific development,
4. Clinicians, health policy-makers, and researchers are unable to participate as equals in global science, and
5. Contributes to the marginalization of majority world, because subscription-based journals rely on subscriber money, and thus have no vested interested in publishing the health issues of the poor areas of the world

Literature is necessary for scientific progress, and scientists working in more resource-poor areas are still working and still need to participate in global discourse. Without very good institutional affiliation, most of the supporting scientific history is out of reach. The lack of access to literature hinders future scientific work from progressing as rapidly and efficiently as it might otherwise.

Yet another of the conflicts surrounding literature access are due to the changing collaboration between scientific authors and publishers in the digital age. Essentially, the production of the manuscript is done for free; or rather, on grant money, but the publisher still profits fairly handsomely. A manuscript travels through several stages.

1. Authors/labs submit their manuscript (*gratis*)

2. Publishers/editors and editors review the paper.
    a) They can either reject outright, or submit for peer review
3. The journal coordinate the peer review of said manuscript, shipping it out to 1-3 other academics in the field.
4. Academics review the paper, give feedback and suggestions and send it back to the journal (*gratis*).
    a) During the months of the process, the submitting author can do nothing else with the manuscript.
5. Revisions by the original writer, and hopefully the journal agrees to publish it.
6. Submitting lab pays a per-figure and/or per-page Article Processing Charge (APC) and signs away their Intellectual Property (IP) rights to the journal.
7. Journal takes the final work as their own and redistribute, typically under restrictive licenses and behind pay-walls

Obviously, financial incentives to publish would only further distort communication practices

The author, after *doing* all the science, receives no monetary kickback On the other hand, commercial publishers (which comprise around 50% of publishers, especially the higher-ranking journals[?]), post enormous profit margins, between 24-54%, to the tune of $1.1 billion dollars profit in 2010 for Elsevier-Reed, the largest scholarly publisher.[?] There is a clear mismatch between those doing the bulk of the effort and the bulk of the profit.

Profits for the publishers also derive not just from scientific labor, but from scientific funding. Half of all basic research in the U.S.[?] * are at least in part publicly funded. The taxpayer-funded National Institute of Health (NIH) issues sustaining, highly competitive multi-year R01 grants to most researchers; these grants pay for laboratory equipment, publication, and salaries of lab heads and those working under them.[?] The results of this publicly-funded research are then made inaccessible behind pay walls – interested readers will have to pay the for-profit publishers to access the research funded by a public institution.

3.2.2 *The speed of research*

Too slow

There is a great deal of concern that science is not fast enough, and that the issues of reproducibility and literature access impede the creation life-saving and life-altering technologies.[?] There's also issues of duplication; spending time chasing scientific relationships that another researcher already investigated, but either didn't publish or didn't publish enough to be useful.[?] Industry access to the literature is also a concern – while big pharmaceutical companies have the monetary means to provide literature access for all of their employees, fledgling bio-tech companies suffer from a dearth of readily available literature.[?]

*And most high-profile research is done in these countries. For more on this, see 5 on page 35

Too fast

Access[?] is also about more than money, extending to licensing issues in the digital age. Journal publications are a continuously and overwhelmingly increasing resource. One group estimated 50 million articles by the end of 2008[?] ; a different method estimated 114 million documents on the web in 2013.[?] The growth rate in the past decade has been between 8-9% on average; dependent on the field;[?] on average, life scientists publish 2 peer-reviewed articles every minute.[?]

While this is consistent with the increases in raw numbers of both journals and publishing authors, that doesn't mean it's any easier to keep up with. While researchers report reading a steadily increasing amount of literature[?] , this precipitous increase in the number of scientific publications has led to the "impossibility of being expert"[?] .

? estimated that for a single recruit to "become expert" in the subspecialty echocardiology, i.e. having read all the relevant papers, "would take 11 years and 124 days, by which time at least 82, 142 more papers would have been added, accounting for another eight years and 78 days." To finally catch up, it would take a net total of 40 years and 295 days. And that's if the interested party could read five papers an hour (one every 10 minutes, followed by a break of 10 minutes) for eight hours a day, five days a week, and 50 weeks a year, for a capacity of 10, 000 papers in one year – and it were still 2010.[?]

The rapidly increasing "data deluge"[?] is part and parcel of new technologies, where papers are based on many datapoints, not just a few.[?] The advent of machine-readable text and linked networks of scholarly information opens the possibility of managing the literature with text-mining, annotations, and new forms of communication and processing, perhaps making it easier for researchers to stay on top of recent developments. Unfortunately, the pay walled and copy-written scientific literature is both fiscally and legally out of reach for massive semantic processing; scientists cannot employ technology to efficiently manage their reading work flow.[?]

Thus, the scientific literature remains piecemeal – single papers demonstrating single results, where over 100,000 possibly-relevant papers are potentially relevant.

3.3 MEANINGFUL RESEARCH

> "Does the pressure to publish in prestigious, high-ranking journals contribute to the unreliability of science?"
>
> **?**

Citation is the metaphorical currency of science, a way of paying homage to previous work and making sure scientists receive their proper due. It also functions, in a globalized/linked/connected world, as convertible and real currency. Citation counts are a proxy for scientific success, first by those outside the academy, and now as a selection metric for researchers engaged in the "literature deluge".[?] Nominally, choosing papers to read and base future work on is based on purely the relevance and applicability of the literature. However, given the nigh-impossibility of keeping up with everything, other techniques come into play. One strategy employed by scientific audiences in deciding where to invest their reading time is the prestige of a journal; similarly,

when choosing which journal will be the most beneficial venue for their work, those same citation rankings come into play.[?]

Qualitatively, the top of the journal hierarchy in most fields is the biology-focused *Cell*, and the multidisciplinary *Nature*, and *Science* triumvirate; journals that are instantaneously recognizable and eminently reputable.[?] To get a *Cell* paper is to be immediately taken a little more seriously.[?] [†]

Metrics and assessment

Quantitatively, the journal hierarchy is represented by the Journal Impact Factor (IF), calculated for journals by thepublishing house, citation analyzer, and mass-media company Thomson-Reuters, specifically their Science Citation Index (SCI) citation network. The IF was originally proposed as one metric of many to track scientific productivity: a simple mathematical formula reflecting the number of citations of a journal's material divided by the number of citable materials published by that same journal. The original intention to allow comparison of citation rates between different journals to aid librarians in choosing the most appropriate ones.[?]

$$\text{Impact Factor} = \frac{\text{number of citations}}{\#\,\text{citable materials published}} \tag{3.1}$$

Metrics immediately lead to gaming the system.

Like with many metrics, it's applied with a widening and undiscriminating brush. IFs have evolved from one metric of citation rates to a shorthand for journal quality overall, on the premise that a higher citation rate of papers indicates higher quality papers.[? ?] From there, publications in a high IF journal serves as a marker of quality on individual papers and researchers.[? ?]

> "... if someone has multiple publications in a higher-impact journal, it's like getting another set of letters — the peers that reviewed that paper gave it high marks"
>
> **?**

IF effects also shape the decisions of journal editors and publishing administrators, who depend on the popularity of their articles to maintain journal reputation. Editors make estimates of likely citation rates for submitted articles, selecting for "sexy", exciting, and likely-to-be-cited literature[?] Thus, the IF calculation shapes what literature appears in high-impact, highly visible journals..[?]

The IF depends on what article types are deemed citable – the fewer, the better (i.e. lower denominator, higher impact). Since reviews are included, this means highly-cited reviews or just a few very highly cited publications can skew impact factors**?** Journals, to maintain the ideal of selectivity and top-notch research, accept a rapidly decreasing number of manuscripts[?]

Scientists, especially high-profile and competitive ones, choose carefully which journals they'll submit to. It's a game of saying is this research trendy *and* of high enough quality *and* an original idea *enough* to make it in this high-impact journal or another? A manuscript submission takes months and in the intervening time, the manuscript can't be

[†]Sources are: my life, everybody's life, a lot of blog posts, general atmosphere. Like, if I see a *Nature* headliner, I'm more likely to be excited and impressed.

sent out anywhere else. This means choosing a too high impact journal is a loss of months of publication time, not to mention that while you're waiting on a decision, somebody might publish similar results firsts. Publishing in high impact journals for the scientific-administrative needs of research, hiring, grantsmanship, and publishing. High impact journals increase your visibility, lend you a sense of decency, and in some parts of the world counts directly toward hiring practices.[?????]; publishing in a less-cited journal can have serious consequences in these administrative gambols.[‡] It sets up a choice: should one publish in a high-profile, non-specific journal or a lower-profile, but more relevant sub-disciplinary journals?[?]

3.4 PUBLICATION BIAS

> Publication bias occurs when results of published studies are systematically different from results of unpublished studies... Empirical research consistently suggests that published work is more likely to be positive or statistically significant than unpublished research.
>
> [??]

What happens when a scientific project doesn't work? When do we keep pushing, and how do we say "*This* piece of evidence disproves our hypothesis" and that does not? An experiment that is *not* working work (with regards to the current literature) lays its blame on reagents, on the technical skill of those involved, on the time of year.[§] A negative result presents no signal to pick up on, no difference; without the contrast between background and signal, the signal gets lost. Statistically, we can't "prove" the null hypothesis; we can only say "if it does exist, our methods are not sensitive enough to detect it." It's also, quite bluntly, not as exciting.

As a result, the literature has a distinct bias towards positive results. A 1991 *Lancet* issue is typically cited as the first large-scale examination of the issue. **?** reviewed a set of clinical research trials, concluding:[?]

> "Studies with statistically significant results were more likely to be published than those finding no difference between the study groups... Studies with significant results were also more likely to lead to a greater number of publications and presentations and to be published in journals with a high citation impact factor. An increased likelihood of publication was also associated with a high rating by the investigator of the importance of the study results, and with increasing sample size."

The tendency is usually referred to as the "positive publication bias", but it's might be more accurately described as bias towards *interesting* results: a high-profile study refuting another high-profile study can be just as exciting as the first positive results were.[???]

[‡]There's a number of sources denying that IFs are *specifically* counted in any of these, especially in the U.S. But they're certainly powerful tokens in the scientific imaginary, from which reviewers of any kind are hardly exempt.

[§]Of course, the time of year *is* a meaningful factor, re: Otto Loewi and acetylcholine in frogs

In clinical trials, there have been numerous initiatives to address this (i.e. pre-registration with a promise to publish), but the problem remains. The rest of the scientific literature is not much better. Between 1990-2007, the proportion of papers with positive results has steadily increased, starting at 70.2% in 1990 and ending at 85.9% in 2007.[?] The positive publication bias is not limited to clinical trials or the eternal scapegoat of psychology, although it clusters there. The 'harder' sciences (e.g. ecology[??], animal studies[??],physics, molecular biology, and chemistry[?] show a similar,if decreasingly prevalent, trend.[?]

Where does this stem from? On the one hand, researchers are likely to choose research practices that lead to positive results, often without realizing it (again, bad at statistics).[??] This is particularly noticeable in fields with flexible and extensive data processing, like functional MRI (fMRI). In 243 papers, researchers chose the analysis method that makes the data work, using almost as many analysis pipelines as there are data sets.[?] This pre-emptively biases scientific results, even before writing a paper.

In addition, papers with negative (non-significant) results are less likely to be published and receive, overall, less citations.[?] This is in large part due to scientific reticence, with authors unwilling to put in the necessary and extended effort in attempting to publish a paper with negative results,[?] instead focusing on "wonderful" results.[?] While journal editors show no bias in their acceptance of negative versus positive results papers[????], this is perhaps more attributable to the fact that submitted negative papers tend to be of higher quality rather than any editorial high-mindedness.[?] Peer reviewers are more likely to recommend a positive-results paper be published, award positive-results papers better methodological scores, are more critical of and detect more errors in papers with non-significant results, and may request new or different forms of statistical analysis.[??] As measured by citation rates, readers are less interested in negative results papers[?], and for-profit funders of larger-scale trials have a vested interest in specific (positive) results, as in the case of industry-funded nicotine and cigarette trials in the 1990s.[?]

3.4.1 *File Drawer Effect*

Many studies in a given research area may be conducted, but are never reported because of the publication bias. This creates a set of journal articles largely unrepresentative of the actual conclusions of conducted research. In the extreme case, if the null hypothesis is "true" (i.e. the relationship being studied does not exist), but the 5% of studies that by *chance* show statistical significance are published, the rest of abandoned data stays hidden in a researcher's file drawer.[?] This biases the state of the field, and in **?**'s words, "claimed research findings may often be simply accurate measures of the prevailing bias".[?] More realistically, this has serious consequences for synthesizing the results of a given field, leading to an overestimation of effect sizes[??] and the continued wasted efforts based of researchers on papers that failed to replicate, but never had the failed replication published.

Science is, in theory, self-correcting. Even if the initial conclusions are wrong, subsequent experimentation reveals some of the limits and misinterpretations – but only if it's published.[?] The file drawer effect interferes with this, by hiding the decline effect. Because the first papers

to describe results are often under-powered and thus over-exaggerate the magnitude of an effect, subsequent studies often find non-significant results; because these are negatives, they are harder to publish and self-correction takes longer.[?]

3.4.2 *Other forms of dissemination*

Papers from the file drawer might see the light of day in other ways. Results of research may also be presented at conferences, submitted to clinical authorities, or shared privately between researchers; while these count as communication of a sort, they have limited accessibility and reach, and are typically not as straightforward as those published in peer-reviewed journals.[?] The *de facto* dissemination system for scholarly production, is not representative of the research that's actually happening, which naturally has consequences for the theories we test going forwards.

3.5 REPRODUCIBILITY

The principle of the elusive scientific method is reproducibility. Researchers document their methods and results to such an extent that any other researcher is able to replicate their data independently, or, more ideally, build experiments atop the results of their colleagues. With reproducibility, two different labs should produce similar types of results (e.g. protein-protein interactions) with different methods (e.g. protein inhibitors, mutagenesis studies).

Like the access crisis, however, there is a perception of a reproducibility crisis in science. Certainly the most high-profile beginning to the discussion was a 2005 article authored by John **?**, provocatively titled *Why Most Published Research Findings Are False*. **?** proposes a statistical proof that the likely false positive rate in the published bio-medical literature clocks in at >50%.[?] The responses were heated and numerous,[???] but in the end most contributors concluded, based purely on statistical considerations, one can expect a percentage of the medical literature to be a false positive (50% according to **?**' calculations, 14% in **?**'s calculations).[?]

More than just statistical theorizing, researchers regularly encounter similar hurdles. In a survey, ~50% of respondents responded that they had difficulty reproducing at least one set of published results[?] One academic lab repeated the exact same genome-scale small interfering RNA (siRNA) gene screening 5 months apart. Reproducibility ranged from 39% to 49% in terms of target hits; this is due in part to the stochastic nature of biology, but also partly to the variety of ways two different data sets responded to the same methodologies.[?] Animal research consistently differs in translation to clinical trials.[?]

Bio tech and pharmaceutical companies trying to monetize those discoveries also demonstrate the practical scope of the problem. The rate of effective translation from basic research into clinical drug treatmentshas always been low, but the increasing costs of drug development and renewed focus on research reliability has prompted drug companies to join the conversation with data. The in-house target validation studies run by most bio-medical companies provide a unique data set on the reproducibility of bio-medical, cancer-focused research. Amgen's researchers attempted to reproduce the results of 53 high-profile 'land-

Drug developments costs increasing largely due to Food and Drug Administration (FDA) restrictions

mark' cancer studies over 10 years; results could only be recapitulated in 6 of the cases, an 11% success rate.[?] Researchers at Bayer tracked the fate of 67 validation projects; in 2/3 of the cases, the validation data was so inconsistent with the published literature that the project was significantly delayed, or more commonly, entirely terminated.[?] . At Bayer, this did not correlate with fields, experimental conditions, model systems, or journal impact – it's just that most research could not be reliably reproduced at industrial labs.

In many other ways, however, most researchers know how temperamental science can be.Scientific work draws on the "tacit knowledge" of researchers, specific to times and places, and failed replication is not usually due to malicious case of fraud. In one case, a Berkeley, CA lab and Boston, MA lab, collaborating on a Fluorescence Activated Cell Sorting (FACS) project, discovered that even with identical protocols they had consistently different results. In a laborious year-long process, the two labs (or rather, the primary researchers in both labs) isolated the difference in their experimental results to the speed of agitation at an early step of the organ isolation process. While the results initially *seemed* irreproducible and incommensurable, their end conclusion was principally that biological research is at such a level of complexity that even minor changes from lab to lab in the micro-environment can "break" an experiment.[??] It's not completely clear when unreplicated turns to unreplicable; as one researcher put it, "most failures to replicate exhibit incompetence."[?]

Thus, the "crisis" in reproducibility may not be new to science, particularly. It may just be gaining increased exposure.

3.5.1 *Statistics*

Full disclosure: this author is also not very good at statistics

High powered animal studies are prohibitively expensive

Part of **?** proposal rested on the improper use of statistics in biomedical research. Scientists, as a whole, are just not very good at statistics, in either analyzing their own data or understanding other people's.[??] As a result of these misunderstanding, along with funding issues, studies are often woefully under-powered (low sample sizes, small effect, or both), leading to unreliable findings. Even when all other research conditions are ideal, under-powered studies have a low probability of discovering 'genuinely true' effects, a low Positive Predictive Value (PPV), and typically exaggerate the magnitude of an effect.[?] Even in supposedly high-impact high-intensity journals, statistical standards remain relatively low.[??]

PPV - *probability that a positive research results reflects a true positive; depends on the prior probability of it being true, the statistical power, and the level of significance*

Since researchers must publish to succeed, and statistical significant and clean results are more likely to be published, researchers have incentives to "engage in research practices that make their findings publishable quickly".[?]

3.6 RETRACTION

On the other hand, positive results are sometimes not as positive as they should be. Processes of peer-review and editorial jurisdiction are supposed to ensure that post-review articles are scientifically sound. The retraction of those articles represents an enormous reputation cost to both journal, who earlier lent their seal of approval, and author. In the short term, the author becomes notorious; in the longer-term, there is a distinct and significant drop in citation rates to the author's

12.5% over five years post retraction

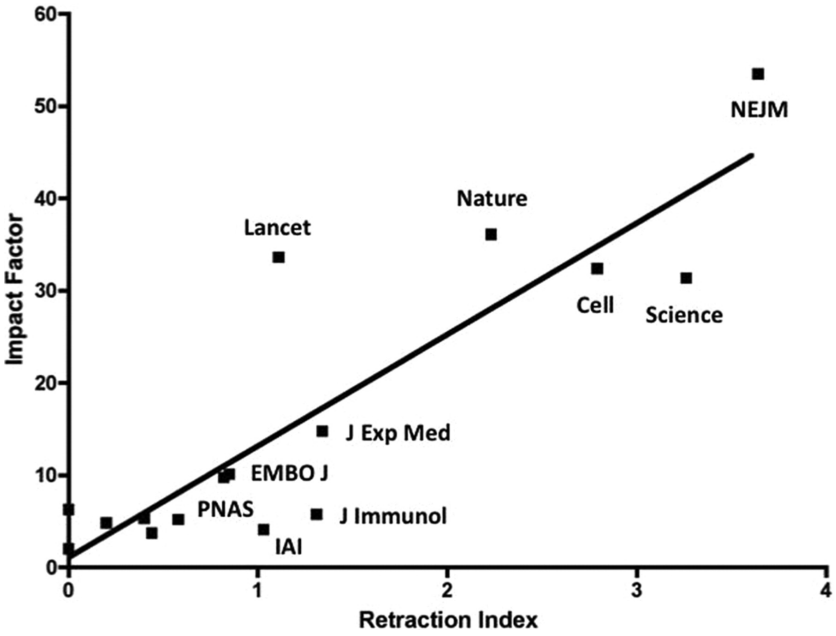


Figure 1: Correlation between impact factor and retraction index.(**?**)

prior work.[?] ¶Retraction may not always be bad (for reasons discussed momentarily), but it is notable. In 2008, **?** concluded that

> "...in the period between 1990 and 2006, we found a significant increase (r = 0.55, p = 0.02) [in retractions]... retraction rates are still on the rise.
>
> **?**

Not only is the overall rate of retractions increasing, but they're increasing in the journals we respect the most. In a 2011 *Infection and Immunity* publication, **?** found a "strikingly robust" correlation between a journal's "retraction index" and its impact factor (Figure 1).[?] This is, of course, concerning for those of us interested in the reproducibility, and those using IF as a gating mechanism for scientific reproducibility.

3.6.1 *The role of fraud*

Lurking at the outskirts of all of this – publication bias, reproducibility issues, and rising retraction rates – is the spectre of scientific misconduct, the willful perpetration of scientific deception. Some researchers propose the pressure to publish, increasingly important to funding and hiring decisions, is enough of push for scientists to produce flawed manuscripts at a higher rate.[?] This is consistent with the results of some analyses, indicating the number of retractions due to research misconduct (i.e fraudulent data) has trended significantly upwards.[?] There have been some extremely high-profile cases of deliberate fraud in the past several years.[||] Scientists report observing misconduct in colleagues 5-33% of the time; as a conservative estimate, about 2% of

¶This is only in cases of non-self-reported retractions; if an author voluntarily steps forward, their citation rate typically briefly increases

[||] Tracked at `retractionwatch.com`, which maintains a list and analysis of all retracted articles

scientists admitted to have fabricated, falsified or modified data or results at least once.[?]

The other possibility is that that flawed manuscripts are simply being identified more successfully in processes of post-publication peer review, in which case science is perhaps fulfilling its self-correcting ideals. While the numbers of retractions and proportions is undoubtedly increasing, it's not completely clear why. **?** examined not just numbers of retractions, but *why* articles were being retracted. Of the 4,449 retracted articles found in 42 of the largest bibliographic databases from 1928-2011, the reasons behind retraction were usually relatively benign, with only 20% of retractions attributed to alleged misconduct**. In both **?** and **?** analyses, "repeat offenders" accounted for many of the retractions. Uncovering deliberate fraud prompts re-examination and often retraction of the whole cohort of papers they may have worked on.[??]

While even in**?**'s otherwise-hopeful analysis there is a growth in retractions by a factor of 11.36 (excluding repeat offenders and adjusting for literature growth), the researchers assert that the retraction rate is likely due to social factors, not decreases in peer review rigor or intentional deception on the part of researchers.[?] The reproducibility issue isn't really affected by this – it still exists, even if researcher's are not intentionally deceptive.

3.6.2 *The Remains of Retractions*

An additional problem remains; once an article has been retracted, there is no reverse dissemination. In the case of highly controversial papers, retractions are usually due to high-profile fraud. In less obvious cases, however, retracted papers continue to be cited long after their nominal removal, potentially biasing scientific progress to come.[??]

3.7 COMMUNICATIONS IN CRISIS

So the *validity* of scientific communications is in questions, largely due to the nature of the unit of published literature, and the pressures on scientists to create certain specific kinds of knowledge. There is issues of access to the literature; but even that literature does not fill all the knowledge gaps. It is subject to funding whims, human biases in selection criteria, concerns about prestige, often statistical bunk, occasionally outright fraud that isn't always caught on. Publishing is the outlet for most of these, but the problems run much deeper, into the very beginnings of scientific projects. What kinds of systems could re-create a production ecosystem that was not subject to these things, or at least remained flexible enough to continually re-prioritize the accuracy of scientific work and the, ahem, pursuit of truth?

**

47% alleged publishing misconduct

20% alleged research misconduct

42% the usage of questionable data or interpretations

4

CRACKING SCIENCE OPEN

> Science is based on building on, reusing and openly criticizing the published body of scientific knowledge... For science to effectively function, and for society to reap the full benefits from scientific endeavors, it is crucial that science data be made *open*.
>
> The Panton Principles

pantonprinciples.org, 02/16/2015

> Knowledge is open if anyone is free to access, use, modify, and share it — subject, at most, to measures that preserve provenance and openness.
>
> The open definition

opendefinition.org/od, 02/16/2015

When applied to the different "problem" areas of 3, open becomes a ragtag team of co-existing, largely collaborative initiatives.

Scientific knowledge seems limited, disparate, disorganized, and unreliable; it lives behind digital pay walls contrived to keep science in the realm of the fiscally elite and educationally privileged, and hides tucked into papers full of jargon. Science doesn't replicate well, even when it's purely 1's and 0's: the reliability of computer programs (to present stimuli, record data, crunch numbers) is limited to the labs writing the program, and sometimes not even then. Attempts at getting access to the generative programs fail almost every time. When scientifically-minded readers try to look deeper into statistical manipulations, datasets typically fail to materialize;[?] when they are available, they're often disorganized or poorly documented, unusable to the intrepid data miner. Fears about tenure, funding, prestige, and scientific sex appeal shape research courses and successes, while academic research is regularly shuttered by the funding whims of the NIH. Research is no longer about the pursuit of truth, but just trying to keep head above competitive waters. Publishing groups are increasingly commercial and hold an unnatural kind of power by determining what *counts* as good, interesting, novel, *publishable* science.[?]

None of this is new *to scientific communication; Fleck observed all of this as merely the sociological nature of science. I tend to agree.*

The increasingly-popular solution - open science - to these problems relies on the Internet and technical know-how, geared towards a generation that grew up on Napster and the Pirate Bay. The vision is one of scientific transparency – making the inner workings of science not just visible, but modular, mine-able, and usable by anyone who cares to try. We expect science to be something to tinker with, whenever we have the time or the ideas. At its best, "open" is geared towards reorienting the whole culture of academic research towards a more sharing-and-caring system.

Open science starts with the already published literature, and a long-standing movement to make journal articles accessible to more than just wealthy university subscribers. Then, advocates wade deeper, demanding not just the results the authors choose to highlight, but the data powering authorial interpretation. But how did they acquire the data? If they did it with a program, then we need that too.

Note Not all specifications apply to all fields; different norms about data, access, code, and process prevail in different areas. Physics has been a leader in accessible publishing since the founding of the arXiv; crystallographers have been sharing crystallography data since the field's inception. Ecology, on the other hand, is notoriously poor at sharing data, likely due to the incentive structure of the field.

The arXiv is a massive repsitory containing almost every pre-print from physics research.

4.1 LITERATURE ACCESS

The problem with access is thought to be largely fiscal and partially legal. Open access scholarly publishing addresses the barriers to accessing peer-reviewed scholarly journal articles, barriers that are thought to be both a scientific hindrance and an infringement on moral rights. An exclusively digital invention, Open Access (OA) literature is

> "digital, online, free of charge, and free of most copyright and licensing restrictions. Ideally, it removes both removes price barriers (subscriptions, licensing fees, pay-per-view fees, i.e. gratis) and permission barriers (copyright and licensing, i.e. libre)."[?]

Subject, at max, to crediting the proper sources in your scientific remix

More succinctly, "true" OA literature has free availability and allows unrestricted (re)use of the text, images, graphs, and supplementary info.

4.1.1 *Implementing Open Access*

Implementations of open access are a rapidly growing part of the scientific publishing system.[?] The "gold" OA model is followed by journals publishing articles under a share-and-share alike license, typically as freely available digital objects. "Green" OA refers to the deposition, by authors, of some version of their article into either institutionally-managed repositories (e.g. the Div III archive at Hampshire) or centralized ones (PubMed, the arXiv). Both versions allow access to the information by anyone with a sufficiently fast Internet connection and the intellectual wherewithal to read scientific jargon; they also allows text scraping and content mining by automated scripts.

Open also means less profit for scholarly publishers from subscription costs.[??] In most industries, this is the barrier to IP access. Who has the rights to remix music and movies? What does it mean to re-use characters from published literature in new stories? Is pirating software wrong? It depends on who you ask, but the argument against free culture usually boils down to: IP should cost money because the producers need to be paid. Musicians, artists, authors and filmmakers make their living via royalties or direct sale of their work.*

Scientific authors and their publishers, on the other hand, occupy a specialized realm where the actual release of knowledge is unaccompanied by any direct movement of money into the author's pockets. Scientific authors move forward without any expectation of direct payment ("royalty-free literature"); they write for impact, not for money, and because advancing knowledge in their fields also advances their career.[?]

*Although this is already troubled...fellowships and grants go to the art world etc. And to be clear, I don't think the copyright terms *there* are really great either.

This puts the debate about open access in a different place than contemporary movements for copyright-free cultural production in other realms; what exactly *are* subscribers paying for, if not to feed and clothe the producers?

Scholarly journals do provide a number of services – one list by a publisher at *Science* listed 82 hats for publishers, from social media outreach to wrangling referees to ensuring articles disclose conflicts of interest.[?] Publishers *also* used to provide delivery of a hard copy of the journal to subscribers, giving them ownership. One assumed subscription costs largely went to the paper-and-ink printing costs; paying substantial fees for ownership of the physical product was only reasonable.

Now, though, what are subscription costs paying for? The physical costs of production are cheaper than they used to be, and libraries have largely downgraded from owning paper copies to leasing digital access. If journal authors, editors, and referees aren't being paid, why are journal publishers still profiting so handsomely? In moral terms, if the goal of publishing is to disseminate information and advance science, why should other other scientists, or potential scientists, be barred from the universal pool of knowledge by an artificially-constructed digital profits barrier?

Practical concerns

OA literature is not necessarily different from closed-access literature in any way, except for who's paying the bills. Literature is not free (of cost) to produce; publishers do play a role. This does not foreclose the possibility of making it free of charge for users and readers. "Related" issues of predatory publishers charging APCs and fake or sub par peer review[?] are issues pervasive to scientific publishing, and not specific to open access models. Open access is a viable financial model; the OA literature has grown remarkably over the past 10 years, now comprising 17% of articles published in 2011[?]

Publishing OA provides benefits to authors, allowing a broader range of individuals to potentially access, use and eventually cite their work. In some analyses, freely available literature correlates with increased citation rates and usage, especially in physics,[? 66? ?] , but this not necessarily the case.[? ?]

annotated bib of citation advantage `http://www.istl.org/10-winter/article2.html`

It also allows the recipients of biomedical work to obtain information about drug treatments or promising new therapies, while clinicians in the U.S. and abroad to access information they might not otherwise have access to.[? ? ? ? ?]

UNIVERSAL V. OPEN Even after implementation of OA policies, access barriers remain. These include, but are not limited to:[?]

- filtering and censorship (by governments or service providers)
- language barriers
  - English publishing
  - scientific jargon, e.g. "Is it science or alchemy?"[?]
- handicap access (e.g. not following guidelines for disability access)
- connectivity (the so-called "digital divide" of unequal broadband Internet)

Open access then, provides partial solutions to the issues of literature access, and the speed of science. It also, idealistically, opens up science to a broader range of "curious minds."

4.2 DATA AND CODE

Code and data are inextricably linked; they rely on each other for usefulness. As the products and basis of scientific conclusions, open data and open code provide a mechanism for encouraging reproducible research and increasing the speed of discovery.

The distribution of data and code is largely argued for in less moral and more practical terms; re-use of data and code has immediate and practical benefits for the speed of science. It introduces a different quality of interdisciplinarity, however. The people producing data (clinicians, ecologists, biologists, anthropologists) may not be the same people using it in analyses. Thus, while sharing data does not necessarily benefit one's own work, it does promote the progress of "science" overall.

4.2.1 *Open data*

Data is the heart and soul of science; "let the data speak" is the clarion call in any argument where you just want the *facts.*

data a set of values of qualitative or quantitative variables collected during scientific activities

The call is for scientists to "free your data", meaning release not just aggregated data analyses, but the full data set that conclusions are based on. It comes from "the belief that biological data have value beyond the purpose for which they were originally acquired."[?] The broad availability of "raw" data can be used in addressing the statistical unreliability of science and in accelerating the rate of discovery by computational/data-based methods.[?] Again, the advent of digital storage and connections has enabled data sets of all shapes, sizes, and kinds to be readily available. While not all data sets are deeply meaningful, the point is to open the information up to the possibilities of the crowd.[?]

This is by no means a new concept or activity in scientific communication. In the early 20th century, aggregated 'pure' data points on elemental melting points, colors, and densities, collected by many scientific workers, were the foundations for Mendeleev's proposal for the periodic table of elements.[??]

Open data in the here and now on a massive scale has been notably successful.[?] As the government was gearing up for the Human Genome Project (HGP) in 1988, they also founded the National Center for Biotechnology Information (NCBI), whose entire mission was to "design, develop, implement, and manage automated systems" for bio-molecular data. Deposition of genetic data by researcher has been successful, at least in terms of usefulness; in 2013, there are "3 million visitors daily to its website, [and] approximately 27 terabytes of data downloaded per day."[?] Genomic data deposition, while not at 100% for researchers, is not unusual or unexpected, and is reused on a massive scale.[?]

Every night in astronomy, the Sloan Digital Sky Survey (SDSS) releases around 200 GB worth of data. Since 2000, the project has collected

imaging data of over 35% of the sky, with "photometric observations of around 500 million objects and spectra for more than 3 million objects". As of this writing, there 6,333 peer-reviewed papers drawing directly on the data; those papers have been collectively cited more than 280,000 times.[?]

Open data initiatives, of course, are not just aimed at enormous public works projects like the HGP. It requires "individual scientists and laboratories [to] embrace a culture of archiving and sharing" for the full benefits.[?]

4.2.2 *Open code*

Programs and scripts control how and when information is collected, what kinds of metadata we track how we parse, smooth, and manipulate data, the final presentation of data on our screens and the figures we submit to journals. From computational biology scripts to psychology stimuli, from graphing ecology datasets to standardizing microscope exposures and image processing, code, in a very real way, *is* the science.

The use of software poses both problem and solution to reproducibility. if a scientific paper relies largely on computer programs to generate results, *not* releasing the program source code raises needless and confusing roadblocks. If, on the other hand, code is released, it potentially saves time and effort for other researchers, and can pinpoint errors in scientific results much more specifically.[?]

4.2.3 *Benefits*

Reliability and reproducibility

DATA Sharing data and code improves the reliability of scientific evidence. In If some proportion of the scientific literature is, as **?** argued, mostly false, one way to address the issue is by providing raw research data. With this, the choices researchers make about data points that could potentially lead to biases – which ones to use or not use, what kind of tests to run, when to stop collecting data – are exposed in the data. Since willingness to participate in informal data sharing is correlated with the strength of statistics in a paper,[?] it also seems reasonable to assume that mandatory data deposition would lead to stronger statistical choices. In the case of questionable or surprising results, re-analysis of full data could help verify conclusions – thus both protecting researchers from accusations of fraudulent data and lending credence to 'paradigm-shifting' results.

Meta-analyses, as well, would benefit from raw data deposition. Instead of relying on aggregated numbers generated by a variety of methods, writers of systematic reviews and meta-analyses could compute their own results, ultimately increasing the statistical power of their conclusions and providing a measure of confidence in the results.[?]

CODE Even if code is described perfectly in precise formal terms, the actual code always has errors, at a rate of 1-10 errors per 1000 lines of code.[?] Especially damaging to scientific purposes is the insidious semantic errors. Not all coding errors manifest with outward syntactic issues where the code won't actually produce anything. Instead, bugs are type errors, or misplaced loops: semantic errors can systematically

and insidiously warp results. Debugging, perhaps in science especially, is non-random and biased towards seeking positive, confirmatory results.??? † These issues might only appear when the same code is used on a different data set.

A mistake you don't make after using Linux

Additionally, code is not subject to peer-review; not that it necessarily should be. However, many scientists treat code and software as infallible tools. Code than exists as a trusted "black box" of processing, rather than a step in the research process that can and does change outcomes.??

The public good

Open data and open code is a "research accelerator."? Data-driven discovery and synthesis plays an increasing role in many fields: machine learning, the improvement of classical statistical methods (based on large data sets),? the neurosciences??? Bio-informatics as a field exists only because of large-scale data collection. All of the fields that draw on data also draw on computer code to handle increasingly massive data sets.

Open data extends the useful life of data collections. In genomics, most researchers re-use datasets and publish within 2 years; third-party users continue to do so for at least six years.? In fields with highly complex and non-repeatable data sets, like archaeology or ecology, there is both a need to preserve irreplaceable data sets and an increased need to share them.? And last, as with open access, if data is created by taxpayer funding, shouldn't taxpayers have access?

In code, we know the relative speed of science is slow; the speed of a single researcher is even slower. While re-using the code of others can be a risky proposition, it can also be an important stepping stone to bigger and more advanced project, or a teaching tool. While not all code is meant to be reused (and that's okay!), seeing how other researchers approached a computation problem can be a guide.?

4.2.4 *Debates*

Implementing open data and code

Like with open access literature, the sharing of data is associated with an increased citation rate to papers in a variety of disciplines[42]

Even while other reformers push for more flexible and realistic assessments of scholarly contributions, open science modes cans still be slotted into current incentive structures. Code and data can be cited; hosting repositories like `Figshare` or `Dryad` provide Digital Object Identifiers‡ for uploaded information and instructions on how to incorporate data citation in a variety of formats.[60]

figshare.com

dryad.com

Although intriguingly, not as a dominant feature in even open-source citation managers and citation files

"NOT GOOD ENOUGH" One of the biggest reasons cited to *not* publish data and code is that it's not good enough for the public eye, not well-documented, or disorganized. But if you used it, it's probably good

† e.g. if you use an int type number in Python, python will round the results. This error will produce approximately accurate results – but certainly not with the calculated specificity, and might introduce other small-but-meaningful errors.

‡ A digital object identifer acts as a permanent short URL for easy and reliable web access; reliable access on the web is, of course, *extremely* tenuous, even for nominally archived and maintained piece of scholarly work.

enough. Not all software *needs* to be re-used; collecting and annotating datasets with metadate should be a part of the research pipeline anyway. It's "good enough".[?] Curation is a necessary part of research, but shouldn't take an enormous amount of time in a well-designed scientific work flow.[?]

Practical Issues

WHICH DATA? A PhD student at the Champlimaud Neuroscience Institute studies cuttlefish feeding habits. As part of her dissertation, she's collected hundreds of hours of video of cuttlefish trials; so far, the raw data occupies two terabytes of hard drive space. While she's interested in sharing her data, both to outsource data analysis and to promote reproducibility, it's not technically feasible. More broadly: *which* data, *when*, and in what format? It's on a case-by-case basis, right now, because of the vast heterogeneity of research results.

Data is also a sociological challenge for scientists. Asking researchers to give up their theoretical ticket to publication is a huge risk, especially in fields like ecology where datasets are extremely hard won and be the basis of many publications. While the risks of being scooped are in fact relatively low, concerns about data appropriation still run high.[?]

DATA CONFIDENTIALITY Especially for clinical trials, who does data belong to?[?] For sensitive information (biomedical data, interviews, location of rare bird or plant species, etc.), there are additional concerns that might

4.3 OPEN NOTEBOOK SCIENCE

> "Open notebook science is the practice of making the entire primary record of a research project publicly available online as it is recorded. This involves placing the personal, or laboratory, notebook of the researcher online along with all raw and processed data, and any associated material, as this material is generated."
>
> -Jean Claude-Bradley[?]

Notebooks are, plausibly, the closest thing to heart and spine of the scientific process. In addition to computer collected data, a good lab notebook tracks the experimenter. Researchers capture their in-progress thoughts, the reasons behind experiments, their day-to-day protocol adjustments, notes on dropped tubes or hastily drawn sketches of experiments. Notebooks are ground zero for wet lab science.

All of the elements so far of OS – data, methods, conclusion, code – are (theoretically) documented and organized somewhere, in some combination of paper and digital record-keeping. The simplest solution might just be to make notebooks open from the start. In an ideal world, this would tracks not only eventually successful projects, but shows other researchers where failure likely lies. A documented and constantly updating notebook makes it easy to trace the more realistic scientific process, one of fits and starts and ad hoc modifications, why *this* Taq was used instead of *that* one, a process where sometimes a single step takes 25 tries.

An accessible scientific notebook complicates the eventual scientific paper, giving future researchers a better idea of how reliable results might actually be. To some extent, open notebook science precludes the possibility of the file drawer problem; it's much harder to tuck results away if they're already online.

5 REPRESENTATION AND ITS DISCONTENTS

A key question missing from the scientific ecosystem is the classic question of representation. How many women and people of color* are in the workforce? How many of the Forbes 500 companies are headed by women?† In this work, that means questions about who gets to make science, and who gets credit for their work.

In the U.S. and Western Europe, since the rise of a modern social consciousness in the 1960's, the push for more women in science is one of our early introductions to the endemic problems of representation. Where are the women in science? Who is producing knowledge in the scientific ecosystem? More generally, which kinds of people and bodies does scientific research include, as subjects, researchers, and audiences?

5.1 THE TROUBLE WITH REPRESENTATION

> When I sat down with one of my senior professors in Durban, South Africa to talk about my Master's thesis, he asked me why I wanted to write about women resistance fighters.
>
> "Because women made up twenty percent of the ANC's militant wing!" I gushed. "Twenty percent! When I found that out I couldn't believe it. And you know – women have never been part of fighting forces –"
>
> He interrupted me. "Women have always fought," he said.
>
> "What?" I said.
>
> "Women have always fought," he said. "Shaka Zulu had an all-female force of fighters. Women have been part of every resistance movement. Women dressed as men and went to war, went to sea, and participated actively in combat for as long as there have been people."
>
> *We Have Always Fought,* Kameron **?**

The narratives around the participation of marginalized groups paint a world where those groups have *never* participated in XYZ activity. This accomplishes the complicated task of burying erasure by *our* culture in the invisibility and repression perpetrated by *their* culture. To talk about the absence of women in science and technology over the past 100 years is a disservice to the exceptional individuals who *did* participate. It is not on them, but rather on us, to recognize the histories we tell will, without serious work, elide the many and diverse Black, Brown, and White wo/men/of color. Women have always fought; it's not their fault we refuse to count them.

The other trouble is more deeply embedded, but fundamental to more adaptable feminist projects. We can ask where are the queers, but queer, like woman or black, is not an inherently meaningful category. Statistical questions about proportions of gendered peopleminorities to White, or tall to small reinstate (re-inscribe?) recently developed

*"Women" is not meant as just white cis-women, but is inclusive of those assigned, identifying as, or read as female, of all races. People of color is not just men of color, but the women of color subject to the 'double-bind' of racism and sexism. **?**

†24, for a whopping total of 4.8%; and only 1% are black, and *none* are openly gay

social relations; race has not always defined us.[?] Analyzing society on a large scale based on these tropes of natural categories presumes their biological and cultural naturalness. In Donna Haraway's words,

> "There is nothing about being 'female' that naturally binds women."
>
> *A Cyborg Manifesto*, Donna **?**

Her argument in *A Cyborg Manifesto* for "building coalitions through affinity, not identity"[?] is a counterpoint to early feminist beliefs that more women would inherently lead to a more "feminine" and responsible science. To some extent, that's true – Researchers who have to cross gender boundaries might be less likely to presume the existence of "male" and "female" hormones. Black and Brown researchers may be less likely to assume the default of White histories for guiding their research in biological paradigms. But on the whole, there is a divide between the goals of women *in* science i.e. representation and women *and* science i.e. the gendered and value-driven nature of knowledge.

Nonetheless, knowing more about who is making and participating in science is a necessary layer; it also helps to complicate . The history of science is a line of Great White Men; our current role models are usually Great White Men, with the possible exception of Marie Curie.

Notes

The focus on biomedical literature and representation derives largely from where meta-research has been done. Clinical trials are prioritized as study objects, plausibly because the effect is more clear – studying a medicine in only men blatantly ignores the other 50% of the population who might succumb to a disease; studying breast cancer as solely a women's problem carries the same issue. Testing malaria medications in a "developed"country is clearly not particularly generalizable to a country with a completely different infrastructure. That's just good science; of *course* clinical research is flawed when different bodies aren't taken into account.

Clinical trials and biological research are also lower on a "Hierarchy of Sciences", which predicts that as we move from simple systems (particle dynamics) to complex (human behavior), researchers reach less definite conceptual and methodological consensus.[?] Biomedical research has more variable elements – subjects – to manage and is thus more susceptible to critiques of who those subjects are. In high-energy physics, it shouldn't really matter where the research capacity is, so non-feminist studies don't seem to focus on it as much.

5.2 REPRESENTATION

5.2.1 *Are bibliometrics global?*

Bibliometrics or scientometrics is the meta analysis of scientific relationships, expressed through formal networks of citation and references. Much of the systematic data on under-representation derives from citation databases, usually the Web of Science (WoS) database of 10,900 "core" journals curated by Thomson-Reuters, but sometimes Google

gray literature: conference papers, pre-prints, other quasi-published scholarly work

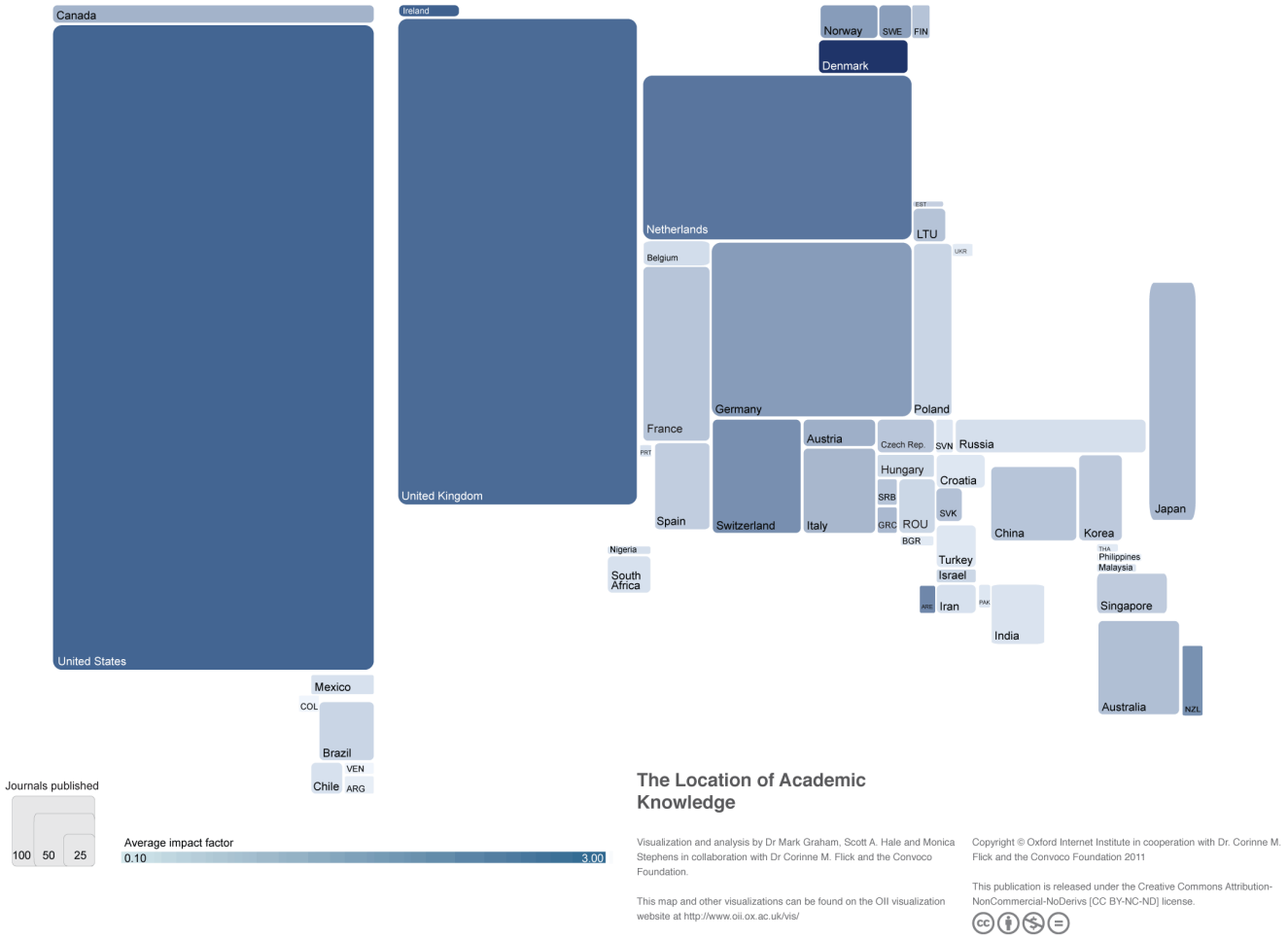


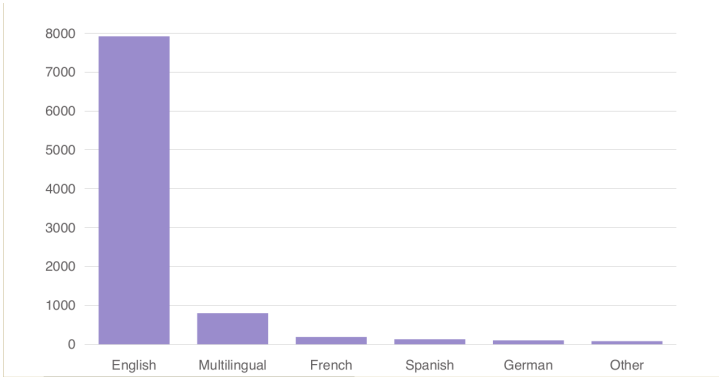
Figure 2: The location of academic knowledge

Scholar (100-160 million documents, including "gray literature"), CrossRef (55 million records), Scopus (53 million), PubMed (>23 million) or JSTOR (4.2 million).[?] Each database provides a different depth and purpose; some include largely biomedical, some all fields of "science", and some the whole breadth of academic endeavors.

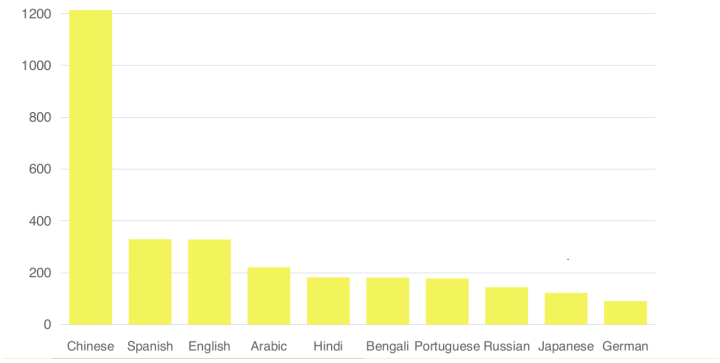
The Thomson-Reuters database, the generator of the IF, is the most commonly used database for bibliometric analyses. It indexes around 10,900 journals[?], capturing the vast majority of highly cited literature.[?] Because of its comparative breadth of information and the IFs use as a tool for filtering information, it also provides a good snapshot of literature visibility – not productivity or quality, but visibility.

e.g. WoS includes full author names and institutional affiliation

Nearly all of the most Thomson-Reuters respected journals are published from the U.S. and the U.K., despite rapidly increasing scholarly production from the rest of the world.[?] InFigure 2, a 2011 analysis of the "location of academic knowledge", the U.S. and U.K produce more SCI indexed journals than the rest of the world combined; Switzerland dwarfs by a factor of 3 the *entire* continent of Africa. Not only do the formerly-colonized countries of the majority world fare poorly in



(a) language of WoS journals



(b) Number of native speakers, in millions

Figure 3: 2011 data language comparison

quantity, their citation rates, as measured by the IF, are systematically lower.[??]

This is less surprising in light of the Thomson-Reuters standards for quality and inclusion in SCI indexing, and thus the assignment of an IF. Thomson-Reuters states:

> *"English is the universal language of science...* There are many journals covered in Web of Science that publish articles with bibliographic information in English and full text in another language. However, going forward, it is clear that *the journals most important to the international research community will publish full text in English.* This is especially true in the natural sciences..." [emphasis mine]

In terms of "regional" journals:

> Thomson Reuters is also interested in excellent regional journals and is able to include a *relatively small proportion* of these each year.

So a major metric, the IF, which is linked to the visibility of literature to other scientists, essentially does not include locally-specific journals and *requires* English-language publication. It is swamped by journals originating from the U.K. and the U.S.„ so the statistics captured by the massive databases used in many bibliometric studies systematically exclude, for example, most of the scholarship emerging from Brazil.[?]

5.3 THE U.S. AND WESTERN EUROPE

The complexities of race in the U.S., and indeed in any country, are hard to overstate and subject to constantly shifting boundaries. White Americans trace ancestry to the British, and later, immigration from the Scandinavian countries and the rest of Western Europe. Black descendants of slavery occupy different social-scientific spheres than recent African immigrants. The response to immigrants and descendants of immigrants from East and South Asia are routinely discriminated against; the increasing representation of Asian and Asian-American immigrants in the sciences hasn't strayed from the "yellow peril"/"model minority" binary since WWII. Latinx groups from South and Latin America suffer their own unique set of injustices, while "indigenous people" comprise a dizzying array of historically different tribal histories on a global and country level scale. That's without accounting for mixed-race individuals, an ever-growing proportion of the population.

Latinx - *a gender-neutral form of Latino/Latina, referring to not race, but merely area-of-origin*

In many ways, gender is cleaner-cut. In the U.S. tradition, there's only two options. While trans scientists do in fact exist, at least anecdotally,[?] , a gendered analysis would account for trans-men as men and trans-women as women. Gender is thus much less heterogeneous, and amenable to large scale analysis.

And, of course, gendered issues are racialized and vice versa. In one small, but in-depth report, 100% of women of color surveyed reported marginalization on gender- and race-based grounds.[?] The "double-bind" of women of color is relatively well-documented; the reality of representational interventions is that "programs intended to serve women disproportionately benefit White women, and programs intended to serve minorities mainly benefit minority males."[?]

5.3.1 *Gender*

> "Although there are more female than male undergraduates and graduate students in many countries, there are relatively few female full professors, and gender inequalities in hiring, earning, funding, satisfaction and patenting persist."
>
> *Global gender disparities in science,* **?**

Since the 1970s and the establishment of equal rights legislation banning outright discrimination against women and minority groups, the proportions of marginalized groups in the academic sciences[‡] has almost equalized, at least in some fields. In 2011, women received 54% of molecular biology and neuroscience PhDs. In physics and computer science women were awarded fewer than 20% of physics and computer science degrees.[?]

The equalizing of representation at entry, although promising, has not fulfilled its promise. While women are even over-represented in many fields at the time of enrollment, the rate of departure from academe for women and people of color is higher at every stage of the academic-scientific career process, leading to an academic landscape where men still dominate most prestigious positions, as in Figure 4.

Unsurprisingly, most of these statistics vary broadly between fields and subfields

[‡]The focus here (and in the literature) is on the academic sciences exclusively, without regard to the women and men who go into industry or other "non-academic field". This is actually a fairly large flaw, since industry and non-academic jobs comprise the majority of career paths for scientifically-trained students

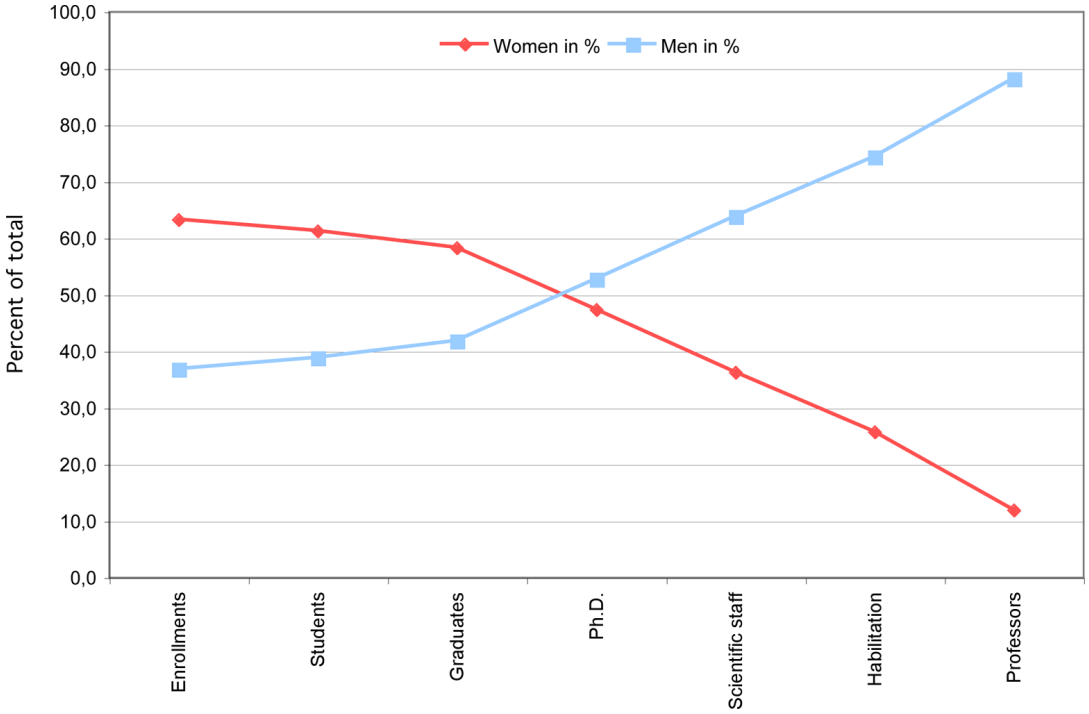


Figure 4: **?**, Scissors Diagram Showing the Gender Distribution within Career Stages in Biological Sciences at German Universities (2003)

Although explicit discrimination is largely legally verboten and culturally unacceptable in much of the world, gender disparities propagate in increasingly subtle, yet meaningful, ways. On average, women publish less often than men; the difference is especially marked in fields with a high research expenditures, like molecular biology and physics.[10]

Duch et al.[10] suggest the lower publishing rate is partially rectified by the overall higher impact of women's publications, in what another researcher called a "highly localized, mono-disciplinary, and dated" stance.[?] While this may be true at the very high levels, since women who succeed are likely to be comparatively exceptional, two massive bibliometric studies of citation patterns and publication databases demonstrate a more complicated pattern.

? analyzed the relationship between gender and research output (proxy: authorship), collaboration extent (proxy: co-authorships) and scientific impact of publications (proxy: citation count) in the WoS database. Between 2008 and 2012, this comprised 5,483,841 research articles and reviews, with 27,329,915 authorships. Of these, women account for <30% of fractionalized authorships, and are outnumbered in first author positions at a 1:1.93 ratio. In the most productive countries, all articles with women in dominant (first or last) author positions receive fewer citations than those with men. Women's publications tend to be more domestic, and thus do not benefit from the increased citation rate accrued by globally-authored papers.[?]

? performed a similar gendered analysis on the JSTOR corpus, an archive of 8.3 million scientific and humanities documents, stretching from 1545 to 2011. Their results are a positive indicator of how far the academy has come, but also of how far we have to go. Prior to 1990, women were largely absent from first author positions (<15%), but from 1990-2011 occupy almost 30%. The gap in last author positions has not

been as successfully addressed. The gap between total female authors and *first* female authorships has been less than 2% since the 1960s – i.e. women, when they're performing lab work, are given credit for their contributions. On the other hand, the discrepancy between total and last authorships remains above 5%, reflecting the same high dropout rate of women seen in Figure 4; they may be in science, but they are not staying there.[?]

5.3.2 *Race*

As with gender, minority group members leave academia at a higher rate than their White counterparts at all stages of the academic research environment.[??] Underrepresented minority groups comprised 28.5 percent of the national population in 2006, yet just 9.1 percent of college-educated Americans in science and engineering occupations.[?]

R01 grants from the NIH underpin a great deal of academic scientific research. Black applicants are 10% less likely than white applicants to receive grant funding, even after controlling for demographics, employers, NIH experience, and research productivity.[?] While Asian Americans represented 23 percent of those holding tenure-track positions, they were only 12 percent of those at the tenure or senior scientist level.[?]

5.4 GLOBAL SUBJECTS

In 1999-2000, just 6.5 percent of research literature in five major medical journals (*BMJ*, *Lancet*, *NEJM*, *Annals of Internal Medicin*e, & *JAMA*) came from the continents of Asia, South/Latin America, Eastern Europe, and Africa. Through the proxy of institutional affiliation, **?** grouped the originating institution of papers into 4 geographic areas:

- UK
- USA
- Other Euro-American Countries (OEAC) Canada and Australia
- "Rest of World" (RoW) the continents of Asia, South America, and Africa, as well as Eastern Europe and Mexico.

Numbers are boring, but wow, are they depressing.

Of the 151 articles RoW-published, 68% included a co-author from a developed country in Europe and in North American; The homogenization of the RoW countries conceals the inequity even there – the vast majority came from Japan and Israel (countries notable for their military establishments)[§], and only 13% came from China and India, the two most populous countries in the world.[?]

That was 2000, of course, and the boundaries have shifted somewhat. Chinese production has skyrocketed, as well as scientific production in the other Brazil, Russia, India, China, South Africa (BRICS) countries.[??] The rest of the world, however, has not equalized, especially sub-Saharan Africa. Despite the rise in absolute terms of published papers, it is falling in comparison to other parts of the world, namely the research capabilities of Northern institutions, as well as China's immense research capabilities .[?]

[§]I don't think the scientific dominance of Japan and Israel is an *accident*, but rather, like the U.S. biomedical-military attachments, a consequence of military aggression and dominance, e.g. Japanese nationalism and Israeli aggression in Palestine.

5.4.1 *Neo-colonial Research*

To return to a much earlier quote about literature access,

> "...Part of the problem is that none of these articles were co-written by a Liberian scientist. The investigators collected their samples, returned home and published the startling results in European medical journals. Few Liberians were then trained in laboratory or epidemiological methods."
>
> Bernice Dahn, Vera Mussah, and Cameron Nutt[?]
> "Yes, We Were Warned About Ebola", *The New York Times*

This is what **?** and **?** called neo-colonial science, or the distressing tendency for wealthy Northern researchers to show up, collect data, and leave without giving credit to their Southern collaborators. In 2003, publications of research from data acquired in the "least developed" countries, do not have co-authorship of local research institutes in 70% of the cases[?] In **?**'s examination of major medical journals, 15 papers used RoW data with no accompanying citation. 15 original papers in the journals used data from RoW countries with no RoW coauthors. Researchers in several Amazonian countries have become more prolific, but there has been a concurrent rise in Amazonian data being published under foreign research leaders.[?]

The lack of researchers – or the lack of acknowledged researchers, rather – has consequences for local health and infrastructure. It contributes to flawed, non-local data interpretations and limits the capacity of countries to build a research community invested in local issues, since all of the "good research" is happening in the U.S. and Western Europe.

5.5 WHICH BODIES ARE IN RESEARCH?

5.5.1 *Globally*

Across the globe, the medical problems most studied are, perhaps unsurprisingly, largely the the problems of the most wealthy and the most privileged. differently based on geography, socio-economics, and race. Pneumonia, diarrhea, tuberculosis and malaria, which together account for more than 20% of the disease burden in the world in 2004, received less than 1% of the total public and private funds devoted to health research."[?] Thus, the:

10/90 gap: less than 10% of global spending on health research is devoted to diseases or conditions that account for 90% of the global disease burden.[?]

Clinical trials of drugs occur in an approximately inverse way to the medical needs of communities. In a 2004 analysis of 286 randomized controlled trials, 43% addressed 1 of the 35 "leading causes of the global burden of disease". Almost half of the diseases weren't studied at all.[?]

What this means, practically, that the global burden of disease falls more heavily on low-income countries, and many fewer economic and intellectual resources go towards research on the medical or infrastructural needs[?] These are largely causes that affect the socioeconomically

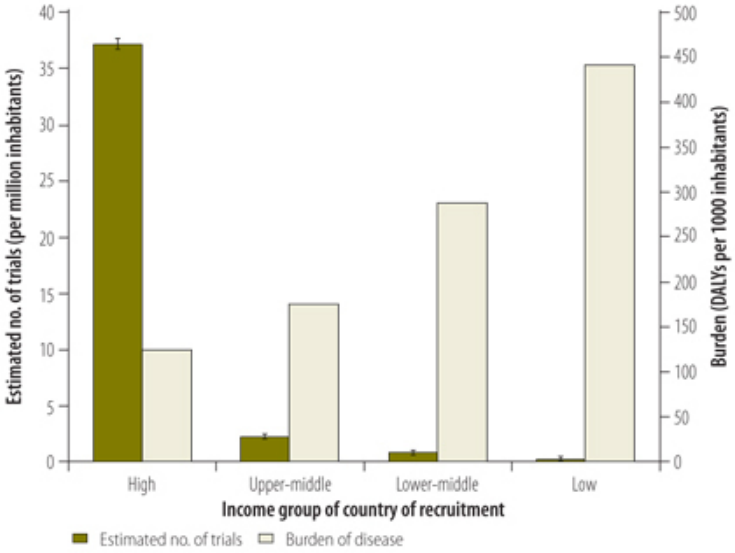


Figure 5: Estimated numbers of trials in the International Clinical Trials Registry Platform recruiting participants in low-, lower-middle-, upper-middle- and high-income countries, 2012 (Fig 4. from **?**)

depressed, which also means disproportionately people, specifically women of color and those in the majority world.[?]

In many ways, this is also an access problem, both to literature and to clinical compounds. Much of the majority world diseases are also diseases of poverty; the minority world largely no longer suffers from tuberculosis because it was eliminated with the use of antibiotics.[?] On the other hand, drug-resistant strains of tuberculosis are emerging in many areas, necessitating a new surge of research and new solutions for the rest of the world.

5.6 HARDLY ANYBODY'S BAD

Many trends are likely not actually markers of overt discrimination against women in *publishing*, 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. Age of the investigator may be *the* determining role; older investigators have had more time to build careers, and had systematic advantages in the past. In terms of bodies studied, this is a changing, albeit too slowly, trend. While men and the minority world continue to dominate on certain indices, there is a large and growing body of scientific literature happening beyond the U.S. and U.K.'s research spheres.

6 MOLECULAR PSYCHEDELICS

psychedelics "mind manifesting"

psychedelics 5-HT_{2a} agonists

Culturally significant and an touchstone for identity at my soon-to-be alma mater, psychedelics – serotonergic* hallucinogens, drugs inducing a profound qualitative perceptual change – loom large as small molecules in the public and scientific eye. They entered the modern scientific frame with with Albert Hoffman's accidental ingestion in 1943 of lysergic acid diethylamide (LSD), synthesized in 1938 from ergotamine.

In the 72 years since Hoffman's discovery of mind-altering properties of LSD, the cultural and scientific relevance of the psychedelic drugs has swung wildly. They have been variously: implicated in CIA cover ups and brainwashing[64]; a foundational of counter-culture movements; effective treatment mood disorders[?] ; a key turning point in the discovery of a major neurotransmitter, and indeed the notion of brain chemistry[37]; and as a field of battle for the rights of indigenous peoples.[?]

The current scientific space of psychedelics is anticipated by human use predating written history. In Europe, prehistoric cave paintings in Spain depict mushrooms, thought to be of the genus *Psilocybe*.[1] In North America, archaeological evidence of mushroom usage from the desert southwest of present-day Texas and Mexico abounds.[7,12,55] A Japanese folktale from the 11th century references "laughing mushrooms" and the hallucinatory and mood-altering effects after consumption.[51] Recipes for "soma" in the ancient Indo-Aryan Rigveda, the ambrosia of the gods, draw on over one hundred ingredients that produce a concoction of psychoactive alkaloids.[30]

In South America, a thriving ayahuasca-shamanistic tradition in the deep Peruvian rain forests is busy modern commerce, gone global in form as the Santo Daime religion.[19][?] The Native American Church, in the U.S. encompasses a broad group of indigenous traditions; across the ocean on the western coast of Africa, the Bwiti practices in Gabon and Cameroon employ the iboga plant as a center of spiritual practice. An estimated 32 million U.S. residents reported lifetime psychedelic usage (17%).[26]

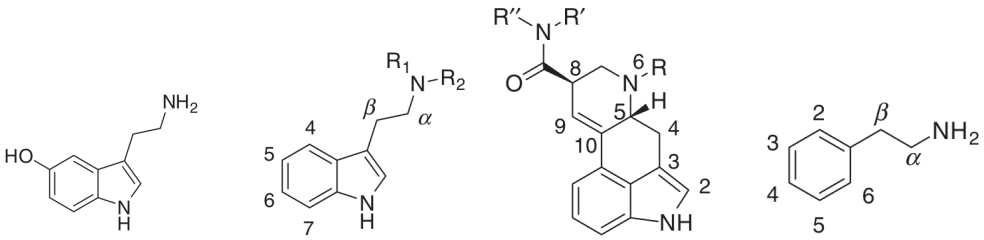
Scientific Psychedelics

After the discovery of LSD, in 1942, the neurosciences were still 20 years in the future.[?] Genetics was in its relative infancy, and would not start gaining steam until the late 1950s and 60s. Psychedelic research focused

*The nomenclature is debated, and depending on who you are will change. I use psychedelics because of it's relative specificity

psychedelics "mind manifesting", popular with (often recreational) followers of Aldous Huxley; typically not inclusive of non- 5-HT_{2A}agonists

hallucinogens drugs causing "profound distortions in a person's perceptions of reality", used largely by scientific researchers; can be for any psychotropic drug



(a) Serotonin (b) Tryptamines (c) ergolines (d) phenethylamines

Figure 6: Chemotypes of 5-HT_{2A} agonists[39]

on strictly psychological effects, i.e. the use of mescaline and later LSD experiences as model psychoses, spiritual healing, or psychotherapy adjuncts.[29]

70 years later, biology is very different. We can track very specifically what happens to bodies (or model systems) on molecular- and cellular-levels, enough to understand that the long-term spiritual effects reported by some psychedelic users?[61] might likely matched by dendritic spine growth on neurons.[20] The potential role of psychedelics as treatments for a variety of bio-psycho-social disorders is gaining global prominence. Psychedelics have therapeutic functions as:

- antidepressants[5,43,59,41]
- in modulating obsessive-compulsive disorder (OCD) symptoms[33]
- addictions to alcohol[25], cocaine[63] and nicotine[6]
- helping individuals cope with anxiety related to life-threatening diseases[43,17,14]
- treatment of excruciatingly painful cluster headaches.[22,56]

And most interesting, in the age of bio-molecular neuroscience, we can tie the alteration of consciousness to biological mechanisms of receptors, signaling, and neural networks.

6.1 THE CLASSICAL PSYCHEDELICS

Serotonergic hallucinogens – psychedelics – are classified according to their chemical structure, mental effects, binding affinities, addictive potential, lethality or lack thereof. The so-called "classical psychedelics" are non-addictive drugs, and users become tolerant after a single effective dose. They are biologically non-lethal, i.e. unlike other common recreational drugs (methamphetamines or opiates), an overdose does not affect critical lower-level biological functions like breathing.[37] The main pharmacological effects are exerted through binding a subtype of serotonin receptor, the 5-HT_{2A} receptor, and structurally most psychedelics resemble the endogenous 5-hydroxytryptamine (5-HT), serotonin. They fall into one of three main chemotypes: tryptamines, which most closely resemble serotonin, ergolines, which can be considered to be rigidified tryptamines, and the phenethylamines (see Figure 6).[38]

psilocin = metabolized psilocybin

The most notorious of the chemicals is the synthetic ergoline LSD. The tryptamines psilocin and *N*,*N*-Dimethyltryptamine (DMT) are, re-

CLASS	TYPE*	CELL RESPONSE
Agonist	full *	maximal activation
	partial *	submaximal response; graded signal
	inverse *	reduction of basal signaling
	functionally selective	ligand induces a conformation that unequally activates pathways
Selective Modulation		ligand can be agonist or antagonist depending on cell type.
Antagonists	competitive, neutral* (surmountable)	no signaling effects; occupies the receptor and thus blocks agonist binding. Agonist signaling is restored with increased concentration.
	non-competitive (insurmountable)	Ligand decreases agonist efficay, but not potency, e.g. signaling permanently modified

Table 2: Types of ligands and their cellular response (Andresen 2011[3])
* = "classic" ligand types, modulating only signal quantity[65]

spectively, the active component of the *Psilocybe* mushroom genus and endogenous to most plants.[4] Mescaline, a phenethylamine, is produced in several species of New-World cacti, notably peyote. The chemical analogues are numerous and endlessly permeable. New ones are synthesized, used in research as highly specific 5-HT_{2A} agonists, filtered out to unofficial (usually recreational) users , and subsequently banned by various governments, beginning the cycle anew.[40]

On the border of the classical psychedelics border is ibogaine and 3,4-methylenedioxy-methamphetamine (MDMA), both of which have some hallucinogenic effects. Ibogaine, although it shares the same tryptamine core as the others, also has an set of substituents that lend it activity at NMDA receptors. MDMA, known recreationally as molly or Ecstasy, does induce psychedelics effects, but it also interacts with the dopaminergic and noradrelinin systems.

6.1.1 *The molecular site of action*

Classical pharmacology has, for 50 odd years, relied on a model of characterizing ligands by the intrinsic functional effects of target interaction. The effects are governed purely by (1) affinity, i.e. the strength of the chemical bond between ligand and receptor and (2) efficacy, the property that allows bound ligands to produce a response. The model assumes if molecule X binds with an affinity Y, the receptor will always effect a signal of quality and strength Z, in a system-independent fashion.[65] The practical implication is the possibility of variety in the *quantity* of a response, but not in the *quality.* Thus, a full exogenous agonist is expected to activate the signaling pathways to the same level as the full endogenous agonist and so on, as in Table 2.

intrinsic activity - *maximum amount of activation*
potency - *ability to induce a response at low concentrations*

The big reveal: that's an oversimplification, and one of the most notable exceptions is the 5-HT_{2A} receptor. Agonist activity and the resultant signaling pathways don't track with the notion of intrinsic

efficacy underlying the classic model; it is one of the foremost examples of a model of ligand-dependent signaling, known as "functional selectivity", "biased signaling", "biased agonism", and/or "agonist-directed trafficking".[65] Many drugs bind to the 5-HT_{2A} receptor as full or partial agonists, including the endogenous serotonin, a number of 'atypical antipsychotics' (which exhibit mixed signaling), and lisuride and ergotamine, but do not induce the behavioral modifications associated with psychedelics. However, agonism at the 5-HT_{2A} receptor by psychedelics is both necessary and sufficient for behavioral responses; off-target interactions typically modulate the behavioral effects of psychedelics, but do not fundamentally turn it on or off.[15,37,16]

Our area of interest is then very narrow: what are the intracellular signaling pathways activated by the stereo-electronic perturbation and conformational movement of specific amino acid residues at the shared binding site of psychedelic hallucinogens responsible for inducing behavioral effects? The grand goal remaining, of course, to explain how a small molecule can (sometimes) irrevocably shake loose long-held notions of self and meaning by activating specific small molecule pathways.

6.2 5-HT_{2A} RECEPTORS

Although other receptors play a role, the accepted main site of action for psychedelics is the 5-HT_{2A} receptor.[18,37] In humans, there is an extremely strong correlation between 5-HT_{2A} receptor affinity and hallucinogen potency in humans, as measured by subjective reports post-trip. 5-HT_{2A} antagonists "ameliorate" (reduce, mitigate, dampen, restrain) the subjective psilocybin experience, as well as block effects on a variety of neuro-physiological measures.[9] In positron emission tomography (PET) studies of binding, the intensity of a psilocybin experience directly correlates to the level of 5-HT_{2A} occupation; again, 5-HT_{2A} antagonists reduce binding and reports of the subjective corresponding experience. As a whole, however, human research with is extremely restricted by the legal status of most hallucinogens; most work is thus done in animals[40]

antagonists
ketanserin:5-$HT_{2A/C}$
risperidone:5-HT_{2A}/D_2

While psychedelic studies in animals somewhat defeat the point of a consciousness-altering drug experience, science must go on. Mice, rats, and rabbits can't report back on their changing views on life, the Universe, and everything. However, in numerous behavioral tests and proxies for psychedelic potential, typically elicited through comparison to known psychedelics (e.g. LSD), 5-HT_{2A} activation is sufficient to produce hallucinogen-like stimulus effects.[18]

Behavioral tests: drug discrimination tests, and a characteristic head twitch response to psychedelics

6.2.1 *GPCRs*

The way these signaling pathways are effected is through the 5-HT_{2A} receptor, a G-protein coupled receptor (GPCR), and one of an extremely diverse class of heptahelical transmembrane signaling proteins. As a protein class, GPCRs are prolifically expressed across cell types and species. They are the endogenous targets of numerous hormones, neurotransmitters, chemokines, local mediators, and sensory stimuli.[8] 30-40% of current pharmaceuticals target just 7% of the available receptor targets.[?]

GPCRs enjoy such a broad range of usage due to their unique signaling capabilities. Ligand binding to the extracellular terminal of a GPCR initiates a conformational change in the protein, modifying the interaction between the intracellular side and an attached heterotrimeric guanine nucleotide-binding protein (G-protein) complex.

apo - ligand free

The G-protein complex consists of an α-, β-, and γ-subunit: in the apo-, canonically-inactive receptor, they associate with each other and the third intracellular loop or tail of the receptor of the receptor, while the α-subunit also maintains a bound guanosine diphosphate (GDP).[31] The conformational shift induced by ligand binding promotes the exchange of the α-bound GDP for guanosine triphosphate (GTP), leading to dissociation of the α-subunit and βγ-complex from each other and the receptor. They are free to diffuse laterally and initiate signaling cascades, until termination of signaling by the innate GTPase activity of the α-subunit and re-association of the resulting GDP-bound α-subunit and β-γ complex, and completing the cycle.[48]

The instability of the γ-subunit means it is almost always found in and exerts effects as part of a dimeric βγ-complex.

To add complexity, at present, the literature references discovery of 16 α-, 5 β- and 12 γ-subunit genes. Dimers form of most, but not all, β-γ possibilities. The units are differentially expressed across the body,[67] thus decreasing the array of possible complexes, which would otherwise stand at $16 \times 5 \times 12 = 960$ options.[8,11] Ligand binding can also trigger a conformational change without subunit dissociation.[47] Additionally, while the βγ-complex was initially regarded as a more passive partner of the G protein α-subunit, perhaps only as a negative regulator, it is now clear that βγ-complexes can act as mediators of signaling in their own right.[24]

6.3 FUNCTIONAL SELECTIVITY

The 5-HT_{2A} signaling pathways bifurcates in a psychedelic vs. non-psychedelic way, complicated by inter-drug variability. The legal status of drugs also shapes the kind of available pathway information. For example, 2,5-Dimethoxy-4-iodoamphetamine (DOI) is currently unregulated, and thus the most common compound. On the other hand, DMT was only placed into Schedule I in 2010, allowing the excellent work by Schmid and Bohn on the role of ß-arrestins in functional selectivity in 2008[54] and 2010[53] at The Scripps Research Institute to go forward, but making follow up work substantially more difficult.

The affinity of ligands for receptor complexes is affected by a variety of factors, expressed as extracellular receptor conformation. The coupled G-protein can affect the receptor conformation,[28] as can β-arrestin binding, membrane potential,[57] phosphorylation, and intracellular scaffolding,[49] to name a few. Ligand binding initiates some number of cascades; this leads to short-term second messenger release and long-term transcriptional regulation.

6.3.1 *G-proteins*

$\alpha_{Q/11}$ SIGNALING Release of α_q activates phospholipase C (PLC) signaling, leading to hydrolysis of membrane phospholipids to inositol triphosphate (IP_3) and diacylglycerol (DAG) . IP_3 mobilizes of intracellular Ca^{2+}; both DAG and Ca^{2+} release activate protein kinase C (PKC).[46] PKCs are long lived active enzymes. Among their targets are phosphory-

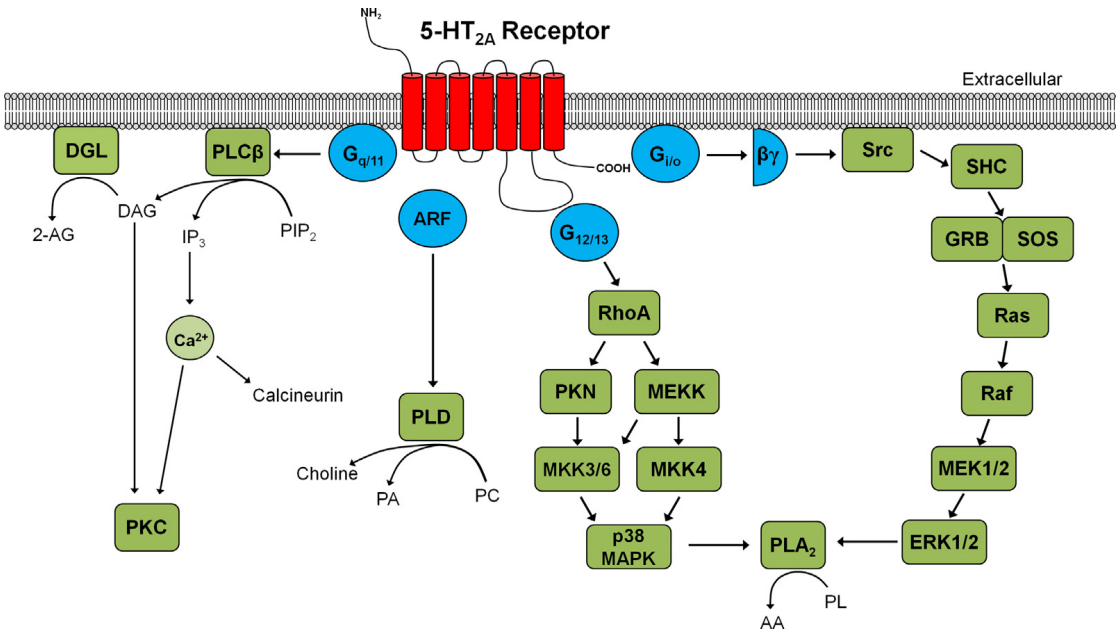


Figure 7: 5-HT$_{2a}$ pathways (Fig 4 from Halberstadt , 2015[18])

lation of other GPCRs (heterologous desensitization) and transcriptional up regulation.

Non-canonical

$\alpha_{I/O}$ SIGNALING Both the pertussis toxin (PTX)-sensitive $\alpha_{i/o}$protein and the associated β-y complex catalyze or directly act the activation tyrosine-protein kinase Src (c-Src). In turn,c-Src can activate a phosphoinositide 3-kinase (PI$_3$K)-protein kinase B (PKB) pathway. More well established is c-Src activation of the Mitogen-activated protein kinase (MAPK)\ERK1,2 pathway, which eventually leads to activation of (notably) ribosomal s6 kinase 2 (RSK$_2$), arachidonic acid (AA), among other transcriptional- and scaffolding effects.. PKB and RSK$_2$

$\alpha_{12/13}$ SIGNALING The least well associated pathway, $\alpha_{12/13}$is primarily associated with the activation of Rho GTPases. Rho signaling up regulates the p38MAPK, converging with the $\alpha_{i/o}$ MAPK\ERK1,2 activation of phospholipase A2 (PLA$_2$). The β-y subunit can also activate PI$_3$K and thus PKB, another intersection with $\alpha_{i/o}$.

6.3.2 *Regulation*

Signaling cascades activate a number of kinases, which in turn phosphorylate the receptor and regulate function. Phosphorylation patterns on receptors can act as a GPCR "barcode", directing β-arrestin scaffolding and signaling, and promoting certain receptor conformations over others.[31]

The phosphate groups also hinder the re-association of the G-protein complex, preventing further signal transduction (desensitization), and recruit β-arrestins to the receptor. Canonically, β-arrestins als desensitize the receptor and induce internalization, promoting the formation of a clathrin-coated "pit" and targeting the receptor to the endosome. Once there, the receptor can continue to signal while re-sensitization

(β-arrestin and phosphate removal) and recycling back to the surface occurs, or degradation by proteases.[3]

β-arrestin activation can also regulate signaling independent of its inhibitor functions, including kinase and transcription factor activation;[44] receptors can also be re-sensitized without recycling certain situations and in certain cell lines.

5-HT_{2A} receptors are targeted to dendrites by the scaffolding protein PSD-95; β-arrestins also play a structural role apart from their recycling function. PSD-95 is essential in transmitting signaling information and receptor processing.[50,31]

6.4 MEASUREMENTS

6.4.1 *Transcriptional 'fingerprints'*

The acute immediate signaling events – second messengers, structural regulation – are reflected in transcriptional and gene changes, providing a mechanism for the longer term effects of psychedelics. The induction of a transcriptional response also provides a way to measure the response to drugs as a combination of many pathways, rather than arbitrarily selecting one or two second messengers. A number of studies have demonstrated the dynamic nature of the LSD transcriptional response in inducing plasticity-related immediate early genes (IEG), notably *arc* and *c-fos*.[36,35]

The Sealfon and Gonzalez-Maeso labs at Mt. Sinai School of Medicine developed a method to measure the fold change in transcription of IEG, taking a so-called "transcriptome fingerprint". Using a panel of relatively high-affinity, structurally related 5-HT_{2a} agonists in both 5-$HT_{2a}^{+/+}$and 5-$HT_{2a}^{-/-}$mice, they found each agonist elicited a reproducible and specific IEG response. All of the agonists induced expression of 5-HT_{2a} - and $\alpha_{q/11}$- dependent *c-fos* expression. However, only the hallucinogenic agonists[†] induced the plasticity-related *egr-2* expression, through an $\alpha_{i/o}$- dependent mechanism.[16]

6.4.2 *Phosphorylation*

Much of the signaling cascade eventually focus around kinase activation, notably PKC (via $\alpha_{q/11}$), PKB (via $\alpha_{12/13}$and $\alpha_{i/o}$), and RSK2 (via $\alpha_{12/13}$and/or $\alpha_{q/11}$), and subsequent receptor phosphorylation. In HEK-293 cells, Karaki et al. found hallucinogenic compounds DOI and LSD led to phosphorylation of Ser^{280}on 5-HT_{2a} , while non-hallucinogenic congeners promoted a different phosphorylation pattern. This psychedelic-specific phosphorylation is PKC-dependent and $\alpha_{i/o}$-independent.

The "bar-coding" of the receptor likely has nothing to do with any intrinsic Ser^{280} affinity, but rather is an effect of distortion of the receptor by the still-bound psychedelic ligand, thus making the Ser^{280} site accessible.[21]

[†] DOI,LSD, mescaline, psilocin
2,5-Dimethoxy-4-methylamphetamine (DOM)
2,5-Dimethoxy-4-bromoamphetamine (DOB),

6.4.3 *De-sensitization and recycling*

The biased phosphorylation pattern has a direct effect on processing of the receptor. In the wild-type receptor, 1-hr pretreatment with LSD and DOI has relatively little effect on either 5-HT-induced IP_3 production or Erk1/2 signaling. This slow desensitization by hallucinogenic drugs is abolished by an alanine substitution, which cannot be phosphorylated. A phosphomimetic substitution at Ser^{280}, however, mimicking a constitutively phosphorylated receptor, causes a hallucinogen-like slow desensitization response to all drugs..[21] This is consistent with other data on desensitization where both 5-HT and DOI induce receptor recycling in a PKC-dependent and G-protein coupled receptor kinase (GRK)-independent manner. 5-HT-induced recycling, however, is complete within 2.5 hours of binding , while DOI takes a full 7.5 hours to be recycled back to the surface.[45]

6.4.4 *β-arrestin*

Ser^{280} has one more role to play in β-arrestin recruitment. $Ser^{280}$is located in the i3 loop, involved in β-arrestin binding. Ergotamine and lisuride recruit more β-arrestins to the receptor than LSD or DOI.[21] This is itself consistent with data on β-arrestin-mediated signaling of DMT and 5-HT. Both compounds provoke a behavioral head-twitch response at high enough doses. However, the 5-HT response is dependent on a β-arrestin/PI3K/c-Src/PKB pathway – inhibition of any member of the scaffold significantly reduces the response. DMT, on the other hand, induces a behavioral response independently of this pathway, and is intensified in β-arrestin KO mice.[53,54]

6.4.5 *Second messengers*

Activation of the $\alpha_{q/11}$pathway is measured by PLC-IP_3 or Ca^{2+} accumulation, while PLA_2-AA release acts as a proxy of $\alpha_{i/o}$ activation.

However, the second messenger pathways coupled to G-proteins exhibit a receptor reserve phenomenon: the concentration at which 50% of receptors are occupied is higher than the concentration producing 50% of the maximum response. Essentially, there are "excess" receptors on the cell surface. Receptors that couple to multiple pathways may have different signaling reserves; thus, the practice of only using one metric (e.g. IP_3 accumulation) as an assessment of agonist efficacy may not capture the varieties in signaling.[23]

In NIH3T3 cells, the PLC-IP_3 and PLA_2-AA pathways are differentially activated by 5-HT_{2a} agonists. Excluding LSD, the rest of the psychedelics tested (psilocin, DOB, 5-MeO-DMT) show increased efficacy and potency at PLA_2 over PLC.[28] More or less potent psychedelics typically induce a corresponding amount of PLA_2 response; while this seems to be roughly correlated with hallucinogenic potential, the trend does not remain consistent enough across drugs to provide a full explanation for their effects.[34,32]

6.4.6 *Subunit signaling*

Finally, G-protein pathways. Both behavioral and transcriptional responses to DOI are dependent on 5-$HT_{2a}$$\alpha_q$ -mediated activation of PLC signaling;[13] the behavioral LSD response is also modulated other receptors.[52] MAPK-mediated transcriptional response to hallucinogenic drugs relies entirely on $\alpha_{i/o}$ induces c-Src. .[16] AA release is mediated by both $\alpha_{i/o}$ and $\alpha_{12/13}$ release, since inhibition of just one does not abolish PLA_2-AA signaling.[27]

6.5 UNIFIED MECHANISM?

Despite the bits and pieces of gathered evidence, the link between functionally selective 5-HT_{2a} activation and behavioral response remains unclear. Clearly, there is the involvement of multiple receptor states and complicated feedback loops; many of these are psychedelic-specific. The 5-HT_{2A}model, although it remains the dominant receptor, does not include the documented involvement of 5-HT_{2C}receptors, a popular theory regarding MGlu2 heterodimerization, or the plethora of other interacting properties of the cell.

6.6 PROJECT OUTLINE

An issue with many of the studies on functional selectivity is the cell-lines, especially for an effect that is highly-dependent on so many factors. While some are done on mice and primary cortical neurons, many more are done with transient transfections into HEK293 (human kidney/adrenal), C6 glioma (rat astrocyte), NIH-3T3 (mouse embryo), or CHO (hamster ovaries) cell lines, as well as *Xenopus* oocytes. None of these reproduce the structural regulation of dendritic spines, and may not express the same intracellular signaling milieu. On the other hand, a cell line that *did* reproduce some aspects of neuronal structure (as far as *in vitro* can) might more accurately mimic *in vivo* signaling effects.

So, the original intention (as of January 2015):

1. Clone the receptor from rat cDNA into a plasmid that is also expressing a large fluorescent protein (GFP), an antibiotic resistance gene, and promoter region to force expression of the DNA.

2. Transfect HEKs to test expression of the construct, and then into P19 mouse stem cells

3. Induce neuronal-like differentiation into the transfected P19s, and see if the cell is capable of reconstructing a dendrite with localized serotonin receptors

Part III

CONTROLLING & MAKING KNOWLEDGE

7 CASE STUDIES IN METRICS AND NOTEBOOKS

As a firm believer in putting (some) ideas into action, it seemed worthwhile to not just talk about open science and representation, but actively engage with the concepts. I came to two conclusions, and subsequent courses of action.

1. Open science was not just an ideal to be thought about – it was something that I could and should be doing. Thus, an open notebook.

2. Representation was also not an ideal to be pined over – the undercitation of women is not just something that happens, but is again, powered by researchers making decisions. I wondered whether, as someone who tries to be equitable and fair minded, and who thinks of themself as someone who fights for ~equality~, I was doing any better than the vast majority of the literature. Hence, bibliometrics on my division III.

7.1 OPEN NOTEBOOK

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. From June until December of 2013, I kept an 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.

7.1.1 *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?

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 , it's frustrating and tiring to have to re-type and revisit a protocol run just earlier, and translate from paper to digital.
    b) The lack of *drawing* abilities is a serious hindrance; annotation via text is significantly less effective than writing in red pen next to it
    c) 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. I would venture to say the increased feeling of failure upon revisiting the entry is one of the most demoralizing things
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.
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 – makes you more likely to be careful with your records and scientific choices
    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

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.

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

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.

7.1.2 *Suggestions for Surmounting Notebook Challenges*

Some thoughts: Since being open is *not* the same as being accessible, transparent, or even useful; 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, but 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" typical of scientific papers. 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.

7.2 BIBLIOMETRICS

I think it's important that when we talk about representation, we don't abstract it to be just numbers. Citation networks, like everything else,

*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*.

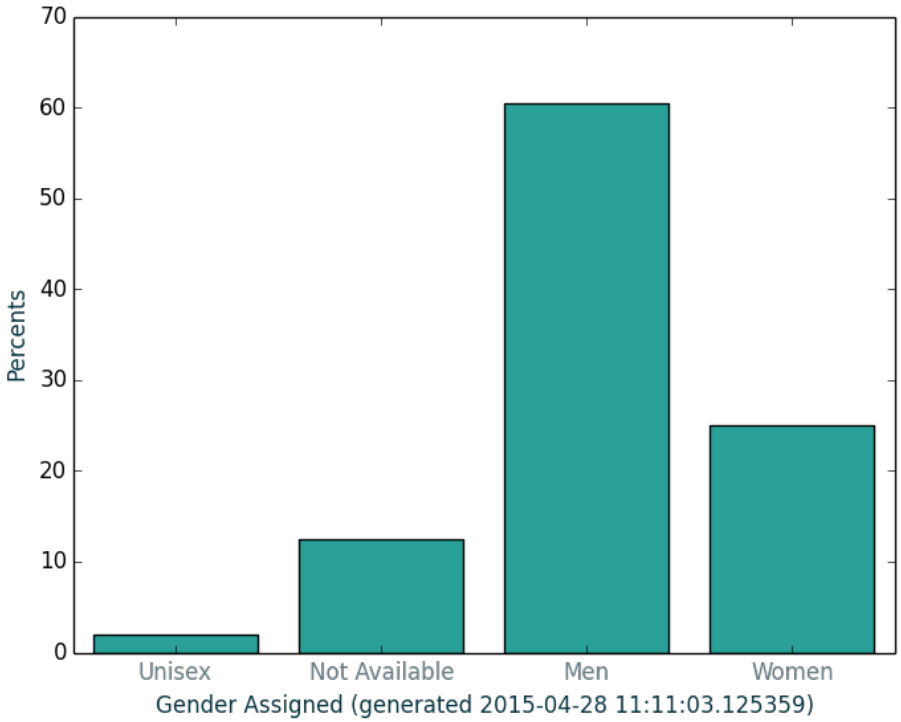


Figure 8: Gender distribution all potential references

are the result of human decisions; I think a program or script analyzing gender in specific fields or reseacher libraries would be a useful tool and yield interesting results. I took preliminary steps towards coding this, making a small script that runs a crude bibliometric analysis on my citation list.

7.2.1 *Methods*

The script is a available as a hacky Github repository, at https://github.com/kathleenleeper/bibmetrics. It is written entirely in Python, version 2.7.5 (https://www.python.org/download/releases/2.7/). It uses a number of packages, all available free of cost and largely of licensing:

1. GenderComputer, a Python library that uses a database of names from different countries to guess gender based on national statistics, licensed under the LGPLv3 (available at https://github.com/tue-mdse/genderComputer)

2. PyZotero, a library that accesses collections from the reference manager Zotero and allows manipulation of the data structures, licensed under the GPLv3 (available at https://github.com/urschrei/pyzotero)

3. Matplotlib, a standard plotting package, licensed to be BSD-compatible and based of the Python Software Foundation license (available at http://matplotlib.org/)

The program (in its current iteration) runs through a .bib file and extracts the title and authors. If no author is found, it prints the title of the entry and the message "no author available". If the author

cannot be assigned a gender by GenderComputer, it prints the author entry. Typically, these are cases of (1) initials (e.g. (2) organization (e.g. "The PLoS Medicine Editors") or (3) names that do not appear in the available databases, usually those of non-Anglo origin or with non-Latin characters.

The script adds 1 to the appropriate array (man, woman, unisex, unassigned) until it is done running through the database, and then calculates the proportions of each category compared to the whole, generating the chart in Figure 8.

7.2.2 *Results*

Unisex names are a relatively insignificant portion, comprising <2% of the total names.

Although in an uncleaned database, the "Not Available" would hover at closer to 20%, almost all bibliographic entries have full names attached to them. The missing N/A names are largely corporations, non-Anglo names, or solitary initials, and published long enough ago that no bibliographic database retains their full name.

The real heart of the matter is the men and women. Close to 60% of the authors in my database are assigned male; only 30% female. This divide would change dramatically, I'm sure, if we broke it down by subject matter – feminist science and philosophy vs the other disciplines in my Division III.

8

TEMPERING OPEN

> "Do we really believe, for instance, that the problem of global injustice is one of lack of access to technology?...
>
> Are we really ready to stand behind the suggestion that recorded information — the document, central as it is to our profession — is a sign of inherent cultural superiority?"
>
> "Unpacking 'Information Inequality"', Dave **?**

This is a hard section to write, not least because it is a critical-reflective sketch of a movement drawn largely in terms of a moral call to arms**? ?** I swallowed hook, line, and sinker several years ago. *If* science is good, science should be more accessible; *if* knowledge is power, knowledge should be more broadly available. *If* everyone has knowledge-power-science, then we have made vast strides towards rectifying a multi-dimensional power inequities.

Most of the suggestions comprising "open science" centers around assumptions about access, knowledge, and distribution. The more interesting and radical ideas toy with re-envisioning whole new systems of scholarly production and communications; the more sedate merely push for scientific knowledge as a public good. So what am I pushing for? Underlined, circled, and highlighted in my notebook is this question:

> Am I criticizing open science, open science, or open science?

Critiques of *open* are the same critiques of free software and open software, a good angle, but not quite right. Critiques of *science* are already largely covered, representationally in Chapter 5, conceptually in Chapter 2 and Chapter 9. But the third option, a reflexive discussion of *open science*, is different from those, and requires a special framing.My key(s) to this haphazard and preliminary analysis of science that is open are in two observations.

1. In the sense that the varieties of open science are merely digital science, **open *is* the direction Science, Technology, Engineering, and Math (STEM) fields are moving**, and in a way that is not necessarily true for analogous open movements based around more corporate interests.

   The NIH, a major funder of research in the U.S., requires all of the published articles based on NIH funding be made available, free of charge, within one year of publication. The Wellcome Trust, the second largest non-governmental biomedical funding source, also requires scientists make their publications *gratis*. *Nature*, the world's most high-profile multi-disciplinary journal, has recently updated their publication policies to "strongly encourage" data deposition and require statements about code availability**?** . Data repositories are popping up at an alarming rate; open notebooks have received attention at the highest levels of publishing.**?**

2. Advocates are unabashed in their vision of science: **help people, do cool stuff along the way**. This is achieved by both accelerating

scientific research and sharing results more broadly, thus both discovering more and enabling participation.

biomedicine: Jean Claude-Bradley, an open science "giant", founded his Useful Chem malaria project to accelerate the discovery of malaria cures. Many advocates for the publication of *all* clinical trial results argue it is a patient's right to know the full scientific history of their medication.

geology: Geology and earth sciences are tightly linked to policy decisions about environmental concerns. International scientific scandals like Cimategate are supposedly "rooted in the resistance of climate scientists to accede to requests from members of the public for data underlying some of the claims of climate science"**?** , open data could mean the difference between the public's trust in scientific goodwill and the State of Florida's unofficial ban on the phrase "global warming" for employees.**?**

Climategate: a breach of university emails that climate change critics used as proof of scientific conspiracy

With those, we can start to ask our questions. If we achieve the stated goals of an OS system, what new problems does that present to the feminist and reconstructive observer and participant? If open science continues on its present course, what values comprise our new, open world? What parts of the current open science ethos should we strive to keep or work to excise?

8.1 "THE FUTURE IS OPEN": WHAT ARE WE BUILDING?

First and foremost, the solutions promised derive from specific kinds of problems – e.g. those outlined in Chapter 3. This set of assumptions guides the problems, what kinds of solution are tenable, and beliefs about what the consequences of those actions will be. They make assumptions about scientific knowledge and about who and how knowledge will benefit. What are those assumptions, and how will they affect science/systems going forward?

8.1.1 *Open, not free*

The strongest proponents of open science are people who treat software like they want science to be – intractably frustrating, but open to experimentation and manipulation by anybody who wants to, and driven by the needs of the community. Correspondingly, the nomenclature of *open* science is telling, drawing on a dichotomy of software licensing. In the closely affiliated free/libre open source software (FLOSS) movement, there's a sharp ideological divide between "free"-*libre* and "open" *gratis* licenses.

> "…'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."
>
> "Free as in sexist?" Free culture and the gender gap"
> Joseph **?**

Advocates of the libre licensing focus on free software as social imperative, with the benefits of distributed information and production a

secondhand benefit. User freedom and the call to rights, as laid out in the founding document of the Free Software movement (the GNU General Public License (GPL)) and the Free Software Foundation (FSF) logo, is paramount.

FSF slogan: "Our mission is to preserve, protect and promote the freedom to use, study, copy, modify, and redistribute computer software, and to defend the rights of Free Software users."

> "The licenses for most software and other practical works are designed to take away your freedom to share and change the works. By contrast, the GNU General Public License is **intended to guarantee your freedom** to share and change all versions of a program–to make sure it remains free software for all its users. . . When we speak of free software, we are referring to freedom, not price."
>
> The GPLv3

Richard?

"Open source", on the other term, as a term and a licensing model, derives from an explicit attempt to side-step the social values and ideological connotations of the term "free software". It instead has a narrow focus on the access to and production of source code - i.e. the 'practical' benefits of distributed production.

From the outside, this distinction often seems trivial. n the case of *open* science, I think it's telling of the ambivalent moral aspects and the ways open science draws on both rhetorics.? One, the same rhetoric of the morality of freedom – the *public has a right to know* and it is scientific *duty* to share as much as possible, in the same way that software users have a right to know what their technologies are doing. In many ways, this harkens back to Mertonian ideals of scientific values.? Allowing more people to access more information is simply the right thing to do. On the other hand, scientists are not altruists, we're just people. Scientific publishing happens to disseminate and spread the good word of knowledge, but it's also used to bolster careers and mark intellectual property boundaries; open access publishing can only go well for authors.?

Open science is no different. The intent of open science, like open source, is to modify the *mechanisms* of production, making more reproducible, more reliable, and more powerful science. It pays no intrinsic attention to content or subject.

In software, open source has a rich history now of taking community-driven labor and spinning it back into commercial and exploitative technologies. In science, the parallel might be projects that pitch themselves as community-driven citizen science. In an alternative construction, they might just be a way to shift labor from cheap graduate students to even cheaper laypeople. I have no doubt of the ability of corporations and governments to perform a similar machinations on researcher-derived works; the removal of price and licensing barriers and the work of building knowledge aggregators by scientists is easily translated into more efficient government-military usage.

Global definitions of "open" and "free"

Free software and open science are built on European/U.S. legal, moral, and social codes, stemming back to John Lock? . The power of the Free Software License comes from its copyleft nature. Using the current globally-dominant IP systems, it *requires* users to share freely, under copyright terms. Without our notions of property and copyright, the

legal strictures underlying open-ness science would have no power – but it also might not need that power.

Guaranteeing products will be under the minority world's copyright law forces those using it to engage and participate in said legal system. This also shapes what kinds of (scientific) knowledge *can* be copy-written under this. Notoriously, but not irrelevantly, shamanistic and indigenous plant knowledge is *not* patentable, because it's cultural knowledge. Once homogenized into official (published) science, however, it can be – and then re-opened as a scientific discovery, *libre* free to all, but under a new copyright regime.

8.1.2 *Return to the past*

Much of the open science movement talks abut a "broken" scientific ecosystem, as if it had been whole in the past and we must find our way back, somehow, to the good days of pure scientific exploration. Proponents proposes open science as a fix, as in this 2013 editorial:

> I think that fraud has increased since I came into scientific research 40 years ago, as the challenges... have increased. In the not-so-recent past, we did not have cutthroat competition to publish in the most prestigious journals as we do today, and grant funding flowed freely. There was enough reward to go around. The life of a scientist was relatively simple, so there were fewer incentives to cheat..."
>
> **So what can we do to return to how things once were?**"
>
> "Sound the Alarm: Fraud in Neuroscience"
> Stephen**?**

I am not the only one to note this. In *Biohackers: The Politics of Open Science,* Alessandro Delfanti describes how:

> "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 and 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."
>
> Alessandro **?** , p. 5

One effect of this narrative is to allow the construction of a mythical past where open science has been involved in every one of our beloved scientific histories. The belief is that "science... has always been special because of its true openness for the sake of knowledge."**?** In this past, to be Isaac Newton, Dmitri Mendeleev, Sydney Brenner, or one of the 98 men listed in *100 Most Influential Scientists***?** is to have been an (open) scientist, given the limited tools of the time. Having an illustrious history helps lends legitimacy to the practical and moral appeal of open science.

While forty-five years ago may have been the hey-day of scientific funding, it was also the time of, again, the Tuskegee Syphilis study. Those famous scientists, forerunners of physics and biology and computer science, existed in a scientific world populated (on paper) almost exclusively by men.* Before the "evil corporations" privatized science, it was privatized in effect by a "meritocracy" that relied on a college education, on skin color, and on money, which was outright denied to women and minority groups. Earlier, the gentleman scholars of the Victorian era that laid the groundwork, like Darwin's *Beagle* voyage, were the wealthy Victorian men who had both time and resources to fiddle with the world instead of surviving.

8.1.3 *Representation redux*

Prerequisite knowledge

In a the Do It Yourself (DIY) culture of open science, where making things legally and financially accessible is the goal, who has intellectual access to literature/data/code? Making things *open* does not equate with "accessible"; accessible literature does not an empowered populace make. To interact or use the newly-legally accessible data and code, one already has to be engaged in the scientific sphere that uses them. For scientific creation, individuals need hardware, physical access, digital access, and the free time to spend messing up before they get it right.

Who participates?

As with science as a whole, forms of (visible) open science are likely dominated by white men, and white men from the usual minority world countries. In free software communities, men outnumber women to a much greater degree than in more traditional development structures[?] ; this derives in part from the assumption that code and software is race- and gender-agnostic. Large-scale, collaborative, and decentralized community structures like those in FLOSS thus usually fail to include any direct safeguards or rules about what kinds of behavior are acceptable – misogyny and racism run rampant, without the checks of corporate human resources department and laws to restrain them.[??]

There is essentially no data on whether this is true in open science. In the North, 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. The only available data is one extremely informal study of the self-reported gender of participants in Open Worm, a project to build a digital model of *C. elegans.* 11% of their contributors are women.[?]

In terms of production of literature, this is hard to distinguish from the visibility problem of the global science sphere. Open access journals are prolific in the rest of the world, and in a variety of languages. they are not, however, regularly indexed in the SCI, are not assigned an IF, and thus remain 'peripheral' in the 'mainstream' of science[?]

*While women contributed as assistants, they were rarely given full credit for their work[?]

8.2 "FOR THE GREATER GOOD": THE MAKING(S) OF OPEN SCIENCE

I stated earlier that the "need" for open science is couched in strong ethical terms. If open science advocates believe it's doing good, what does that entail and assume? The moral high ground of open science advocates is not just scientific reliability, but the inclusion of "curious minds" who would otherwise not have access.[?]

Two major players arise from this – one, a public populace who is now empowered by access, and two, researchers across the world in poor institutions, who would otherwise not have access to the sum of human knowledge.

8.2.1 *The mythical Public*

The division between science and layperson is very real in the imaginary realm, and very blurry in the real world. Who, exactly, is the public that is funding research and thus needs access to the results? Apart from the prerequisite knowledge that circumscribes participation, the "public" may not be equipped or interested. Additionally, while they may be interested, the need for scientific jargon to impress other scientists renders the literature completely incomprehensible.

8.2.2 *Majority world participation/needs*

It is not just that "more scientists" will have access, but a specific *kind* of scientist – the ones located in the socioeconomically lower areas of the world. This plays into the truism of the the necessity of science and technology for the "development" and betterment of the majority world nations.

To demonstrate, a selection of quotes from the past several years:

> Scientific progress in developing and emerging countries is greatly hampered by their inability to afford essential journals. . . The development of the Open Access (OA) movement offers hope for information-deprived scientists."[?]
>
> "All peoples, no matter what the economic nature of their society, need the opportunity to access scientific knowledge. . . One major challenge facing many developing countries is that their researchers have very little access to contemporary scientific literature ."[?]
>
> "These [access] tolls bring enormous profits to the traditional corporate publishing industry, but they make it impossible for most people worldwide — particularly in low and middle income countries — to access the biomedical literature. . . "[?]
>
> "Indeed, the digital divide contributes not only to the exacerbation of this gap but also to the deprivation suffered by researchers in developing countries"[?]

This discourse, the need for the majority world to access the minority world's knowledge in order to proceed is nearly identical to the 1950s. The "developed" countries have always needed to help the "developing" countries reach their standards.[?] It relies on two narratives of information inequality, where information is a quantifiable and useful product that is assumed to be:[?]

1. generated through the technological advancements of the West's information "revolution," and
2. largely (if not completely) absent in the majority world — an absence that, in turn, accounts for the "underdevelopment" of such communities.

This sets up important consequences for consumer-producer dichotomies, legacies of neo-colonialist research, the value of different communication forms, and the types of knowledge we accept.[?]

Reification of power structures

Access to scientific literature is important to scientific production; it is however inadequate to rectify the global inequalities in production and visibility on its own, linked as they are to economic-political-military power positions. Majority world participation in *science* is marginalized for a whole host of other factors unrelated to scientific access to literature.

Open science focuses so much on dissemination of already-done-science, and much less on the production of science, except insofar as dissemination (of literature, data, code) allows for more production – "even in resource-poor countries, where they can't collect data".

Positioning the majority world as in need of information does nothing to challenge the image of the majority world as consumers, not yet ready to produce on their own, which only serves to obscure the *current* research and the actual infrastructural needs to perform more research.

The written word

The focus on open communication through digital means also precludes the possibility of other forms of communication, re- and continuously prioritizing the scholarly document as the height of globally-applicable knowledge.

Indigenous sciences and local biologies

OS also relies on the same globalized notions of broadly, unilaterally applicable research. *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, or co-opted into the bigger framework, as the case may be.. 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.

8.2.3 *The right kind of knowledge*

The major scientific problems in Chapter 3 are all based around outside institutions of restriction – publishing houses, funding institutes, The State, incentives that prioritize *this* kind of production on scientific

[†] Again, *if* science is local, there is no homogeneous global community of science/tists. There isn't one anyway tho.

projects. The "science" itself, the pipetting or data collection, only needs modification to the extent that it should be automated, modified, and modular. In this model, the biggest thing holding science back from solving the world's problems of disease, pollution, and infrastructure is scientists and their culture. Changing the culture to one of sharing and openness would, necessarily, make the science *faster* and therefore better – since science is already doing so well. The issue is never scientific production itself, but the speed at which and for how many purposes we can use it.

It makes no strides towards more a humane, culturally-engaged science. It offers accessibility as bait, not to anyone in particular, but to the whole world. It puts no focus on collecting different *kinds* of information (feminist karyotypes, or examining neglected tropical diseases), or reshaping the input we accept into the scientific process. Openness still requires the same types of conclusions, the same processes, the same types of intellectual, financial, and technical resources.

i.e. There's no point in OA literature if it doesn't address your disease

9 MAPPING PSYCHEDELICS

Psychedelics are pharmacologically, historically, and conceptually interesting. In my frame of reference, they are small but notorious molecules. As compounds with a cultural history They are inseparable from their 'practical' applications in therapies and on people.

I've spent a lot of time writing about scientific communication, which ultimately comes down to the control of knowledge. Psychedelic research is similarly bound up in networks of scientific prestige, values, conceptualizations, and of community organizing and different knowledges. I

1. I am a strong advocate for the value of different knowledges and different ways of approaching them. We all have ways of navigating the world. Of particular interest (for me) is the cultures around psychedelic drugs. I roughly separate them into:
    a) the scientific and laboratory, where they are chemical structures
    b) the recreational-North usage, where they are acid tabs and dried fungi bought on the deep Web
    c) traditional usages, where drugs are one component of deeply complicated spiritual practices, and moreover, it is no longer the *drug*, but plant preparations
2. The increasing rise of biomedicalized understandings of disease has serious and far-reaching consequences for people and policy, some good, some bad. I also have deep concerns about the complicity of biomedical researchers in the United State's constant, ever-shifting war machine, and psychedelics are no exception.

If we (the scientific establishment) recognize recreational or indigenous psychedelic usage as a valid form of knowledge, we also assimilate and incorporate it into our technoscientific complex. So who should control the flow of psychedelic knowledge? Who are the stakeholders in this?

9.1 SCIENTIFIC USERS

The initial scientific appearance of psychedelics focused on medical-military psychological explorations*, all with the belief that the subjective experience was key to their outcomes. Regardless of their goals, the projects were not molecularly-focused.

In the intervening 70 years, two trends in medicine set the stage for the re-entry of psychedelics as scientific objects.

The first are processes at the heart of medical sociology, bioethics, and medicine. For 40 years, the idea of:

medicalization the process by which aspects of life previously outside the jurisdiction of medicine come to be construed as medical problems; exerting control over medical phenomena

*e.g. Timothy Leary's spiritual explorations, the Central Intelligence Agency (CIA)'s mind-control projects, early attempts at reducing addictions

has guided notions around analyzing health, medicine, and society. In the late 90s, Adele **?** and other sociologists extended the idea of medicalization in order to account for new "conditions of possibility", leading to a theory of

biomedicalization increasingly biological-scientific aspects of the practices of clinical medicine; that is, technoscientific practices of basic life science ("bio") are increasingly part of applied clinical medicine; increasingly not just curative, but preventative and focused on optimizing the human experience

Biomedicalization means deviations from the norm is now not just a psychiatric issue of bad morals or childhood influences, but a chemical problem to be solved by chemical means. While typically presented as an intrusive diagnostic by the medical establishment**?** , it can be a positive step for many (e.g. permitting individuals to self-diagnose and shift blame, giving a voice to unrecognized issues).**?**

Biology, and now by extension medicine, turned molecular. In parallel, the neurosciences were born in the 1960s. By 1990, it was the "Decade of the Brain",[29] and neuroscience had evolved, in a biomedicalized fashion, to be increasingly neuromolecular.**?**

9.1.1 *Biomedicalized psychedelics*

This pharmacological disease model of various formerly-social ills and the new dominance of brain science re-opened the door for careful and scientific psychedelic research. Most of the serotonergic hallucinogens are Schedule I drugs; the U.S. government's official stance is:

1. The drug or other substance has a high potential for abuse.
2. The drug or other substance has no currently accepted medical use in treatment in the United States.
3. There is a lack of accepted safety for use of the drug or other substance under medical supervision.

However, the loosening of government strictures on research indicates a changing focus. The biomedicalization of psychedelics allow them new clinical/medical configuration and applications; a space opened up for pharmacological interventions into the lives of those with PostTraumatic Stress Disorder (PTSD), addictions, and depression.The changing medical boundaries – what is and is not a molecular problem, and the increased focus on the mind as a site of intervention – give psychedelics a new purpose. Scientifically, they are no longer mind-opening, or drugs of abuse, but compounds characterized primarily by their neuromolecular effects. Constructed biochemical boundaries very deliberately eliminated other forms of psychoactives, from designer opiates (ketamine) to very traditional fungi (*Amanita muscaria*). Psychedelics were re-imagined and redrawn as as 5-HT_{2a} agonists.

Addiction

The framing of the problem affects the solution, and vice versa. (Bio)medicalization of mental health can be empowering – attributing clinical depression to a chemical imbalance can be a helpful way to move forward, instead of blaming themselves.**??**

Similarly, alcoholism as a disease implies the possibility of healing and the movement of blame from individual choices to a genetic inheritance and accident of environment. It also, however, reduces a psychological-bio-life-complex of chemical/societal/habitual dependency to a one-off pharmacological intervention.b?

If, on the other hand, we frame addiction as a social concern – one that users are driven to by a lack of options and by a lack of satisfying community interactions – the solution may becomes quite different. In many cases, taking care to place users back into supportive and meaningful environments is often an effective way to help them cope with the psychological toll of addictions.

Psychedelics, in particular ibogaine[2] and LSD[25], have shown efficacy in treating addictions (opiods and alcoholism, respectively). But in many cases, merely stopping the cravings for a drug isn't enough. It must be also paired with something to replace the need for heroin or alcohol. Thus, a pharmacological cure to addictions (and other psychedelic applications) retains a sense and need for the personal.

> "In other words, if you don't want to quit—and if you don't have a new life purpose like promoting an addiction cure (!) or at least some social support—ibogaine won't do much more than any other type of detox. It's not exactly nothing to have a psychedelic experience and come through detox without suffering physical withdrawal. But that's not all you need to end most addictions."
>
> Szalavitz[62]

Scientific workers fulfill biomedical needs and framings, deliberately distancing themselves from a second set of recreational uses.

9.2 RECREATIONAL USERS

The re-introduction of psychedelics into the clinic and lab goes hand-in-hand with a systematic devaluing of recreational users, at least in the formalized literature and the public/media's eyes. This is partially a political maneuver. For psychedelic research to be legitimate, researchers must explicitly and implicitly separate themselves from their communities.

Hallucinogens have amazingly well-documented and supportive informal communities. Taking psychotropics is, for many, a spiritual experience requiring no little amount of preparation. Users are often hyper aware of biochemical effects, possible interactions with medical conditions or other drugs, how to set good experiential scenes,and how to guide their mental state in meaningful ways. In short, recreational users are *good* at taking psychedelics, and do them sometimes just as carefully as scientists. They are not accredited, but they are consumers of an age where everything is suspicious; recreational users have very high "ethos of vigilance."?

http://www.erowid.org

Erowid The "non-profit, harm reduction organization" "documenting the complex relationship between humans and psychoactives" is a main resource users of psychoactive drugs. They have a dizzying and expansive archive of peer-reviewed scientific literature (marking it pay walled

or not), pharmacological information, health risks, well-documented testimonies on drug use (other drugs in use, dosage, time and duration of experience, mental/physical health histories, *ad. infinitum*).It is a mix of hard scientific information about binding affinities and drug interactions, practical usage and safety information (both pharmacologically and mentally), proposals for chemical syntheses, meditations on spirituality, cultural histories, law and policy suggestions, art pieces and so on; a tremendous resource built by and for psychoactive communities.

Erowid and related recreational-knowledge based sites do not, unlike the scientific literature, paint the potential of psychoactives with a one-sided brush. Users post good experiences and bad; some say it is very important to them personally, but always with the large and constant caveat of 'mileage may vary'. In many ways, the information on Erowid is much more realistically oriented – towards clinical applications – than the nominal cutting edge of science. It neither makes grand claims about everybody's experiences nor relegates psychoactives to the realm of the purely dangerous Schedule I.

> Perhaps community itself is the most important "lab apparatus" of contemporary psychedelic practice, a large-scale, dissipative structure for the ongoing investigation of the mind.
>
> *Darwin's Pharmacy : Sex, Plants, and the Evolution of the Noösphere*

9.3 FUNDING

An important link between recreation users and researchers in the psychedelic fields is funding. Funding for psychedelic research in the U.S. comes largely from

1. Various drug enforcement agencies, with a vested interest in promoting psychedelics as drugs of abuse
2. Various philanthropists and private funders with a vested interest in the therapeutic potential of psychedelics
    a) recreational users with money

This means any research conducted has an *extremely* vested interested in casting psychedelics one way or another; thus, their assays, experimental choices, and conclusions are all prone to fall into one of two camps.

Intriguing as well is the lack of the usual drug developers. Since the compounds are already known, pharmaceutical companies don't stand to make very much money off of already well-known drugs, and so there's little motivation to develop them. At the same time, they are undoubtedly psychologically/scientifically interesting, and used by enough recreational users to maintain a low level, but constant, stream of well-documented self-experiments.

9.4 INDIGENOUS SCIENCE

Psychedelic experiences exist in indigenous cultures globally, the same indigenous cultures threatened by an ever-rising tide of globalized economies and corporate states.

Indigenous knowledge is also under constant threat from not just globalization, but the tendency to prioritize Western styles of thought to the exclusion of all.

9.4.1 *Complexity of indigenous rights*

Psychedelics exist in most cultures; it is a classic scientific and U.S. feminist simplification to leave it at that. In reality, indigenous groups are a vastly heterogenous group.

In South America, ayahuasca ceremonies are relatively large business, but my first instinct was to cry "cultural appropriation." The business aspect is actually consistent with historical precedent, where shamanistic services were always part of the indigenous economy.[19] On the other hand, the Native American Church practices psychedelic usage as an intensely community-oriented practice; outside participants are rarely invited in, and only on special occasions. So each country, and group, requires specific knowledge and careful intent.

9.4.2 *Historical colonialism*

Psychedelic use in Mexico was outlawed in by Spanish conquerors in the the 1600s, and stayed alive in small, isolated villages. In the 1950s and 60s, the first (white, male, and then white, female) pilgrims from the United States made their way to isolated Mexican villages to first take drugs in the spiritual shamanic context, and then started using them recreationally.

In addition,, women often held botanical and plant knowledge because of the distribution of gender roles. When colonialism showed up in the Americas and in Africa, the subsequent destruction and theft of botanical knowledge was principally from *women*, not just indigenous groups as a whole.?

9.4.3 *Ecological destruction*

When we say these plants and compounds have cultural histories, what that means is that they literally – grow or grew somewhere; and growth is not a constant.

The peyote cactus is, for exampled, endangered; the Native American Church considers it their duty to maintain and cultivate it.. The Amazonian rain forest where the *Banisteriopsis Caapi* and its ayahuasca brew cohorts is under ecological attack, being denuded at a rapid rate (5,000 km2 in 2014, a 20% loss since 1970).

To become a major treatment option, those plants either have to be produced on a massive scale (reducing genetic diversity, bringing in issues of labor movements and ethics, appropriating new farmland) or synthesized (bringing in green chemistry issues), both of which raise issues in and of themselves.

9.5 RESISTANCE TO CO-OPTION

The quality (and thus long term effects) of a psychotropic experience is created through the *interplay* between environment and individual; like Fleck's facts, it doesn't wholly reside in either.g Trying to pull out

the environment-person-biological interplay out in a lab environment, is not but a full fledged transformation such that the ayahuasca in the lab is only nominally related to ayahuasca in (shamanistic) practice is related to recreational DMT usage.

I like psychedelics, specifically, because they do not lend themselves well to wide-spread or easy application. While their therapeutic potential *may* not be entangled with their perceptual effects, in the here and now, we have not yet synthesized the anti-addictive, non-hallucinogenic counterpart to LSD. So therapists are stuck with the re-assertion of the individual, in combination with biological factors.

I find this particularly intriguing in the case of PTSD. The U.S. military has an interest in PTSD cures. It affects many in the service, hindering their continued contribution to the war effort(s), and more importantly, reflects badly on the U.S. government for their abysmal treatment of veteran's. At the same time, the psychedelic "cure" for PTSD, while effective, is based on deep introspection and psychotherapy; it seems unlikely to help in the production of American citizens re-socialized into being killing machines. So it seems likely, simply by virtue of their "off target" effects, that psychedelics cannot be used simply in assisting the U.S. war machine.

9.5.1 *Bioprospecting*

Of concern for many indigenous knowledges is the transformation and patenting of herblore into medicinal compounds by pharmaceutical companies.[58] Bioprospecting relies on patenting plant compounds collectively discovered in biodiverse areas, and patenting and marketing the isolated drug. Many psychedelics, however, are no longer within the time-frame of a patentable drug; legally, they cannot be made into solely profit-generating compounds.

9.6 MOVING FORWARD

I promised – or wanted to find out – who had stakes in knowledge, and who had rights to control it. I still don't know, obviously, but I have a better idea. Open science provides specific solutions to specific scientific problems; it's also a contributor to the potential marginalization of the majority world and does nothing to move away from old narratives of development.

Psychedelics are pharmacologically fascinating and clinically difficult; the subjectivity of human experience presents frustrations for potential capital projects. They are also emblematic of a constant tug-of-war between spirituality and science, a divide I still fall squarely on the science side of. The most obvious space that I see (or think I see) going forward is the need for me to understand how to continue to link the biological to the subjective, and preserve the essential role of *people* and ceremonies in the scientific usage of psychedelics. Going forward, questions that I think will shape my work:

1. Activism on the side, e.g. being aware of the current state of psychedelics "in nature" (ecologically) and "in culture" (legally, as tools)

2. Communicate "better" directly with members of the recreational community. Psychedelics are going to stay, and recreational practitioners use scientific information in ways scientists may not anticipate

3. Policy work to increase representation of indigenous practitioners as valid members of the scientific community

    a) As well as understanding the limits and power of Intellectual Property to protect said knowledge, ideally without placing indigenous knowledge under any boundaries it does not already have.

4. Ending D.A.R.E., the U.S.'s woefully ineffective "harm prevention" program, and advocating for healthier, "well-ness" oriented programs in school that teach about how to do drugs safely, rather than not at all

5. Consider the role of gender and race in both the biological subjects that I study and the community at large, and understand which groups *cannot* participate in psychedelic culture because of

    a) Employ "cultural controls" in research; tailor each scientific psychedelic experiment to the specifics of the situation

6. Understand *specific* histories in the way the anthropologists or community-story tellers do, not in the offhand secondary way that scientists refer to counter-cultural histories or indigenous traditions.

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