

# Journal of Undergraduate Research

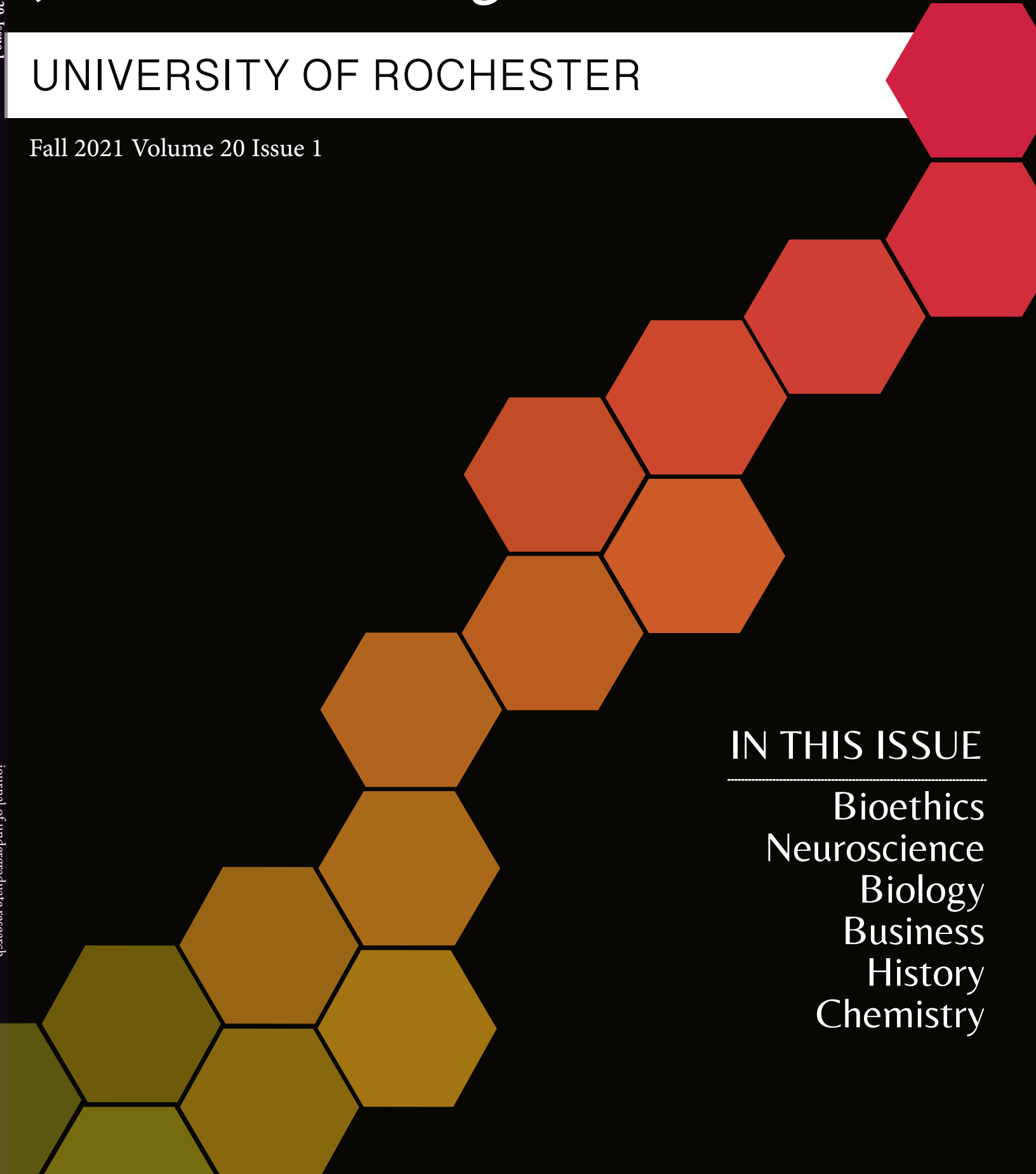
UNIVERSITY OF ROCHESTER

Fall 2021 Volume 20 Issue 1

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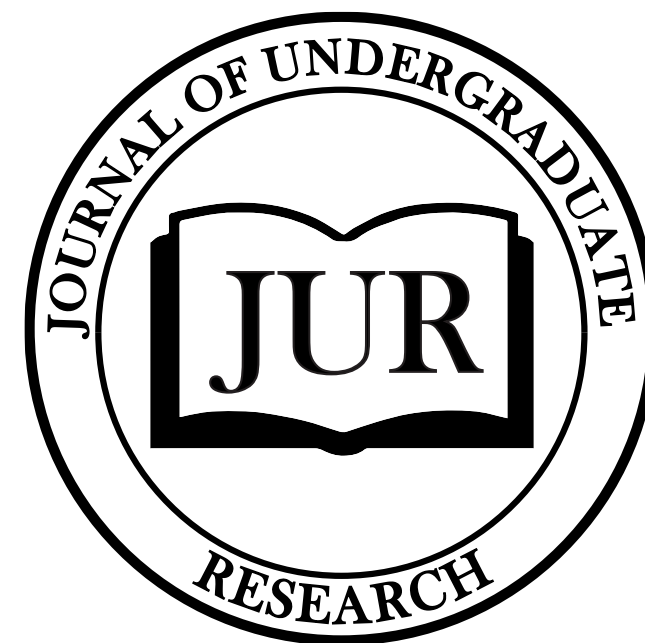
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# Journal of Undergraduate Research



*Volume Twenty, Issue One  
Fall 2021*



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*The Journal of Undergraduate Research (JUR) is dedicated to providing the student body with intellectual perspectives from various academic disciplines. JUR serves as a forum for the presentation of original research, thereby encouraging the pursuit of significant scholarly endeavors.*

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## Letter from the Editors

To all of our readers, faculty, and staff, we are very excited to present the Fall 2021 issue of the Journal of Undergraduate Research, an extraordinary collection of work accomplished by undergraduate students here at the University of Rochester. Each semester, we are amazed by the caliber of submissions we receive. It is evident within each page the level of dedication, academic rigor, and sophistication that is required to write and prepare these articles. Many of these data were collected and arguments synthesized during a time of uncertainty (the COVID-19 pandemic), thus we applaud the author's efforts to continue in their academic pursuits.

In this issue, we highlight six articles that showcase the wide breadth of diverse research being conducted at the University. From Matthew Burgess' investigation of the consequences of Soviet economic policies under Joseph Stalin to Carolyn Kocheck's examination of novel neuroprosthetic approaches to relieving phantom limb pain, we believe that the research in this issue demonstrates the creative, innovative and intellectual capacity of our undergraduate student body. Additionally, we want to highlight the abstracts from students who presented at the Undergraduate Research Expo in May, 2021. We hope that the upcoming articles in this issue inspire our readers to think critically, investigate fully, and be courageous in their academic pursuits.

We would especially like to thank our layout team and managing editors who assembled the journal and worked to ensure our articles were of the highest quality. Additionally, we thank our dedicated faculty who put in the time and effort to review each submission with great care and consideration. Our journal would not be possible without the support of the Undergraduate Research Office. Once again, thank you to our authors, faculty, and editorial team for making this publication possible. Every single contribution is prized and appreciated. Finally, to our readers, we hope you enjoy this collection of interdisciplinary works from our undergraduate research community.

Sincerely,

*Nisha Arya & Jocelyn Mathew*

*Editors-in-Chief*

# Journal of Undergraduate Research

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This issue of the Journal of Undergraduate Research was assembled on macOS Big Sur using Affinity Publisher. Microsoft Word and Google Docs were used for text editing and review. Fonts used include Minion Pro, the main font for body text, and Myriad Pro, the main font for headings and decorative text. This physical version of this journal was bound by Emerald Print Management of Rochester, NY.

# On the Use of Information from Past Unethical Research

Samuel Streicher '23, *Bioethics*

Advised by William FitzPatrick, PhD, *Department of Philosophy*

## Introduction

Certain progressions in research ethics have directly followed severe moral transgressions: the Nuremberg Code, as one example, emphasized the importance of informed consent in response to experiments performed by German doctors on concentration camp prisoners during World War Two ("History"). Of course, these developments do not retroactively erase ethical violations, and as a result, subsequent researchers might find themselves in a peculiar position: they may be able to identify the immorality of a past study but simultaneously recognize the data's potential to inform current, otherwise moral, work. A study's problematic history makes current use controversial. While the use of information from unethical research may indeed be controversial, I argue that it is morally acceptable to make careful and qualified use of such information if significant benefits are at stake.

I first critique central counterarguments and then describe a counter argument that proves to be more compelling – Dr. Aaron Ridley's concern involving deterrents and incentives (Ridley 1995). Although Ridley claims that an analysis of deterrents and incentives forces him to reject the use of information from unethical research, I believe his idea merely serves as another reason to *restrict* - but not completely prohibit - the use of such information.

To clarify, my argument is specific to supporting *careful* and *qualified* use of information from previous unethical work. By 'careful,' I mean a use that is plausibly necessary for the realization of significant benefits from the unethical research in question (plausibly, and not certainly, since a guarantee would be difficult or near impossible to achieve). Later in section IV, I further explain my use of the term 'significant' by responding to certain claims made by the American Medical Association. By 'qualified,' I mean a use that is accompanied by an acknowledgment of any past immorality underlying the relevant data. By 'use' of research, I mean to include:

**i:** any employment of medical knowledge or therapy derived from the unethical research in question or

**ii:** any action that reasonably causes future work to be informed by the unethical research in question, including but not limited to the reading, re-analysis, and publication of the immoral experiment's data.

Moreover, while certain discussions distinguish between the terms 'ethics' and 'morality,' I use both interchangeably in reference to the rightness or wrongness of an action (Singer 2021). Regarding the phrase 'unethical research,' I speak broadly of medical research, including human and animal studies. The morally questionable status of the investigation may stem from issues of consent, abuse, wrongful discrimination, or other concerns.

## Assessment of Typical Concerns

A potential worry regarding the use of information from unethical research is that such an action honors the researchers who acted wrongly or perhaps indirectly condones the research itself (Higgins et al. 2020, 679-680).

However, with careful use of the information at hand, both worries might be alleviated. For instance, if a publication explicitly noted that certain data pieces were obtained through unethical means, it need not be the case that the previous researchers are accepted or their projects condoned. In fact, by drawing attention to the past unethical research, the relevant wrongdoings might be more publicly condemned.

Still, some might worry that if society uses unethical data to develop extraordinarily beneficial innovations, the immoral researchers might be viewed as the parents of this development. As a result, these researchers may receive intellectual praise. This case does little to challenge my primary claim because intellectual strength does not directly reflect moral character. In other words, while the use of information from unethical research might show intelligent sides of unethical individuals, it does not erase their moral record.[1] If such a case stands as our primary concern about using information from unethical research, then our attention should be on accurately portraying the historical narrative of characters - intelligence and moral blemishes together - rather than banning the use of information derived from past immoral work.

The above argument also addresses the concern that the use of information from ethically tainted research inherently disrespects the suffering of victims (Higgins et al. 2020, 680-681). Again, with the careful use of information, purposeful acknowledgment of past injustice, and accurate portrayals of historical narratives, it is not clear that disregard for the victims' suffering may follow from using such information. If, however, little benefit can be extracted from the unethical work or the data might be replaced with an ethical study, the issue of disrespect indeed becomes more complex. For this reason, further suggestions for the careful and qual-

ified use of information from immoral research are discussed in section IV.

As a separate concern, current scientists might claim that drawing on information from past unethical work could sully their own reputation in that they might be viewed as morally "complicit" (Higgins et al. 2020, 680). A more extreme claim follows a similar thread but further asserts that the reputation of medicine itself is at stake when using information from immoral studies (680).

In the introductory remarks of his work "Ill-Gotten Gains: On the Use of Results from Unethical Experiments in Medicine," Ridley describes the proposal that information cannot be ethically bad or good (Ridley 1995, 255). While the method of extracting information might be immoral, it is not the information itself that is ethically marred. Therefore, the use of such information does not inherently stain the moral record of other researchers who are not responsible for the original wrongdoing. The same might be said for the institution of medicine itself. It should be noted that Ridley merely describes this idea and does not necessarily endorse it himself. Readers may be dissatisfied with the preceding rebuttal: they might grant that information is not ethically bad nor good yet still claim that using information from past unethical experiments can nonetheless put researchers at risk for complicity in past immorality. For instance, in an article assessing Chinese transplant studies, Higgins et al. cite Dr. Gregory Mellema's work on complicity to suggest that moral complicity is possible when people fail to show appropriate regard for causing "subsequent" (Higgins et al. 2020, 680) suffering from their actions.

However, the use of unethically obtained information does not necessarily demonstrate current researchers' lack of caution for "subsequent" harm (680). In fact, as noted above, researchers who effectively highlight the moral flaws of unethical experiments, thus understanding the weight of using such information, could initiate greater public awareness and desire to prevent similar future wrongdoings. Therefore, with proper disclaimers alongside their use of such information, researchers (along with the institution of medicine) should not *immediately* be viewed as morally complicit in past unethical behavior. There are cases, as noted in section IV, when scientists *might* be complicit if they improperly use unethically obtained information or if they make insufficient efforts to highlight past injustices in ways that are insensitive and plausibly harmful.

In response to some experiments, like those performed by the Nazis during WWII, many scholars have noted that the degree of immorality can be so severe that the experiments' results are consequently invalid and should not be utilized (Cohen n.d.; Moe 1985, 273). The dissolution of validity can stem from either or both of the following: the questionable general integrity of the researchers or the limiting design of the experiment (Cohen n.d.; Moe 1985, 273). Arnold Relman, a past editor of the *New England Journal of Medicine*, seems to comment on the former source of invalidity, claim-

ing that the studies performed by the Nazis, or perhaps at least those described in the relevant citation, "are such a gross violation of human standards that they are not to be trusted at all" (Moe 1985, 273). Dr. Allen Buchanan expands on the validity concern: in his experience contributing to a review committee for the University of Minnesota, he found that "experiments that [were] ethically unsound [were] also scientifically unsound" (Moe 1985, 273). With respect to Nazi hypothermia experiments, for example, researchers may discredit the physiological data sets since they reflect a tortured, malnourished group rather than a healthy population. Therefore, the resultant data cannot be generalized to the greater public (Cohen n.d.; Moe 1985, 273).

Irrespective of the source of validity concerns, unethical studies - even terribly inhumane experiments - are not always invalid in a technical sense (Freedman 1992, 141-142). For instance, if an investigator lied to randomized control trial participants about the risks of using a newly developed drug, it is unclear why all resultant medical data would be innately flawed. Regarding the issue of Nazi hypothermia experiments representing only narrowly defined study populations, the problem here stems from concerns of experimental design, not from morality (though this statement is not intended to validate the data of Nazi experiments). Although Buchanan finds that unethical experiments are often scientifically unsound, this pattern may simply be coincidental; it is unclear why the pattern would hold true in all cases. Moreover, this focus on practical validity issues largely skirts our moral question: the rationale offers little explanation on the morality of using information from past immoral work (141-142). Therefore, this argument should not be the fundamental moral principle that prohibits the use of information from unethical research (141-142).

## Ridley's Strongest Concern Involving Incentives and Deterrents

The previous rebuttals can be summarized by one or more of the following ideas:

**A:** The careful use of information, the meaningful admission of injustice, and a full depiction of researchers - including their moral record, rather than a plain focus on intellectual achievements - largely protects against misplaced respect for immoral investigators or possible disregard for the suffering of victims.

**B:** Information itself may not have a moral status (Ridley 1995, 255). Even if this idea is wrong, the use of unethically derived information does not necessarily exhibit current researchers' carelessness towards the risk of future harm, and therefore need not, at least immediately, sully the record of current researchers.

C: The practical concern of validity does not address our fundamental moral question regarding the use of unethically derived information.

Ridley, however, brings a concern that withstands rebuttals A, B, and C. His concern about using unethically obtained information revolves around a “conceptual connection between the use of such results and the performance of future unethical experiments” (Ridley 1995, 258, emphasis original). To portray this concern, Ridley describes a theoretical experimenter, the Ideal Experimenter, who is a specific type of utilitarian, entirely driven to act in a way that produces the greatest amount of happiness via medical studies. In this sense, even if an experiment, experiment Z, were unethical with respect to non-utilitarian standards, the Ideal Experimenter would proceed with study Z if its production of human happiness via medical results would be greater than the study’s associated harms (258-260), assuming all alternative study methods did not yield greater sum utility than study Z. [2]

To effectively prevent the Ideal Experimenter from conducting unethical studies, a deterrent must push his happiness-harm calculation to total greater harm. However, if the potential benefits from the study are so great, little will be able to shift the calculation sum away from utility. Ridley clarifies that personal threats to the Ideal Experimenter - both to the experimenter’s reputation or even physical health - will not deter the Ideal Experimenter, assuming the benefits of the study are great enough. The only meaningful way to deter the Ideal Experimenter is to dissolve his fundamental utilitarian-based incentive - that his datasets will be used to yield large benefits (Ridley 1995, 260-262). As Ridley puts it as, “if the ideal experimenter can be brought to believe that any experimental result obtained in contravention of non-utilitarian standards will *not* be used to benefit anybody (i.e. will be suppressed, destroyed if possible, outlawed), then he will have been given a powerful reason to conform to those standards” (261, emphasis original). Notice that rebuttal A and B might actually support the Ideal Experimenter’s propensity to perform a beneficial but unethical experiment. If society accepts rebuttal A and B, the Ideal Experimenter will know his results will be more readily used, even if unethically obtained (261-262). Rebuttal C does not apply here since the case grapples with utilitarian versus non-utilitarian ethics and different conceptions of morality or justice.

Ridley anticipates that readers might perceive his concern as overly theoretical since real researchers, for the most part at least, will not equate to Ideal Experimenters. In other words, very few individuals could be likened to the Ideal Experimenter (Ridley 1995, 263). However, Ridley explains that such an objection avoids the problem population: those who are most likely to conduct immoral studies in the first place are the very selective few who are comparably similar to the Ideal Experimenter (264). It is also worth noting that a real researcher need not be a *perfect* utilitarian in order for Ridley’s concern to hold weight. If the benefits to be gained from

the unethical research are very great, some researchers would be compelled to carry out the work, rendering them similar enough to the Ideal Experimenter. Thus, Ridley’s concern is not isolated to an elaborate theoretical figure. Indeed, when the benefits to be gained are great, Ridley’s Ideal Experimenter becomes progressively less theoretical and increasingly tangible (264).

In response to Ridley’s concern, readers might ask the following: if the benefits at stake are so great, would it not be justified to pursue the otherwise unethical experiment? In other words, do the ends not justify the means? However, such a perspective is highly problematic, largely due to issues associated with utilitarianism. As an example, researchers who adopt this ends-based approach might be willing to cut ethical corners - such as the obtaining of meaningful informed consent, or an explanation of risks to study participants - in order to secure a test population for beneficial experiments. I assume this sort of behavior does not align with most people’s conception of morality.

Ultimately, Ridley claims that the use of unethically obtained information provides enough incentive for immoral experiments to take place. He concludes, then, “the results of unethical experiments in medicine ought not to be used, even, or especially, when their use might be expected to yield large benefits” and that his claim should be “taken as a practical recommendation” (Ridley 1995, 264). For Ridley, such an approach is the “only sure way of getting the message across to those for whom it is intended” (266). In response to a likely objection, Ridley describes how his conclusion could be practically implemented (265-266). As noted, Ridley’s argument cannot be resolved by the strategies used in section II.

I agree that the most fundamental deterrent against future immoral studies would be the complete prohibition of use of any information from unethical experiments, no matter how beneficial the information may be. Nevertheless, it is a mistake to suggest that society is *morally obligated* to pursue this route. If Ridley’s general argument is arranged into premise-conclusion format, the mistake becomes more apparent. A simplified version of Ridley’s argument can be formulated as follows:

**Premise 1:** Doing X is the maximally effective means to preventing unethical research.

**Premise 2:** We are morally obligated to take the maximally effective means to preventing unethical research, regardless of the costs.

**Conclusion:** Therefore, we are morally obligated to do X, regardless of the costs.

The structure of the argument is valid in that the conclusion follows from premises 1 and 2 together. Although Ridley’s work thoroughly supports premise 1, the overall argument is not sound because premise 2 is not true; our moral obligations to prevent unethical research are not boundless. Moral

obligations must be weighed against other morally relevant considerations - with one example here being the potential obligation to use already available medical knowledge to aid those in need. Indeed, if doing X in the name of maximally preventing immoral research imposes incredibly heavy costs or sacrifices other important goals, our moral obligations might not include X. Rather than streamlining efforts towards one moral goal exclusively, an alternative strategy might better align with society’s *collective* set of goals and values. An analogy clarifies this idea:

**Premise 1:** The maximally effective means to preventing suicide is the surveillance and forceful confinement of all individuals at risk for suicide for the entirety of the time that they are at risk of harming themselves, even if this risk is small (note that the exact method of prevention here is not important; the important elements are Premise 2 and the Conclusion).

**Premise 2:** We are morally obligated to take the maximally effective means to preventing suicide, regardless of the costs.

**Conclusion 1:** Therefore, we are morally obligated to surveil and confine all individuals at risk for suicide for the entirety of the time that they are at risk of harming themselves.

While we may *wish* to prevent suicide and look out for our fellow human beings, the cost of taking such a drastic approach would be too high. Of course, in a case where some individuals are a threat to themselves, and you are in their immediate vicinity, you likely have a moral obligation to call for help, ensure they reach a hospital, or gain assistance. Nevertheless, you are not morally required to stop all other life activities and monitor these individuals for however long necessary to most effectively prevent an upsetting occurrence. The maximally effective approach outlined above challenges other important considerations - such as privacy and liberty of the individuals at risk, practicality, and resource availability - without supplying enough benefits overall, compared to less drastic alternative solutions. On the whole, other approaches might serve our collective range of goals more effectively.

Ridley’s argument forgoes this sort of thinking, and as a result, his requirements are too restrictive (FitzPatrick 2004, 111). Consider if Ridley’s policy were to apply to current medical knowledge. In a separate article related to citations of unethical research, Dr. Allen Buchanan explained that “[i]f you exclude from use all the experiments now viewed as unethical, you’d have to tear up half the medical textbooks. There may have to be some kind of concession [to] the fact that we are evolving standards of acceptability” (Moe 1985, 274). Even if Ridley only intended to apply his suggestions moving forward with future data, it is not difficult to imagine cases where some tremendously beneficial medicine had been developed, only to be shunned because its experimental

background was unethical. Additionally concerning, the degree of ethical transgression does not seem to matter here; even if the experimental methods underlying this miracle medicine were only marginally unethical, it would seem that the data for the intervention would have to be disregarded nonetheless. Moreover, forbidding the use of such data potentially violates the freedoms of other people’s access to information that is plausibly beneficial to them. Sacrificing real and significant benefits for others in order to construct a theoretical blockade to future immoral research may be a very poor tradeoff - perhaps *wrongful* to those who stand to benefit from the information in question, especially if it turns out that Ideal Experimenters are even more unusual than Ridley suggests. Overall, although Ridley’s argument is strong, it is not sound, and its ramifications are troublesome.

While I do not claim to have specific guidelines for delineating where our moral obligations end, I believe the following procedures are steps in the right direction: enacting laws and regulations to prevent unethical research shows some recognition of the moral importance of the situation; legal consequences for unethical research may also serve as some adequate form of deterrent against immoral studies; and the careful use of information from immoral investigations, described in section IV, also demonstrates sensitivity towards the issue.

Although Ridley’s argument contains a mistake, the underlying idea of deterring scientists from conducting immoral studies still serves as a reason to limit - but not prohibit - the use of information from unethical research. To clarify, without limiting the use of information from unethical research, the public could readily use experimental data regardless of its derivation. As a result, scientists would not have to incorporate the issue of public hesitance into their utility calculations for study design. Consequently, these scientists might be *too* willing to cut moral corners for small medical gain (though these scientists would only do so if the small gain would be greater utility-wise than the associated moral cost and if the total utility would be greater than that of all other available options). Overall, abandoning limitations on the use of information from unethical research bolsters utilitarian-esque justifications for proceeding with distasteful studies (and I again assume that most readers would largely object to a utilitarian system of experiment ethics).

### Suggestions for the Careful Use of Information & Conclusions

In section I, and throughout this discussion, I qualify my argument: I claim that it is morally acceptable to make careful and qualified use of information from past unethical research if *significant* benefits are at stake. I recognize that abiding by arbitrary qualifications for significance could catalyze issues for exceptional cases. Therefore, it might be more effective for international ethics bodies to collectively suggest *general* guidelines for determining whether significant benefits are at stake. Nonetheless, I build on the following statement from

the American Medical Association (AMA), specifically requirement 3, to call for a more encompassing use of the term 'significant.'

In a short publication titled "Release of Data from Unethical Experiments," the AMA specifies three criteria that must be met in order to publish or use information from immoral studies ("Release of Data" n.d.):

- 1: The unethical data sets must not be replaceable by any morally obtained data sets.
- 2: The unethical data sets must be subjected to robust examination to ensure validity.
- 3: Without using the information from the immoral study at hand, "human lives would certainly be lost" ("Release of Data" n.d.).

From requirement 3, it seems that the AMA might hold the benefit threshold at the undoubted loss of human lives. However, I suggest that the threshold for 'significant' benefits should not be so stringent. Such a strong restriction disregards multiple cases where there would still be a strong motivation to use unethically obtained information, even when death is not a concern. For instance, perhaps unethically obtained information could lower or eliminate discomfort for those living with a painful condition. Moreover, I suggest that we include both animal and human conditions within this consideration.

Regardless of the precise method used to determine the 'significance' threshold, I purposefully incorporate both the 'careful' and 'significant' qualifiers in my argument to prevent trivial use of immorally obtained information; along the same vein, I also support requirements 1 and 2 from the AMA excerpt above. If AMA requirement 1, requirement 2, or any of the suggested qualifiers are violated, the possibility of disrespecting experiment victims grows (Higgins et al. 2020, 680-682; "Release of Data" n.d.). These violations are related to complicity as well (Higgins et al. 2020, 680); in disregarding the aforementioned considerations, researchers might be demonstrating insufficient sensitivity to past immorality, and a lack of sensitivity plausibly degrades efforts to prevent the relevant wrongdoing.

Lastly, I do not argue that unethical research must be *continued* for the sake of data. In this sort of case, the harm is ongoing and dependent on our current use of data. Such a scenario is different from the context intended for the above discussion; in our intended cases, some harm has already been done via an unethical experiment, and researchers must evaluate whether it is morally appropriate to use any information from this experiment. Ultimately, I suggest that, when significant benefits are at stake - though these benefits need not reach the life or death threshold - it is morally acceptable to make use of information from past unethical research when the realization of the aforementioned benefits require the use of such information.

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## Footnotes

[1] To clarify, those who call for prohibiting the use of information from unethical experiments are not suggesting denying or ignoring the fact that such experiments have occurred. In fact, those who do not support the use of information from past unethical research would still likely grant that, in certain instances, it may be necessary to allow general experiment information to be accessible in order to ensure that people can obtain an adequate education on the subject matter.

[2] It is important to highlight the latter portion of the claim regarding alternative study methods. Simply because a study produces more happiness than harm does not mean the Ideal Experimenter would carry out such a study. For the Ideal Experimenter - a utilitarian driven by happiness produced by medical results - a study design must yield greater total utility than *other possible study approaches*, after accounting for the harm factor in utility calculations. For instance, study design

X may be grossly harmful, but may also provide bountiful medical goods to just tip the scales towards net happiness. Study Y may only provide modest medical goods, but could still offer greater net utility than study X if the harms of study Y were significantly less than the harms of study X. In this sort of case, the Ideal Experimenter would be drawn to perform study Y based on a total calculation of harms and benefits. For the purpose of this discussion, I consider a case where the experiment of greatest net utility, among all available study methods, is still considerably unethical.



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# Review: An Investigation of Neuroprosthetic Treatments of Phantom Limb Pain

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## Background & Significance

Phantom limb pain (PLP) is a condition in which individuals perceive pain from a previously amputated limb. PLP is a result of nerve damage that occurs during amputation (Petersen 2019), impacting both the peripheral and central nervous system. The peripheral nervous system is composed of cranial and spinal nerves, which receive information from the environment as well as generate motor responses. The central nervous system includes the brain and spinal cord and interprets the information received from the peripheral nervous system. Individuals affected by PLP have pain ranging from mild to severe which can be described as “stabbing, shooting, piercing, tingling, throbbing, and/or burning,” (Petersen 2019).

PLP impacts the peripheral nervous system in that during amputation there is damage to the nerves outside of the brain and spinal cord. Nerve fibers have to be ligated or resected (Petersen 2019) and the injured neuron axons swell and form an “end-bulb” from which new axon “sprouts” begin to grow (Petersen 2019). Due to the amputation, the Schwann cells that align to help cells regrow axons do not align properly. As a result, the sprouting neurites have nowhere to grow which in turn causes them to form a tangled knot called an amputation neuroma. The sprouts spreading to nearby tissue as well as the neuroma formations make the surrounding tissues much more sensitive to what would normally be harmless physical stimuli (Petersen 2019). In addition, the neuromas formed are hyperexcitable due to the upregulation of sodium channels and exert a constant “barrage” of electrical signals constantly (Petersen 2019). This can be linked to the phenomenon of neuropathic pain, in which nothing is actually damaging the body, but the neurons are still firing as if there was. The mechanism of neuropathic pain involved in the peripheral nervous system is that of hepatic transmission in which the demyelinated A $\beta$  axon fibers, responsible for pain and temperature sensory stimuli, become demyelinated and induce action potentials in neighboring C axon fibers. Thus, the damaged area not only becomes much more sensitive to stimuli but also signals pain when there is none. Another major route of phantom limb pain is the ectopic activity, or activity coming from the wrong place, in the dorsal root ganglion (DRG) (Petersen 2019). The same upregulation of sodium channels that causes hyperexcitability of neuromas also contributes to the ectopic activity in the DRG. It is believed that the majority of the ectopic activity that causes neuropathic damage is in the DRG (Petersen 2019).

In the central nervous system, sensory remapping and the body’s neuromatrix representation of itself are considered responsible for the pain in PLP. After the loss of a limb, or any other sensory input, the neurons that originally corresponded to that area, now respond to adjacent areas of the body (Petersen 2019). Thus, after an amputation, the neurons that originally served that limb will remap and try to respond to adjacent tissue areas. But, this adjustment can cause a misinterpretation of stimuli. Additionally, there seems to be another mechanism of neuropathic pain: central sensitization in which the chronic pain and spinothalamic neurons become extensively responsive. This causes the release of more neurotransmitters, specifically N-methyl-D-aspartate (NMDA) (Petersen 2019) in the spinal cord and eventually results in long term potentiation and permanent rewiring of the central nervous system.

Non-neuroprosthetic treatments do exist, one of which is pharmaceuticals. Anti-seizure medications such as gabapentin and pregabalin are used as they reduce the frequency and intensity of neuropathic pain (Collins 2018). Opioids are also used to reduce the cortical remapping and reorganization in the somatosensory system after amputation occurs and sensory input is lost (Collins 2018). Unfortunately, opioids have severe side effects including high rates of addiction as well as dizziness, constipation, and nausea (Collins 2018). NMDA glutamate receptor agonists are also used to prevent the neuropathic pain in PLP by blocking NMDA release. Besides pharmaceuticals, there are also surgical options including ablative surgery and dorsal root entry (DREZ) lesioning. Ablative surgery can be used to remove neuromas when all other treatment methods have been exhausted (Petersen 2019) and patients have made complete recoveries. DREZ lesioning uses radioactive current to destroy the pain trigger nerve cells along the dorsal root. Most patients report immediate relief of PLP pain after DREZ lesioning and some even report relief for years after the procedure. However, results vary drastically from patient to patient (Petersen 2019). Surgical techniques are highly invasive and there is a high risk for other, unintentional damage as results that do not guarantee full PLP recovery. One non-invasive technique used is mirror therapy. Part of the reason for PLP is that post-amputation, the brain still sends signals to the missing limb but does not receive sensory signals confirming movement back (Petersen 2019). In mirror therapy, the individual watches a reflection of their voluntary movements in order to create a visual stimulus, or “illusion”, that the voluntary movements are not painful (Petersen

2019). Thus, no phantom limb pain occurs as the body gets a form of sensory stimulus that the limb is moving. While it has seen success, mirror therapy is not considered a “first-line treatment” (Petersen 2019).

Phantom limb pain affects thousands of individuals. There are currently 1.9 million amputees living in the United States (Collins 2018), and up to 85% of amputees (Petersen 2019) have phantom limb pain. It is important to note that amputations are common and are caused by a variety of conditions including cancer, trauma, infection, and diabetes mellitus, all on top of combat related injuries (Collins 2018). Thus, phantom limb pain can affect almost anyone and is more common than one might think.

## Summary and Critique:

### APPROACH #1: DORSAL ROOT (DRG) STIMULATION

The dorsal root ganglion plays a large role in the neuropathic pain associated with phantom limb pain. This study examines the targeting of the DRG for stimulation as a treatment for phantom limb pain. The approach uses electrodes placed in the areas surrounding dorsal root ganglions in order to deliver electrical stimulation (Eldabe 2015). This stimulation creates a paresthetic sensation that serves to numb and relieve the pain caused by PLP (Eldabe 2015). The Spinal Modulation Axium device is an implanted neurostimulator (INS) composed of four quadripolar percutaneous leads and a wireless programmer device (Liem 2013). The leads are placed at varying levels on the spinal cord depending on the amputation type. There is an initial trial period that employs an external trial neurostimulator (TNS) for 3-30 days (Liem 2013). If the TNS is found to be successful, the INS neurostimulator is implanted.

The INS quadripolar neurostimulator leads are steered into the intervertebral foramen near the DRG using fluoroscopic guidance (Liem 2013). For each patient, the appropriate lead position is determined using intraoperative device programming. This ensures that the paraesthesia stimulation from the INS overlaps with the patient’s painful areas and provides optimal pain relief based on patient controlled intensity (Eldabe 2015). The paresthesia serves as sensory feedback to the brain thus blocking pain signals that occur when the brain sends out a signal. A source of pain is produced when signals are sent to the amputated limb region, but the brain gets no sensory feedback in return. By providing sensory feedback, this problem is resolved. For the lower extremity amputee patients, leads were placed at L3-S1 DRGs and for the upper extremity amputee patients, leads were placed at C6-C7 DRGs (Eldabe 2015).

Measurements taken include baseline PLP characteristics and pain/quality of life post implantation of the DRG neurostimulation device (Eldabe 2015). Baseline PLP data included prior pain management techniques and pain intensity as measured by a visual analogue scale (VAS - 0mm = no pain, 100mm = worst pain imaginable) (Eldabe 2015). All

eight patients found over 50% pain relief in the trial period and all received the permanent implanted device (Eldabe 2015). Program settings were: 20-40 Hz in frequency, 200-420 us in pulse width, and 150-1800 uA in amplitude (Eldabe 2015). Post-implantation measurements were taken 9.0  $\pm$  6.3 months afterwards (Eldabe 2015). The baseline VAS average was 83.55  $\pm$  10.5mm (Eldabe 2015) and the follow up VAS average was 38.1  $\pm$  27.1mm (Eldabe 2015). The average percent pain reduction was 52.0  $\pm$  31.9% (Eldabe 2015). One patient achieved complete pain relief and two others saw significant quality of life improvements (Eldabe 2015).

This neuroprosthetic had great results in reducing phantom limb pain in amputee patients. Neuromodulation of the DRG is more effective than traditional SCS stimulation. SCS places leads over the dorsal columns instead and paresthesia distributions are much larger than the actual PLP pain regions (Eldabe 2015). Thus, the paresthesia is not as direct and less effective. The device also applied paresthesia effects to not only the stump surface area but also to each patient’s individual phantom limb pain areas.

Thus, the device treats individual pain as opposed to only applying treatment to the stump. By just applying treatment to the stump, not all pain sites may be covered as often patients have PLP sensations in regions other than the stump due to the amputation impacting neuron growth. In terms of patient individuality, each patient was evaluated based on their own pain regions. As a result, the device can be “fit” to each patient to ensure the best results. The neuroprosthetic was also found to be successful in different types of amputation. Lower extremity amputee patients saw an average pain relief of 50%, with one patient achieving full pain relief. Upper extremity amputee patients saw a pain relief of 67.8%, but one patient’s data was unavailable. Also important is that the patients had varying reasons for amputation including non-biological events such as motor accidents and biological events such as arterial embolisms. There then appears to be no difference in effectiveness based on why an amputation occurs.

While overall, the neuroprosthetic seemed to work well, it is important to note how particular the device is regarding implantation. Two patients with leads placed sub-optimally saw a gradual lessening of effectiveness of the prosthetic. Because the results are highly sensitive to the device placement, it seems that slight movement of the lead would lower the device accuracy. Additionally, it is unknown how long the prosthetic will continue to ease patient pain. Most patients are still taking pain medications post implantation. So it is important to note that the prosthetic does not completely solve PLP and patients still need the use of medication for their pain. The DRG stimulation is not yet a “stand-alone” treatment. While DRG’s patient individuality can be seen as a strength as it ensures the best results for each patient, it can also be seen as a weakness because positive results may be difficult to reproduce. The fact that DRG is personalized also



increases the time and money that patients must spend before seeing results

The study itself did have many strengths. Before implanting a permanent stimulation device, an external device was used to test the effectiveness of the lead placements. If there was less than a 50% pain relief, the permanent device was not implanted. The study also included patients with varying amputation types, this showing that the device can be used across all amputation types. Another important consideration is the variation in years post implantation. The patients ranged from 1-18 years post amputation, this variation allowing the prosthetic to be evaluated based on its ability to treat amputees whose limbs have had longer opportunities to remap their somatosensory systems. The study's patients also varied in their reason for amputation, this allowing the effectiveness of the prosthetic to be evaluated based on whether or not the amputation was due to a biological defect or an accident. The study also noted the patient's use of other medications. This is important as it shows that although this prosthetic does bring major pain relief, it is not yet able to stand alone as many patients were still using pain medication in conjunction with the prosthetic.

The study layout also had weaknesses. The study itself was retrospective and some data was unavailable; the result being that it does not detail as much as a trial study would. The study also only examined eight patients. And while the prosthetic was found to have significant success, it would need to be studied at a larger scale. The average post implantation follow up time was  $9.0 \pm 6.3$  months. Thus, the lifespan of the prosthetic is not known as measurements were not taken longer than 2 years post implantation. Another issue was the inconsistency of the follow up times which ranged from 5 to 24 months. For more effective comparisons of results, multiple measurements should be taken at the same times for all patients. A final weakness was the use of a VAS scale system. This system relies on patient feedback to determine pain level. This does not account for possible variation in the participants' tolerance to pain. In some ways, this is not detrimental as the device is regulating each patient's pain individually. If there was a more normalized scale, each patient might have a different level of relief to the same levels of stimulus.

#### APPROACH #2: BRAIN MACHINE INTERFACE TRAINING

This study employs the use of a brain-machine interface training based on real time magnetoencephalography (MEG) signals in order to reconstruct hand movements of a robotic hand. This device works based on the principle/theory that phantom limb pain is caused by the inadequate plasticity of the sensorimotor cortex (Yanagisawa 2016). By restoring function, the device hopes to reduce pain by retraining the brain. Brain-machine interface systems (BMIs) work to reconstruct motor function as well as create plastic cortical activity changes (Yanagisawa 2016). In order to do this, the BMI decodes the neural activity created by a mental action to

move a part of the body and then converts this decoded phantom movement into a signal for a robotic neuroprosthetic (Yanagisawa 2016). The BMI system includes a robotic hand, a decoder (of varying type), and sensors to detect MEG signals.

All patients in the study participated in BMI training to control a robotic hand. Measurements of cortical plasticity were taken by comparing the same offline task performance before and after each training session (Yanagisawa 2016). Pain was measured with a visual analogue (VAS) scale (Yanagisawa 2016). The BMI training for the control of a robotic hand was done as a randomized crossover trial consisting of two training sessions on two different days, employing the use of different decoder types each time (Yanagisawa 2016).

First, patients performed an "offline task" pre-BMI in which they were instructed to control a prosthetic hand by moving their phantom hands without looking at their arms (Yanagisawa 2016). While they performed this task, MEG signals were taken using 84 sensors. The signals were then averaged and each patient's pain was evaluated. In order to estimate the cortical representation during the offline task, cortical currents were estimated from MEG signals using variational Bayesian multimodal encephalography (VBMEG) (Yanagisawa 2016). The z-scored cortical currents were compared between two types of movements using two way ANOVA and it was found that contralateral sensorimotor cortex cortical currents varied between movement types (Yanagisawa 2016).

When the phantom decoder was introduced, the F-values of the z-scored cortical currents increased in the contralateral sensorimotor cortex and pain scores increased from  $38.2 \pm 18.5$  mm to  $45.8 \pm 18.4$  mm (Yanagisawa 2016). On a different day, the BMI training with a random decoder found little to no changes before and after training (Yanagisawa 2016). Therefore, the phantom decoder increased the ability of cortical activity to discriminate against different phantom hand movements, but it increased pain levels of patients (Yanagisawa 2016). Another training experiment was performed with a real hand decoder constructed from MEG signals obtained while moving their intact hand (Yanagisawa 2016). This training involved a similar offline task to control the neuroprosthetic hand by moving their phantom hand (Yanagisawa 2016). This caused the patients to associate the movement of their phantom hand to the movements of the robotic hand; but, the robotic hand was actually being controlled by a decoder that was classifying the MEG signals based on the intact hand movements (Yanagisawa 2016). It can be understood from this that the patient was associating the phantom hand movements with the cortical representation of the intact hand movements (Yanagisawa 2016). This real hand decoder decreased the phantom hand F-values in the contralateral (to the phantom hand) sensorimotor cortex and decreased pain scores from  $38.3 \pm 15.5$  to  $34.6 \pm 14.8$  mm (Yanagisawa 2016).

The study demonstrated that with MEG based BMI training to control a neuroprosthetic hand, the pain levels of a patient with PLP can be changed. This change was seen in different decoder types. When the real hand decoder was used, the plasticity of the cortical representation of the patient's phantom hand movements in the contralateral sensorimotor cortex decreased, as did pain. With the phantom decoder, cortical representation of the patient's phantom hand movements in the contralateral sensorimotor cortex increased and thus pain increased. Thus, phantom limb pain was found to be directly proportional to cortical sensorimotor plasticity (Yanagisawa 2016).

There were many strong aspects of this neuroprosthetic. One major strength was that it rewires the brain in order to decrease cortical plasticity of the phantom limb, stopping the pain altogether as opposed to just blocking it. The device is also not as invasive compared to other treatments as it only requires the patient to attend training sessions in which they retrain their brain without anything being implanted into it. It is important to note that the device has patient individuality as each patient's individual MEG signals were used. The device also makes an important link between plasticity and pain that can really further the studies of PLP treatment. Finally, it was a huge success in patients who had tried and had little success with DREZ lesioning and mirror therapy, both of which are normally highly effective.

In terms of neuroprosthetic weaknesses: only one type of amputation was studied; the device was used on some patients who still had slight sensory control of their upper arm muscles; the device had an unknown lifespan; and, it was much more effective in the contralateral hemisphere. The prosthetic was only used for those with upper arm sensory loss and thus its effectiveness in treating PLP in other amputation types is unknown. Also important is the fact that some patients were still able to "slightly contract" their upper muscles (Yanagisawa 2016), indicating there was still some level of sensory input. Additionally, it is unknown as to how long one must use this device. The prosthetic was also much more effective in the contralateral hemisphere than the ipsilateral hemisphere. It is unknown how large of a role the ipsilateral hemisphere plays in PLP. It could still impact the patient's pain.

The study had many strengths in its layout. The use of multiple decoders is important as the real hand and phantom hand decoders demonstrate the two sides of the link between cortical plasticity and PLP while the random decoder serves as a type of comparison. The study based its cortical current measurements of accurate structural MRIs using Freesurfer software. It also performed extensive statistical analysis when determining MEG signals for each patient. Another strength is the consistency of not only the offline task the patients were asked to perform, but also the measurements that were consistently taken for each patient at the same times before/after training sessions.

There were several parts of the study layout that could be improved as well. Having only studied those with upper arm

sensory loss, the prosthetic was only used for those with upper arm sensory loss and thus its effectiveness in treating PLP in other amputation types is unknown. Nine out of ten patients had the same reason for sensory loss thus it is unknown if this device will work for other ailments/causes for sensory loss. All of the subjects were male, lacking variety in the subjects that were studied. In addition, some patients still had some degree of sensory input in their upper arm muscles. After the study was completed, other measurements were not taken. As a result, it is unknown how long this cortical remapping prevented pain.

#### Comparison

When comparing these studies, the DRG Stimulation device study tested eight patients with PLP with an average age of  $52.2 \pm 20.0$  years. Three patients had an amputation of a lower extremity while the other two had an amputation of an upper extremity. Patients with digit amputations were not included (Neuromodulation: Technology at the Neural Interface 2015). Patients with lower extremity amputations received leads in L3-S1 DRGs and for the upper extremity amputee patients' leads were placed at C6-C7 DRGs (Collins 2018). In the BMI study, ten patients were examined, nine of which had the same condition and all of which had an upper arm extremity amputation. In terms of subject selection, the DRG had much more variation in the types of amputation and reasons for amputation. The BMI study was very limited in its subjects which raises the question of whether this method can be applied to all types of amputation patients. In terms of component parts and setup, the DRG study utilized a much more invasive device as it had to be physically implanted in dorsal root ganglions of the patients where the BMI system used training tasks which required no invasive surgery. The DRG study did see a much larger change in pain reduction though. The average percent pain reduction was found to be  $52.0 \pm 31.9\%$  (Collins 2018). The baseline VAS average was  $83.55 \pm 10.5$ mm and the follow up VAS average was  $38.1 \pm 27.1$ mm (Collins 2018). In the BMI study, there was an average pain decrease from  $38.3 \pm 15.5$  to  $34.6 \pm 14.8$  mm (Yanagisawa 2016). For the most part, the studies reported consistent data. The only issue in the DRG study was that not all patients received follow ups consistently. Post-implantation measurements were taken on average  $9.0 \pm 6.3$  months afterwards with a range from 2 to 24 months (Collins 2018).

#### Future Studies

In the future, there are many directions that can be taken. Regarding the DRG Stimulation device, the article suggests two possible future investigations. First is the mechanical manipulation of neuromas in order to find a link between this manipulation and the development of PLP (Eldabe 2015). This would be done both with and without DRG neural stimulation. The other suggestion is employing the use of DRG stimulation before the amputation (Eldabe

2015). By applying this device before the amputation, phantom limb pain might be avoided altogether (Eldabe 2015). As for the BMI device, the BMI training should be applied to other amputation types. The idea that phantom limb pain is directly proportional to cortical sensorimotor plasticity should be further explored. If it is possible to “re-train” the brain and use the body’s natural neural plasticity in order to ingrain a new nerve pattern that will reduce pain, that is a much safer and less invasive option. The BMI study also suggests the idea of BMI training accompanied with sensory feedback which would essentially create a sensorimotor loop in order to manage persistent pain (Yanagisawa 2016). Another issue that has to be solved is whether or not the BMI training has to be repeated. Our bodies do have a “use-dependent” nerve system. Thus, if the brain is retrained, how long do the effects of the training last? The BMI study did not take follow up measurements but these measurements could be essential for determining if these training will be permanent.

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# Characterization of B Cell states with respect to BCR and HIF-1 $\alpha$ Pathways using discrete-state modeling

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## Abstract

B Cell Receptor (BCR) signaling and B cell O2 level response play a crucial role in B cell activation, migration, and proliferation during infection, vaccination, and several other diseases, with Hypoxia Inducible Factor 1 (HIF-1  $\alpha$ ) regulating the latter. Consequently, investigating BCR activation and HIF-1  $\alpha$  response is critical to understanding B cell response to different diseases. To characterize B cells by their activation of BCR and HIF-1  $\alpha$  activity, Single-cell RNA sequencing (scRNA-seq) and a discrete state modeling algorithm called Boolean Omics Network Invariant-Time Analysis (BONITA) was utilized. Different clusters of B cells from breast cancer tissue were found to map distinctly to separate RNA expression states/attractions, implying regulatory differences in B cells before and after neoadjuvant chemotherapy. Distinct mapping of different B cells clusters was also observed in cells obtained from Lung cancer tissue further pointing out to certain regulatory differences in lung cancer cells compared to normal cells.

## Introduction

RNA sequencing (RNA-seq) is a genetic approach that has been used to study the expression profiles of different populations comprised of thousands of cells assumed to be homogeneous. Despite the success of RNA-seq in providing insights into clinical and translational research, this method ignores cellular complexity and heterogeneity within tissue samples and might overlook essential details at the cellular level. For example, the different specialized receptors and functions of lymphocytes in a population of immune cells cannot be distinguished in bulk RNA-seq. Differentiation during embryonic development, which also depends on interactions between a population of heterogeneous cells, are ignored in bulk RNA-seq. Furthermore, averaging the expression profile of a population of cells may overlook rare cells in such populations that play important roles in disease progression and treatment-resistance, such as malignant tumor cells in tumor tissue.

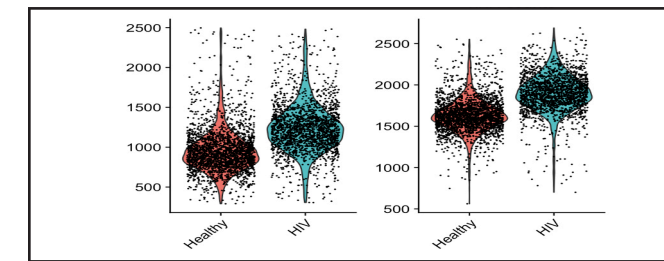


Figure 1a: RNA features and counts of B cells isolated from HIV vs Healthy Patients

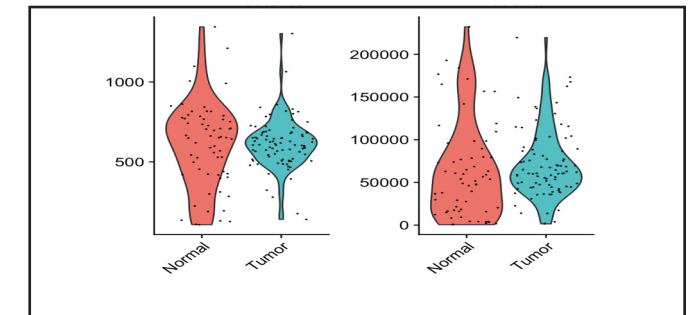


Figure 1c: RNA features and counts of B cells isolated from healthy vs Lung Tumor infiltrated tissue

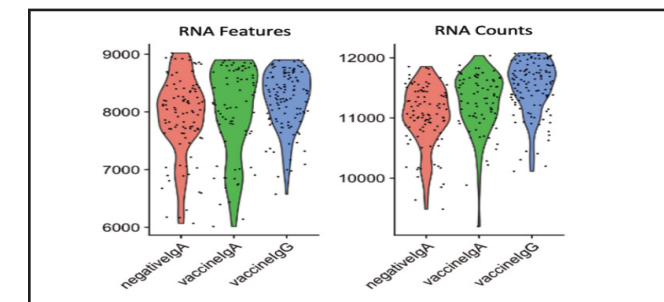


Figure 1b: RNA features and counts of three clonally related groups of B cells following influenza vaccination

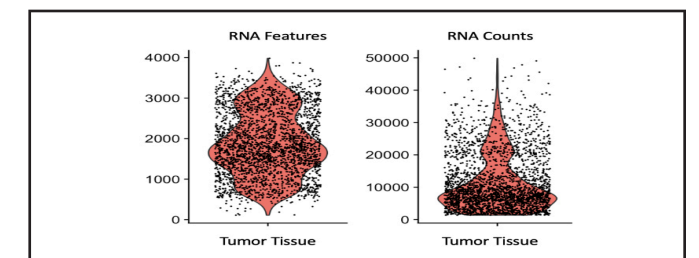


Figure 1d: RNA features and counts of B cells isolated from Breast Cancer tissue before and after neoadjuvant chemotherapy

New advancements in biotechnology have allowed for the development of single-cell RNA sequencing (scRNA-seq), which gained scientific interest due to its ability to provide insights into cellular heterogeneity in normal and diseased tissues. By analyzing the expression profile of each cell in a population separately, scRNA-seq uncovers distinct cells within a population that might have different functions, histories, or stochastic alterations. Moreover, by avoiding the averaging of cellular signals and by providing a large number of expression states, single-cell transcriptome data allows for the reconstruction of gene regulatory networks across several conditions.

Gene regulatory networks are directed graphs where edges connect between regulators of genes and their target genes. Several algorithms have been developed to infer how these regulatory relationships influence and determine the expression of genes in a cell, many of which use binary models to account for an on or off state of genes in a network. Logic gates (AND, OR, NOT) that describe how genes influence each other are used to determine the states of all genes in a particular network, thus providing insight into the most important genes in gene expression in a cellular network. In this experiment, the gene regulatory networks for HIF-1  $\alpha$  and BCR pathways were inferred using the algorithm Boolean

Omics Network Invariant-Time Analysis (BONITA).<sup>1</sup> Unlike other algorithms that do not take convergent regulatory relationships into account, BONITA infers logic gates that depict synergy for HIF-1  $\alpha$  and BCR networks' topologies, which account for signal integration in convergent interactions. Nevertheless, using single-cell transcriptome data to infer the logic gates governing the interactions between genes is not a direct problem with only one solution. Rather, several logic gate sets, also referred to as equivalent rule sets (ERS), are possible. In this experiment, these ERSs were used to simulate B cell expression states (attractors or steady states) with respect to BCR and HIF-1  $\alpha$  activity. Different cells in a population could map to distinct attractors or steady states, which might imply the presence of distinct states of genes' regulation in these cells.

### Methods

Single-cell RNA sequencing data of isolated B cells was obtained for four studies from the Gene Expression Omnibus (GEO) repository. The isolated B cells were obtained from healthy patients as well as HIV patients,<sup>3</sup> influenza vaccinated patients,<sup>6</sup> Lung Cancer infiltrated tissue,<sup>4</sup> or Breast cancer infiltrated tissue.<sup>5</sup> These datasets were preprocessed using the Seurat toolkit implemented in R. Initially, the datasets were separately normalized and filtered based on the

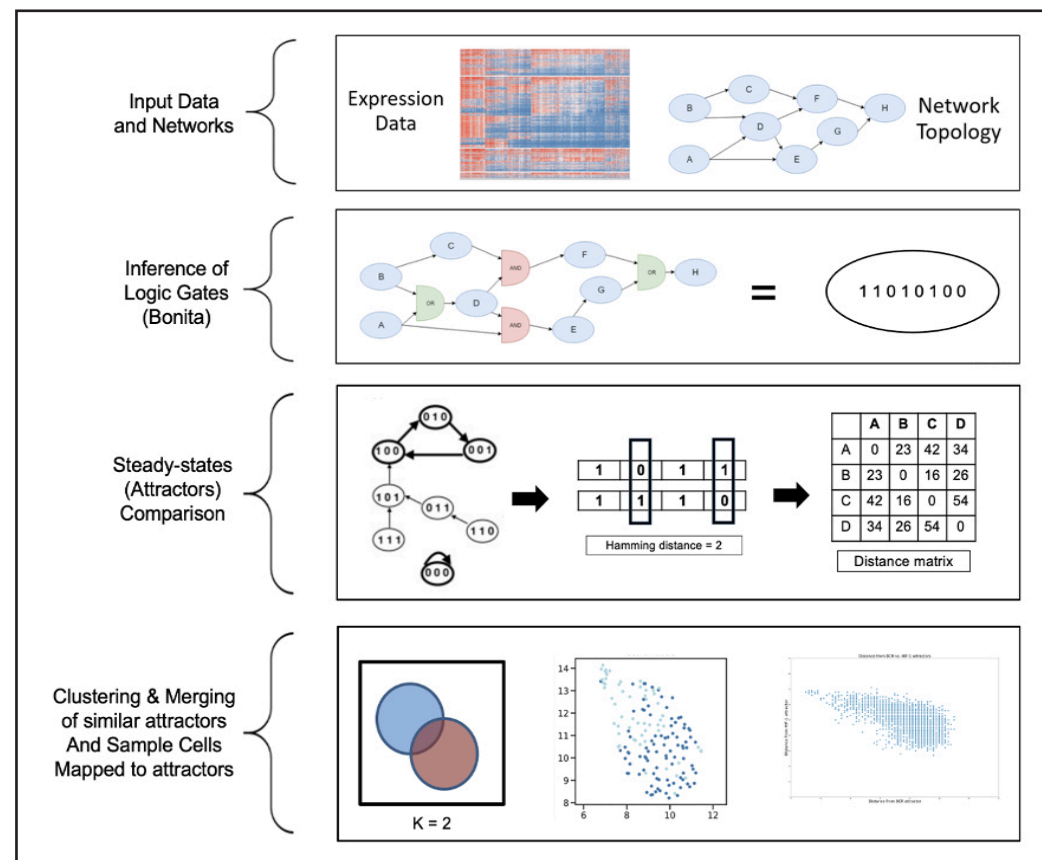


Figure 2: Flowchart of HIF-1 and BCR networks' analysis

Attractors in BCR Network	Number of Cells
0	40
1	111

Figure 3a: Frequency table for the number of B cells per attractor in BCR network

	Tumor Tissue	Normal Tissue
Attractor 1	63	48
Attractor 0	25	15

Figure 4a: 2X2 table for the identity of B cells and their associated attractor in BCR network

Attractors in BCR Network	Number of Cells
0	195
1	763

Figure 5a: Frequency table for the number of B cells per attractor in BCR network

RNA count, RNA features, and mitochondrial gene count as shown in Figures 1a-1d. Thresholds for filtration were based on comparison between the cells of different experimental groups. Primarily, cells with high count of mitochondrial genes were omitted since this indicated apoptosis and cells with high counts or features of RNA were also omitted since these indicated technical errors during scRNA sequencing in which more than one cell could have been sequenced simultaneously. After preprocessing, the clustering of cells in each dataset was evaluated using the dimensional reduction techniques Principal Component Analysis (PCA) and Uniform Manifold Approximation and Projection (UMAP); each cell was given a label based on the cluster to which it mapped.

To investigate the cells' regulatory states across different conditions, network analysis and rules inference were performed on all four datasets; however, only two datasets, breast cancer and lung cancer datasets, provided meaningful mapping between cells and rule sets. As a result, further analyses primarily focused on these two datasets. Initially, the inference of Boolean rules for the BCR and HIF-1  $\alpha$  networks used the BONITA algorithm. Using network topology while accounting for signal integration in convergent cellular

Attractors in HIF-1 Network	Number of cells
0	114
1	37

Figure 3b: Frequency table for the number of B cells per attractor in HIF-1 network

	Tumor Tissue	Normal Tissue
Attractor 1	28	9
Attractor 0	60	54

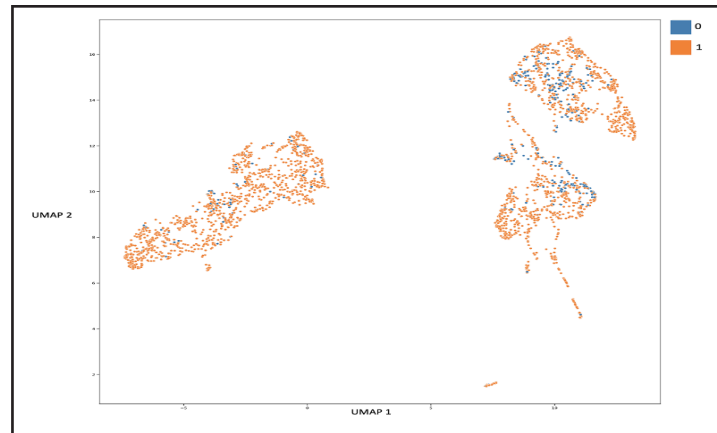
Figure 4b: 2X2 table for the identity of B cells and their associated attractor in HIF-1 network

Attractors in BCR Network	Number of Cells
0	2348
1	320

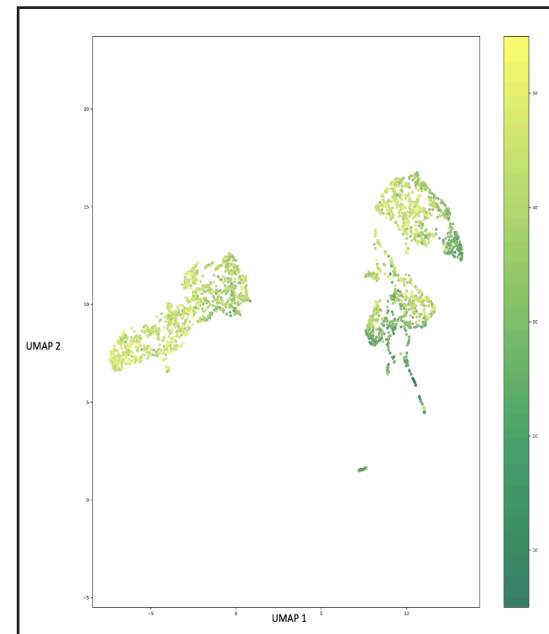
Figure 5b: Frequency table for the number of B cells per attractor in HIF-1 network

pathways. Obtained from the WikiPathways database, this algorithm required the BCR and HIF-1  $\alpha$  network topologies. This algorithm was also provided with the Seurat-filtered and -normalized scRNA expression data as shown in Figure 2. Each dataset was run on the University of Rochester Medical Center Linux cluster, BlueHive, where several possible ERS were obtained.

After the sets of possible logic gates (ERS) are generated, each ERS could be used to simulate how an initial gene expression state of a cell would change with time. Using a synchronous update algorithm<sup>2</sup> running the logic gates of that ERS simultaneously on a cell's initial gene expression state at time  $t$  and obtaining a successor state at time  $t+1$ . Continuing to run the ERS on each successor state, new states will be obtained in a pattern that projects that cell's static initial expression state into a dynamic behavior through the time governed by that specific ERS. Eventually, specific sequences of gene expression states, attractors, will keep reoccurring whenever the ERS is simulated, as shown in Figure 2. These recurring states are hypothesized to be biologically relevant. Therefore, these attractors were chosen for further analysis.



**Figure 6:** UMAP plot of all sample cells color-coded based on the attractor they are closest to in the BCR pathway



**Figure 7:** UMAP plot of all sample cells color-coded based on distance from their respective attractor in the BCR pathway.



**Figure 8:** Heatmap of on vs off genes between attractors in the BCR pathway

To identify steady states of the cells with respect to the BCR and HIF-1  $\alpha$  network activities, 10 random ERSs were used in each network to identify attractors. First, the hamming distances between the obtained attractors were calculated and a distance matrix was generated as shown in Figure 2. Next, the matrix was fed into the k-medoids clustering algorithm implemented in Python in order to cluster attractors by finding similar network states. The attractors in each cluster were then merged together, and the hamming distances

between the resulting attractors and the cells' initial states were calculated. Finally, each sample cell was then mapped to the attractor closest to its initial expression state, allowing for further filtering to exclude those which less than 5% of the sample cells mapped to.

To visualize the number of cells per attractor, frequency tables were generated for each network in each dataset. Additionally, PCA embeddings and cluster labels per cell sample were obtained using Seurat, which were used to generate two

types of UMAP figures. The color coding of cells in these figures was based on the attractor labels they mapped to or the hamming distance between these cells and the attractors they mapped to. Furthermore, heatmaps were generated to show the differences in gene expression between attractors.

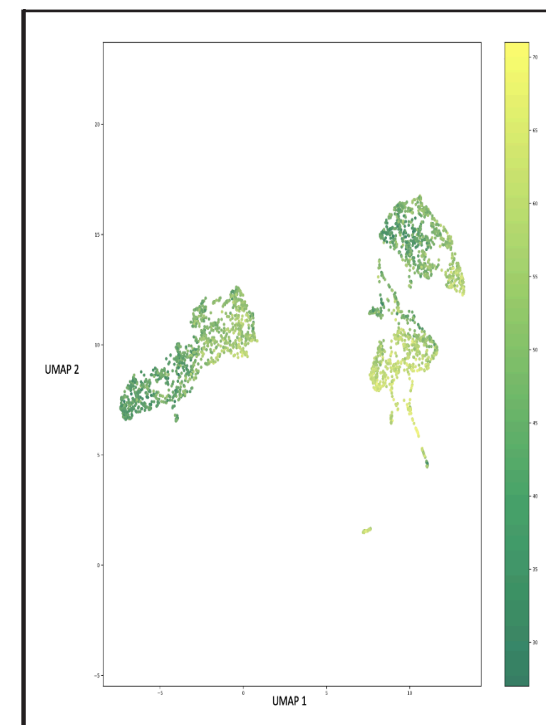
### Results and Analysis

Despite the fact that network analysis was performed on all four datasets, only the breast cancer and lung cancer datasets provided meaningful mapping between cells and rule sets. Therefore, further network analyses primarily focused on these two datasets.

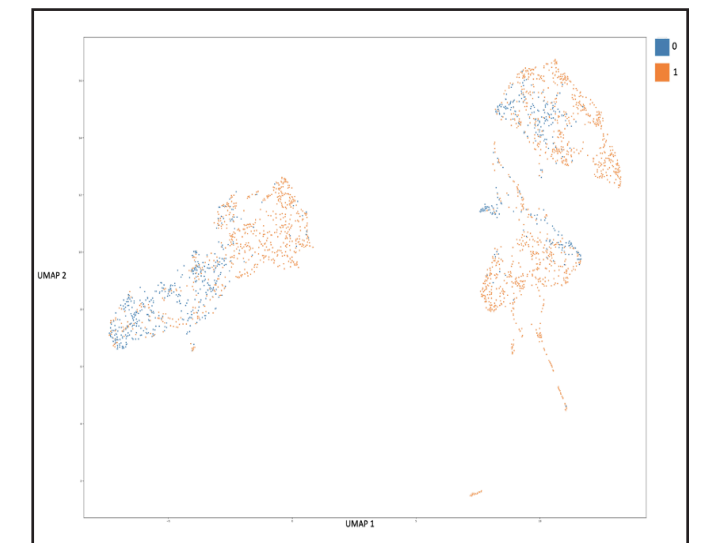
In the breast cancer dataset, network analysis provided two attractors for the BCR and HIF-1  $\alpha$  networks. B cells from both experimental groups, before and after neoadjuvant chemotherapy, were then mapped to one of these two attractors in each network based on the hamming distances between attractors and cells' initial expression states. The frequency tables shown in Figures 5a and 5b show that more cells were mapping preferably to one attractor over another in both BCR and HIF-1  $\alpha$  networks respectively. Our interest

was to see if B cells from breast cancer before and after neoadjuvant chemotherapy mapped differentially to one attractor over another. The breast cancer dataset did not provide the identity of cells on GEO. Nevertheless, further in-depth network analysis was performed in order to direct future analyses. In the BCR pathway, Figure 6 shows specific clusters of B cells mapping to distinct attractors. These results might suggest differences in BCR network's regulatory state across the two experimental groups studied or among B cells in a population. Furthermore, comparison between Figures 6 and 7 demonstrates that the initial states of the cells mapping to attractor 1 (orange) were close (dark green) to this attractor. This further supports that this specific subpopulation of B cells might be expressing and regulating genes in a specific pattern as specified by attractor 1. However, cells mapping to attractor 0 (blue) showed further distances.

Similarly, in the HIF-1  $\alpha$  pathway, Figure 9 shows a small number of cells mapping to distinct attractors (blue) with more than 86% of cells preferentially mapping to attractor 1. The mapping distinction implies differences in the HIF-1  $\alpha$  network's states across the two experimental groups studied,



**Figure 10:** UMAP plot of all sample cells color-coded based on distance from their respective attractor in the HIF-1 pathway.



**Figure 9:** UMAP plot of all sample cells color-coded based on the attractor they are closest to in the HIF-1 pathway



**Figure 11:** Heatmap of on vs off genes between attractors in the HIF-1 pathway

preferences to a specific state of the HIF-1  $\alpha$  network, and potential differences among B cells themselves within a specific population. Comparison between Figures 9 and 10 shows that several clusters of cells congregated close to the attractors they were mapped to (dark green), while a few clusters of cells, all of which mapped to attractor 1, showed larger distances (yellow).

These discrepancies suggest the existence of more than two attractors or states that need to be considered for these cells. Therefore, future work will focus on investigating the existence of such additional states. In addition, the differences between attractors 0 and 1 specifically pinpointed using a heatmap shown in Figures 8 and 11 uncover several genes that are differentially on versus off in the two identified attractors. Future work will focus on investigating the interactions between these genes and their functional roles in order to determine the nature of differences in gene regulation in the BCR network or the HIF-1  $\alpha$  network between B cells from breast cancer tissue before and after neoadjuvant chemotherapy.

In the lung cancer study, network analysis provided two attractors for the BCR and HIF-1  $\alpha$  networks. B cells from lung cancer and normal tissue were then mapped to one of these attractors based on the hamming distances between attractors and cells' initial expression states. The frequency tables shown in Figures 3a and 3b show that more cells were mapping preferably to one attractor over another in both BCR and HIF-1  $\alpha$  networks respectively. Our interest was to see if B cells from tumor versus healthy tissue mapped differentially to one attractor over another. Each B cell's source (tumor versus healthy tissue) and the attractor that each B cell mapped to in each network (attractor 0 versus attractor 1) was collected in a 2X2 table and used to perform a chi-squared test, as shown in Figures 4a and 4b for BCR and HIF-1  $\alpha$  networks respectively. The chi-square statistic for the BCR network was found to be 0.3989 with a p-value of 0.53 > 0.05, suggesting no significant mapping differences in the BCR network. However, the chi-square statistic for the HIF-1  $\alpha$  network was found to be 6.1007 with a p-value of 0.014 < 0.05, suggesting that there might have been expression differences of interest in the B cells obtained from lung cancer tissue versus healthy tissue. To verify the importance of these results, future work will focus on collecting more lung cancer datasets and pinpointing the genes on versus off in attractor 1 or attractor 0.

## Conclusion

B cells play important roles in responding differently to various infections and vaccinations. Here, we focused on investigating differences in the regulation of BCR and HIF-1  $\alpha$  networks in B cells across different conditions. To investigate these differences for each B cell in a population separately, scRNA-seq and a discrete state modeling algorithm (BONITA) were used. In-depth network analysis showed several clusters of B cells from breast cancer tissue mapping to distinct regulatory states, alluding to distinct on and off

specifications of genes (attractors) in each network. These findings support further investigation of more datasets in order to pinpoint what the regulatory changes in B cells are in response to neoadjuvant chemotherapy, which could prove essential to finding better chemotherapies with less side effects. Furthermore, other B cells from breast cancer tissue mapped to other regulatory states not investigated here. Therefore, this finding urges future work to pursue additional regulatory states governing the expression of B cells isolated from breast cancer tissue. Additionally, regulatory differences between B cells from lung cancer tissue and healthy tissue showed statistical significance. Thus, future analysis could pinpoint specific differences in the regulatory pathways in B cells, which are potential targets for anti-cancer drugs.

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# Reducing the Gender Gap in Technology through an Entrepreneurial Network

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## Introduction

The software industry has a rapid growth rate of 21% (US Bureau of Labor Statistics, 2019). In fact, 3.5 million new computing-related jobs are expected in the next six years (Department of Labor Statistics, 2018). However, women represent only 25% of the tech workforce (Graf, 2018), 5% of CEOs in Forbes' Top 100 Digital Companies List, and 10% of executive positions in Silicon Valley (Ben, Fenwick, 2019). The lack of gender diversity in this industry is also present in academic settings: only 1.4% of female first-year college students intend to major in computer science (NCWIT, 2020), and women represent only 19% and 21% of bachelor's degrees granted in computer science and engineering, respectively (NCSES, 2016).

The gender gap in the information technology (IT) industry is concerning not only because women are being left out of these opportunities but also because women-led tech startups report a 35% higher return of investment (ROI) (Boston Consulting Group, 2018). Therefore, the lack of gender diversity in the IT industry reduces the opportunity for economic growth, affecting both women and men.

The present paper aims to provide a potential solution to increase female representation in this field. In particular, the reasons for the lack of female entrepreneurship in technology and how this affects women's decision to pursue a career in tech will be analyzed.

The economic literature suggests that a relevant problem for women entrepreneurs in high-growth sectors is the lack of venture capital funds. Venture capital is a form of funding in which investors provide capital to companies that are expected to have high-growth returns in exchange for a certain percentage of ownership of the business. There are several reasons for this funding gap involving social and cultural factors, complicating the issue. In this paper, I analyze two main causes: the lack of women investors and the impact of implicit bias.

The lack of venture capital funds for female entrepreneurs is significant, as it reduces the number of young women choosing careers in IT because of the absence of role models. Role models help develop a sense of belonging within a field and break gender stereotypes associated with it, which opens more possibilities for those around them. This is known as the role-model effect, which will be discussed later.

To reduce the gender gap in IT, I propose to create a platform that connects young women with entrepreneurs and

investors, allowing them to build their entrepreneurial and professional network at the beginning of their careers.

## The Struggle Of Female Founders In Technology

High-growth businesses are those that grow sales and employment by at least 20% per year. Companies under this category generally belong to the internet and software development artificial intelligence, energy development, and biotechnology industries. To a large extent, women are underrepresented in high-growth entrepreneurship; 10% and 15% of high-growth startups are founded by women (Ewens, Townsend, 2019). This gender gap exists due to the difficulties female founders have in raising capital from investors, which limits the success of the female-led startups in the market. In fact, female founders are 63% less likely than male founders to receive venture capital funding (Guzman, Kacperczyk, 2019), and only 2.2% of all the venture capital in 2017 was invested in female-founded companies (*Pitch-Book, 2018*).

One of the main factors contributing to this problem is the lack of female investors. 90% of venture capitalists are men (Ewens, Townsend, 2019), and they usually invest in entrepreneurs who a) belong to their professional and personal networks and b) they feel identified with. Venture capitalists invest in early-stage companies where there exists a high-risk of failure. In order to minimize the risks, investors are more likely to invest in people they know, trust, and connect with. Male investors usually bond better with male entrepreneurs. This is caused by homophily and in-group preference, which refers to the act of associating and treating more favorably those who share similar characteristics (Guzman, Kacperczyk, 2019). These biases are particularly concerning for female-led startups because of the lack of women in the finance sector, suggesting that more female investors are necessary to have more female-funded entrepreneurs (Ewens, Townsend, 2019).

Additionally, implicit bias, which is the act of unconsciously having stereotypes and prejudices against certain populations, may further exacerbate a gender gap. In this case, women entrepreneurs experience implicit gender biases from male investors. The study, *Are early stage investors biased against women?*, establishes two types of gender biases: taste based discrimination and miscalibrated beliefs. Taste based discrimination refers to male investors experiencing less satisfaction from investing in female entrepreneurs, while mis-

calibrated beliefs means that they generally hold "an incorrect stereotype about entrepreneurs of the opposite gender" (Ewens, Townsend, 2019). These biases stem from the perception that entrepreneurship is a male activity and that masculine traits are associated with high-growth ventures (Guzman, Kacperczyk, 2019). Because women are a minority in the high-growth sector, male investors tend to question their competence and future performance. For example, women-led startups that are under the support of incubator programs, seek lower amounts of capital, or run in female-related markets are at a disadvantage because investors tend to perceive these characteristics as signs of less ambition and risk-seeking (Ewens, Townsend, 2019). Meanwhile, male entrepreneurs operating under the same conditions, do not face these disadvantages.

Usually, male investors are not aware of these biases, thus there is intense controversy in the industry around this topic. A common counterargument to the gender gap is that investors invest in the startups with higher financial returns, regardless of the founder's gender. However, female investors and male investors respond to women entrepreneurs in opposite ways (Ewens, Townsend, 2019). The fact that a gender gap exists "is already suggestive of gender bias because if investors...were strictly analyzing a deal from a financial perspective, then we would expect investors of both genders to respond similarly" (Ewens, Townsend, 2019). This hypothesis is confirmed by the analysis of the investors' opinions on comparable women-led and men-led startups. In general, "female and male investors agree on which deal is better when comparing both-men or both-women entrepreneurs," showing that both types of investors have a similar way of evaluating deals. But, "they tend to disagree if the entrepreneurs are one woman and one man," proving that they might be biased towards their same gender (Ewens, Townsend, 2019). When analyzing the long-term performance of the deals, the male-founded startups supported by male investors were no more financially successful than the female-founded ones. This supports the idea that reducing the gender gap in tech entrepreneurship and supporting more female-led startups will lead to economic growth in the overall industry. It also implies that male investors do not look solely at financial returns, and only invest in female startups if they are too promising to reject. Interestingly, there is no proof of the same behavior in female investors, reaffirming that male investors are implicitly biased against female founders (Ewens, Townsend, 2019).

It is clear that there are several sociocultural and economic aspects of the funding problem faced by women entrepreneurs in the IT sector. In order to solve this issue, it is important to understand the roots of the problem and study potential policies that could reduce these barriers. More female investors are needed, as they are much more likely to fund female entrepreneurs than male investors. Moreover, women interested in tech entrepreneurship need more visibility in the startup ecosystem and access to investors' networks before the funding stage. Younger female generations

might not see tech entrepreneurship as a career path when women are not able to expand their businesses and get recognized in the IT industry. As a consequence, they may not engage in building their network of venture capital investors that would facilitate the investment process in the future. To understand the implications of this hypothesis, it is relevant to analyze whether there exists a role-model effect that impacts young women's career decisions.

## The Effect Of Role Models in Young Women

Because there is a lack of studies addressing the effects of tech entrepreneurs on young women in the current social sciences literature, I will refer to the role model effect that STEM faculty has on female students and extrapolate the results.

Full-time female faculty in Science, Technology, Engineering, and Math (STEM) represent only 18% of the college tenure track faculty in the United States (Young, 2013). This lack of female representation in faculty creates a challenging environment for female students in particular because "people tend to gravitate toward and persist in activities in which they believe they will succeed" (Young, 2013). In addition, research shows that female students with female STEM professors "were more likely to automatically identify themselves with

science; and second, they automatically associated science with women more so than with men" (Young, 2013). These results confirm the influence that role models have on young women.

Increasing the amount of female professors in a certain field also impacts the amount of girls taking classes in that field. Female students were twice as likely to take advanced STEM courses if they had initially taken an introductory class with a female professor (Bettinger and Long, 2005). Additionally, the likelihood of a female student completing a STEM major increases when the number of female professors teaching the introductory courses increases (Serra and Porter, 2018). These findings are key contributions to the gender gap problem because they imply that early access to female role models in STEM increases the probability of retaining women in these fields.

Even though female professors have a positive effect on female students, their scope is limited only to students taking their classes. Chief Executive Officers (CEOs) and business founders are able to reach and positively impact a much larger audience, including females who have never been exposed to technological education. While young men have public figures in the IT industry such as Bill Gates, Jeff Bezos, and Mark Zuckerberg to look up to, women do not have nearly as many females in tech with the same level of global influence. Therefore, applying the role model effect to female founders in the tech sector would increase the amount of young women interested in a technology career.

## The Solution

Given the analysis provided above, I identify three main pillars of the gender gap in IT entrepreneurship: the lack of capital invested in female-led startups, female entrepreneurs in tech, and role models for young women. Clearly, these pillars are related to each other. These shortcomings have created a cycle that is very challenging to stop. For this reason, I propose the creation of a networking platform that connects young women with female founders and investors.

Lack of access to the startup network composed of entrepreneurs and investors is one of the basic problems. Connecting with a large number of investors and building professional relationships allows entrepreneurs to obtain funds. In order to reduce the gender gap in tech entrepreneurship, women need to have access to these connections. However, building this network needs to start from an earlier stage or else challenges will increase over time. Young women need to connect with a network of experienced female entrepreneurs and investors that can provide resources and mentorship, easing their entry into the startup world.

Therefore, I propose the creation of an online networking platform designed for female college students and recent graduates to connect with mentors in the industry. This platform would allow them to have access to mentorship, resources, and connections, and establishing these mentorship opportunities from an early stage of their careers would increase female retention in tech entrepreneurship. As the industry gains female founders, more young women would have role models who would help them to develop a sense of belonging and inspire them to follow these careers. Thus, creating this platform would reduce the gender gap in IT.

Additionally, through this platform, young women would also build connections with investors. This not only provides them the space to bond with investors and consequently have access to more funding opportunities but also to gain insights about the finance sector and what investors are looking for. This implies that women would be more prepared to raise capital in the future, which would ultimately reduce the gender gap in this field as well.

Given the reasons presented above, it is important to develop this networking platform because in the short term it tackles the lack of female role models and entrepreneurs in tech and in the long-term it tackles the lack of capital invested in women-led tech startups.

## Conclusion

The problem of the gender gap in the IT industry is complex. It is a cycle that starts from a young age due to a lack of role models, continues to adulthood when a female enters the workforce, and perpetuates further for those who choose the entrepreneurial path. The funding barriers that female tech

entrepreneurs face causes the gap to continue expanding, because without these role models, less women opt to study or work in technology. By cultivating and supporting the female tech entrepreneurial spirit at an earlier stage, more women would be attracted to this field. As a potential solution to this, I propose the development of an online networking platform for young women to connect with female entrepreneurs and investors who would serve as role models. This would result in an increased interest in IT and entrepreneurship in young women, and eventually an increase in female founders. It would also address the lack of venture capital invested in women-led companies,

as young women would be able to build their connections with investors early and gain knowledge about the finance world. Ultimately, it is important to develop this online networking platform because it is an integral solution that addresses the gender gap in IT from both the entrepreneurial and the investment sides.

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## For the Sake of the Future: The Soviet Economy and a Surfeit of Shortages

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"They send all the bread out of the country, and we ourselves are here with no bread while our party leaders holler about achievements. We work eight hours at the factory, then stand four or five hours in breadlines. And there you have a thirteen-hour workday."<sup>1</sup> Sentiments like these echoed throughout the Soviet Union. Workdays were extended unnecessarily by waiting in long lines to purchase the most mundane items when supplies ran low. People learned to live with the consequences of government choices in which they had no say, such as an intentional reallocation of the grain required for making bread to satisfy other priorities. Such scarcities made the inconvenience of occupying the queue an all too familiar one, and citizens believed corrupt or inept bureaucrats were behind these shortages of life's necessities. While malfeasance accounts for part of the problem, pervasive shortages also indicate the existence of something more profound, a byproduct of the Stalinist economic system implemented early in the nation's political and economic maturation process that allowed shortages to continue.

This essay examines the Soviet nation's recurrent shortage phenomenon, a consequence of the economic policy in effect between 1928 and 1953. This examination will focus primarily, however, on the Soviet Union's economic experience in the years between the commencement of the First Five-Year Plan (First FYP) and the German invasion of the Soviet Union during Operation Barbarossa. The Soviets viewed shortages as an acceptable trade-off in securing national industrial modernization and gaining economic strength. This essay considers the impact of that exchange along three lines of inquiry: Stalinist economic policy programming, including nationalization and implementation of Stalin's intermediate goal programs (the Five-Year Plans, or FYPs), the hierarchy of access to goods, and the disparity in policy implementation between the nation's urban and rural areas. Shortages impacted Soviet citizens at nearly every socio-economic and political level and were instrumental in defining efficiency or inefficiency across all sectors of the economy. Therefore, in addition to secondary literature, this essay utilizes news reports, historical interviews, and first-person narratives to explore how this surfeit of shortages inherent in the national economic policy impacted the daily lives of Soviet citizens, how they created workarounds where possible, and how they did without when there was no other option.

At this point, a few words about the subject of shortages and related financial constraints in a socialist economic system are in order. Noted Hungarian economist János Kornai has spent much of his career unpacking the economic system of

socialist nations. He has identified the socialist economic experience of a "reproduction of shortage" as deficits that are not "temporary, provisional, [or] occasional events but ... a complex of phenomena that constantly reproduces itself under specific circumstances."<sup>2</sup> I have also adopted Kornai's interchangeable terminology schema for "socialism" and "communism." Kornai writes comprehensively on the existence of this "reproduction of shortages" in applying socialist economic theory to the real world, and he argues that such shortages did not result from high-level planning errors.<sup>3</sup> Instead, he contends that they reflect an imbalance in a supply-demand equilibrium inherent and accepted in socialism. In essence, Kornai describes a glaring flaw in the socialist economic system when viewed through a capitalist economic lens. The system ignores the demands of the marketplace in determining what goods to produce. Instead, it aligns its output with the dictates of a central planning apparatus removed from the demand side of the supply-demand equation. The imbalance in this equation results in repeated gluts of unwanted goods and persistent shortages of necessary or desired items. The overriding principle is that if it is more expedient for the national economic program to produce widgets than it is to produce loaves of bread, then widgets it is.

While the focus of this essay remains on the Soviet experience with a shortage economy, an essential corollary to the concept of reproduction of shortages is Kornai's construct of budget constraints. He proposed the idea of "soft budget constraints" (as opposed to "hard budget constraints") in the late 1970s and applied it to economies in a phase of transition from capitalist to socialist.<sup>4</sup> Amidst the relationship between shortfalls and soft budget constraints in transitional economies, the government (or any organization providing funding to an enterprise) does not strictly control that enterprise's spending, and it covers any budgeting shortfalls at the enterprise level.<sup>5</sup> Alternately, in a relationship governed by "hard budget constraints," the enterprise is limited in its activity by a budget that prohibits cost overruns.<sup>6</sup> The linkage between soft budget constraints and the reproduction of shortages inherent in transitioning socialist economies formed early in the Stalinist economic schema. As scholars Paul Gregory and Mark Harrison noted, "[the soft budget constraint] originated in Stalin's industrial drive and was perpetuated by his inability to commit to financial discipline."<sup>7</sup> These soft budget constraints sacrificed fiscal prudence on the altar of industrial growth.

Protracted shortages that existed in all economic spheres — ranging from the collection of raw materials to the manufac-

ture of finished goods, including labor involved at each step of the production process — were tolerated at the enterprise level because the government would cover any expenditures over budget. Under Stalin, the Soviet's overarching directive was to meet production quotas, regardless of cost and perhaps, common sense. If amassing raw materials in one economic sector meant a dearth of those materials elsewhere, the latter suffered shortages, and the former dealt with a glut in the supply. This practice extended beyond just the primary industrial concerns, such as blast furnaces and dams competing for massive quantities of concrete; it also enveloped light manufacturing firms and factories, like those of the Chelyabinsk and Stalingrad tractor plants.

Firms sought to accumulate as much tangentially relevant material as possible, including labor, to ensure they met rigid construction and production quotas. Industrial managers recklessly hoarded goods like steel and rubber. This was observed in tractor factories where the amassing of consumer goods unrelated to the production of tractors was an unexpected occurrence in the larger hoarding trend. Factory managers used these seemingly extraneous goods as incentives to create larger labor pools by offering workers additional perquisites (e.g., food, clothing, and housing). These enticements allowed factory managers to secure a large enough labor supply to meet a government timeline or quota regardless of how little time remained before the deadline.<sup>8</sup> A labor glut in one area virtually ensured a shortage in another, but this was a battle where those prepared were the victors. Shortages and soft budgets were exchanged for industrializing the Soviet economy on Stalin's timeline and found an affinity for obscene overages at various points in the production process. By comparison, the nationalization of the private sector and collectivization of privately held farmland was a matter of growth by consolidation.

### The Rocky Road to Nationalization

The first inklings of the future economic issues to face the Soviet state, including the nationalization of privately-owned industries and agricultural holdings, appeared during the Russian civil war under War Communism. Nationalization continued to increase exponentially after Soviet victory. "In November 1920, the government nationalized even small industry ... in theory the whole sphere of production was now in the hands of Soviet power."<sup>9</sup> One carryover the Soviets inherited from the previous regime was the frustrating issue of "peasants [who] were unwilling to sell [bread/food-stuffs] when there were almost no manufactured goods on the market to buy."<sup>10</sup> At the Civil War's conclusion, victorious, the Soviets stood atop the pile of social and economic debris symbolic of the battered nation. One of the first changes Stalin made upon solidifying his control within the Politburo was rescinding the hated economic policy of War Communism. He followed this by rescinding Lenin's implementation of the New Economic Plan (NEP) in 1921. State capitalism grew under the NEP to mitigate the nation's previous central planning economic policy missteps. One compo-

nent of this growth was the rise of the *kulaks* (comparatively large landowning peasant farmers) and a new capitalist class - the NEPmen. These were business people who took advantage of some aspects of the NEP, including exercising the small freedoms tolerated in private enterprises as a form of state capitalism.<sup>11</sup> Unlike those who succeeded him, Lenin saw value in progressing methodically through the theorized stages of communism and building a robust industrial base before advancing to the following theoretical economic and political steps. With no one left to oppose him or his vision, Lenin set about rebuilding the USSR as he saw fit.

In Lenin's view, socialism equated to the hypothetical Marxist stage of the Dictatorship of the Proletariat, where the workers, under the guidance of the party, would hold the political power. Under full communism, of course, all class distinctions (i.e., peasants, poor, proletariat, bourgeoisie, and elites) ostensibly disappeared. Lenin's regime realized significant success in the traditional economic zone of agriculture, which continued as the primary economic sector of the new Soviet state. According to historian Lewis Siegelbaum, the "grain harvest was nearly 40 percent above the previous year's level ... the tax burden ... fell from 17.8 percent to 15.5 percent ... notwithstanding the fact that the state received 366 million puds[pounds] of grain in tax, or almost three times as in 1921/22."<sup>12</sup> The economy swiftly recovered post-war, and by the late 1920s, production levels had returned to those of 1913.<sup>13</sup>

A newly re-energized agricultural economy that existed within the state but lay outside its direct control was not what Lenin's successor had in mind. By the time of Lenin's death in 1924, Josef Stalin had already inserted himself into the halls of Soviet power and had set about putting his stamp on the Soviet economy. Despite rapid growth resulting from the NEP, several unforeseen factors contributed to a reversal of the nation's economic course. State tax collections fell as the *kulaks* held onto grain rather than sending it to market. They did this anticipating a reduction in the supply, an increased demand, and higher potential profits. In part, the decision to withhold grain was also motivated by the reality that few consumer goods were available for purchase, and the *kulaks* did not need ready cash.<sup>14</sup> As Osokina notes, "they stashed away cash at home in piggy banks, stockings or mattresses because there was nothing to spend it on. They would rather hoard grain that grew daily in value than trade it for depreciating money."<sup>15</sup> Concerned over increasing prices and a growing fear of famine, Stalin reversed the economic course in 1928 and returned to the forced collectivization of farms.

### Stalinist Economic Policy

Following the turn away from the NEP's model of state capitalism, Stalin implemented the first of his FYPs. In a 1931 speech to business leaders, Stalin called to push the Soviet industry to a level that matched western powers: "We are fifty or a hundred years behind the advanced countries. We must make good this distance in ten years. Either we do it, or we

shall go under."<sup>16</sup> However, his all-consuming desire to create a new heavy industry sector from scratch effectively starved the existing, predominantly agricultural, economic base. Nevertheless, Stalin pressed on. Key industries vital to the First FYP were identified, with the idea that it was essential to concentrate the construction of such industries in discrete locations to increase efficiency. Magnitogorsk was among the best-known of these super sites; historically, it was a small, backwater steppe town destined to become the archetype for future socialist utopias. The Magnitogorsk planners, intending for it to rival the great steel towns of the American Midwest whilst becoming a critical industrial center in the process, set about erecting blast furnaces at a breakneck pace.

Historical analyses, first-person narratives, and even historical fiction about the days of the construction at Magnitogorsk abound. Among the most compelling are Valentine Ketaev's *Time, Forward!*, John Scott's *Behind the Urals*, and Stephen Kotkin's *Magnetic Mountain*. Each of these works resonates with the fallout from pervasive shortages of raw materials, finished goods, and even labor. For example, *Time, Forward!* is a cornerstone of the literary genre of Soviet Realism. Nevertheless, such early Soviet literature needed to portray Soviet "reality" in a way that was acceptable to the powerful. As a result, Ketaev never openly criticizes the persistent lack of goods in the novel, and he mentions dwindling supplies and inequality of access to goods in passing as if that experience was quite ordinary. Early in the narrative, Ketaev describes the constituent members of a crowd gathered in a Magnitogorsk office as a hodgepodge of humanity, the shortages of goods implicit: "in bast shoes, barefooted, in overalls, without overalls; in shoes, tow-headed ones, those who had washed themselves ...."<sup>17</sup> The inference of shortages (and of class differences) is subtle but noteworthy.

Comparably, Scott's *Behind the Urals* is a first-person account of an American engineer, initially a true believer in socialism and its promise of equity and a classless society, who traveled to Magnitogorsk to help construct the facility. What he found instead was a cataract where socialist ideals slammed against the rocks of an inequitable reality. For example, Scott recalls a meeting concerning the difficulties with erecting one of the centerpieces of Magnitogorsk, the giant blast furnace. As a prisoner specialist named Tishenko explained, "A riveter froze to death last night. Cold and malnutrition. This morning four of the girls we have heating rivets didn't show up ... The compressor is working badly."<sup>18</sup> The labor shortage might seem the most surprising issue at the construction site considering the city's draw for those looking for work, but the shortages also extended to supplies of food, clothing, fuel for workers, raw materials, and construction components to complete the project.

It was possible to blunt the impact of shoddy compressors and unheated rivets, but the lack of warm clothing and nutrition compounded all other issues facing construction crews. Intensive labor in harsh conditions, like those found in Magnitogorsk, required adequate food supplies, clothing

capable of handling the wind and the cold, and fuel to provide respite from the elements. These necessities were in ample supply for some of the workers, party members, foreign experts, and supervisors required to keep the construction on schedule. Those with skills required in the industrial makeover of the country and those holding the reins of the nation's power were critical for success, and the pressure to meet their needs was palpable. They could not suffer shortages that were otherwise acceptable to foist upon those outside this core group who possessed necessary knowledge or power. Scott demonstrates that most workers made do, cannibalizing materials from other areas: "Within five minutes the stove was full of scraps of wood, most of which had been taken from a pile of railroad ties outside."<sup>19</sup> In this case, the immediate need was for warmth, and workers willingly relinquished any future use of the railroad ties to satisfy the urgent requirement for heat. However, in its early days, the most critical shortage at Magnitogorsk was adequate housing for the workers, and sometimes whole families, who arrived in the city to work on the construction or operation of the plan. This need would eventually be satisfied, as Kotkin describes in his opus on the city of steel.

Kotkin's *Magnetic Mountain* weaves a historic structure into the narratives of those who experienced the triumphs and frustrations of Magnitogorsk's construction program. Magnitogorsk, including its surrounding environs (collectively, *Magnitostroi*), was the archetype of a modern socialist city representing the Soviet's utopian ideal. In some respects, *Magnitostroi* was a marvel in the Soviet hinterlands in its time with, among other luxuries, a cinema that seated thousands, a circus, and state-provided housing. Kotkin's narrative emphasizes how party bureaucrats pushed relentlessly and sometimes heedlessly toward lofty goals, ignoring the system's apparent chasm between planning and an achievable reality. Their policies were reliably consistent, and the outcomes reliably chaotic. However, Kotkin offers that despite familiar chaos, many supported the socialist system because it seemed more equitable than life under the Romanovs: "The plenum [December 1936] concluded with a tribute dashed off to Stalin in which the participants exclaimed, 'we cannot express in words the full force of our love for you,' and pledged their readiness to 'meet the enemy.'"<sup>20</sup>

Common goals initially fostered the comradery necessary for Soviet progress, but soon enough, cracks began to appear in this façade of equality, indicating that some people were "more equal" than others. Collectively, Kotkin's narrative captures the cost of communal and individual pressures of unreasonable construction and production schedules amid the general scarcities endured by an overworked and often underfed workforce. Implementing the ideals of building a new socialist utopia began at the local level at Magnitogorsk and then expanded to the entirety of the Soviet Union. However, the people of the Soviet Union had difficulty in achieving the standards of the "New Soviet Person" which included virtue, a strong work ethic, and a strong sense of



comradery with fellow citizens symbolized by Moscow's *Worker and Kolkhoz Woman* monument.<sup>21</sup> Unfortunately, the comradery that developed was alternately energized or strained by burgeoning socialist competitiveness. Some workers continued to believe in the common cause of their efforts. Their supervisors, who likely benefited materially from meeting and exceeding quotas set by the state, championed goal-oriented efforts as the means to achieve a better standard of living for themselves and their families. By comparison, those who provided for their families in relative obscurity on small farms for much of Russian history found themselves targeted by Stalin's ambitious modernization mandate.

### Collectivization of Farms and Implementation of the FYPs

The ability to feed its people was critical to the economic wellbeing of the Soviet Union. Nevertheless, the Soviets regularly struggled to produce or acquire enough food to accomplish that goal. To a significant degree, Soviet famines resulted more from human-made economic policy than from natural causes. Osokina argues the transformation under Stalin was: "... the final step in the destruction of the market and the race to famine."<sup>22</sup> The institution of Stalin's First FYP meant not only the end of the NEP and the death of the private sector but also widespread starvation due, in part, to the collectivization of farms. Previous attempts to collect and then forcibly confiscate grain failed, incentivizing the collectivization of farms: "... peasants would remain producers but would not own that product."<sup>23</sup> In addition, workers in the cities employed in the industrial sector of the economy came higher in the social hierarchy than peasants in the heartlands. As Osokina argues, "... exports and cheap bread for workers came at the expense of famine for millions of peasants."<sup>24</sup>

Soviet intent sat in stark opposition to the reality that unfolded within the agricultural sector. Three primary goals were at the core of the reimplementing of farm collectivization efforts: first, to bring the agricultural sector under a state-controlled communist model; second, to accelerate the destruction of the *kulaks* as a social class; and finally, to feed/fund the growing industrial complex and its workers. Osokina describes the results of the First FYP, not dizzied by success, as Stalin had characterized, but dizzied by hunger.<sup>25</sup> First, the Soviets dealt with the immediate issue of the government's inability to outbid its citizens in the marketplace. As a result, "widespread repression against private traders began in 1927-1928."<sup>26</sup> As a consequence of these reprisals and the coerced procurement of grain, "The grain market was the first one destroyed, and the first rationed item was bread ...," the most basic food in the Russian diet.<sup>27</sup> Osokina notes: "The grain question was settled in the interests of industrialization ... the success of the campaign to beat grain out of the peasantry in 1929-1930 allowed for an increase in the supply of bread that brought workers in other industrial centers up to the norms in Moscow and Leningrad."<sup>28</sup> While the West

was busy rebuilding Europe after the First World War through a fragile series of loans, shipments of food, and equipment, the Soviet Union turned towards an isolationist stance historically held by the Russian state.

The Soviets distrusted the international community; the international community felt the same. This mutual distrust aggravated an already tense and tenuous situation. A post-war economy, handicapped by financial issues handed down from the imperial era, combined with an unstable currency and little in foreign reserves, put the new nation under intense economic pressure. The Soviet Union possessed vast natural resources, but most of them were still locked in the ground and would remain there until the Soviets either constructed or purchased the machinery required for industrialization. Thus, grain became the chief export for trade, no matter how counterintuitive it seemed for a nation gripped by famine. Moreover, when the Soviet Union needed to produce more grain, it ramped up grain seizures and attacks against the *kulaks*.<sup>29</sup> Opinions on the fate of the *kulaks* ranged widely at the beginning of collectivization: "the conference was not able to settle this disagreement, nor was the special commission composed of first-rank figures."<sup>30</sup> Siegelbaum notes in support of this observation that "The party's attitude toward the kulak, and the question of the fate which was to be reserved for him in the course of transformations which were being prepared, is characterized by hesitations which reflect an uncertainty and lack of clarity about the real social character of the kulaks."<sup>31</sup> Nevertheless, the commission eventually made its decision: "liquidation of the kulaks as a class."<sup>32</sup>

Not surprisingly, the state tracked all sorts of data while executing the grain procurement program. Shockingly, that included the abuses committed by state agents:

"After the general assembly, they detained several citizens and denied them food and drink for three days ... they hung boards with insulting inscriptions ... and spat in their eyes ... they jabbed each one in the sides [with bayonets]" ... [and] in the villages of Yavlenka, Aleksandrovka, and Ilinka ... they boarded up the windows ... of those citizens who had been declared boycotted. Then they took kerosene and matches and placed a guard by the door so that no one could get out of the house ... this went on for three days."<sup>33</sup>

This escalation of violence against the kulaks and the peasants gained traction, raising alarms in the West:

"The Commissariat of Workers' and Peasants' Inspection ... is a body for unearthing graft and corruption ... [yet] this much-dreaded organization seems to consist of a corps of somewhat snooping individuals who cast terror into the hearts of the just as often as the unjust. This [commissariat] consists in part of volunteers who ... go out and call somebody else to order. If prison or Siberia is the result, what of it!"<sup>34</sup>

These observations were made by economist Alzada Comstock on assignment in Moscow for *Barron's* financial newspaper. They succinctly captured the commissariat's opinion, and therefore, the opinions of Stalin and other elites. Ultimately, the primary objective results had more to do with the industrial advancement of the USSR than they did the wellbeing of the Soviet people.

In early January 1933, Stalin spoke to the innermost circle of the party about the results of the First FYP and plans for the Second. Newspaper coverage in *The New York Times* reflected an international interest in Stalin's policies and the plight of Soviet citizens and shortages of food: "The people now are experiencing a food shortage which is growing worse and which presages dire results this Spring and Summer unless drastic action is taken ... corrective measures ... will be in the form of alteration or modification of the present procedure applying to these policies rather than an actual change in the policies themselves."<sup>35</sup> However, Soviet plans were still heavily focused on industrialization at all costs. As a contemporaneous observer S.P. Turin concluded in his report on the Second Year Plan, "The Five Year Plan has transformed Russia from an agricultural into an agricultural-industrial country; 57.5 percent ... of the national income of the USSR has been derived from industry, transport, and the building industry, and only 22.9 percent ... of it comes from agriculture."<sup>36</sup> The industrialization mandate had crossed a Rubicon, and the die had been fully cast.

The reliance on agriculture as the nation's economic driver diminished, but at what cost? In line with the Soviet policy of controlled criticism and admission of minor failures, perhaps to obscure bigger ones, Stalin and the Soviet government espoused the many significant successes of the First FYP, as they set about planning and implementing the Second FYP. Turin noted: "the inadequate development of transport was considered by the Conference to be one of the chief failures of the First Five Year Plan. As a remedy for this, Molotov suggest[ed] the laying down of 25 to 30 thousand kilometres of railway track and a yearly output of 400 thousand motor-cars ..."<sup>37</sup> Consequently, the Second FYP focused more on primary industries not covered in the First FYP as well as further integration and infrastructure advancement, all while glossing over the people's plight.

The Third FYP centered around the sustained buildup of heavy industry and military armaments as the world moved closer to global conflict with the rise of German nationalism under the command of Adolf Hitler. As the industrial focus continued to turn its back on consumer goods to focus on military goods, "defense spending [increased] to 18 percent of GDP, in 1940," forcing the already weak consumer goods sector to falter while "the living standards of workers and employees stagnated and may have even fallen by 1941."<sup>38</sup> In 1942, foreign minister Vyacheslav Molotov addressed the Eighteenth Congress of the Communist Party of the Soviet Union on the progress made during the Second FYP and the outline of the upcoming Third FYP. A description of results

reported the amount each industry exceeded the set goals. One stood as an outlier: consumer goods ("plan fulfillment was only 85 percent of consumers' goods").<sup>39</sup> Examining the primary focus of the first ten years of industrialization— heavy industry development—the Soviets still lagged "well behind in the production of electric power, pig iron, steel, coal and cement ... [and] behind in the per capita output of manufactures like cotton and woolen fabrics, leather footwear, sugar, paper, soap and some others."<sup>40</sup>

Despite this weaker-than-intended outcome, on likely inflated consumer goods numbers, the continued gap in heavy industry proved more vital. That remained the primary focus of the Third FYP: "The Third Five-Year Plan provides for tremendous advance in all branches of the national economy ... first and foremost in our heavy industry and defense industry."<sup>41</sup> Molotov acknowledged the workarounds to meet the increased energy quota despite the non-concurrent power plant growth through his statement that there was "somewhat excessive load on the existing electrical power stations."<sup>42</sup> As a result of this excessive loading, power stations became another critical goal according to Molotov: "Our task is to bring about the utmost expansion of the production of articles of general consumption."<sup>4</sup>

Total Capital Investment: 181 Billion Rubles |100%

Industrial Development: 103.6 Billion Rubles |57.24% of total

Industry Producing Means of Production: |48.18% of total 87.2 Billion Rubles

Industry Producing Means of Production: |9.1% of total 87.2 Billion Rubles

Industry Producing Articles of Consumption: |5.9% of total 16.4 Billion Rubles

Agriculture Development: 10.7 Billion Rubles |2.8% of total

Machine and Tractor Stations: 5 Billion |2.8% of total<sup>44</sup> Rubles

Soviet officials witnessed their people beset by shortages in all areas of life. Instead of allocating a more significant percentage of the budget to alleviate those shortages, they enlisted the cooperation of most of the population to push toward continued industrialization. In hindsight, this decision to prioritize industrialization may have been critical in preparing the nation for the Second World War.

At that war's end, the Soviet Union turned to rebuild the nation and its economy. The Fourth and Fifth FYPs represented a partial transition from wartime to peacetime industry. Despite the devastation, the war represented a chance to transform the Soviet economy and lead to sustainable growth and improved economic conditions. However, as Gregory states, "... [the FYP] was revived at the war's end. Its persistence suggests that the [model of the] five-year plan remained of value to the Soviet leadership."<sup>45</sup> This persistence mani-

fested in the Fourth FYP, one meant to drag the shattered economy back to levels reached a decade before the war:

“... only in the coal industry does the new Plan even pretend to set goals above the pre-war levels ... The comparative figures ... provide decisive proof of how the war devastated key branches of Soviet industry; how despite all the pillaging and looting in the regions occupied by the Red armies, Soviet economy remains in a highly critical condition.”<sup>46</sup>

In addition, the rail network set quotas such that “the Kremlin itself [knew] that even these extremely modest goals [values similar to and below the Third FYP] cannot and will not be attained.”<sup>47</sup> The dire news hit even closer to the agricultural health of the nation with the admission that it lacked available tractors: “The conclusion is inescapable: under the best conditions, bread, the staple food of the masses, will continue not only scarce, but dear, in the next immediate period.”<sup>48</sup>

Germane to the analysis in the essay, however, is the continued lack of attention to the nation’s consumer goods sector: “Even by 1950 the Soviet masses will not get the quantity (let alone the quality) of the consumers’ goods they obtained as far back as in 1937.”<sup>49</sup> A comparison of the 1950 control figures to stated production levels in the previous FYPs indicates that the production quotas set to be met by 1950 for “... cotton fabrics ... woolen fabrics ... [and] other mass consumers’ goods were lower than the corresponding figures not only for the Third but also the Second Five-Year Plans.”<sup>50</sup> In contrast to the rebuilding of the economy with a robust light industry base and intensified buildup of heavy industry, the Soviet Union continued its policy of placing the needs of industry above the needs of the people.

Stalin died in 1953 and did not witness the completion of the Fifth FYP, the goals of which most closely aligned with those of the Fourth FYP. The rebuilding of Soviet heavy industries, such as the production of pig iron, coal mining, and oil exploration and refining, to pre-war levels, was accomplished and new goals were set by the committee: “The overall volume of ... the means of production has been doubled and in some branches surpasses that of 1940.”<sup>51</sup> This recovery was not limited to heavy industry, however, as “Production of cotton textiles per capita [had] increased 20% in relation to 1940; woolen fabrics more than 60%; paper more than 70% ... [and] ... the total harvest of the most important food crop, wheat, 48% bigger than in 1940.”<sup>52</sup> Pushing through economic recovery, the Soviets had ready to propel the nation again down the well-worn path of the previous FYPs with stated objectives like, “The [goal] of the means of production is to increase around 80% and the production of articles of consumption roughly 65%.”<sup>53</sup> While these numbers appear to signal a positive change for the Soviet populace in increased consumer goods, the article of consumption with the most significant increase (220%) was cement. Ironically, the vast amount of cement produced belied the fact that there was still an “acute housing shortage.” And pre-war con-

sumer goods production improved, although at a geologic pace.<sup>54</sup>

The termination of the NEP in 1929 and the commencement of the FYPs that guided Soviet economic policy for decades stymied the hope of most people for widespread access to goods until the 1960s under the leadership of Leonid Brezhnev. Many Soviet citizens found ways to exploit the socio-political system and offload the pain of these repeated shortages onto those around them. Some Soviet citizens sought to elevate themselves and improve their lifestyles through assimilation into the existing socio-political structure of the party, thereby mitigating the impact of the shortages they experienced personally before party integration. While the concept of social mobility (the ability to move from one social class to another through personal effort or contact with individuals with influence) standard in the United States gained a modest, if unacknowledged, toehold in the Soviet Union, it was perhaps not for long.

### Hierarchy of the Access to Goods

“From each according to his ability, to each according to his needs.”<sup>55</sup> This maxim is perhaps the most recognizable of Marxist-Leninist theory. It envisions a classless society where each member of the society is guaranteed access to goods and services unrestricted by membership in, or exclusion from, a socially constructed class. In flagrant opposition to this belief, new social classes were established under Stalin with a significant degree of heritability developed between generations. However, before a new socio-political structure blossomed, Stalin purged the ranks of the intelligentsia, military officers, and bureaucrats in the Great Terror, leaving those classes previously loyal to him decimated. Those who survived agreed to create pro-Soviet propaganda and tow the party line. Consequently, Stalin granted them priority access to goods and services and their children priority consideration for admission to universities and other perquisites.<sup>56</sup> This hierarchy of survivors was, as a group, wily, paranoid, and determined to maintain their positions, regardless of cost.

At its most elemental level, a hierarchy is a stratification of individuals and groups, the structure of which relies upon various predetermined criteria. For our purposes, a standard pyramid represents the hierarchy of individuals, while an inverted pyramid represents the access those individuals have to goods. The relationship between the two indicates that those at the top of the Soviet hierarchy had the most significant access to consumer goods, and those at the bottom had the least. As Fitzpatrick argues in *Everyday Stalinism*, the hierarchy of consumption had more to do with people’s relationship to the state, not their relationships to one another.<sup>57</sup> Those closest to the inner circle of the Soviet power structure were able to access consumer goods almost without restriction. The further citizens resided from the core of power, the more their access to goods diminished. Such a structure recalled some of the dreaded aspects of life under the Romanovs where the nobility experienced access to items of

culture and wealth, and most everyone else lived in abject poverty.<sup>58</sup> However, exposure to the very existence of consumer goods, even if restricted in access, was entirely new for most citizens, including those pushed to the city by the confiscation of individual farms for collectivization and industrialization.<sup>59</sup>

Based on their proximity to the Soviet power structure, Soviet citizens had differing access to goods, including the quality and selection available in retail shops with different stores restricted to elites and party members. In a U.S. government-sponsored project, Harvard University interviewed more than one hundred Soviet emigrés living in Munich, Germany, in 1950. In his interview, a former Soviet soldier offered:

“If you know a man, let’s say, a director, you can say that you are almost sure that he is a party member. In fact, everyone in a superior position is almost sure to be a party member ... Furthermore, the material conditions are different. If a man occupies a better post, as he will if he is a party member, he will get more money, he will be better dressed, he will have a better apartment, his children will be better taken care of.”<sup>60</sup>

A politburo member or his family could access items every day that a low-ranking party apparatchik in the Urals might be able to purchase only once or twice a year. A different interview subject, a former Russian peasant woman, responded to the interviewer’s question on differences in treatment of citizens: “We lived in a cellar. All workers lived there. The people who had good apartments were members of the NKVD, Party members, and officers. They had special distribution stores. As for the bulk of the population, there was nothing to make up for that.”<sup>61</sup> Many of the peasants were relatively oblivious to the variety of manufactured goods in the modern era. Just a few years before, the “Bolsheviks tried to increase grain deliveries by offering the peasants manufactured goods instead of money in exchange ... [and] so the food crisis in turn worsened, barter became a base form of exchange, and money lost its value... wages and salaries were being paid partly in kind ....”<sup>62</sup> Among the most privileged members of everyday society were factory workers in critical cities like Moscow. However, that privilege made surprisingly little practical difference in their ability to acquire goods compared to the peasants in the countryside: “Industrial workers in Moscow were the most privileged, but again, the advantages were not especially significant.”<sup>63</sup> A bit more cotton, an additional bar of soap, and additional fuel every month meant that “Muscovite workers had to buy less at the markets than the average Soviet worker. This small difference constituted the privileges of the industrial vanguard in the distribution of non-food items.”<sup>64</sup> Nevertheless, small luxuries, even those offered as an occasional employment incentive, were only dreams for most factory workers or office clerks.

According to historian Julie Hessler, “citizens spent increasing amount[s] of their income in the remnants of the private

sector (sometimes termed the black market) and spent increasing amounts of time both buying and selling goods.”<sup>65</sup> Despite this elevated activity within the private sector, “Soviet society [did not] become a consumer society; the preoccupations with marking status and expressing individuality through consumption choices, identified by several commentators as essential components of modern consumerism, remained restricted to a small minority of the buying public.”<sup>66</sup> In essence, their inexperience with consumption as a marker of status meant that most Soviets were not particularly motivated to expend more significant effort to achieve access to a wider variety or better quality of merchandise. While those in urban centers were able to develop and partake in a private market, “Rural consumers were left out of these developments, both for reasons of poverty and because of their limited access to goods,” which only stood to widen the gap between those in the cities and those in the hinterlands.<sup>67</sup> For example, in turning back to *Time, Forward!*, those at differing levels within the hierarchy in Magnitogorsk had different lodgings, clothing, and freedoms than one another.

### Urban/Rural Disparity

Prior discussion of nationalization and collectivization and the hierarchy of goods and services overlap the necessary discussion of the disparity in policy implementation between urban and rural areas, yet a few critical points remain. Marxist theory dictates that a nation must implement a dictatorship of the proletariat to move towards a communist society. In the Soviet Union, that posed a serious issue due to the lack of a true proletariat. Stalin implemented policies that pushed for both the rapid growth of the urban population and economy at the expense of the rural population and economy. As discussed previously, the crackdown on private trade negatively impacted the peasantry far more than urban workers. “After two good harvests in 1925 and 1926, however, peasants surely became a more noticeable presence in the urban queues for manufactured goods.”<sup>68</sup>

Nevertheless, it was a presence that lacked any economic power under these new policies.<sup>69</sup> While the cooperatives that previously sold goods might have welcomed peasants for trade, the new “... response on the part of cooperatives was to refuse to sell to peasants.”<sup>70</sup> To these cooperatives, and even the Soviet higher-ups, the “peasants [were seen] more as a source of raw materials than as a potential consumer base ... [they were to] wait patiently in the wings for the products of industry, while continuing to provide raw materials at a submarket price.”<sup>71</sup> In addition, rural residents cried out to the Soviets to bring beneficial displays of their power to country villages: “Step by step the countryside is falling behind the cities ... the village is still in no condition to build new Red reading huts – it is too poor ... for the lack of a reading room, we have no books.”<sup>72</sup>

City dwellers were not always in a more favorable position. Waiting in the breadline meant that at least the shopper had money to make purchases. However, not everyone was lucky

enough to have money in their pockets. Hard hit were those among the former bourgeoisie class. When they ran out of money, they were unable to purchase even the barest necessities. Desperate to overcome not only the shortages that plagued the state but their inability to buy food, they sold their last few treasures to raise money:

“Outside this mass of junk stand men, women, and young girls of all ages, mostly belonging to the upper and middle classes ... here they stand ... for hour after hour in the hope of selling the few remaining articles left in their homes ... many are ... paralyzed with hunger and cold, and all have a dumb, expressionless, resigned look, as if all hope had long since departed from their souls.”<sup>73</sup>

This devastating recollection enforces the realization that once these people liquidated the entirety of their possessions, more desperate measures were needed to avoid starvation. Citizens abrogated the system through “illegal registration for rations, [becoming] ‘people with sacks,’ and theft,” redistributing goods outside the system’s parameters to overcome shortages of food and goods rather than starve to death.<sup>74</sup>

## Conclusion

Millions of Soviet citizens endured shortages, sometimes stoically, sometimes grudgingly, for reasons greater than satisfying their personal needs: “For the sake of the future many people were ready to make sacrifices, overlook any abominations and justify loathsome behavior.”<sup>75</sup> Stalin intended to remake the Soviet Union to align with his vision once he consolidated his power in the late 1920s. Eliminating the state capitalism introduced less than a decade before under Lenin, Stalin set the nation on a path that included pervasive shortages, forced collectivization, a new hierarchy antithetical to a theoretically pure communist society, and growing disparities in the treatment of urban and rural populations.

A fascinating part of unpacking these documents and reviewing previous research has been that, as Kornai knows firsthand, these shortages are reproducible throughout the socialist experience, regardless of geographic location, when the system transitions from a capitalist economy to a socialist one. Perhaps they were more pronounced in the former Russia because it had previously been so backward-looking in its economic planning. Its geographic size and population density (at least in the cities) made it second only to Communist China in the potentiality of the impact of modernization on the nation and its people. Shockingly, Stalin’s actions robbed his nation of the human potential that might have meant a different outcome for the nation. Perhaps that was the most significant shortage of all – and it had nothing to do with soft budget constraints. Ultimately, Stalin’s economic machinations, good and bad, dragged the Soviet economy from agricultural stasis to relative industrial parity with other nations in just over a generation, five years at a time.

## Footnotes

<sup>1</sup> A complaint from a worker referenced in a report compiled by the OGPU (*Obedinennoe Gosudarstvennoe Politicheskoe Upravleniye*, a forerunner of the KGB) in Elena Osokina, *Our Daily Bread: Socialist Distribution and the Art of Survival in Stalin’s Russia, 1927-1941*. Trans. by Kate Transchel and Greta Bucher (Armonk and London: M.E. Sharpe, 1999), 30.

<sup>2</sup> János Kornai, *Contradictions and Dilemmas: Studies on the Socialist Economy and Society* (Boston: MIT Press, 1986), 7.

<sup>3</sup> Kornai’s corpus of work on socialist economic theory and its application, including his ideas on the “reproduction of shortages,” are extensive and include, but are not limited to, works such as *Contradictions and Dilemmas*, referenced above, *Economics of Shortage. Vol. A of Contributions to Economic Analysis* (Amsterdam and New York: North Holland Publishing Co., 1980), and *The Socialist System: The Political Economy of Communism* (Princeton: Princeton University Press, 1992).

<sup>4</sup> Kornai, Eric Maskin, and Gérard Roland, “Understanding the Soft Budget Constraint,” *Journal of Economic Literature* 41 no. 4 (2003): 1095. <https://www.jstor.org/stable/3217457>.

<sup>5</sup> Kornai, “The Soft Budget Constraint,” *Kyklos* 39, no. 1 (1986): 3. <https://doi.org/10.1111/j.1467-6435.1986.tb01252.x>.

<sup>6</sup> Kornai, “The Soft Budget Constraint”: 3-4.

<sup>7</sup> “Paul Gregory and Mark Harrison, “Allocation Under Dictatorship: Research in Stalin’s Archives” *Journal of Electronic Literature*, (2005) 43, no. 3: 723.

<sup>8</sup> Matthew Lenoe, “HIST332 – Stalinism,” Class Lecture,

<sup>9</sup> Sheila Fitzpatrick, *The Russian Revolution: Updated Edition* (Oxford: Oxford University Press, 2017), 81.

<sup>10</sup> Fitzpatrick, *The Russian Revolution*, 81.

<sup>11</sup> Lewis H. Siegelbaum, *Soviet State and Society between Revolutions, 1918-1929* (Cambridge: Cambridge University Press, 1992), 86.

<sup>12</sup> Siegelbaum, *Soviet State and Society*, 90.

<sup>13</sup> Siegelbaum, *Soviet State and Society*, 103.

<sup>14</sup> Matthew Lenoe, Email to Author, May 4, 2021.

<sup>15</sup> Osokina, *Our Daily Bread*, 17.

<sup>16</sup> Josef Stalin, “The Tasks of Business Executives,” Speech Delivered at the First All-Union Conference of Leading Personnel of Socialist Industry, February 4, 1931, Marxist Internet Archive, <https://www.marxists.org/reference/archive/stalin/works/1931/02/04.htm>.

<sup>17</sup> Valentine Kataev, *Time, Forward!* (1932) rev. ed. (Evanston, IL: Northwestern University Press, 2005), 29.

<sup>18</sup> John Scott, *Behind the Urals: An American Worker in Russia’s City of Steel* (1942) (Bloomington and Indianapolis: Indiana University Press, 1989), 23.

<sup>19</sup> Scott, *Behind the Urals*, 12.

<sup>20</sup> Stephen Kotkin, *Magnetic Mountain: Stalinism as Civilization* (Berkeley, Los Angeles, London: University of California Press, 1995), 280.

<sup>21</sup> Maja Soboleva, “The Concept of the ‘New Soviet Man’ and Its Short History,” *Canadian-American Slavic Studies* 51, no. 1 (2017): 66.

<sup>22</sup> Osokina, *Our Daily Bread*, 42.

<sup>23</sup> Osokina, *Our Daily Bread*, 43.

<sup>24</sup> V. P. Danilov, “Kollektivizatsiya sel’skogo khoziastva v SSSR,” *Istoriia SSSR*, no. 5 (1990): 7-30 in Osokina, *Our Daily Bread*, 43, n.3.

<sup>25</sup> Osokina, *Our Daily Bread*, 42.

<sup>26</sup> Osokina, *Our Daily Bread*, 22.

<sup>27</sup> Osokina, *Our Daily Bread*, 24.

<sup>28</sup> Russian State Archive of Political History, f.17, op.3, d.769, 11. 7-8 in Osokina, *Our Daily Bread*, 43, n.2.

<sup>29</sup> “Document 139 – Letter of Denunciation from Young Pioneers and Komsomol members to director of forestry department, Sep. 1936, *Tsentral’nyi Komitet DMO*, f.1, op. 23, d. 1888, l. 102. Typewritten copy,” in Lewis H. Siegelbaum and Andrei Sokolov, *Stalinism as a Way of Life: A Narrative in Documents*, abridged (New Haven and London: Yale University Press, 2004), 274-276.

<sup>30</sup> “Document 139,” in Siegelbaum and Sokolov, *Stalinism Way of Life*, 274.

<sup>31</sup> Moshe Lewin, *The Making of the Soviet System: Essays in the Social History of Interwar Russia* (New York: Pantheon Books, 1985), 138.

<sup>32</sup> Lewin, *Making Soviet System*, 139.

<sup>33</sup> “Document 119 – Excerpt from an account of ‘excesses’ committed in the course of grain procurement campaign, April 1929, State Archive of the Russian Federation, f. 1235, op. 141, d. 113, s. 91-122. Typewritten copy,” in Storella and Sokolov, *Voice of the People*, 304-305.

<sup>34</sup> Alzada Comstock, “Soviet Policy – The 1931 Revision: The Stalin ‘Speech’ Supplants the ‘Plan,’” *Barron’s*, August 24, 1931, 7. <https://tinyurl-com.uc.idm.oclc.org/yedrrad4>.

<sup>35</sup> “Stalin’s Address Awaited Tensely: Russians on Edge to See Text of Speech made Saturday to Party Executives. New Measures Expected: Moves to Deal with Shortages and Stimulate Peasants are Held to be Essential,” January 9, 1933. <https://search-proquest-com.ezp.lib.rochester.edu/historical-newspapers/stalins-address-awaited-tensely/docview/100646014/se-2?accountid=13567>.

<sup>36</sup> S. P. Turin, “The Second Five-Year Plan.” *The Slavonic and East European Review* 11, no. 31 (1932): 63. <https://www.jstor.org/stable/4202738>.

<sup>37</sup> Turin, “Second Five-Year Plan”: 59.

<sup>38</sup> Martin McCauley, *Stalin and Stalinism*, 3rd ed. (London: 55 Karl Marx, “Critique of the Gotha Programme.” (1875), first

published in *Die Neue Zeit* 1, no. 18 (1890-1891), Marxist Internet Archive, <https://www.marxists.org/archive/marx/works/1875/gotha/index.htm>.

<sup>39</sup> Vyacheslav Molotov, *The Soviet Union in 1942: The Third Five-Year Plan For the National-Economic Development of the USSR: Report Made to the Eighteenth Congress of the Communist Party of the Soviet Union (Bolsheviks) And Reply to the Discussion March 14 and 17, 1939*. (New York: Workers Library Publishers, Inc., 1939).

<sup>40</sup> Molotov, *Soviet Union 1942*, 20-21.

<sup>41</sup> Molotov, *Soviet Union 1942*, 27.

<sup>42</sup> Molotov, *Soviet Union 1942*, 34.

<sup>43</sup> Molotov, *Soviet Union 1942*, 35.

<sup>44</sup> Transportation and other unidentified “investments” comprised the remainder of the budget. Molotov, *Soviet Union 1942*, 44.

<sup>45</sup> Paul Gregory, *The Political Economy of Stalinism: Evidence from the Soviet Secret Archives*. (Cambridge: Cambridge University Press, 2004), 119.

<sup>46</sup> “The Fourth Five-Year Plan and the Crisis in Soviet Economy.” *Fourth International* 7, no. 9 (1946): 262. <https://www.marxists.org/history/etol/newspaper/fi/vol07/no09/v07n09-w70-sep-1946-fourth-int.pdf>.

<sup>47</sup> “Fourth Five Year Plan”: 263.

<sup>48</sup> “Fourth Five Year Plan”: 263.

<sup>49</sup> “Fourth Five Year Plan”: 263.

<sup>50</sup> “Fourth Five Year Plan”: 264.

<sup>51</sup> Michel Pablo, “The 19th Congress of the Russian CP (December 1952),” *Fourth International*, 13, no. 6 (1952): 169. <https://www.marxists.org/archive/pablo/1952/12/19congress.htm>.

<sup>52</sup> Pablo, “19th Congress Russian CP”: 170.

<sup>53</sup> Pablo, “19th Congress Russian CP”: 171.

<sup>54</sup> Pablo, “19th Congress Russian CP”: 171.

<sup>55</sup> Karl Marx, “Critique of the Gotha Programme.” (1875), first published in *Die Neue Zeit* 1, no. 18 (1890-1891), Marxist Internet Archive, <https://www.marxists.org/archive/marx/works/1875/gotha/index.htm>.

<sup>56</sup> Matthew Lenoe, “HIST332 – Stalinism,” Lecture, University of Rochester, Rochester, NY, n.d.

<sup>57</sup> Sheila Fitzpatrick, *Everyday Stalinism: Ordinary Life in Extraordinary Times: Soviet Russia in the 1930s* (New York: Oxford University Press, 1999), 11-13.

<sup>58</sup> Fitzpatrick, *Everyday Stalinism*, 11.

<sup>59</sup> Fitzpatrick, *Everyday Stalinism*, 12.

<sup>60</sup> “Case 18 (Interviewer R.F., Type A3), Male, 34 to 45, Great Russian, Bookkeeper, chiefly in Army,” (Harvard Project on the Soviet Social System, Schedule A, Vol. 2), Conducted

September 28-30, 1950, Munich, Germany, Harvard University – Slavic Division, Widener Library, <https://iif.harvard.edu/manifests/view/>.

<sup>61</sup> “Case 107 (Interviewer A.D., Type A4), Female, 57, Great Russian, Peasant, housewife, unskilled worker,” (Harvard Project on the Soviet Social System, Schedule A, Vol. 8), Conducted September 28-30, 1950, Munich, Germany, Harvard University – Slavic Division, Widener Library, <https://iif.harvard.edu/manifests/view/>.

<sup>62</sup> Fitzpatrick, *The Russian Revolution*, 81.

<sup>63</sup> Osokina, *Our Daily Bread*, 92.

<sup>64</sup> Osokina, *Our Daily Bread*, 92.

<sup>65</sup> Julie Hessler, *A Social History of Soviet Trade: Trade Policy, Retail Practices, and Consumption, 1917-1953* (Princeton: Princeton University Press, 2004), 11.

<sup>66</sup> Hessler, *Social History Soviet Trade*, 11-12.

<sup>67</sup> Hessler, *Social History Soviet Trade*, 12. Routledge, (2008), 51.

<sup>68</sup> Hessler, *Social History Soviet Trade*, 145

<sup>69</sup> Hessler, *Social History Soviet Trade*, 145.

<sup>70</sup> Hessler, *Social History Soviet Trade*, 145.

<sup>71</sup> Hessler, *Social History Soviet Trade*, 145.

<sup>72</sup> “Document 34 – Letter to *Krest'ianskaia Gazeta* from the peasant A. Stikharyov requesting more cultural aid from the cities, 1925. Russian State Archive of the Economy, f. 396, op. 3, d. 43, l. 41, Original manuscript” in Storella and Sokolov, *Voice of the People*, 124.

<sup>73</sup> Osokina, *Our Daily Bread*, 103.

<sup>74</sup> Osokina, *Our Daily Bread*, 106. Osokina identifies these “people with sacks” as rural Russian emigrés who arrived in the cities every day carrying all their possessions in a sack. Osokina, *Our Daily Bread*, 105.

<sup>75</sup> “Document 59 - Letter of Appreciation from F. M. Postnikov to *Krest'ianskaia Gazeta*, 1936, RGASPI f.17, op. 120, d. 232, ll.58-59. Typewritten copy,” in Siegelbaum and Sokolov, *Stalinism Way of Life*, 137-138.

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# Manganese Promoted Oxidative Radical Addition Reactions

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## I. Introduction

### Single Electron Transfer (SET) Chemistry in Asymmetrical Synthesis

The ongoing discovery of the importance of stereochemistry in drug action has led to a significant increase in the demand for asymmetric synthetic strategies to access molecules enriched with stereochemical elements. For instance, despite the abundance of cases where the two enantiomers of a chiral drug display distinct pharmacological behavior in their selectivity and affinity for receptors, transporters, and enzymes, a considerable fraction of commercial drugs is still only available in racemic mixtures.<sup>1</sup> As a result, the search for synthetic methods with versatility, stereoselectivity, operational simplicity, and efficiency has been a burgeoning field of research.

Accessing molecules with the level of topological complexity comparable to and compatible with biological systems in a stereoselective fashion requires a strategic approach that overcomes the limits of conventional methods and emulates the stereocontrol exerted by enzymes. The incorporation of single electron transfer (SET) chemistry in synthetic pathways is a potential solution. These reactions, often initiated by a one-electron redox event, proceed through short-lived radical intermediates with kinetic selectivity. Therefore, they are less sensitive to steric and stereoelectronic effects compared to their two-electron counterparts. These characteristics have led to recent studies on the applicability of SET chemistry in generating congested stereocenters and complex polycyclic molecular frameworks, particularly those with unusual ring sizes and structures as shown in Figure 1. Among various organometallic catalysts that have been employed to carry out such reactions, this project identified

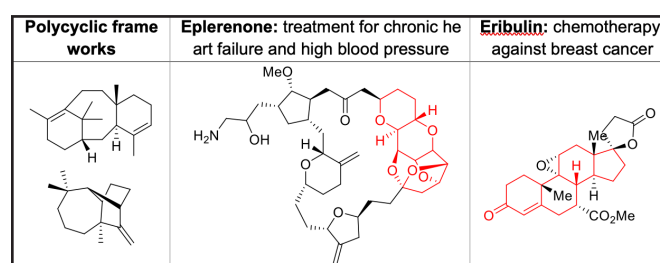
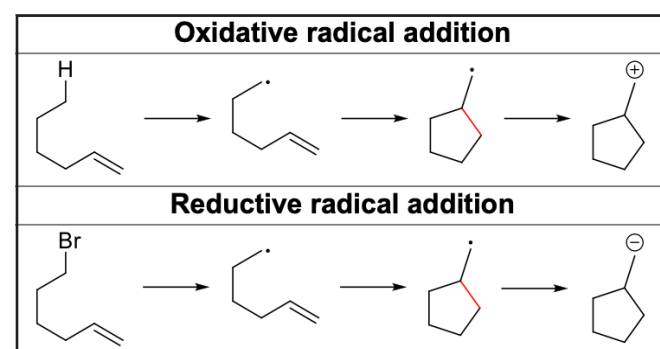


Figure 1. Examples of molecular frameworks conceivably accessible by SET reactions.

chiral manganese carboxylate complexes as a promising mediator for the enantioselective synthesis of small molecule intermediates for compounds with potential pharmaceutical utility. The plethora of cyclization and addition reactions mediated by manganese(III) acetate reported in the literature, in addition to the relative abundance and low cost of the metal, motivated this choice.

## B. Radical Addition of Alkenes



Scheme 1. Oxidative and reductive mechanisms of radical cyclization of alkenes.<sup>2</sup>

The radical cyclization of alkenes has been established as a facile type of SET reaction particularly valuable for the synthesis of cyclic compounds. Such reactions may proceed through either the oxidative or reductive pathway shown in Scheme 1 depending on the transition metal reagent. The oxidative pathway involves the generation of a radical intermediate through the loss of a proton followed by one-electron oxidation of the resulting carbanion; this process is often described as proton-coupled electron transfer. The reductive pathway, on the other hand, produces a radical species through the one-electron reduction of the carbocation generated upon the loss of a leaving group, typically a halide. The cyclization step of these pathways proceeds through the same SET mechanism followed by the termination step which differentiates them from one another. While reductive termination requires the delivery of a proton, limiting the synthetic use of this approach to relatively unfunctionalized products, the carbocation generated upon oxidation of the cyclized radical intermediate in the oxidative pathway may undergo several different pathways of termination. The carbocation's ability to react with heteroatom donors, in particular, gives the oxidative method an upper hand in accessing highly functionalized and versatile products.<sup>2</sup> Manganese(III) carboxylate complexes, a group of strong one-electron oxidants, were employed for this project

## C. Asymmetric Induction

Enantioselective synthesis requires the introduction of chiral elements into the reaction, which may bias the formation of one enantiomer over another. The stereo-directing groups may be attached to the substrate as a cleavable auxiliary or to the reagent, often an organometallic catalyst, as a ligand. The former option entails the covalent attachment of an optically pure chiral residue to the substrate. The absolute configuration of the newly created stereocenter is dictated by the stereochemistry of the chiral auxiliary, which is cleaved from the substrate following the asymmetric induction step.<sup>3</sup> Conversely, the latter approach relies on the catalyst bearing an enantiopure chiral ligand coordinating with the substrate over the course of the reaction and exerting stereocontrol.

Fine-tuning these asymmetric synthetic methods to industrial-scale production of pharmaceutical ingredients often magnifies the advantages and disadvantages of each method. When using a chiral auxiliary, for instance, the removal, recovery, and reuse of the stoichiometric equivalent of the cleaved segment must be deliberately outlined in order to reduce the cost and waste of the overall process. These diastereoselective methods, however, are typically less sensitive to minor perturbations and have rather straightforward purification steps due to the differing chemical properties of diastereomeric pairs. Enantioselective catalysis, on the other hand, avoids the risk of losing the newly formed stereocenter to racemization or epimerization, which may occur during the cleavage of the chiral auxiliary in the earlier approach. However, optimizing the steric and electronic properties of the chiral catalyst to the substrate of interest may be an exceedingly complex and somewhat unpredictable process.<sup>3</sup>

The chiral auxiliary-controlled method of asymmetric induction has been applied to both the oxidative and reductive radical cyclization of alkenes. The precedents shown in Figure 2 both utilized 8-phenylmethyl ester moiety to induce stereo-facial differentiation in their substrate. The oxidative cyclization of the diene shown in the top example demonstrated good diastereoselectivity (86% d.e.). The removal of the stereo-directing segment was found to leave the stereochemistry at the new stereocenter unchanged, translating the

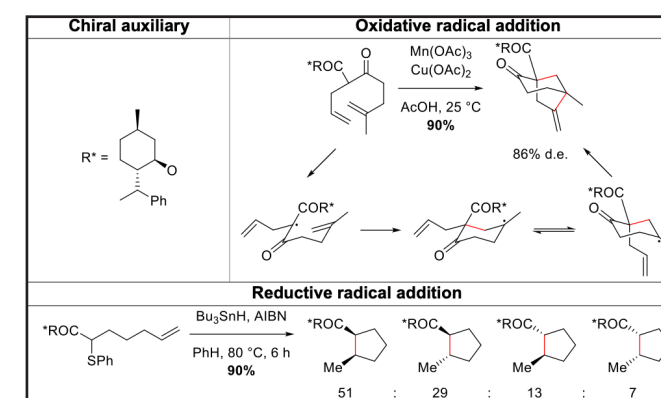


Figure 2. Chiral auxiliary-controlled asymmetric induction in radical cyclization of alkenes.<sup>4,5</sup>

observed diastereoselectivity to enantioselectivity.<sup>4</sup> The reductive cyclization of the alkene in the rear illustration exhibited relatively poor diastereoselectivity, although the elimination of the preexisting stereocenter converged the diastereomers to an enantiomeric pair, yielding higher enantioselectivity.<sup>5</sup> Compiling such patterns of stereoselectivity in the presence of a diverse set of chiral elements is an inevitable step of optimization in the current methods of asymmetric induction, in not only the auxiliary-controlled processes but also in the catalyst-controlled approach, which this project sought to achieve.

## D. Chiral Manganese Carboxylate Complexes for Reagent-Based Stereocontrol

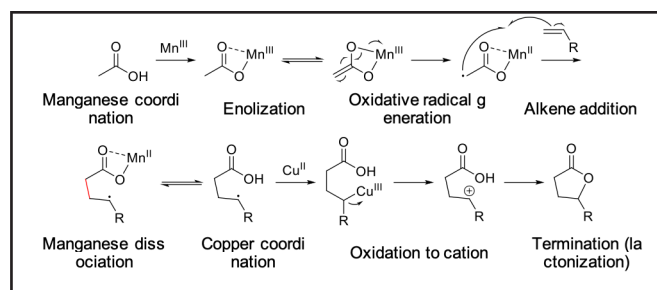
The foundation for employing the one-electron oxidant manganese(III) acetate in the oxidative radical addition of alkenes was laid in 1968.<sup>6,7</sup> In this method, the carboxymethyl radical generated from heating the reagent in acetic acid was added to various alkenes as proposed in Scheme 2. At first, the resulting radical intermediates were further oxidized with a second equivalent of manganese(III) acetate to yield  $\gamma$ -lactones through intramolecular nucleophilic attack. Then, in 1971, the use of copper(II) acetate as a cooxidant was found to accelerate the rate of the termination step with its remarkable efficiency in oxidizing primary and secondary radicals.<sup>8</sup> These findings standardized two equivalents of manganese(III) acetate and one equivalent of copper(II) acetate in mediating similar reactions.

Efforts towards understanding the mechanism of this newfound reactivity led to several discoveries. For instance, the enolization of acetic acid promoted by the oxo-centered manganese(III) triangle was found to be the rate-determining step of the proposed mechanism as illustrated in Scheme 3.<sup>9</sup> Above other findings, such mechanistic studies provided evidence for the coordination of manganese(III) with oxygen atoms of the substrate throughout the course of these reactions. The theorized presence of manganese-bound  $\alpha$ -acetate radical intermediates revealed the potential for enantiocontrol using chiral ligands bound to the metal.

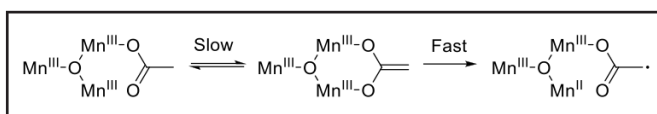
The abundance of commercially available enantiopure chiral carboxylate compounds, some of which are shown in Figure 3, encouraged the pursuit of this hypothesis. Employing a series of chiral ligands with varying steric and electronic properties was envisioned to enable catalyst control over reaction outcomes with regard to enantioselectivity.

## E. $\beta$ -Dicarbonyl Substrates

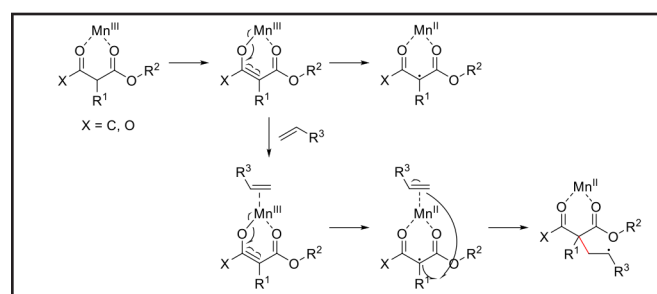
Inspired by a plethora of studies conducted on the various patterns of chemoselectivity in the oxidative radical addition of alkenes to  $\beta$ -keto esters,  $\beta$ -diketones, and malonate esters, this project set  $\beta$ -dicarbonyls as the system of investigation. With these substrates, the carbonyl oxygen atoms were predicted to coordinate with the metal center. Additional coordination of the alkene to manganese would amplify stereocontrol in the delivery of various alkenes to the manganese-bound radical intermediates as shown in Scheme 4.<sup>10</sup>



**Scheme 2.** Proposed mechanism of oxidative radical addition of alkenes to acetic acid.<sup>7,8</sup>



**Scheme 3.** Relative rates of manganese-bound  $\alpha$ -acetate radical generation.<sup>9</sup>



**Scheme 4.** Proposed mechanism of oxidative radical addition of alkenes to  $\beta$ -dicarbonyls.<sup>10</sup>

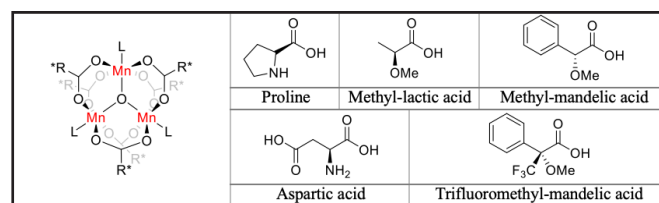
## II. Results & Discussion

### A. Intramolecular Cyclization of Unsaturated Malonate Esters

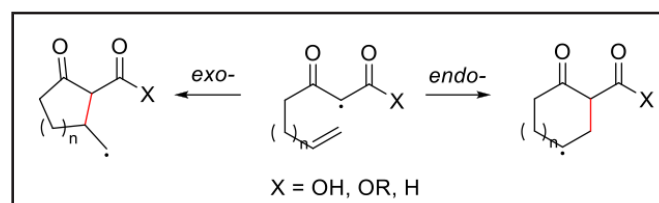
The primary scope of this project was the intramolecular cyclization of malonate esters with an alkene tethered to one end of the molecule. The design of the initial substrate considered the following factors to form predictions regarding the reaction outcomes. First, the cyclization of these substrates could result in either *exo*- or *endo*-cyclization, leading to the formation of different sized rings even when the same starting material was used, as illustrated in Scheme 5.<sup>2</sup>

The *exo*:-*endo*-cyclization selectivity in  $\beta$ -dicarbonyls was known to be predominantly determined by the substitution pattern of the alkene. While 1,2-disubstituted alkenes or alkenes with highly substituted distal carbon were found to generally favor *exo*-cyclization, alkenes with highly substituted proximal carbon typically produced *endo*-cyclized products.<sup>2</sup> Monosubstituted alkenes exhibited a higher degree of promiscuity generating a rather indiscriminate mixture of *exo*- and *endo*-products upon the cyclization of the  $\beta$ -keto ester in Scheme 6.<sup>11</sup>

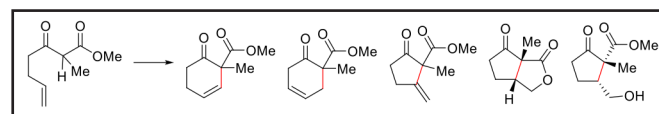
The reaction illustrated in Scheme 6 also emphasized the



**Figure 3.** Structure of chiral manganese carboxylate complexes with ligands of choice.



**Scheme 5.** *Exo*- and *endo*-cyclization of unsaturated  $\beta$ -dicarbonyls.<sup>2</sup>

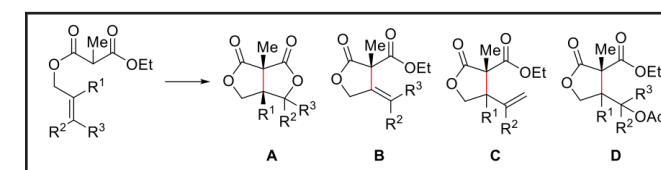


**Scheme 6.** *Exo*:-*endo*-cyclization selectivity in  $\beta$ -keto esters bearing a monosubstituted alkene.<sup>11</sup>

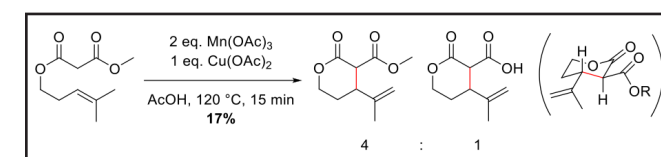
importance of understanding termination patterns after oxidation of the cyclized radical intermediate. In the case of the substrates designed to form lactones and lactams, an exclusive preference for *exo*-cyclization was exhibited, but the substitution pattern of the alkene determined the preference for various termination pathways. The cyclization of the malonate ester shown in Scheme 7 could form the bicyclic moiety seen in **A** from the intramolecular nucleophilic attack initiated by the ester oxygen. Depending on the availability of abstractable protons, different elimination products, **B** and **C**, could be produced. In addition, an external nucleophile available in the reaction mixture, an acetoxy group in the case of **D**, could react with the carbocation intermediate. From the monosubstituted derivative of the model substrate drawn in Scheme 6, 53% of **A** and 20% of **B** were formed. The disubstituted alkenes ( $R = \text{Me}$ ) exclusively chose one termination pathway; the 1,1-disubstituted substrate produced 21% of **A**, and the 1,2-disubstituted substrate produced 54% of **C**. The trisubstituted alkene ( $R = \text{Me}$ ) yielded a mixture of 30% **C** and 17% **D**, and the substrate with a phenyl group attached to the distal carbon formed a mixture of 20% **A** and 43% **D**.

Based on these known patterns of chemoselectivity, this project was launched by investigating the malonate ester substrate shown in Scheme 8. The cyclization was carried out

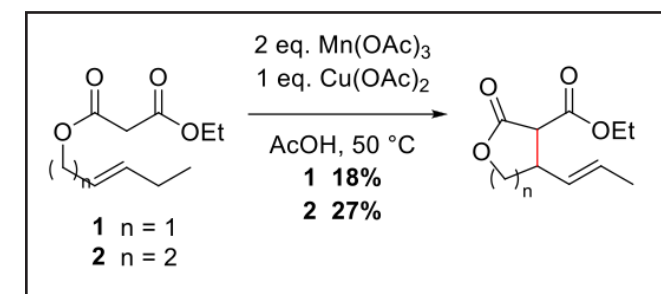
using stoichiometric amounts of manganese(III) acetate and copper(II) acetate in acetic acid. The substrate was predicted to undergo *exo*-cyclization to produce a 6-membered lactone moiety, and the absence of exogenous nucleophiles in the reaction mixture was expected to result in the exclusive formation of the elimination product with a terminal alkene (such as **C** from Scheme 7). The length of the tether was inspired by the literature precedent shown in Scheme 9, where a significant increase in yield was observed when the substrate was designed to form a 6-membered ring rather than a 5-membered ring.<sup>13</sup> Conducting this reaction in lower temperatures (50-80 °C) only yielded trace amounts of the cyclized products even after several days, rendering them extremely challenging to isolate and characterize. It was only when the reaction was run at temperatures higher than 100 °C that the reddish brown tint of the active manganese(III) species completely disappeared, indicating the full consumption of the oxidant and yielding a detectable amount of the lactonized products. The elevated reaction temperatures successfully shortened the reaction time to about 15 to 30 minutes, but the cyclized products underwent rapid decomposition; the desired ester product was hydrolyzed to the acid derivative even when the reaction was terminated prematurely.



**Scheme 7.** Oxidative termination pathways in cyclization of unsaturated malonate esters.<sup>12</sup>



**Scheme 8.** Cyclization of a malonate ester bearing a trisubstituted alkene.

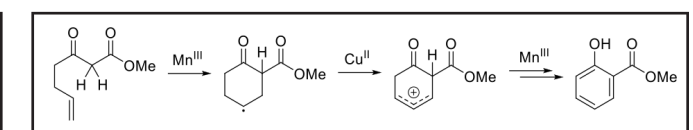


**Scheme 9.** Literature precedent for cyclization of malonate esters.<sup>13</sup>

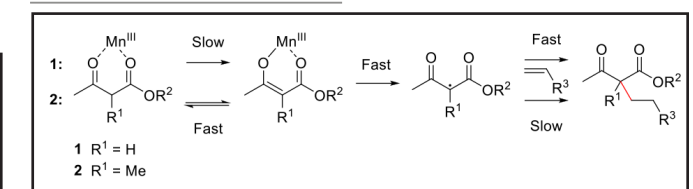
Although a series of optimization efforts improved the collective yield of the cyclization of the initial substrate to 17%, this result was far from ideal for the screening of chiral ligands in non-coordinating solvents, considering that similar substrates exhibited a decrease in yield when the acetoxy group was replaced with other polar aprotic solvents or carboxylate ligands. A few strategies to improve these results were devised: substituting an  $\alpha$ -hydrogen of the malonate ester moiety with a methyl group was predicted to prevent unwanted oxidation exemplified in Scheme 10,<sup>14</sup> and replacing the gem-dimethyl substitution of the alkene with a phenyl group was proposed to improve chemoselectivity by promoting lactonization.

Pursuing the first plan of action in modifying the substrate design required the understanding of the difference in reaction kinetics between  $\alpha$ -unsubstituted  $\beta$ -dicarbonyls versus their  $\alpha$ -substituted derivatives. The rate-determining step of the cyclization of the  $\alpha$ -substituted derivatives, unlike that of their  $\alpha$ -unsubstituted congeners, was found to be the alkene addition step (Scheme 11).<sup>10</sup> The removal of an abstractable proton at the  $\alpha$ -position accelerated and induced reversibility in the enolization process.

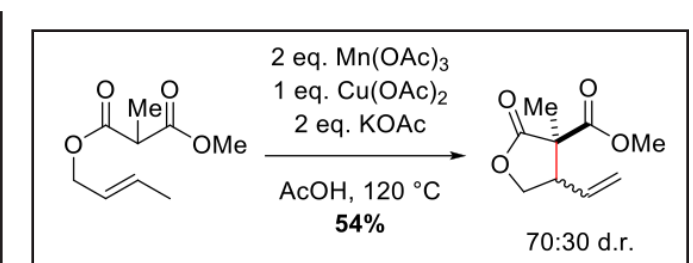
This change was speculated to contribute to the observed



**Scheme 10.** Oxidation of an  $\alpha$ -unsubstituted  $\beta$ -keto ester in extra equivalents of manganese(III).<sup>14</sup>



**Scheme 11.** Difference in cyclization kinetics of  $\alpha$ -unsubstituted and substituted  $\beta$ -keto esters.<sup>10</sup>



**Scheme 12.** Literature precedent for cyclization of  $\alpha$ -methyl malonate esters.<sup>15</sup>

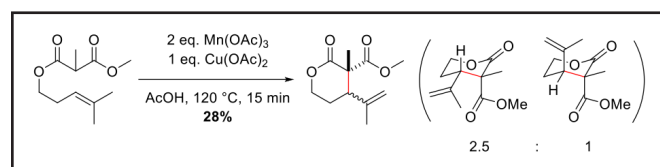
increase in yield with  $\alpha$ -substitution reported in the literature example shown in Scheme 12.<sup>15</sup> The cyclization of the  $\alpha$ -methyl derivative of the initial substrate occurred with improved yields (28% upon optimization) and reduced mass balance issues (Scheme 13). The cyclized product did not undergo hydrolysis under the reaction conditions necessary for the desired reactivity, indicating its superior stability compared to its  $\alpha$ -unsubstituted analogue.

However, the diastereoselectivity of the cyclization of the  $\alpha$ -methylated substrate presented another hurdle. While the initial substrate exhibited the preferential formation of the diastereomer with the alkene fragment in equatorial conformation, the cyclization of the modified substrate yielded a mixture of a diastereomeric pair with poor selectivity. Such observation has precedent in the literature example shown in Scheme 14. Depending on whether the configuration of the substituents on the alkene of the starting material was *cis*- or *trans*-, the ratio between the major and minor diastereomers of the cyclized product fluctuated.<sup>16</sup>

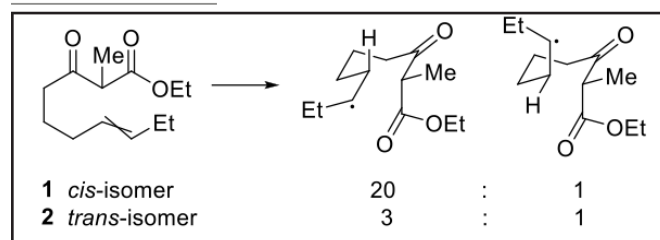
Despite the observed decrease in diastereoselectivity, the promising results demonstrated by the  $\alpha$ -substituted substrate, particularly in terms of the yield of cyclization, led to the screening of a series of polar aprotic solvents, including MeCN, DMF, and DMSO. Searching for any evidence of reagent-based induction of enantioselectivity in either diastereomer took precedence over optimizing the system for improved diastereoselectivity. As alluded earlier, acetic acid had to be replaced by a non-coordinating solvent in order for

chiral manganese carboxylate complexes to be introduced to mediate these reactions; the possibility of ligand exchange had to be eliminated. The reaction achieved comparable relative yield in DMSO when monitored by gas chromatography. Chiral manganese methyl-mandelic acid complex, which yielded auspicious results with the substrates investigated by other members of the research group, was prepared using the enantiopure form of the carboxylate ligand as illustrated in Scheme 15. The ligand exchange of the manganese precursor occurred with moderate yield. Unfortunately, no cyclized products were detected even after 25 hours of reaction in the presence of the complex. The reaction profile only showed steady decomposition of the substrate as noted in Scheme 16.

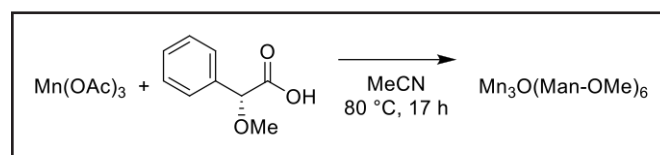
Cyclization of the phenyl-substituted relative of the initial substrate was carried out as an alternative approach to adjust the substrate design to improve the chemoselectivity of the original reaction. Pursuing this pathway additionally converged the scope of this project with other ongoing works within the research group exemplified by the reaction shown in Scheme 17. The attachment of an aromatic group to the tethered alkene was anticipated to stabilize the cation intermediate through conjugation, promoting secondary lactonization. As indicated in Scheme 18, however, this starting material did not exhibit the desired reactivity even in the presence of achiral metal reagents; only cleaved fragments and decomposed debris, including the fragment shown in parentheses, were isolated regardless of the reaction temperature or duration.



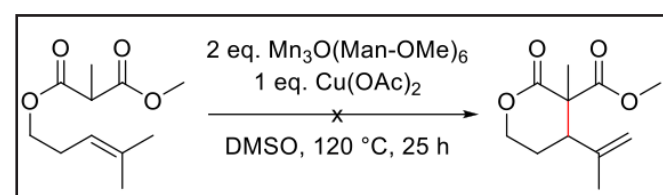
**Scheme 13.** Cyclization of an  $\alpha$ -methyl malonate ester bearing a trisubstituted alkene.



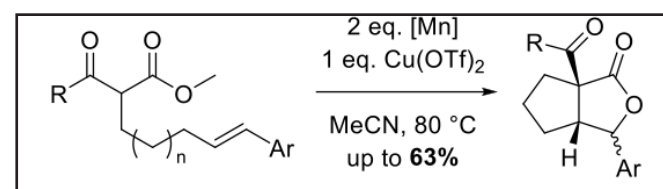
**Scheme 14.** Diastereoselectivity in cyclization of  $\beta$ -keto esters.<sup>16</sup>



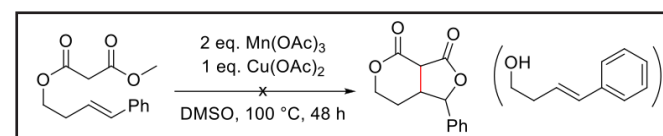
**Scheme 15.** Preparation of chiral manganese methyl-mandelic acid complex.



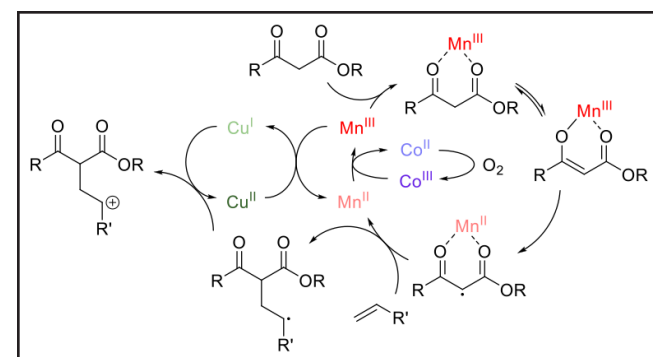
**Scheme 16.** Introduction of chiral manganese methyl-mandelic acid complex.



**Scheme 17.** Cyclization of  $\beta$ -keto esters with an  $\alpha$ -tethered alkene.



**Scheme 18.** Cyclization of a malonate ester bearing a phenyl-substituted alkene.

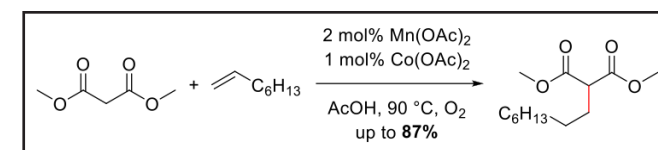


**Scheme 19.** Proposed catalytic cycle of manganese/copper/cobalt.

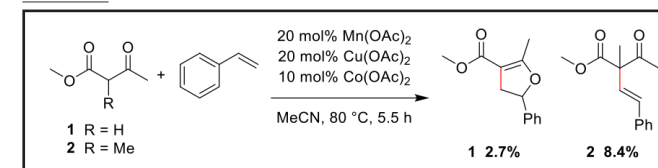
### B. Intermolecular Addition of Aryl Alkenes to $\beta$ -Keto Esters

The unsatisfactory results obtained from the intramolecular cyclization of malonate esters motivated a shift in this project to examine the intermolecular addition of aryl alkenes to  $\beta$ -keto esters. This substrate class complemented the investigation of the same reaction using malonate esters administered by another member of the research group. Both projects sought to move away from the stoichiometric loading of valuable chiral manganese carboxylate complexes. In order to reduce the amount of metal reagents used, cobalt(II) acetate was introduced to achieve the regeneration of the active metal species and complete the proposed catalytic cycle illustrated in Scheme 19. The incorporation of the cobalt species was inspired by the literature precedent in Scheme 20 where the intermolecular addition of an octene to a malonate ester was conducted in as low as 2 mol% loading of manganese(II) acetate. The generation of the active manganese(III) species was speculated to occur through a cascade of oxidation starting with the oxidation of cobalt(II) at the expense of gaseous oxygen, a readily available oxidizing agent. Then, the reduction of cobalt(III) was coupled with the oxidation of manganese(II) to manganese(III).<sup>17</sup> Unlike the previously studied intramolecular cyclization reactions, which were carried out under an inert atmosphere, these catalytic reactions were conducted open to ambient air.

The intermolecular addition of styrene to methyl acetoacetate and its  $\alpha$ -methyl derivative was conducted using reaction conditions optimized for the partner project as a starting point (Scheme 21). The trend extrapolated from the earlier studies regarding the number of acidic  $\alpha$ -protons abstractable from the  $\beta$ -dicarbonyl moiety was once again observed; the collective yield of the additional products improved with  $\alpha$ -methyl substitution. However, these reactions demonstrated unforeseen promiscuity and unpredictable chemoselectivity, producing several products, including the *cis*- and *trans*-isomers of the elimination product and the lactonization products formed from nucleophilic addition by either the keto- or ester-oxygen. These results were unsuit-



**Scheme 20.** Literature precedent for manganese/cobalt catalytic system.<sup>17</sup>



**Scheme 21.** Intermolecular addition of styrene to  $\beta$ -keto esters.

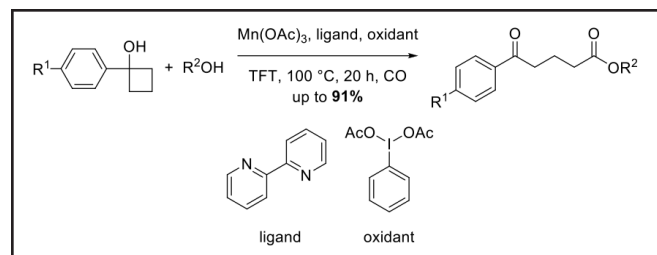
able for the introduction of chiral manganese carboxylate complexes.

### III. Future Directions

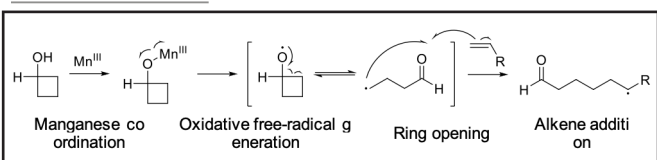
The failure to identify a model system to test the hypothesized reagent-based stereocontrol in the oxidative radical addition of alkenes to  $\beta$ -dicarbonyls using chiral manganese carboxylate ligands motivated the search for a new class of manganese-mediated or catalyzed reactions. Inspired by the recent reports on manganese-catalyzed cyclopropanol and cyclobutanol ring-opening reactions in the literature exemplified by Scheme 22, the investigation of the applicability of the manganese/copper/cobalt catalytic system to these reactions is an exciting direction this project could take. In this precedent, the active manganese species generated *in situ* through ligand exchange mediated the efficient construction of 1,5-ketoesters from various aryl cyclobutanols.<sup>18</sup>

The mechanism of these ring-opening reactions was proposed to proceed through the oxidative generation of a free-radical species which undergoes a series of SET events, opening the strained cyclic moiety.<sup>19</sup> The resulting radical could react with a diverse set of nucleophiles, some of which could be various alkenes as illustrated in Scheme 23.

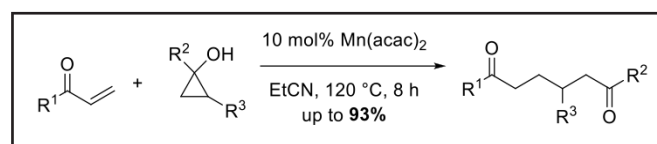
Aryl enones were the alkenes of choice in the literature precedent shown in Scheme 24. The manganese-catalyzed formation of 1,6-diketones showcased operational simplicity and wide substrate scope, rendering it a reasonable starting point for the project's new direction.<sup>20</sup> Inspired by this report, the oxidative ring-opening of phenyl cyclobutanol with various aryl enones and silyl enol ethers shown in Scheme 25 was chosen as the initial scope of investigation. The introduction of stereo-directing elements to these substrates or the ligands complexing with manganese could elucidate unexplored trends in chemo-, regio-, and stereoselectivity in these processes.



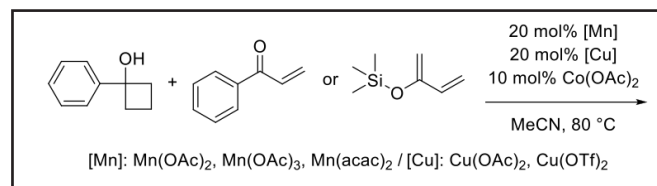
**Scheme 22.** Recent report of manganese-mediated ring-opening of aryl cyclobutanols.<sup>18</sup>



**Scheme 23.** Proposed mechanism of oxidative radical ring-opening of cyclic alcohols.<sup>19</sup>



**Scheme 24.** Literature precedent for ring-opening of cyclopropanols with aryl enones.<sup>20</sup>



**Scheme 25.** Ring-opening of phenyl cyclobutanol with aryl enones and silyl enol ethers.

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## Abstracts from Undergraduate Research Exposition 2021

### Accounting for New York State's Sports, Samiksha Vittalraj '20

Economic disadvantage is known to be associated with large reductions in the performance and participation of students in school. In this study, we investigate the extent to which the sports participation gap between rich and poor schools is explained by a reduction in sports available (extensive margin) versus a reduction in sports team sizes (intensive margin). We used data from the New York State Public High School Athletic Association (NYSPHSAA) to measure athletic participation, and data from New York State Education Department (NYSED) to measure school participation. We use the Blinder-Oaxaca decomposition method to explain the proportion of participation gap due to poorer schools providing fewer sports versus those schools having lower sports participation in the available sports. Our research suggests that the participation gap is not largely due to poor schools having smaller sports teams but offering the same sports choice set for students; what happens instead is that the poor schools have fewer sports available altogether. Overall importance of teams in our analysis is highly dependent on the definition of the sports offering; we have chosen to look at public schools that state that they offer certain team sports. Even though the overall importance of teams varies, depending on the definition used, there are a few sports, including lacrosse, field hockey and track, that consistently play sizable roles in contributing to the gap between rich and poor schools. Therefore suggesting that these teams are important. These findings shall be helpful to inform policies to boost athletic participation in poor schools.

### Analysis of North American Quitsites: Resources for Electronic Cigarettes and Vaping Cessation, Manpreet Kaur '20

Vaping is an epidemic and manufacturers of Electronic Nicotine Delivery Systems (ENDS) such as JUUL or PuffBarr are currently addicting a new generation of young people through their design, flavors, and marketing tactics (FDA). Youth engaging in vaping may be unaware of or misinformed about the harms of vaping and flavor toxicity. However, the North American Quitline Consortium (NAQC) includes a directory of quitsites for each state, province and territory within Canada and the USA. These quitsites provide information and resources for smoking cessation. The extent to which information on resources for vaping cessation are provided by each website has not been studied previously. Accordingly, this project has involved a thorough analysis of vaping-related information present on these quitsites and the type and amount of information and resources were compared across all sites. Only one third (21 of 66; 31.8%) of NAQC quitsites had specific sections or pages dedicated to vaping. Although one half (33 of 66; 50%) presented information on the harms of vaping, only 12 sites (18.2%) had messaging to indicate that flavors are harmful. Of the 22 sites with cessation resources, only two of them (New York State and the Province of Newfoundland) recommended speaking to a health care provider (although some websites included information and resources targeting healthcare providers and patient referral). In late 2019 and early 2020, there have been increased regulations on the vaping industry, including a partial ban on flavors (FDA). Information on the harms of vaping (particularly the harms of vaping flavors) remains lacking, and messaging across these publicly available websites is not consistent in terms of facilitating and supporting vaping cessation.

### LinkedOut: Co-designing Technologies with Returning Citizens, Rukimani PV '20

LinkedOut is a collaborative project between returning citizens (formerly incarcerated persons), researchers, city government, and an NGO. The project resulted in an online resource directory for returning citizens and 2 co-design workshops focusing on digital literacy and securing employment. In sum, the project lasted 10 months, and provided reflection on the inclusivity of technological design.

### Impact of Race and Socioeconomic Status on Diagnostic Age of Children with Autism Spectrum Disorder, Andrea Lopez '21

This study looks at the impact of race and socioeconomic status (SES) on the age of diagnosis for children with autism spectrum disorder (ASD). As the prevalence of ASD has risen over the years, it has become increasingly important to understand different aspects of ASD including the health disparities and differences in age of diagnosis which impacts whether or not a child can access resources and treatment in the critical developmental time period. This pilot study analyzes archival data from the Developmental Neuropsychology Laboratory's research database within the University of Rochester's Department of Psychology to examine the relationship between SES, race, and age of ASD diagnoses. From this dataset, 56 of the participants were processed and analyzed. Data collected includes child's SES, race, severity of the child's symptoms, and the date and location of the child's diagnosis. A child's SES was calculated using the Hollingshead Four-Factor Index of Socioeconomic Status based on parental education, parental occupation and marital status (Hollingshead, 1975). ASD symptom severity was calculated using the Social Responsiveness Scale, 2nd edition (SRS-2). Information regarding the child's age of diagnosis was obtained via parent interview. Results from the sample indicated a mean age of diagnosis of 5.15 years. Pearson correlation results did not indicate a significant association between SES and diagnostic age. However, one-way ANOVA results indicated that the mean age of diagnosis for the children of color (n=13, 6.31 years) was notably higher than for white children (n=43, 4.85 years). While this effect was not statistically significant (F= 2.041.74, p=0.1) in this sample, the size of this effect is clinically meaningful. This difference in diagnostic age between groups means white children in our sample, on average, were diagnosed approximately 1.5 years earlier than children of color creating a health disparity in access to early treatment for children with ASD who are of a racial minority. Future research should continue evaluating disparities and barriers different populations face in accessing healthcare for children with ASD.



**In-store and Online Advertising Messages for Tobacco Products in a Western New York Metropolitan Area, Astghik Baghinyan '22**  
Smoking has been established by the CDC to be harmful to smokers and the people around them that inhale the second-hand smoke (CDC). However, smoke-shops still have the right to sell tobacco products to the public and we were interested in finding out what are some of the online and in-store advertising features they use to sell their products. For these reasons, a qualitative research method "windshield survey" collected words on-site from 6 smoke-shops' store-fronts to generate a word cloud where the size of the words correlates with the frequency of their usage. The second part of the research included gathering words from the 10 most recent Facebook posts of 15 smoke-shops to generate a world cloud. Using open coding qualitative methods, 15 themes were developed from these Facebook posts to generate a pie chart. For the in-store advertising, out of 50 unique words, the most frequently occurring words were "smoke" (n=5), "accessories" (n=3), and "vape" (n=3). For the Facebook advertising, out of 346 unique words, the most frequently occurring words were "stock" (n=28), "vape" (n=27), and "cigar" (n=26). The themes that emerged the most were the following: accessories (23.0%), novel (14.4%), and deals (9.2%). Overall, we observed that for both in-store advertising and online Facebook advertising the main focus of smoke-shops is on vapes and accessories. Additionally, other commonly used words such as "stock" and "in stock", which appeared 47 times in total, indicate the smoke-shops' tendency to advertise the variety of products they sell.

**Formation of Carbon Dioxide Adducts from Carboxamide Anions Generated During Gas-Phase Fragmentation of Anions Derived from Capsaicinoids, Annie Wang '22**

Novel chemical reactions that consume CO<sub>2</sub> as a reactant are widely sought through research today because increasing levels of CO<sub>2</sub> in the atmosphere is the cause to many environmental problems. One known reaction is the CO<sub>2</sub> addition reaction, which can be used as a diagnostic structural probe for gaseous anions under mass spectrometric conditions. In our research, we experimented with capsaicinoids, the active ingredients in chili peppers that contribute to the pungency. Daughter scan experiments on all deprotonated capsaicinoids were conducted either in ion mobility mode with mobility cell filled with CO<sub>2</sub> or ToF mode without CO<sub>2</sub> in the mobility cell. We found that upon activation, all capsaicinoids lose a 136-Da 2-methoxy-p-quinone methide unit to generate a carboxamide anion. The presence of the hydroxyl group at the para position of the vanillamine moiety is crucial for this specific fragmentation to take place. Moreover, the carboxamide anions generated by this fragmentation undergo a nucleophilic addition reaction if they encounter carbon dioxide, and form respective alkylcarbamate anions. To verify the role of the hydroxyl group attached to the para position in the fragmentation mechanism, we further experimented with N-4-hydroxybenzylbutyramide and N-benzylbutyramide. We found that upon activation, the anion of N-4-hydroxybenzylbutyramide lose a 106-Da fragment for p-quinone-methide to form a carboxamide (m/z 86) which readily react with CO<sub>2</sub> to generate a carbamate ion (m/z 130). In stark contrast, the anion from N-benzylbutyramide did not form a CO<sub>2</sub> adduct because for the initial p-quinone-methide elimination, the participation of the para hydroxy group is necessary. Thus, we report that for the CO<sub>2</sub> adduct formation, a hydroxyl group must be at the para position of the benzene ring bearing the -CH<sub>2</sub>-NH-COR moiety.

**Do Implicit Negative Appraisals of Anxiety Moderate the Relationship Between Anxiety and Depression?, Hannah Duttweiler '20**  
Decades of research consistently documents pronounced comorbidity between anxiety and depression (e.g., Lewinsohn, 1997; Mineka et al., 1998); however, more research is needed to better understand mechanisms underlying high rates of co-occurrence between the two disorders. A body of research suggests anxiety disorders develop prior to depression in the majority of comorbid cases (e.g., Wittchen, et al., 2000; Essau, 2003). However, little is known about specific conditions under which anxiety leads to later depression. The negative anxiety response style (NARS) model (Starr & Davila, 2012; Starr et al., 2016) suggests that the tendency to make hopeless inferences and ruminate about anxiety moderates co-occurrence between anxiety and later depressive symptoms. However, some may lack insight to their tendency to engage in NARS. Dual process models (Haefel et al., 2007) theorize that many processes operate in both explicit (under conscious awareness) and implicit (instantaneous, unconscious processes) modes. The current study examined negative implicit judgements as a possible moderator in the relationship between anxiety and depression in a college sample. A sample of 173 participants (Mage= 20.2, 75.9% female) were recruited through an undergraduate participant pool. Participants completed a novel version of the Implicit Associations Task (IAT; Greenwald et al., 1998), which paired associations between "anxiety" versus "calm" with "bad" versus "good" (drawing stimuli from existing IATs). Anxiety and depression were assessed with the Depression Anxiety Stress Scales (DASS; Lovibond & Lovibond, 1995), and explicit NARS was assessed with the Response to Anxiety Questionnaire (RAQ; Starr & Davila, 2012) and face valid questions. Participants re-completed questionnaire measures 1 month following baseline. The novel IAT scoring algorithm by Greenwald et al. calculated a D score, which is the difference between response latencies for the two critical category pairing conditions, divided by the standard deviations across all blocks (2003). The final D score was used in analysis to represent implicit judgements such that more negative D scores imply more negative judgments of anxiety. Analysis revealed that, although 99.4% of participants endorsed negative associations with anxiety, there was substantial variation with a normal distribution (M= -0.945, SD= 0.303, skew= .852, kurtosis= 1.23). However, the D scores did not correlate with explicit measures of NARS (ps > .05). Further, preliminary cross-sectional analyses showed that the IAT did not significantly moderate the association between anxiety and depression (p>.05). The explicit measure for negative associations of anxiety was a marginally significant moderator of the relationship (b=.005, SE=.003; p= .076), in the predicted direction (i.e., higher explicit negative anxiety response style,

stronger associations between anxiety and depression). Although these results failed to support the dual process model of the NARS theory of comorbidity, it is possible that adjustments to the novel anxiety IAT are needed to ensure the implicit associations are being accurately captured.

**Exploring the relationship between overgeneralized autobiographical memory, impaired social problem solving, and stress generation, Emma Cho '20**

Prior research suggests that depressed individuals are more likely to experience stress generation, or stressful life events that are dependent on their own characteristics or behavior (Hammen, 2006; Liu & Alloy, 2010). A possible unexplored contributor to stress generation is overgeneralized autobiographical memory (OGM), or the tendency for depressed individuals to give nonspecific memories in response to prompts for specific, personal memories (van Vreeswijk & de Wilde, 2004). Less specificity in memory recall is correlated with decreased effectiveness in social problem solving (Evans et al., 1992; Raes et al., 2005; Sidley et al., 1997). OGM may interfere with an individual's ability to access memories of previous social problem-solving attempts, leaving them less able to learn from their mistakes and more likely to experience the same interpersonal difficulties. Thus, in a sample of 173 undergraduate students (Mage = 20.2, 75.9% female, 41.5% Caucasian), this study explored a novel mechanism by which a deficit in social problem-solving skills mediates the relationship between OGM and stress generation at a one-month follow-up. OGM was not significantly correlated with the reported frequency of dependent or independent life events at follow-up, nor was it significantly correlated with social problem-solving ability. Both OGM and social problem-solving ability did not significantly predict stress generation at follow-up when controlling for depression ratings and reported frequency of dependent events at baseline. These results are inconsistent with both prior research and the proposed model, potentially because of the high level of functioning within the sample; future research in clinical samples is needed.

**Role of Pore Structure on the Sintering Effect of Pt Diesel Oxidation Catalysts, Natalie Ramesh '21**

The USDRIVE Low Temperature Oxidation Catalyst Test Protocol recommends an accelerated aging test for Pt diesel oxidation catalysts (DOCs) to be performed at 800 °C in flowing air. However, at such high temperatures, Pt sinters readily to form large particles due to significant vapor phase transport of PtO<sub>2</sub>. One approach we used to slow the rate of Pt sintering was by alloying Pt with Pd. A second approach was to trap the mobile Pt species with an oxide such as PdO that reacts to form Pt-Pd bimetallic particles, or using CeO<sub>2</sub>, which traps Pt in atomically dispersed form. Recently, we have explored the role of pore confinement to determine if it was possible to slow the vapor phase transport of PtO<sub>2</sub>, and therefore, the rate of Pt sintering. Since PtO<sub>2</sub> vapor has negligible binding to silica, it provides the ideal support to study the role of pore structure. We studied MCM-41 and SBA-15 as silica supports and found that, although they slowed the rate of Pt sintering after aging at 800 °C, the resulting Pt DOCs was not very reactive due to blocking of the pores by the Pt particles, which in turn blocked accessibility of the smaller Pt particles retained inside the pores. This inaccessibility is due to high pore diameter to length ratios of MCM-41 and SBA-15. Here we explore other silica with a more open pore structure, such as silica spheres which have much lower aspect ratios. We found that we could slow the rate of Pt sintering and improve the reactivity using a model reaction, such as CO oxidation. The results are then compared to Pt on a commercial Davisil silica support, which we use as the control for this study.

**Constructive Absorption and Reflection for Light Propagation Through a Cholesteric Liquid Crystal Film, Baris Eser Ugur '21**

Circular Dichroism demonstrated by Cholesteric Liquid Crystals (CLC) is crucial for creating circular polarizers that can be used in the optics industry and the military. In this project the Good-Karali theory is extended to simulate composite CD through a cholesteric stack by incorporating chromophore's selective absorption and cholesteric stack's selective reflection. This allows the modeling of optical circular polarizers to maximize the polarization ratio and isolation ratio of incident light for optimized performance. The developed theory is capable of modeling the transmission, absorption, reflection and the polarization ratio which allows the optimization of various parameters for a given CLC film for device development. It has been shown in the theory that selective absorption of light plays a dominant role over selective reflection, providing a new area of circular polarizers with isolation ratio to be used for novel night-vision technology.

**Polynomial Generalizations of Knot Colorings, Matthew Zevenbergen '21**

In the mathematical field of knot theory, knot invariants are properties preserved across all embeddings and projections of the same knot. Fox's n-coloring is a classical knot invariant which associates to each knot projection a system of linear equations. Our research looks to generalize Fox's n-coloring by using two, not necessarily distinct, polynomials which we call a (g,f)<sub>p</sub> labeling. We have found that the cubic 2x<sup>3</sup>-y<sup>3</sup>-z<sup>3</sup> forms a valid (g,f)<sub>p</sub> labeling, when p is 2 modulo 3. Furthermore, we have confirmed a family of pairs of linear polynomials that together form a valid (g,f)<sub>p</sub> labeling. Finally, we have proven that there are no possible pairs with a quadratic polynomial which form a valid (g,f)<sub>p</sub> labeling.

**Toxicovigilance of Novel Psychoactive Substances using Social Media and Forum Data, Cameron Fredriksen Isaacs '21**

Novel psychoactive substances (NPS) refer to classes of substances which have been either newly synthesized or involve pre-existing substances that are being abused in novel ways. NPS have become an increasingly abused class of drugs in the United States in part due to their ease of access, availability on the internet, higher potency, and sometimes a loophole bypassing DEA regulations. NPS are also commonly developed in clandestine labs and manufactured with variable concentrations. As a result, abusing these substances is associated with a high potential for morbidity and mortality. Due to the rapid development of new substances and the inability to screen for them, there is little epidemiological, pharmacological, and clinical information on these substances. In order to understand NPS trends, between 2016 and 2018, we reviewed over 4,000 posts on Reddit containing user's self-reported experiences after using a specific NPS. Of the 4,000 posts, there were 900 users included in the study. To be included, each user had to mention using at least one NPS and provide data about their experience. We found that the most commonly abused class of NPS were psychedelics followed by stimulants and that the most common substance was 4-AcO-DMT or Psilocybin. The most common route of administration was oral. Lastly, approximately 51% of all users reported that this was their first time using that substance. These results were similar to previous studies on NPS.

#### **Stroke prediction using Carotid Artery CFD simulations, Leonor Tales '21**

Stroke is a leading cause of death and is often prevented through carotid stenting, a surgery performed for patients with 70-90% artery blockage. However, when a patient's artery blockage is below this threshold, other predictive methods are necessary. Blood flow models can therefore aid these medical care decisions. This project is a collaboration between the Departments of Chemical Engineering and Neurosurgery with the goal of understanding whether computational fluid dynamics (CFD) can be used to predict strokes in patients with coronary artery disease. The project focuses on computationally simulating patient's specific blood flow patterns based on computerized tomography angiography for geometry and ultrasound for velocity and pressure data. CFD enables the analysis of each patient's blood flow patterns, focusing on their geometry, velocity profiles, streamlines, and pressure gradients. This is beneficial for quantifying the differences between velocity profiles given stroke outcomes. The purpose of this project is to ultimately create a model that predicts the onset of stroke in patients based on their carotid artery geometries coupled with ultrasound data.

#### **Regenerative capacity of ataxia-telangiectasia mutated deficient alveolar epithelial cells following injury in mice, Molly Behan '21**

In the alveolar space, the alveolar epithelial type II (ATII) stem cell works as the progenitor cell for alveolar epithelial type I (ATI) cells, which together help to maintain lung function. In the airway, the critical progenitor cells are the club cells, they also are important for maintaining lung homeostasis. Unfortunately, the mechanisms involved in controlling the proliferation, expansion, and quiescent following injury for these cells are not fully understood. In previous studies, the cyclin dependent kinase ataxia-telangiectasia mutated (ATM) has been hypothesized to play an important role in the mechanisms involved in airway stem cell repair, as club cells were shown to lack the ability to sufficiently regenerate following injury when ATM deficiency was modeled in mice. Here, ATM's role in regulating the alveolar epithelial progenitor cells is studied using wildtype and ATM-null mice. The levels of genes expressed specifically by ATI and ATII cells were analyzed in ATM null and ATM WT mice using qRT-PCR and immunohistochemical staining before and after injury by infection or exposure to hyperoxia. Although, no changes in expression of ATII cells genes were detected, we observed lower levels of ATI specific genes in ATM-null mice prior to injury. This suggests that ATM may still be involved in development of the ATI cells but not in development or repair of ATII cells. Our findings suggest ATM is required in progenitor cells that regenerate the airway epithelium following injury and in alveolar cells required for postnatal lung development.

#### **Exogenous Attention at the Foveal Scale, Yue Zhang '20**

The effects of exogenous attention in the visual periphery have been studied extensively. Yet, it is not well-known if this type of attention can be fine-tuned in the foveola, the 1-degree foveal region where visual resolution is the highest. Here, we addressed this issue by investigating the temporal dynamics of foveal inhibition of return. This phenomenon is typically associated with exogenous attention, and involves the suppression of a stimulus that had been recently attended to.

A classic spatial cueing paradigm was used. The entire stimulus array was scaled in size to fit within the 1-degree foveola. Observers (n=9) fixated on a central marker throughout the trial. After a brief exogenous cue, high-acuity stimuli, tiny bars tilted 45 degrees, appeared at four locations 11° away from the central marker. Following a variable inter-stimulus interval, a response cue appeared pointing to one location. Subjects were instructed to determine the orientation of the stimulus previously presented there. Trials had 50% probability of being valid, i.e., when the exogenous and response cue matched. To eliminate the confounding factor of fixational eye movements, which would otherwise shift the stimulus array on the fovea, we used retinal stabilization; the stimuli remained immobile on the retina, and only trials without microsaccades were selected for analysis.

Our findings show that for shorter inter-stimulus intervals (~60 ms), subjects' ability to discriminate fine details was enhanced at the attended location and reduced at the unattended locations ( $d'$  difference between valid and invalid trials; 0.50,  $p < 0.01$ ). We also report a temporal modulation resembling inhibition of return, characterized by higher performance at the unattended locations with longer intervals ( $d'$  difference between valid and invalid trials; -0.61,  $p < 0.01$ ). These results indicate that involuntary attention can be fine-tuned at the foveal scale, contributing to the enhancement of high-acuity vision.

#### **Fourier Processing of Partially Coherent Fields, Benjamin Nussbaum '21**

Techniques for the Fourier processing of entirely coherent or incoherent optical radiation are well known; we extend these techniques to spatially partially coherent light and verify the theoretical predictions of Opt. Lett. 42, 4600 (2017). We implement an optical system to generate a spatially partially coherent field by passing a coherent laser beam through a rotating ground glass diffuser. We examine the effect upon this beam of a spatial filter in a 4f system, the canonical optical processor, and quantify the degree of spatial coherence by measuring the interference fringe visibility resulting from a subsequent Young's experiment. We demonstrate control of the degree of spatial coherence with respect to the spatial filter pinhole diameter, in agreement with the theorized result. Future work could include the development of more intricate Fourier plane amplitude and phase filtering to generate arbitrary coherence profiles. This process of controlling coherence profiles could provide better imaging quality in such applications as astronomy, microscopy, lithography, medical imaging, and automotive sensing. Other extensions of this work could include examining the manipulation of polarization in partially coherent fields.

#### **The Impact of Interparental Conflict and Sensitive Parenting on Children's Cognitive Functioning, Maya Koven '20**

Interparental conflict has been demonstrated to have substantial implications for the family system including parenting and children's development. This study examined the indirect relationship of interparental conflict and children's cognitive functioning through sensitive parenting. Participants included 235 families (mothers, fathers, and their child) who came for annual visits for three waves of data collection. Assessments of interparental conflict were derived from observational tasks coded for negativity and conflict and problem solving and cooperation. Assessments of sensitive parenting were derived from observational tasks coded for sensitivity. Children's warm problem solving was assessed during a puzzle box task. Children's working memory and cool problem solving were assessed during the administration of two subtests of the WPPSI-IV. Results show a direct significant relationship between interparental conflict and children's warm problem solving. Additionally, results suggested two indirect relationships between interparental conflict and children's cognitive functioning, such that there was an indirect relationship between interparental conflict and children's cool problem solving through paternal sensitive parenting, and an indirect relationship between interparental conflict and children's working memory through maternal sensitive parenting. These findings were significant over two waves of data collection. Results suggest that interparental conflict has direct and indirect effects on children's problem cognitive functioning.

#### **The Interaction Between Maltreatment and Teacher Warmth and Effects on Peer Relationships and Emotion Regulation, Erik DuShane '20**

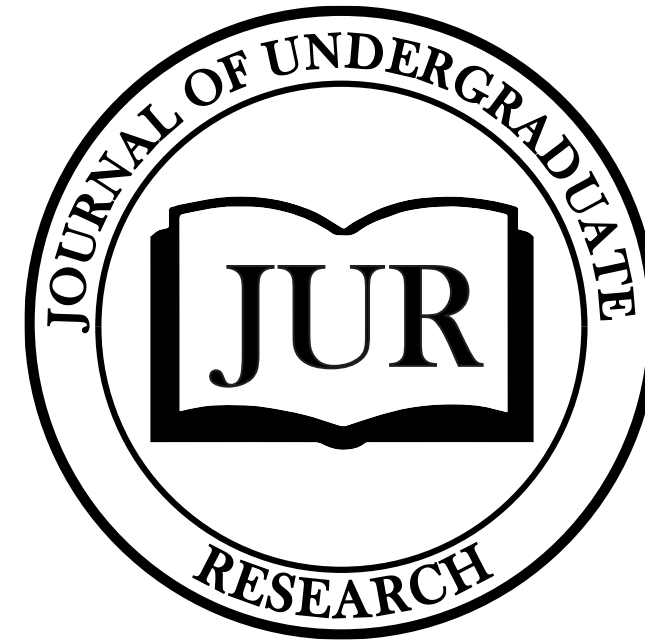
Maltreatment can have a number of deleterious effects on the social and emotional development of children. Because these experiences can result in a wide range of adverse outcomes in different domains of their lives, it is important to identify protective factors for children who experience maltreatment. The current study examined the impact of child maltreatment on peer relationships and emotion regulation as well as the role student-teacher relationships play. Participants included 115 high-risk urban children (ages 8-12) with histories of maltreatment. Results indicated that higher number of maltreatment subtypes was a predictor of increased peer victimization. Moreover, there was evidence of an interaction between extensive maltreatment and teacher warmth that affects emotion regulation such that low teacher warmth was associated with lower levels of emotion regulation for multiply maltreated children. Higher teacher warmth is also associated with more prosocial behaviors towards children with less extensive maltreatment histories, but not for children who were multiply maltreated. The role student-teacher relationships can play for maltreated populations are discussed in terms of intervention in the school environment.

#### **Experimentally Increasing the Thermotolerance of *S. uvarum*, Haley Cohen '21**

Many species have adaptations to temperatures in which they are found, but the genes and pathways by which such adaptations have evolved are widely unknown. *Saccharomyces* yeasts offer distinct advantages as a model system in which to study thermal adaptation. *Saccharomyces* yeasts are of particular importance to humans, as they are central to the production of beer, wine, bread, and even biofuels. These yeasts can help us understand general principles of microbial evolution. Here, we intend to determine: whether temperature-sensitive species can adapt to high temperatures, and if so by many small steps, few large steps, or something in between; and whether high temperature adaptation has a cost at low temperature. Eight strains of *Saccharomyces* yeasts, differing in baseline thermal growth profiles, were experimentally evolved under three different temperature conditions. After approximately 100 generations of evolution, lineages of *S. uvarum* appeared to have improved their thermal tolerance, most without a cost to growth at lower temperatures. Some areas that desire further investigation include the effects of repeated UV mutagenesis, heat shock, and a constant heat stress on experimental evolution.

#### **Emotion Recognition Skills & Social Motivation Among ASD and Control Children, Hanqiu Li '21**

Babies develop emotion recognition skills starting from 3-6 months (Camras & Allison, 1985). The social motivation theory of autism spectrum disorder (ASD) posits that individuals with ASD find social stimuli less rewarding than do people with neurotypical activity. The current research tested whether there exists a relationship between emotion recognition skill and social motivation among children with and without ASD.



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## Featured in This Issue

### On the Use of Information from Past Unethical Research

*Samuel Streicher '23, Bioethics*

This piece argues that it is morally acceptable to make careful and qualified use of information from past unethical research if significant benefits are at stake. The discussion begins with a critique of common counterarguments, followed by a description of a counterargument that proves to be quite compelling - Dr. Aaron Ridley's concern involving deterrents and incentives. Although Ridley claims that an analysis of deterrents and incentives forces him to reject the use of information from unethical research, his case merely serves as another reason to restrict - but not completely prohibit - the use of such information.

### Review: An Investigation of Neuroprosthetic Treatments of Phantom Limb Pain

*Carolyn Kocek '22, Neuroscience*

Phantom limb pain (PLP) is a result of nerve damage that occurs after amputation. The amputation can result in neuroma formation and incorrect cortical mapping resulting in pain. This condition impacts the lives of 85% of all amputees. This article examines two neuroprosthetic approaches to relieving PLP: a dorsal root ganglion stimulation and brain machine interface training.

### Characterization of B Cell states with respect to BCR and HIF-1 $\alpha$ Pathways using discrete-state modeling

*George Kassis '22, Microbiology and Immunology*

B cell activation, migration and proliferation depend upon B Cell Receptor (BCR) signaling and response of B cells to O<sub>2</sub> levels. The latter is regulated by Hypoxia Inducible Factor 1 (HIF-1 $\alpha$ ), thus the investigation of BCR activation and HIF-1 $\alpha$  response is critical to understand B cell response to different diseases. To characterize B cells by their activation of BCR and HIF-1 $\alpha$  activity, here we utilized Single cell RNA sequencing (scRNA-seq) and a discrete state modeling algorithm called Boolean Omics Network Invariant-Time Analysis (BONITA). In-depth network analysis characterized several clusters of B cells from breast cancer and lung cancer tissues.

### Reducing the Gender Gap in Technology through an Entrepreneurial Network

*Maria Fernanda Sesto Carballo '23, Business*

The problem of gender diversity in technology reduces the opportunity of having economic growth in the industry, affecting both women and men. This research paper aims to provide a potential solution to increase the female representation in this field. In particular, the lack of female entrepreneurship in technology is analyzed by studying the reasons why it happens and how it affects younger women's decision to pursue a career in technology.

### For the Sake of the Future: The Soviet Economy and a Surfeit of Shortages

*Matthew Burgess '22, History*

From assembly line to breadline, Soviet citizens under Stalinism frequently spent days waiting for basic necessities, learning to live with the consequences of government choices in which they had no say. Citizens believed corruption and incompetence lay at the heart of these imbalances, yet the problem was more acute, an outcome of purposeful choices within the Stalinist economic system that accepted the existence of shortages. This essay examines the recurrent shortage phenomenon and the impact of exchange along three lines of inquiry: Stalinist economic policy programming, the hierarchy of access to goods, and the disparity in policy.

### Manganese Promoted Oxidative Radical Addition Reactions

*Yeonseong Seo '21, Chemistry*

The theorized manganese-bound radical intermediates in manganese promoted oxidative addition reactions present an interesting opportunity for achieving chemo-, regio-, and stereoselectivity by tuning the steric and electronic properties of the chiral ligands bound to the metal center. The substrate scope of manganese mediated (or catalyzed) intramolecular cyclization, intermolecular addition, and ring-opening reactions was investigated for the introduction of elements that may result in the preferential formation of the desired product over the other(s). implementation between the nation's urban and rural areas.



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