

# thurj

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*Spring 2024*  
*Best Manuscript Award*

## Rose Chen Giroux

Rose Giroux is a member of the Class of 2026 and grew up in the Boston area. She is pursuing a degree in the History of Art & Architecture and East Asian Studies with a focus on China and Japan. Her academic interests range from European and Asian print culture to late 19th-century graphic design. Most of her academic work and research thus far centers around attempts by male artists to depict and harness female sexuality. Rose is also passionate about arts education and directs the Chinatown Afterschool Program (CHAP) through the Phillips Brooks House Association. She is spending this Spring and Summer as the Alexis Gregory Intern conducting research in Boston and abroad on Aubrey Beardsley and Japonisme for the Harvard Art Museums.

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April 2024

Dear Harvard Community,

It is my pleasure to present the Spring 2024 issue of The Harvard Undergraduate Research Journal (THURJ), a student-run biannual publication dedicated to showcasing exceptional research from the Harvard undergraduate community.

Since reestablishing THURJ in the fall, our team has been hard at work creating, editing, and refining this new issue. It is with immense pride that we unveil the largest issue in THURJ's decades-long history. This edition showcases a diverse and eclectic collection of research spanning social justice, HIV discoveries, mental health, scientific advocacy, and even "zombie" fruit flies. We are especially pleased to honor Rose Giroux '26 with this semester's Best Manuscript prize for her exceptional work merging philosophical and anthropological perspectives in the analysis of witch hair's historical depictions.

This spring, the THURJ Executive and Associate Boards have launched several key initiatives, marking significant advancements for our journal. Among the highlights are our successful acquisition of Digital Object Identifiers (DOIs) for all manuscripts and articles in addition to our new partnership with the Harvard Libraries to showcase our journal in both print and digital mediums. We have also initiated a cross-institute research journal summit as a collaborative space for undergraduate researchers, reintroduced the Best Manuscript award to honor outstanding works, launched our high school research program and competition to inspire young researchers, and welcomed Professor Andrew Berry as our new and invaluable faculty advisor. Finally, a comprehensive revamp of our website has enhanced its functionality and accessibility, ensuring that a wider audience can engage with our content. Through these efforts, we are committed to promoting undergraduate research, extending THURJ's influence within Harvard and beyond, and maintaining our role as a leader in the Harvard College academic community.

This publication, however, would not exist without the incredible efforts of the Spring 2024 General Board, whose immense efforts in creating this unprecedentedly large issue are both visible and tangible. In addition, we would like to thank our faculty contributors, the Office of the Dean of Sciences, the Office of the Dean of Arts and Humanities, and the Office of the Dean of the Faculty of Arts and Sciences for their continued support.

All of us in THURJ are incredibly excited and proud to present our newest issue to the Harvard community. Please enjoy!

Sincerely,

A handwritten signature in black ink, appearing to read 'Ellie Shin', with a stylized, flowing script.

Ellie Shin  
Editor-in-Chief



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Research Journal

## About Us

The Harvard Undergraduate Research Journal (THURJ) showcases peer-reviewed undergraduate student research from all academic disciplines. As a biannual publication, THURJ familiarizes students with the research publication process. This process not only stimulates faculty student collaboration and provides students with valuable feedback on their research, but also promotes collaboration between the College and Harvard's many graduate and professional schools. In addition to publishing original student research papers, THURJ keeps the Harvard community updated on and provides an important forum for discourse on the cuttingedge research that impacts our world today.

## About the Cover

Natalie Zhang '27

This issue's cover art delves into the theme of justice, exploring the complexities and contradictions surrounding the concept in our society. A sculpture resembling Themis, the Greek Goddess of justice, takes center stage, adorned with a transparent veil rather than her usual blindfold, prompting reflection on whether justice is truly impartial in our world. Adjacent to this sculpture, a window reveals a cold and unforgiving pair of eyes, symbolizing the unyielding indifference of unjust systems that persist today. In the background, a silhouette of the ideal, blindfolded Themis serves as a poignant reminder to envision a world where justice truly prevails.





# Research

# Blasted, Bound, and Bald: the Abject Properties of Witch Hair

Rose Chen Giroux  
Harvard College '26

The witch's blasted hair in Early Modern visual culture is moving and evolving. Her hair is untamable, animated by a wind and a force unknowable to the viewer. The artists who captured this "blasted" hair in the 16th century, including Hans Baldung Grien, Hans Sebald Beham, and Albrecht Dürer, found themselves working in opposition to what appears, at first glance, a formidable "other:" women's agency and sexuality, frozen in bodily form as strands of hair. Little research has been dedicated to an earnest analysis of the witch's amorphous hair so this paper consists primarily of original research and the application of philosophical and anthropological theory. Julia Kristeva's theory of abjection is a key tenet of this paper's central argument. The witch is not an "other" directly opposed to a mainstream, she is a third intermediary thing: Kristeva's "abject." She is a personification of the skin on the surface of sour milk, instilling disgust in the potential consumer. She is the abject precisely because she is embedded in the object; her hair is the most explicit vehicle for this argument. Friedrich Spee von Langenfeld's accounts of forced hair removal and contemporary literature from Raymond Firth, Barbara Baert, and E.R. Leach inform this reading of witch hair as the abject. This paper concludes that the visual translation of blasted hair is an attempt to remove it and its female sexual connotation from the imagination to a more accessible visual medium. The artist's renderings are meant to turn the abject into an easily digestible object, a complete "other."

## Introduction

In Hans Baldung Grien's *The Witches* (**Figure 1**), a cohort of witches perform a vague ritual, limbs shaded and curved in the same fashion as the air, trees, and animals that surround them. Of particular note is the tree that rises on the right side of the print — distinctly fleshy and made up of the same mild curves that constitute the witches. The witches themselves wear their hair in a way that mimics the waves of air that unfurl around them. They are fully integrated into their environment: the central witch's hair moves upwards, disappearing behind a dish and then emerging from it as cloth. Hair is useful as a "manipulable representation of the entire person..." (Firth 1973, 296). At its most basic level, hair is a biological thing and an artistic symbol. It is living and growing, being cut and combed. Hair, and the witch's hair in particular, is not fully tamable by the artist.

As for the artist Hans Baldung Grien, scholar Yvonne Owens writes extensively about Baldung's emotional community and how it informed his depictions of witches and women. Owens extrapolates on Barbara H. Rosenwein's *Emotional Communities in the Early Middle Ages* to inform her reading of Baldung's work. Rosenwein argues that the early medieval period was a bridge connecting the classical tradition of putting words to emotions with modern Western civilization. Owens creates a line of reasoning between the male-dominated artistic and emotional community Baldung occupied with his charged engravings of witches. I argue that this artistic and emotional community, born from the classical tradition and carried through the early modern period, is the same one that later birthed psychoanalytic theory. The men who engraved, painted, and printed witches did so in a misogynistic world that allowed for the violent persecution of witches and went on to originate psychoanalytic theory. In summation, "the themes are always the same" (Didion 1968, 120).

Psychoanalyst Julia Kristeva's theory of abjection is most applicable to witch art because it delineates a distinctly feminine subconscious. Derived from Freud's theories of the unconscious,



**Fig. 1.** Baldung Grien Hans, *The Witches*, engraving, 1510 (The Metropolitan Museum of Art)



Kristeva's abjection relates directly to themes of gender, religion, and terror that permeate most early modern depictions of witches and their hair. Abjection is the human reaction (horror, vomit) to a threatened breakdown in meaning caused by the loss of the distinction between subject and object or between self and other (Felluga). Abjection helps delineate the emotional, primordial, and visceral basis for any argument on the European witch. Witch imagery and the witch's hair are representatives of women's sexuality, and that very sexuality is their most abject property. Situated between private and public symbol, between individual production and collective interpretation, the ambiguous nature of hair makes it an ideal medium for historical and gendered abjections prevalent in early modern Europe.

The technical aspect of capturing hair in art also lends it a unique flexibility and freedom. There is no formal, classical, or "ideal" of a woman's hair during the Renaissance period; it operates outside the constraints of convention. Lines are drawn sans expectations — agency is given to the artist in curves. The artist is "containing" hair, he is capturing it on a metal plate, on a woodblock, or in aquatint. In this process of confinement, the artist who depicts witches finds a mesmerizing predicament. The witch is neither subject nor object, she is that third intermediary "abject." If hair can be taken additionally as a symbol, then it can be argued that hair "not only 'says' something, it also arouses emotion and consequently 'does' something" (Leach 1958, 147). Hair is alive within witchcraft illustrations both through its mobility and through its emotional impact on the viewer. By seeking to harness the witch and her hair, and spinning them into objects, the artist himself is drawn in by the abject through emotional channels. He is ultimately straying from the object and "lead[ing] [him]self away from meaning" (Kristeva 2002, 230).

### Hans Sebald Beham's Eve: Biblical Woman and Witch

Hans Sebald Beham's Eve (Fig. 2) is shockingly petite. A small white margin called a plate mark separates the print from where it was originally situated. The tone of the engraving is produced through the meticulous system of hatching, lining, dotting, and dashing the metal (Niederman 2017, 264). Beham's technique involved great precision — he had to be sure not to draw these marks too closely together to prevent bleeding and overflow. Overabundance of ink and lines pose real threats to the integrity of the work. Eve, who I interpret as a witch, sits on a tree stump, hunched against the trunk of another, living tree. She holds a sphere in her left hand, perhaps an apple and a biblical reference (Genesis III). The flesh of her body is etched in concentric circles and curves, and her hair emerges from behind her body, pushing out from her head in waves, undone curvilinear forms. A snake grasps the branch above her head, also taking on the unstructured, liberated form of Eve's hair. The form of the witch more closely resembles the natural elements than the village. She is the sole human subject of the work, yet perches at a distance as the abject. The witch's back finds symmetry, a mirrored image, and icon in the curved branch above her head. Adam is notably absent.

Beham's print has lived in various collections, and at different times has been labeled both Eve and The Witch (Koerner 2023). This evolving nomenclature is indicative of the unequivocal relationship between Eve and the witch, the woman's biblical role and her pagan one. Kristeva's theory of abjection corroborates this claim and explains necessarily the discomfort of Eve. Abjection



Fig. 2. Beham Hans Sebald, *Eve/The Witch*, engraving, 1519 (Busch-Reisinger Museum)

assumes and is conflated with biblical works because it is primordial. Abjection is an urge that precedes, and in certain instances, supersedes religious structuring (Kristeva, 242). The womanly form, whether it appears as Eve or a witch, is wildly threatening to the artist and viewer. Eve was a woman who crept close to the male form. She was drawn from Adam's torso and considered a crippled, deformed iteration of him just as the woman's body was considered a disfigured version of the early modern European man's (Koerner 2023). The dissonance between man and woman as binary opposites was solidified in Christian doctrine, but following Kristeva's theory of abjection, our discomfort with Eve as a character springs from something besides her being an "other" to Adam and God. Eve is meant to be a creator: a mother of infants, life, and humanity. Under abjection, what disturbs us most about Eve is her destruction of God's expectations by taking that apple and biting it. God, in this context, can be taken as a substitute for our own human and moral consciousness.

Applied to Beham's Eve/The Witch, each visual element is newly sinister. The tree that supports the woman could be the biblical tree of the knowledge of good and evil. The biblical tree could also have been felled, and still appear in the print as the tree stump under a witch's rear. Perhaps the sphere in the woman's left hand is not an apple, and instead represents a connection to the pagan goddess Fortuna (Byrne 2011, 37). The snake above the woman's head could be read as either Satan in animal form or as a witch's familiar, a small demon companion (Britannica 2016). The temporality and setting of this print are also called into question. After being stripped of her immortality, Eve lived



before the buildings etched into the background could have been built. The woman shown in this print is primordial and witch-like because she surveys a European village. She is a historical figure grounded in an early modern European billage, not in the pre-civilized Eden. She wears no clothes, existing up and away from the reach of society and referencing the primordial universe in her nakedness. Both Hans Baldung Grien and Hans Sebald Beham's women have "blasted" hair, vitalized by a force unknowable to the artist and the viewer.

### Dürer's Witches: Wind-Blasted Women

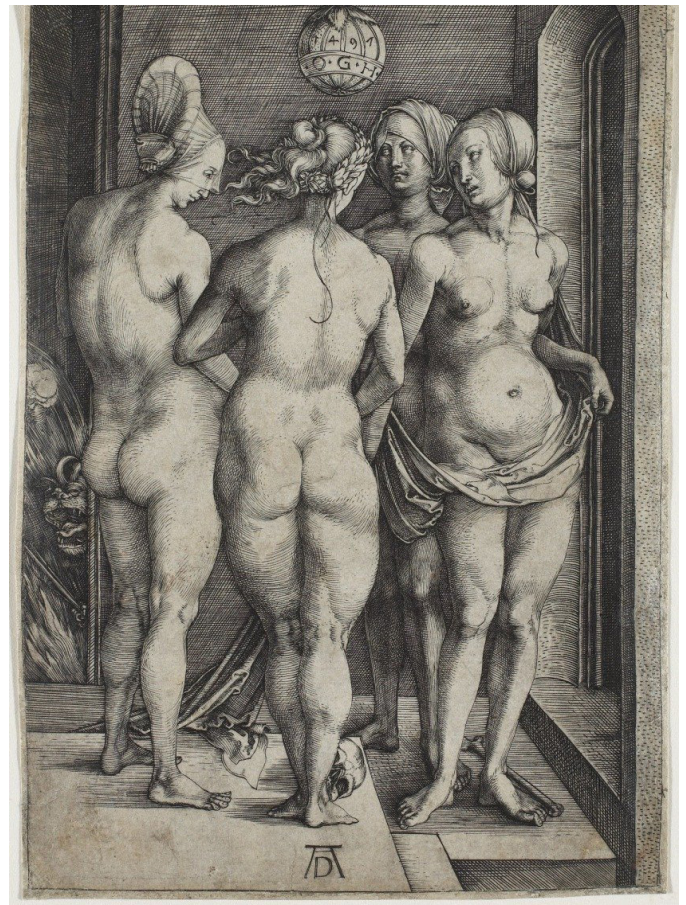
German artist Albrecht Dürer is well known for his depictions of witches, often using the same engraving medium as Hans Sebald Beham. Baldung was a member of Dürer's atelier, and the two artists maintained a lifelong friendship and artistic partnership (Hand 1993, 12-13). Hans Sebald Beham belonged to the generation following Baldung and Dürer, drawing inspiration from the older artists in both style and technique (Stewart 2012, 4). The three men operated within the same emotional community, drawing on shared literature and one another. Dürer, however, carried an outsized influence on the other two artists. Baldung was one of Dürer's proteges, as indicated by a lock of Dürer's hair discovered

in Hans Baldung's estate (Staatliche Kunsthalle Karlsruhe 2023). Beham was accused of plagiarizing Dürer's book on human proportions (Stewart, 4).

Dürer's witch depictions vary in how they treat the female form but are universally dynamic and erupting with movement. *Witch Riding Backwards on a Goat* (Fig. 3) serves as an excellent example of this dynamism. An older witch sits backward on a goat, a cluster of putti forming a circular frame within the rectangular print. Her body differs from the witch of Beham's aforementioned *Eve/The Witch*. This witch is loose and hunched, her flesh and musculature defined and quick to the bone. She directs the viewer towards her crotch with a spindle, a domestic object dramatically incongruous with the wild, outdoor setting of the ritual. Grasping this spindle with a weathered right hand, the witch wears no threaded



**Fig. 3.** Dürer Albrecht, *Witch riding on a Goat*, engraving, 1501-1502 (National Gallery of Art)



**Fig. 4.** Dürer Albrecht, *The Four Witches*, engraving, 1497, (National Gallery of Canada)

clothing. Though the goat and witch seem to move toward the left of the piece, the witch's hair is blasted in the opposite direction, solidifying her magical status. Her hair, of varying chopped lengths, is remarkable as a material and as a symbol. This witch's hair contradicts the custom of her time. In early modern Europe, a girl wore her hair long until late adolescence (Firth, 268). Then, it was tied up into a bun as a sign of maturity and marriageability. Not only is her hair a representative of the witch's status as an "other," but the translation from Dürer's imagination to this print underlines the abject nature of witch hair.

Hair is typically styled as an object in works of art, static with



rare exceptions of movement produced by some external wind that moves universally across the work. Here, the witch's hair is alive and animated. It is moving without reason, and in doing so it defies our expectations and becomes an abject object. Art historian Barbara Baert also connects hair more directly to the abject. Hair is a "dry and aesthetic version" of liquid and more recognizably abject bodily fluids like blood and semen (Baert 2018, 157). Hair is unique because it is simultaneously a part of the physical and aesthetic self while also being abject. Blood and semen are given their abject properties by their private nature; head hair is readily visible. Hair functions as both a private and public symbol. It is an associative medium, gesturing towards notions of gender and power, sex and liberation. Though not shown outwardly in the selected works, body hair also has the additional property of trapping and enhancing the potency of pheromones linked to sexual attraction (Grammer, Fink, and Neave 2005, 135-42). Drawing emphasis to the hair of a witch inevitably draws the artist towards the topic of her sexuality and its allusiveness. The process of binding up hair was traditionally associated with sexual control and maturity.

Dürer's *The Four Witches* (Fig. 4) engraving shows women with this bound hair. The piece immediately invokes the classical iconography of the three graces (Fig. 5). Paragons of beauty, the fourth body is nearly concealed from the viewer save her face and its disinterested expression. She is inaccessible and beyond the reach of the viewer's sight. All four figures come together to ascribe a sense of secrecy and ambiguity to the engraving. These witches are classically beautiful, with rounded flesh and soft features. They are turned from the artist and viewer, though, avoiding the gaze of those who seek to see and understand them. The rightmost figure conceals her genitals with a cloth that flows from her head wrap to drag on the ground in the direction of a monstrous beast in the left corner. All but one woman wears a head covering, indicative of their domestic role and sexual maturity. Face concealed and stance locked in the third position, the central witch wears a partially undone bun. A breeze moves the bun's tail, one unlikely to originate in the women's domestic setting. The unknowable nature of the woman is fortified by the haphazard hairstyle of this central witch. As an indicator of a witch's power, the careful observation of hair reveals the abject strength of the witch in the process of practicing magic. What, then, occurs when hair is removed from our reading of the witch and her power?

### Blasted to Bald: Forced Hair Removal and the Bald Witch

Friedrich von Spee details the witch inquisition and trials in the often-referenced *Cautio Criminalis* (Spee 2003, 148). Most peculiarly, von Spee takes note of forced hair removal during witch trials:

*Before he tortures her, the torturer leads her aside, so that she may not strengthen herself against the pain with some kind of magic charm, he shaves and searches her entire body – even that part by which her sex shows is most impudently searched. Of course to this day nothing has ever been found. . . Once Gaia has been searched and shaved, she is tortured so that she recounts the truth, that is, she simply pronounces herself to be guilty. Whatever else she might say is not the truth, nor can it be.*

The emotional impact of hair removal and its distinct connection with shame weighs heavily on both women and witches. Lucas Cranach the Younger's woodcut print of the *Execution of Four Persons Convicted of Witchcraft* (Fig. 6) demonstrates the fear tactics used in witchcraft trials to induce confessions. The body is different here — it is disjointed, inelegant, and "done in reverse" as a woodcut. As compared to the engraved witches of Beham and Dürer, woodcut emerges as a unique counterpoint to arguments on the witch's power. The negative white space emerges as Cranach applies the diligent and intensive action of scraping and shearing to a surface that will not appear in the print. The viewer's omission or negation is the artist's production or affirmation. The piece's thesis comes about in the places of the print untouched by the artist. Woodcuts pass through the artist's imagination, are translated into their inverse, applied to wood, and then applied to paper. This method is removed from and removes the power of the witch. The convicted witches are angular, not curved. They face the viewer directly and contort their limbs uncomfortably at the



Fig. 5. Unknown, *Les Trois Grâces*, marble, 2nd century A.D., (Musée du Louvre)





**Fig. 6.** Lucas Cranach the Younger, *Execution of Four Persons Convicted of Witchcraft*, woodcut, 1540

top of wooden posts. These are individuals who are not naked as symbolic liberation but as coerced humiliation. Their nakedness is subverted for the viewer and inquisitor.

The convicted witches are bald, presumably having had their hair removed or burnt away as part of their trials. A firm transition from one social state to another is also demarcated here, the “deliberate shaving of the head...has taken on a ritual quality” (Firth 288). Witches lack a clear impetus for their craft because they exist outside the broader society. Perhaps hair removal is an attempt to familiarize the witch, to reign in her abject powers as represented by her hair, and to indoctrinate her into the visual and symbolic culture of mainstream society. This is a futile attempt, for the concept of a witch is already deeply embedded in Christian literature. Applying Kristeva’s theory of abjection more directly, abjection “accompanies all religious structurings” (Kristeva 242). The witch is, again, not an “other” but an abject. The witch and her hair are intimately acquainted with the viewer. Her hair is a public and private symbol, a physical material to be manipulated, harnessed, and removed in lieu of the witch concept. Cranach’s print is disturbing, but not revolting. It is the witch’s inevitable downfall at the hands of social and religious authorities. These four executed individuals are examples of fallen witches, with the artist working as an authority capturing and applauding their demise. Far more disturbing are images of women and witches who lack hair but maintain their abject powers. Francisco de Goya’s images of women, witches, and prostitutes in *Los Caprichos* are notable for their cryptic messaging. In the engraving

*San Fernando ¡Cómo hilan!* (Fig. 7) Goya depicts three prostitutes sitting in a prison cell. Light enters from the left of the etching and falls on the women’s cropped hair. These women were detained, shaved, and made to spin thread to finance the prison system. In the language of the time, “spinning” was a euphemism for prostitution, while the spindle represented a phallus (Fundación Goya en Aragón 2022). The thread also has a fascinating unity with the human hair and women’s agency.

Weaving and thread are easily associated with acts of creation and what Baert characterizes as material emergence from “the liquid darkness of nothingness” (Baert 161). These prostitutes wield



**Fig. 7.** Goya Francisco de, *San Fernando ¡Cómo Hilan!* ink and aquatint, 1794-1797, (Fundación Goya en Aragón)

the same magical powers of creation, reproduction, and sexuality that the witch does, and similarly subvert these abilities. Goya’s juxtaposition of witches and prostitutes is intentional and reflects a general attitude towards women and efforts to reign in their sexuality. Following the ironic theme of *Los Caprichos*, Goya’s spinning prostitutes are practicing their new craft with mischievous eyes, flaunting their spinning and demonstrating the ineffectiveness of the institution that seeks to reform them. Part of this reforming effort reveals itself in forced hair removal, a practice dating back to the emotional community of Baldung, Beham, Cranach, and Dürer and the treatment of convicted witches. In Goya’s work, women and witches retain their sexuality and independence even through the removal of their abject hair that moves without wind.

## Hair as an Abject Object

Hair is above all an individual creation. Hair is a bodily product an individual chooses to grow, nurture and imbue with symbolic meaning. For the witch in art, hair is an explicit sexual metaphor, threatening because it often represents the artist's failed efforts to comprehend and control it. Hans Baldung Grien's witches integrate explicitly into their natural settings with hair as a key vehicle and physical indicator of the process. A witch's hair is established as a malleable representation of her agency and magic. In Hans Sebald Beham's *Eve/The Witch*, a woman demonstrates the blasted hair of a witch while affirming the primordial association between women and the abject through her dual identity as Eve. In either reading of *Eve/The Witch*, the viewer is disturbed principally by the thwarted expectation of the woman's behavior, not by the literal content of her action. Lucas Cranach's bald, convicted witches and Goya's shaved prostitutes offer developing arguments on hair's role as an enhancer or detractor from abjection. Cranach's images present a witch stripped entirely of her power after being recognized and punished for her social and religious indiscretions while Goya presents prostitutes continuing to spin and create their own sexual practices. To Goya's prostitutes, the sex act is not for propagation, a belief abject for an audience of Christians. The prostitute is misusing her sexuality just as the witch does.

These works are visual fictions that do not aim to convey realities in the form of subject and object. Instead, the artist seeks that ambitious abject and the accompanying emotional weight through the strands of a witch's hair. Whether undertaken in engraving, woodcut, or aquatint, this is a process that ultimately endangers the artist himself and reflects the underlying anxiety of his emotional, social, and historical situation. Abjection appears at the time of religion's birth and wcollapse, destined to outlast it and the artist's circumstances (Kristeva, 242). These witch works demonstrate demise, themselves products of witchcraft inquisitions and the seismic shift of the 16th-century Protestant Reformation in Germany and fear of heresy during the Spanish Inquisition (Ledray 2016, 4). Hair, whether blasted, bound, or shaved clean, is indicative of the artist's struggle to imprison, digest, and represent the abject during times of great uncertainty.

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# A Bistable Switch in HIV Disease Outcome for Antibody Treatment Following the Onset of Recurrent Aphthous Oral Ulcers

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Understanding the interplay between the humoral immune response and viral dynamics is critical for developing effective strategies against HIV infection. While verbal reasoning falls short due to the complexity of these interactions, mathematical models offer insight into the dynamics of virus-antibody interactions. This study builds upon previous work conducted by Ciupe et al. 2018 by integrating experimental data with mathematical modeling to investigate the impact of antibody concentration and timing on HIV disease outcomes by exploring the relationship between viral inoculum size and disease persistence in three scenarios of SIV infection. Our findings reveal bistable switches between viral clearance and persistence between  $I(t) = 1.04 \times 10^{12}$  and  $I(t) = 1.05 \times 10^{12}$ , where  $I(t)$  represents the infusion rate of antibodies, measured in units of antibodies per day. Additionally, this paper investigates the effect of initial inoculum size on viral clearance, observing clearance when  $I(t) = 1.04 \times 10^{12}$  and the initial viral inoculum size is  $\leq 18.6/300$  vRNA copies per ml. Although these findings underscore the significance of antibody-mediated responses in controlling HIV infection and suggest avenues for improving treatment strategies, further research into the optimal duration and timing of antibody treatment is essential for enhancing treatment efficacy and refining predictive models.

## Background

When challenged with foreign macromolecules, the humoral immune system produces an efficient response of antibody production (Skerra, 2003). However, the human immunodeficiency virus (HIV) evades CD4 T helper cells, the central component of generating neutralizing antibodies that orchestrate specific responses to a wide range of viruses (Wodarz & Nowak, 2002). When understanding the dynamic between HIV pathogenesis and immune system response, verbal reasoning proves insufficient because of the inherent complexity of the interactions involved. In particular, verbal reasoning may overlook subtle nuances, intricate feedback loops, and nonlinear relationships that are fundamental to comprehending the progression of HIV infection and the host immune response. Thus, mathematical models have proven useful in understanding how virus-antibody dynamics alter the course of HIV infection by capturing a set of assumptions and deducing logical conclusions through altering key parameters.

Many studies have utilized chimeric simian-human immunodeficiency virus (SHIV) as a comparable animal model for HIV pathogenesis (Ciupe et al., 2018). It has been found that broadly neutralizing monoclonal antibodies (bnMAbs) have exceptional in vitro potency against a high-dosage mucosal HIV challenge, but the strength of protection in both high-dose and low-dose challenges is dependent upon the ratio between concentration of bnMAbs and size of the viral challenge (Moldt et al., 2012; Hessel et al., 2009). In simpler terms, the effectiveness of vaccines relies heavily on the balance between the amount and strength of antibodies produced by the immune system and the size of the virus challenge; if there are not enough strong antibodies to fight off a large amount of virus, the vaccine may not be as effective. Therefore, understanding the concentration and avidity of antibodies in relation to the size of viral inoculum proves important in developing vaccines that offer robust protection against HIV.

## Introduction

In Ciupe et al., 2018, a mathematical model incorporating the interaction between virus, recipient and donor antibody, and antibody-virus immune complexes was developed. Previous studies have demonstrated that 20 viral RNA (vRNA) copies from plasma obtained during the ramp-up stage of simian immunodeficiency virus (SIV) infection (7 days after inoculation) are required for establishing persistent infection in recipient rhesus macaques. Contrastingly, a substantially higher count of 1500 vRNA copies from plasma collected during the set-point stage (10-16 weeks after peak viremia) of infection is necessary for persistence (Ma et al., 2009). To test the hypothesis that the ramp-up plasma contains only free virus while the set-point plasma contains antibody-virus immune complexes that can still infect but at a lower infectivity rate, Ciupe et al., 2018 fits viral load data onto a developed mathematical model. This model estimates the long-run concentration of free virus, free donor and recipient antibodies, and donor and recipient antibody-viral immune complexes. The experimental protocol involved infecting rhesus macaques with SIV, collecting plasma at different infection stages, titrating the vRNA copies from each sample, and then using the plasma to infect SIV-naïve rhesus macaques intravenously. Notably, while no donor antibodies were detected in ramp-up stage plasma, they were present in set-point stage plasma, suggesting a potential role of antibody-virus complexes in infection dynamics.

To predict the relationship between viral inoculum size and SIV disease outcome, Ciupe et al., 2018 develops a mathematical model consisting of seven differential equations describing the rate of change of uninfected CD4 T cells, infected CD4 T cells, free virus, recipient antibody concentration, donor antibody concentration, recipient antibody-virus complex concentration, and donor antibody-virus complex concentration. After fitting data to estimate model parameters, Ciupe et al., 2018 predicts the minimum virus inoculum to establish disease persistence in



three different scenarios of infection:

1. In the first scenario, the recipient animal is infected with donor plasma containing SIV virions from the ramp-up stage of infection; a bistable switch between viral clearance and persistence was found at an initial free virus concentration of 17.5/300 vRNA copies per ml.
2. In the second scenario, the recipient animal is infected with donor plasma containing SIV virions from the set-point stage of infection; a bistable switch between viral clearance and persistence was found at an initial free virus concentration of 42/300 vRNA copies per ml and a ratio of 7.8 between initial donor antibody-virus complexes and free virus.
3. To address the effect of antibodies in changing disease outcome, in the third scenario, the recipient animal is infected with donor plasma containing SIV virions from the ramp-up stage of infection with heat-inactivated antibodies from the set-point stage of infection; a minimum of  $7.4 \times 10^9$  donor antibody molecules per ml are needed for viral clearance.

Variables	Description	Initial values
$T$	Target cells (cells $\text{ml}^{-1}$ )	$T(0) = 10^6$
$I$	Infected cells (cells $\text{ml}^{-1}$ )	$I(0) = 0$
$V$	Free virus (virion $\text{ml}^{-1}$ )	$V(0)$ varies
$A_D$	Donor antibody (molecules $\text{ml}^{-1}$ )	$A_D(0)$ varies
$A_R$	Recipient antibody (molecules $\text{ml}^{-1}$ )	$A_H(0) = 3.5 \times 10^8$
$X_D$	Donor immune complexes (complexes $\text{ml}^{-1}$ )	$H_D(0)$ varies
$X_R$	Recipient immune complexes (complexes $\text{ml}^{-1}$ )	$H_X(0) = 0$

Parameters	Description	Values
$s$	CD4 T cell production rate (cells $\text{ml}^{-1}\text{day}^{-1}$ )	$10^4$
$d$	Target CD4 T cells death rate ( $\text{day}^{-1}$ )	0.01
$\beta$	Free virus infectivity rate ( $\text{ml day-virion}^{-1}$ )	estimated
$\beta_1$	Immune complexes infectivity rate ( $\text{ml day-virion}^{-1}$ )	$10^{-8}$
$\delta$	Infected cells death rate ( $\text{day}^{-1}$ )	0.39
$N$	Burst size (virion)	2000
$c$	Virus clearance rate ( $\text{day}^{-1}$ )	23
$\alpha$	Antigen dependent expansion of antibodies ( $\text{ml day-virion}^{-1}$ )	$10^{-9}$
$r$	Antibody division rate ( $\text{day}^{-1}$ )	estimated
$d_A$	Antibody degradation rate ( $\text{day}^{-1}$ )	0.07
$K$	Antibody carrying capacity (molecules $\text{ml}^{-1}$ )	$5 \times 10^{13}$
$k_p$	Binding rate ( $\text{ml day-virion}^{-1}$ )	$1.6 \times 10^{-11}$
$k_m$	Unbinding rate ( $\text{day}^{-1}$ )	100
$c_{AV}$	Immune complexes clearance rate (complexes $\text{day}^{-1}$ )	$10^6$
$M$	Immune complexes where clearance is half maximal ( $\text{ml}^{-1}$ )	500

**Chart 1.** (Ciupe et al., 2018) Parameter values and initial conditions used in the model of recipient-virus interaction. Variables are constantly changing based on the given situation while parameters remain fixed.

A key limitation to this study, however, is that while Ciupe et al., 2018 identifies the minimum number of antibody molecules needed to establish viral clearance at the time of infection, it is not realistic to assume that an animal would receive antibody treatment at the exact time of infection. Therefore, in this paper, I will not only attempt to replicate the mathematical model of recipient-virus infection in Ciupe et al., 2018, but I will also explore how changing the time at which antibodies are administered to the recipient animal will affect disease outcome and the concentration of donor antibodies needed to induce viral clearance.

## Explanation of Differential Equations

Ciupe et al., 2018 uses the following variables and initial conditions stated in **Chart 1**.

When the recipient animal is challenged with donor plasma, Ciupe et al., 2018 assumes that the donor's antibodies,  $A_D$ , and antibody-virus immune complexes,  $X_D$ , are transferred into the recipient. It is also assumed that  $X_D$  can still infect the recipient at a rate  $\beta_1 < \beta$ , a *de novo* antibody response that occurs in recipient animals, and that the recipient antibodies proceed independent of antigens at a maximum proliferation rate  $r$  and a maximum capacity of  $K$ . In simpler terms, the rate at which  $X_D$  can cause infection in the recipient (represented by  $\beta_1$ ) is assumed to be less than the initial infection rate denoted by  $\beta$ .

As a result, Ciupe et al., 2018 obtains the following model:

$$\begin{aligned}
 \frac{dT}{dt} &= s - dT - \beta TV - \beta_1 T(X_D + X_R), \\
 \frac{dI}{dt} &= \beta TV + \beta_1 T(X_D + X_R) - \delta I, \\
 \frac{dV}{dt} &= N\delta I - cV - k_p(A_R + A_D)V + k_m(X_R + X_D), \\
 \frac{dA_R}{dt} &= \alpha A_R V + rA_R \left(1 - \frac{A_R}{K}\right) - k_p A_R V + k_m X_R, \\
 \frac{dX_R}{dt} &= k_p A_R V - k_m X_R - c_{AV} \frac{X_R}{X_R + M}, \\
 \frac{dA_D}{dt} &= -d_A A_D - k_p A_D V + k_m X_D, \\
 \frac{dX_D}{dt} &= k_p A_D V - k_m X_D - c_{AV} \frac{X_D}{X_D + M},
 \end{aligned}$$

**Model 1.** (Ciupe et al., 2018) Model of Recipient-Virus Interaction; Listed as (4) in the article. This model explores the formation of virus-antibody immune complexes and their implications in transmission and defense. It demonstrates a bistable switch mechanism, indicating two distinct states: clearance and persistence.

We are most interested in the differential equations for  $A_R$ ,  $X_R$ ,  $A_D$ , and  $X_D$ , since the other equations build upon a basic Simian Immunodeficiency Virus (SIV) model. In analyzing the differential equations, notice that the assumption that the recipient antibodies reach a carrying capacity  $K$  result in the logistic term  $rA_R(1 - \frac{A_R}{K})$  within  $\frac{dA_R}{dt}$ , therefore indicating that the recipient antibodies cannot reproduce infinitely and thus disease persistence will possibly occur due to this carrying capacity. In addition, note that  $\frac{dX_R}{dt}$  and  $\frac{dX_D}{dt}$  both have terms that include quotients, indicating that these are clearance terms. They describe the change in the rate of the clearance of antibody-virus immune complexes. The variable  $c_{AV}$  sets the maximum possible rate of clearance of antibody-virus immune complexes, so the clearance terms vary between 0 and  $c_{AV}$ . When  $X_D = M$  or  $X_R = M$ , the clearance term is  $c_{AV}/2$ , which

is half of the maximum clearance rate. Theoretically, large  $c_{AV}$  is therefore favorable, as it will allow  $X_D$  and  $X_R$  to decrease faster, thus allowing  $V$  to decrease faster.

Furthermore, it is important to further evaluate the relationship between  $\frac{dA_D(t)}{dt}$ ,  $\frac{dX_D(t)}{dt}$  and  $\frac{dV(t)}{dt}$ . Initially, when Ciupe et al., 2018 sets  $A_D(0) = 7.4 \times 10^9$ ,  $X_D$  experiences an initial surge. However, due to the conditions where  $c_{AV} = 10^6$ ,  $k_m = 100 \gg k_p$ , and  $A_D$  does not drastically change as  $t \rightarrow \infty$ ,  $X_D$  gradually declines over time. Similarly,  $X_R$  follows a trajectory of initial increase followed by a decline over time, with  $A_R(0) = 3.5 \times 10^8$  and  $X_D$  remaining relatively stable over time. As both  $X_D$  and  $X_R$  decrease,  $V$ , consequently, diminishes over time.

A critical aspect lies in the dynamics of  $A_D$ , which decreases due to an association rate  $k_p$  between virus and  $A_D$  forming  $X_D$ , while simultaneously increasing due to a dissociation rate  $k_m$  of  $X_D$  into  $V$  and  $A_D$ . Notably,  $k_m$  is much larger than  $k_p$ , leading to rapid dissociation of donor antibody-virus immune complexes compared to their formation. Therefore, a drastic increase in  $A_D$  would lead to a corresponding surge in  $X_D$ , subsequently elevating  $V$  significantly, owing to the high dissociation rate. This relationship is important when I try to manipulate the model to include a term for a drastic increase in  $A_D$  later in this paper.

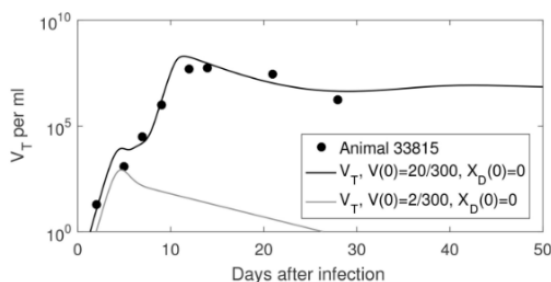
### Replicating the Model of Recipient-Virus Interaction

Aligning with the work of Ciupe et al., 2018 is necessary to validate my model. Through data fitting, Ciupe et al., 2018 estimates  $\beta = 1.34 \times 10^{-7}$  and  $r = 1.95$  for Animal 33815, a recipient animal (rhesus macaques) infected with donor plasma containing SIV virus from the ramp-up stage of infection.

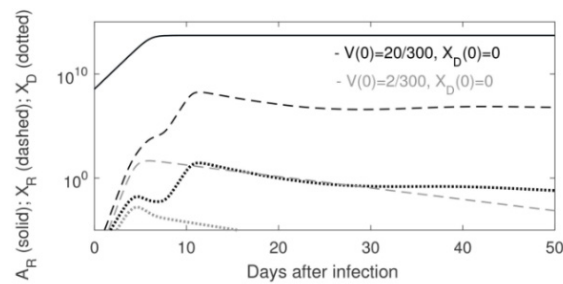
The parameter  $\beta$  represents the rate at which susceptible individuals become infected upon contact with infectious individuals, reflecting the infectiousness of the virus. In the context of the model, a higher value of  $\beta$  indicates a greater likelihood of transmission from infected to susceptible individuals.

On the other hand, the parameter  $r$  represents the maximum proliferation rate of antibodies in the recipient animal's immune response. In the model, a higher value of  $r$  signifies a faster rate of antibody production by the immune system in response to the viral infection. This parameter is essential for understanding the strength and effectiveness of the immune response against the virus.

Thus, the following graphs were obtained (note that the function of total virus with respect to time  $V_T(t) = V(t) + X_R(t) + X_D(t)$ ):

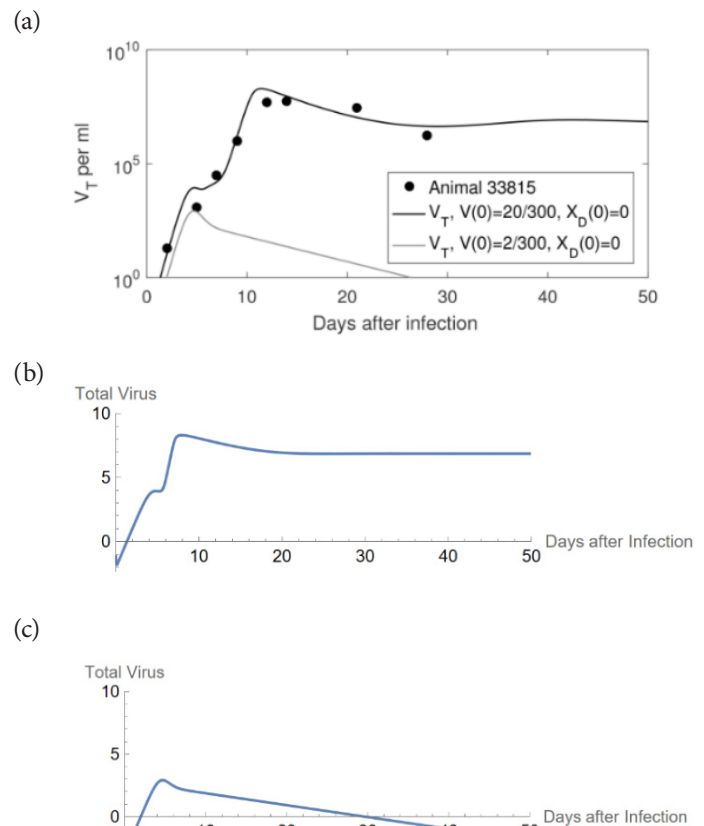


**Fig 1.** (Ciupe et al., 2018) The change in  $V_T$  (total virus) over time given by **Model 1** for Animal 33815, which was infected by donor plasma containing ramp-up stage virions. At  $V(0) = 20/300$ , there is persistence of infection; at  $V(0) = 2/300$ , there is clearance of infection.



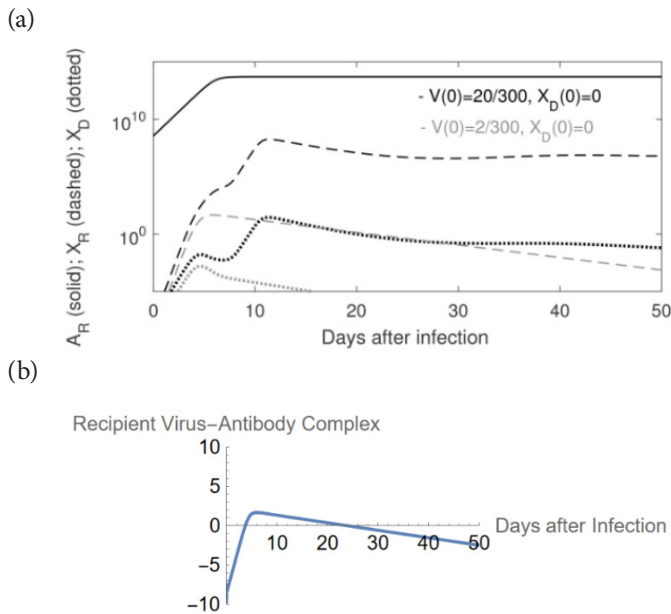
**Fig 2.** (Ciupe et al., 2018) The change in free antibody (solid black line),  $X_D$  (dotted line), and  $X_R$  (dashed line) over time given by **Model 1** for Animal 33815, which was infected by donor plasma containing ramp-up stage virions. The gray lines represent the situation with condition  $V(0) = 2/300$  vRNA copies per ml and the black lines represent the situation with condition  $V(0) = 20/300$  vRNA copies per ml. For  $V(0) = 2/300$  vRNA copies per ml,  $X_R$  increases slightly above 0 and then proceeds back to 0; this is logical because the disease outcome is clearance, so while there is an initial response of recipient antibodies, the concentration of recipient antibody-virus complexes will eventually reach 0 as the virus is cleared.

**Figures 1 and 2** show that at  $V(0) = 20/300$ , the disease and the presence of both donor and recipient antibody-virus complexes persist, while at  $V(0) = 2/300$ , the disease and the presence of both donor and recipient antibody-virus complexes are eliminated (Ciupe et al., 2018). The higher initial viral load (20/300) represents a more severe infection, while a lower initial viral load (2/300) represents a milder infection. Using the software *Wolfram Mathematica* and plugging in the model's differential equations, initial conditions, and estimated parameters for this specific case, I obtained similar graphs:



**Fig. 3.** Generated by *Wolfram Mathematica*. Analogous to the change in  $V_T$  over time given by **Model 1** for Animal 33815, which was infected by donor plasma containing ramp-up stage virions. The vertical axis is on a logarithmic scale.

(a) Duplication of **Figure 1**, the change in  $V_T$  (total virus) over time given by **Model 1** for Animal 33815, which was infected by donor plasma containing ramp-up stage virions. (b)  $V(0) = 20/300$ , comparable to the black line in **Figure 3a**. (c)  $V(0) = 2/300$ , comparable to the gray line in **Figure 3a**.

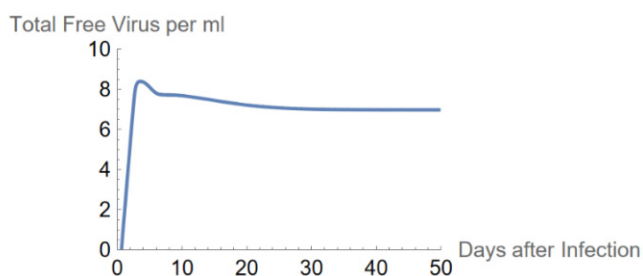


**Fig. 4.** Generated by Wolfram Mathematica.

(a) Duplication of **Figure 2**, the change in free antibody (solid black line),  $X_D$  (dotted line), and  $X_R$  (dashed line) over time given by **Model 1** for Animal 33815, which was infected by donor plasma containing ramp-up stage virions. (b) Analogous to the change in  $X_R$  over time given by **Model 1** for Animal 33815, which was infected by donor plasma containing ramp-up stage virions, for  $V(0) = 2/300$ . The vertical axis is on a logarithmic scale. This is comparable to the dashed gray line in **Figure 4a**.

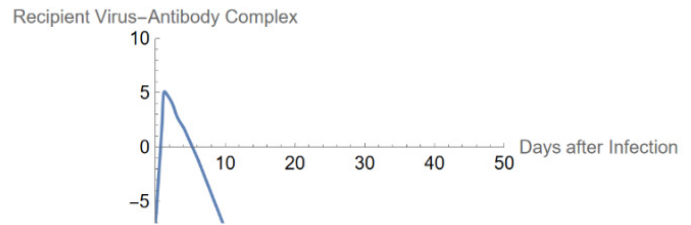
### Verifying the Model of Recipient-Virus Interaction

To ensure that the generated model produces replicable outcomes, we reduce  $c$ , the virus clearance rate, from 23 to 2, while keeping  $V(0) = 2/300$  and all other initial conditions the same. We get **Figure 5**, which indicates persistence of infection. This is logical, as dramatically decreasing the rate at which virus is cleared will result in persistence. It is important to note, however, that while Ciupe et al., 2018 uses  $c = 23$ ,  $c$  can range anywhere between 9 and 36 (Ramratnam et al., 1999).



**Fig. 5.** Generated by Wolfram Mathematica. The change in  $V_T$  over time given by **Model 1** for Animal 33815, which was infected by donor plasma containing ramp-up stage virions, for  $V(0) = 2/300$  and  $c = 2$ . This is a contrast to **Figure 3b**, where  $c = 23$  resulted in virus clearance while keeping all other initial conditions the same. The vertical axis is on a logarithmic scale.

Let  $V(0) = 20/300$  and  $c = 23$ , while keeping all other initial conditions the same. Then, change  $\delta = 0.39$  to  $\delta = 3.9$  to amplify the death rate of infected cells by ten-fold. We get **Figure 6**, which indicates that the concentration of recipient antibody-virus complexes will decrease to 0 over time, therefore indicating clearance of infection. This is logical, as dramatically increasing the rate at which infected cells die will result in clearance.



**Fig. 6.** Generated by Wolfram Mathematica. The change in  $X_R$  over time given by **Model 1** for Animal 33815, which was infected by donor plasma containing ramp-up stage virions, for  $V(0) = 20/300$  and  $\delta = 3.9$ . This is a contrast to the dashed black line in **Figure 2**, where  $\delta = .39$  resulted in the persistence of  $X_R$  while keeping all other initial conditions the same. The vertical axis is on a logarithmic scale.

### HIV Antibody Treatment from Symptom of Recurrent Aphthous Oral Ulcers

While Ciupe et al., 2018 finds that a minimum of  $7.4 \times 10^9$  donor antibody molecules per ml are needed for viral clearance at time  $t = 0$ , it is not reasonable to assume that individuals are treated with antibody treatment at the exact time that they become infected with HIV. In estimating the approximate amount of time between virus contraction and antibody treatment, it is important to determine the specific symptoms that indicate a potential HIV infection and the time elapsed between infection and embodiment of symptoms. Hecht et al., 2002 found that weight loss and oral ulcers were the most specific symptoms for HIV infection, and the best independent predictors for HIV infection were fever and skin rash.

#### Developing an Injection Term for $\frac{dA_p(t)}{dt}$

Due to the relatively high prevalence of oral ulcers, affecting approximately 50% of patients with HIV at some point during the progression of their disease, recurrent aphthous ulcers remain a valuable diagnostic indicator. While the figure may seem modest, it's important to note that even though not all patients manifest this symptom, its occurrence spans various stages of HIV progression, from acute primary infection to advanced disease (Weinert, 1996). This persistence across disease stages underscores its significance in diagnosis despite its seemingly moderate prevalence. The most important oral indicator for HIV diagnosis is when the aphthous ulcer develops on nonkeratinized mucosa; however, it is important to note that other types of ulcers can also occur on non-keratinized mucosa, so an aphthous ulcer must be distinguished by treatment response (MacPhail et al., 1992). Most HIV-infected patients acquire minor aphthous ulcers, which last up to 2 weeks (MacPhail et al., 1992). Therefore, since these aphthous ulcers develop during the acute stage of HIV infection (2-4 weeks after HIV exposure) and last for up to 2 weeks, and recurrent aphthous ulcers extend the experience of oral ulcers through the formation of new aphthous ulcers when old ones heal, we can predict that the earliest indication of potential HIV infection is when aphthous



ulcers last for more than 4 weeks. Assuming a patient receives antibody treatment on the fourth week after HIV exposure, we can insert the same initial conditions that Ciupe et al., 2018 uses for recipient rhesus macaques infected with donor plasma containing SIV virions from the ramp-up stage of infection with heat-inactivated antibodies from the set-point stage of infection, except with  $gA_D(0) = 0$  and  $A_D(28) = I(t)$ , where  $I(t)$  represents the infusion rate of antibodies, measured in units of antibodies per day, and is varied. Therefore, we can manipulate the differential equation for donor antibodies to include an  $I(t)$  term, where  $I(t)$  is an exponential function:

$$\frac{dA_D(t)}{dt} = -d_A A_D - k_p A_D V + k_m X_D + I(t)$$

$$I(t) = \frac{10}{\sqrt{\pi}} e^{-10(t-28)^2}$$

I generated  $I(t)$  as a smooth rather than a discontinuous function to better complement the *Wolfram Mathematica* software, which has a difficult time interpreting a large discontinuous jump of  $\frac{dA_D(t)}{dt}$ . The reason why I used  $\frac{10}{\sqrt{\pi}} e^{-10(t-28)^2}$  is because its integral over the line is exactly 1. Thus, the injection  $I(t)$  parameter is the exact amount of increase that the infusion is delivering.

### Modifying the Model of Recipient-Virus Interaction

In addition, I need to modify **Model 1** developed by Ciupe et al., 2018 in order to account for a sudden drastic increase in  $A_D$ . Theoretically, in **Model 1**,  $X_D$  will increase if  $A_D$  increases. As a result, because  $V_T$  depends on  $X_D$ ,  $V_T$  also increases when  $A_D$  increases. Since Ciupe et al., 2018 begins with an initial condition above 0 and does not add an injection term like the one I propose,  $X_D$  and  $V_T$  do not experience a sudden drastic increase as  $t \rightarrow \infty$ . However, if I keep **Model 1** as it is,  $I(t)$  will lead to an extremely large and sudden increase in  $X_D$ , which will ultimately lead to an increase in  $V_T$  as  $t \rightarrow \infty$ , since  $k_m \gg k_p$ ; however, this is not biologically reasonable as adding a large amount of donor antibodies should not lead to an even greater increase in total virus as  $t \rightarrow \infty$ . Therefore, because **Model 1** developed by Ciupe et al., 2018 may not be applicable to a situation in which there is an injection term – since  $\frac{dV(t)}{dt}$  is designed to interpret a fairly small value of  $\frac{dA_D(t)}{dt}$  and  $\frac{dX_D(t)}{dt}$  (a small change in the rate of change of  $A_D(t)$  and  $X_D(t)$  in comparison to the large change in rate that  $A_D(t)$  and  $X_D(t)$  will experience from an injection term) – I will modify **Model 1** to prevent  $I(t)$  from unrealistically changing the virus outcome. The new model is as follows:

$$\frac{dV(t)}{dt} = N\delta I - cV - k_p(A_R + A_D)V + k_m X_R$$

$$\frac{dX_R(t)}{dt} = k_p A_R V - k_m X_R - c_{AV} \frac{X_R}{X_R + M}$$

$$\frac{dA_D(t)}{dt} = -d_A A_D - k_p A_D V + \frac{10}{\sqrt{\pi}} e^{-10(t-28)^2}$$

$$V_T = X_R + A_D$$

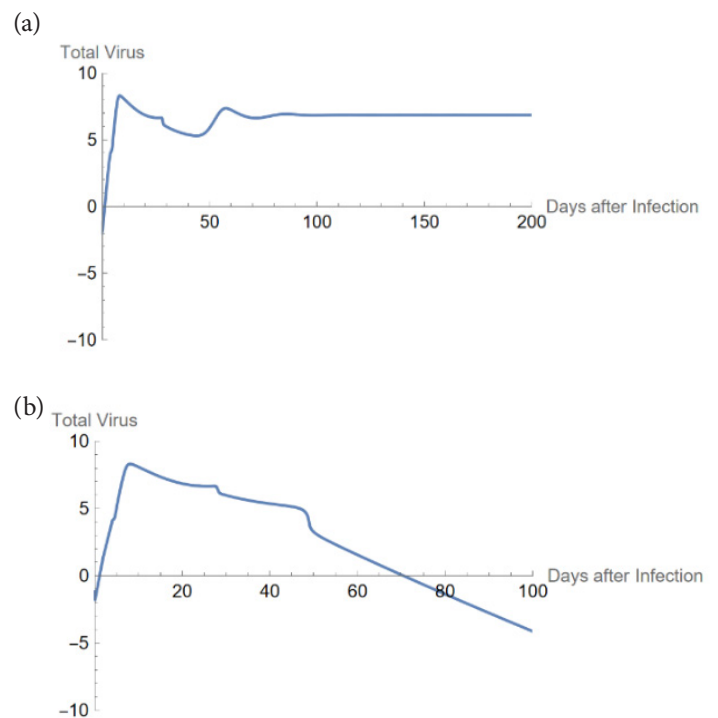
**Model 2.** Modified version of the Recipient-Virus Interaction Model created by Ciupe et al., 2018. It incorporates an injection term,  $I(t)$ , representing the infusion rate of antibodies over time, aiming to prevent unrealistic increases in the virus population. By integrating additional recipient antibodies into the system, the model ensures a more biologically plausible representation of HIV dynamics post-treatment.

I will not focus on  $\frac{dT(t)}{dt}$  and  $\frac{dI(t)}{dt}$  because they are not as relevant to this expansion as the other differential equations since

the emphasis lies on the impact of antibody infusion ( $I(t)$ ) on the virus population and its interactions with recipient antibodies ( $A_R$ ) and donor antibodies ( $A_D$ ). Notice that I completely removed  $\frac{dX_D(t)}{dt}$  and  $X_D$  from **Model 1** because after a patient is treated with an antibody injection, we can assume that these antibodies represent an input of extra recipient antibodies,  $A_R$ , so rather than forming their own antibody-virus immune complexes,  $X_D$ , they become incorporated with the already-present  $A_R$  to form  $X_R$ . This assumption will prevent the model from displaying a biologically unreasonable output from the sudden and large increase in  $A_D$  from the  $I(t)$  term.

### Results

Using the baseline parameters from Ciupe et al., 2018, except with the adjustment of  $A_D(0) = 0$  and  $A_D(28) = I(t)$ , a bistable switch between persistent and cleared virus populations occurs within the range of  $1.04 \times 10^{12}$  to  $1.05 \times 10^{12}$  for  $I(t)$ . **Figure 7** illustrates the corresponding variations in  $V_T$  for different values of  $I(t)$ .



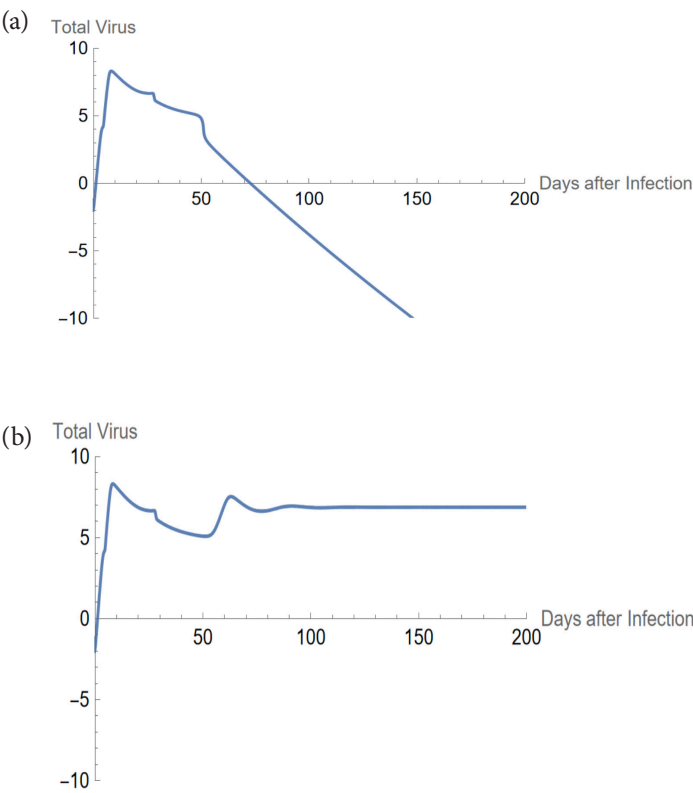
**Fig. 7.** Generated by *Wolfram Mathematica*. The change in  $V_T$  over time for **Model 2**, with  $A_D(0) = 0$ . The vertical axis is on a logarithmic scale.

(a)  $I(t) = 1.04 \times 10^{12}$  (b)  $I(t) = 1.05 \times 10^{12}$

Therefore, **Figure 7a** and **7b** show that there are two different stable equilibrium states that the system can achieve when donor antibodies are injected at  $t = 28$  days. When  $I(t) = 1.04 \times 10^{12}$ , the stable equilibria that the system approaches is  $V_T = 8.5 \times 10^6$ , or viral persistence. When  $I(t) \geq 1.05 \times 10^{12}$ , the system approaches  $V_T = 0$ , or viral clearance, at approximately  $t = 70$  days.

While viral persistence occurs when  $V(0) = 20/300$  and  $I(t) = 1.04 \times 10^{12}$ , manipulating the value of  $V(0)$  will allow investigation of whether changing the initial concentration of free virus will also confer viral clearance. As seen in **Figure 8**, viral clearance occurred for  $I(t) = 1.04 \times 10^{12}$  when  $V(0) \leq 18.6/300$ :



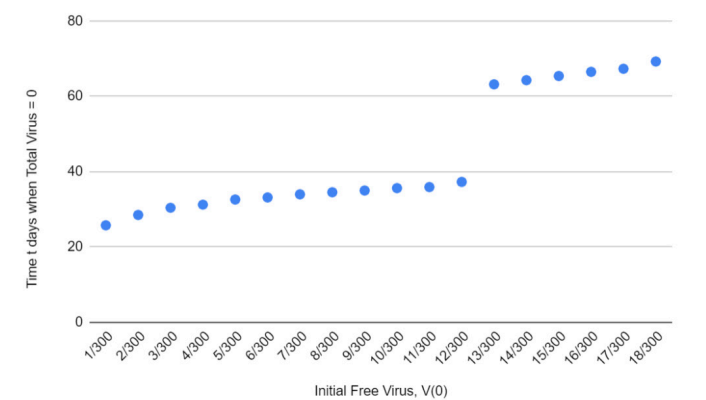


**Fig. 8.** Generated by Wolfram Mathematica. The change in  $V_T$  over time for **Model 2**, with  $A_D(0) = 0$  and  $I(t) = 1.04 \times 10^{12}$ . The vertical axis is on a logarithmic scale. (a)  $V(0) = 18.6/300$  (b)  $V(0) = 18.7/300$

Initial Free Virus, $V(0)$	Time $t$ days when Total Virus = 0
1/300	25.73
2/300	28.48
3/300	30.41
4/300	31.24
5/300	32.62
6/300	33.17
7/300	34.00
8/300	34.55
9/300	35.01
10/300	35.65
11/300	35.93
12/300	37.30
13/300	63.22
14/300	64.32
15/300	65.43
16/300	66.53
17/300	67.35
18/300	69.28

**Table 1.** The values of  $t$  collected when  $V_T = 0$  for  $1/300 \leq V(0) \leq 18/300$  using the “Get Coordinates” feature on Wolfram Mathematica. As  $V(0)$  increases, the time  $t$  days when Total Virus  $V_T = 0$  also increases.

In addition, I collected the value of  $t$  when  $V_T = 0$  for  $1/300 \leq V(0) \leq 18/300$  in order to investigate how changing the initial concentration of free virus can affect when the patient will experience full recovery. I obtain **Table 1** and **Figure 9**.

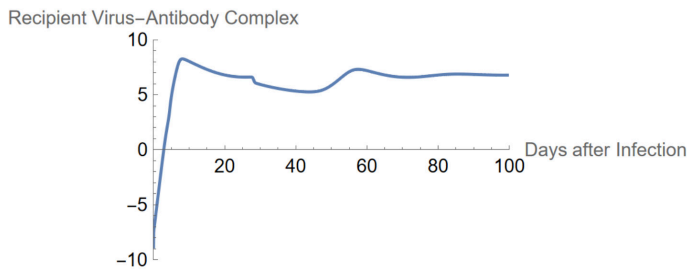


**Fig. 9.** The correlation between the time at which  $V_T = 0$  and an integer value of  $V(0)$  when virus clearance occurs for  $I(t) = 1.04 \times 10^{12}$ . For  $1/300 \leq V(0) \leq 12/300$ , there is a positive correlation between  $V(0)$  and the time at which  $V_T = 0$ , and this positive correlation seems to occur at a decreasing, positive exponential rate.

Discussion

Ciupre et al., 2018 found that a concentration of  $7.4 \times 10^9$  donor antibodies are needed at time  $t = 0$  in order to achieve viral clearance for an animal with  $V(0) = 20/300$ ,  $\beta = 1.46 \times 10^{-7} \text{ ml day} - \text{virion}^{-1}$ , and  $r = 2.14 \text{ day}^{-1}$ . However, rather than simulating a situation in which the animal is treated with the antibody treatment at the exact time of infection, I propose a more realistic situation in which the recipient animal is infected by the HIV virus with  $A_D(0) = 0$ , but then the animal receives antibody treatment on the 28th day after infection, a reasonable estimate for the earliest indication of potential HIV infection when tracking the symptom of recurrent aphthous oral ulcers. I find that an injection of  $1.05 \times 10^{12}$  donor antibodies at 28 days confers viral clearance. More specifically, as seen in **Figure 7**, I predict a bistable switch between viral persistence and viral clearance exists between  $I(t) = 1.04 \times 10^{12}$  and  $I(t) = 1.05 \times 10^{12}$ . The bistable switch separates very different outcomes for similar initial conditions. For example, if  $I(t) = 1.04 \times 10^{12}$ , the system approaches a stable equilibrium of  $V_T = 8.5 \times 10^6$ , or viral persistence. On the other hand, if  $I(t) = 1.05 \times 10^{12}$ , the system approaches a stable equilibrium of  $V_T = 0$ , or viral clearance. If antibody treatment is given at  $t = 28$  rather than  $t = 0$ , we can predict that more antibodies are needed to confer viral clearance; this prediction proves true, as  $1.05 \times 10^{12} > 7.4 \times 10^9$ , the value of  $A_D(0)$  in Ciupre et al., 2018.

It is worth investigating why the patient experiences an overall decrease and then increase in total virus before experiencing viral persistence in **Figure 7**. When the patient receives treatment on Day 28, we observe a sharper decrease in  $V_T$ , which is biologically reasonable because more antibodies means more defense against the virus. However, at approximately Day 50, the patient experiences an increase in  $V_T$  before  $V_T$  approaches an equilibrium of  $8.5 \times 10^6$ . This increase is due to the increase in  $X_R$  at approximately  $t = 50$  days (**Figure 10**), since  $V$  can be generated through the dissociation of  $X_R$  and  $V_T = V + X_R$ , as seen in **Model 2**.



**Fig. 10.** Generated by Wolfram Mathematica. The change in  $X_R$  over time for **Model 2** with  $A_D(0) = 0$  and  $I(t) = 1.04 \times 10^{12}$ . The vertical axis is on a logarithmic scale.

While the biological cause for the increase in  $X_R$  at approximately  $t = 50$  days is not precisely known, it can be inferred that due to insufficient levels of  $I(t)$ , the patient initially underwent damped oscillatory behavior in total virus levels after 28 days before stabilizing into a more persistent equilibrium.

Furthermore, while viral persistence occurs for  $I(t) = 1.04 \times 10^{12}$  when  $V(0) = 20/300$ , I investigate if changing the initial concentration of free virus while maintaining  $I(t) = 1.04 \times 10^{12}$  can result in viral clearance. As seen in **Figure 8**, I find that a bistable switch between viral clearance and persistence exists between  $V(0) = 18.6/300$  and  $V(0) = 18.7/300$ ; I observed viral clearance for  $I(t) = 1.04 \times 10^{12}$  when  $V(0) \leq 18.6/300$ . Consequently, as seen in **Table 1** and **Figure 9**, I find that when viral clearance is observed, changing the value of  $V(0)$  changes the time at which the patient experiences full viral recovery. For  $1/300 \leq V(0) \leq 12/300$ , there is a positive correlation between  $V(0)$  and the time at which  $V_T = 0$ , and this positive correlation seems to occur at a decreasing, positive exponential rate (**Fig. 9**); therefore, changing the concentration of  $V(0)$  at lower concentrations has more impact on the time at which the patient achieves full recovery than changing the concentration of  $V(0)$  at higher concentrations. However, between  $V(0) = 12/200$  and  $V(0) = 13/300$ , there is a much larger increase in the time at which the patient achieves full recovery; as seen in **Table 1**, at  $V(0) = 12/300$ , the patient achieves full recovery at 37.30 days, but at  $V(0) = 13/300$ , the patient achieves full recovery at 63.22 days. Between  $V(0) = 13/300$  and  $V(0) = 20/300$ , the correlation between  $V(0)$  and the time at which  $V_T = 0$  increases gradually as before.

Overall, administering antibodies at 28 days post-infection can still lead to viral clearance, albeit requiring a higher concentration of antibodies compared to immediate treatment. A bistable switch phenomenon, indicating a threshold effect between viral persistence and clearance, exists between  $I(t) = 1.04 \times 10^{12}$  and  $I(t) = 1.05 \times 10^{12}$ . Additionally, altering the initial virus concentration affects the time to achieve viral clearance, with lower concentrations exhibiting a more pronounced impact on recovery time. These findings highlight the complexity of antibody treatment dynamics in HIV infection and underscore the importance of timing and initial viral load in treatment outcomes.

## Future Expansion and Failures

### Future Expansion

In this paper,  $I(t) = \frac{a}{\sqrt{\pi}} e^{-b(t-28)^2}$ , where  $a = 10$  and  $b = 10$ . Here,  $a$  represents the amplitude of the antibody infusion, while  $b$  controls the rate at which the infusion peaks and decays. A key remark about this  $I(t)$  term, however, is that the values for  $a$  and  $b$  may

not realistically represent the time length of one antibody treatment session.

Therefore, by increasing the value of  $b$  and adjusting  $a$  accordingly to maintain the integral of  $I(t)$  as 1, we can effectively shorten the duration of the antibody infusion administered to a patient. This adjustment is crucial as it allows for a more realistic representation of treatment duration, potentially improving the model's accuracy in simulating real-world scenarios. Maintaining the integral of  $I(t)$  as 1 ensures that the total amount of antibodies delivered remains consistent, which is important for accurately assessing the efficacy and impact of the treatment regimen. More research regarding the average time length of antibody treatment for patients with HIV is needed. In addition, it is unclear whether my model can be applied to mucosal virus infections or non-neutralizing antibody responses.

### Difficulties

It is important to note that due to the mediocre occurrence rate of oral ulcers in patients with HIV, using oral ulcers as a proxy may not be entirely accurate.

I initially developed  $I(t)$  as a discontinuous function in order to better replicate an antibody infusion in which all of the antibodies are given at the same time, over a time frame of  $t = 0.1$  days:

$$\frac{dA_D(t)}{dt} = -d_A A_D - k_P A_D V + k_M X_D + I(t)$$

$$I(t) = \begin{cases} \text{some varied dosage, DSG; if } 28 \leq t \leq 28.1 \\ 0; & \text{otherwise} \end{cases}$$

However, the *Wolfram Mathematica* software was only able to sustain low values of  $I(t)$  before breaking and producing unreasonable outputs, such as  $V_T \rightarrow \infty$  at  $t = 28$  days. Thus, I modified the  $I(t)$  term to a continuous function in order to comply with the limits of the *Wolfram Mathematica* software.

In other words, the main failure that I encountered was that I was unable to find a bistable switch without the *Wolfram Mathematica* software breaking when I used a discontinuous function of  $I(t)$ . I attempted to manipulate the other parameters while maintaining a discontinuous function of  $I(t)$  in order to see if I could produce a reasonable result. When the  $I(t)$  was within a range that *Wolfram Mathematica* could handle, I did experience clearance when I significantly decreased  $k_m$ , or significantly increased  $c_{AV}$  or  $c$ , but of course, dramatically decreasing the unbinding rate, or dramatically increasing the immune complexes clearance rate or virus clearance rate, is not biologically reasonable. In addition, I noticed that Ciupe et al., 2018 assumes that antibody-virus immune complexes can still infect but at a rate of  $\beta_i < \beta$ . Because the *Wolfram Mathematica* software broke from the drastic increase of  $X_D$  since  $k_m \gg k_p$ , I realized that if I assume that the antibody-virus immune complexes cannot infect or dissociate (thus allowing the deletion of  $k_m$  and any variables it attaches to in **Model 1**), then the program can produce a reasonable output without breaking. Again, however, this assumption would not be biologically correct, as these immune complexes are still infectious since antibodies are incapable of fully rupturing covalent bonds in viruses (Fox & Cottler-Fox, 1992).

## Conclusion

Recurrent aphthous oral ulcers, prevalent across all stages of HIV infection, stand out as a particularly specific symptom of the condition (Weinert, 1996; Hecht et al., 2002). These ulcers, persisting for at least four weeks or more, serve as a crucial early indicator of HIV infection. This emphasis on oral ulcers is justified by their distinctiveness and reliability in signaling potential HIV infection compared to other symptoms. I modify the recipient-virus interaction model developed by Ciupe et al., 2018, using the same initial conditions that Ciupe et al., 2018 uses for recipient rhesus macaques infected with donor plasma containing SIV virions from the ramp-up stage of infection with heat-inactivated antibodies from the set-point stage of infection, except  $A_D(0) = 0$  and  $A_D(28) = I(t)$ , where  $I(t)$  is varied. In my modification, I remove  $\frac{dX_D(t)}{dt}$  and  $X_D$  by assuming that the infusion of  $A_D$  is interpreted as an extra input of  $A_R$ . I find that a bistable switch between viral persistence and viral clearance exists between  $I(t) = 1.04 \times 10^{12}$  and  $I(t) = 1.05 \times 10^{12}$ . When  $I(t) = 1.04 \times 10^{12}$ , viral clearance can be observed when  $V(0) \leq 18.6/300$ , and a positive correlation exists for  $V(0)$  and the time at which the patient experiences full recovery when  $1/300 \leq V(0) \leq 18/300$ . Although this paper highlights a bistable switch between viral persistence and clearance, shedding light on the dynamics of antibody treatment, further investigation into the optimal duration of antibody treatment for HIV patients is warranted to enhance the accuracy of treatment simulations. Future research in this realm could explore the interplay between treatment timing and efficacy, as well as the incorporation of additional factors influencing HIV dynamics, such as immune response variations and viral mutations. Such inquiries would contribute to refining predictive models and improving treatment strategies in combating HIV infection.

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# Eye to I: Panoptic Muslim Surveillance and Warsan Shire's Poetics of Liberation

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In 1786, French architect Jeremy Bentham envisioned the panopticon, a structure in which prison cells surround an opaque tower where guards surveil the prisoners. In the panopticon, prisoners could be observed by guards without knowing when they were being watched, making them trained for constant vigilance.

My research places this centuries-old theoretical model against contemporary Muslim surveillance, arguing that the panopticon is a way to more deeply and thoroughly understand the omnipresent surveillance weaponized against Muslim communities after 9/11. More broadly, I refuse to dilute the impact of internalized and externalized policing on marginalized communities. I investigate how post-9/11 surveillance in Nairobi places Muslim communities into a prison-like structure in which they are repeatedly watched, affecting their internal psyche—the art form of poetry written by these marginalized groups allows for a deeper viewing and dissection of this surveillance. Invoking French philosopher Michel Foucault, who drew from the panopticon in his literary theories on discipline, with first-hand ethnographic research on Muslim surveillance from contemporary scholars living in Nairobi, Kenya, I pose a literary-ethnographic stance regarding how we can view the lasting impacts of Muslim surveillance.

In analyzing the detrimental conditions of surveillance in postcolonial Kenya, I also investigate how a key contemporary poet, Warsan Shire, breaks free from these boundaries through her artistic work, which focuses on the generational and haunting implications of surveillance in her own Muslim community. Shire herself was born in Kenya and migrated to the United Kingdom with her family when she was a young child. Her poetry, both spoken and written, has now reached global audiences in North America, Germany, and South Africa and has influenced the contemporary literary canon. Catechizing Muslim surveillance through meshing literary and anthropological research, I hope to dismantle the post 9-/11 prison-panopticon of inspection, emphasizing the role of artistry in liberation and resistance.

*"Assimilation" by Warsan Shire*

*We never unpacked,  
dreaming in the wrong language,  
carrying out mother's fears in our feet—  
if he raises his voice we will flee  
if he looks bored we will pack our bags  
unable to excise the refugee from our hearts,  
unable to sleep through the night.*

*The refugee's heart has six chambers.  
In the first is your mother's unpacked suitcase.  
In the second, your father cries into his hands.  
The third room is an immigration office,  
your severed legs in the fourth,  
in the fifth, a uterus—yours?  
The sixth opens with the right papers.*

*I can't get the refugee out of my body,  
I bolt my body whenever I get the chance.*

In her first full-length published poetry collection, *Teaching My Mother How to Give Birth*, the refugee poet Warsan Shire frames her experience moving from Nairobi to London, feeling isolated in her identity and her body:

*No one leaves home unless home is the mouth of a shark. I've  
been carrying the old anthem in my mouth for so long that  
there's no space for another song, another tongue or another*

*language. I know a shame that shrouds, totally engulfs. I tore  
up and ate my own passport in an airport hotel. I'm bloated  
with language I can't afford to forget. I don't know where I'm  
going. Where I came from is disappearing. I am unwelcome. My  
beauty is not beauty here. My body is burning with the shame  
of not belonging, my body is longing. I am the sin of memory  
and the absence of memory (Shire, 2011).*

In these lines, Shire explores the gravitational pull between memories of her Kenyan homeland and her current condition of unease and longing. Shire's words illuminate the paradox of her poetic identity, a creative process that hinges on melding a sinuous influx of words to create a deeper narrative and truth. As a daughter of refugees, her poetic expression navigates the feeling of being "bloated with language" and how it can fully encapsulate her diasporic experiences. Poetry cannot fully articulate the depth of the stories in her bones, yet perhaps it remains the only medium that can come close; its ability to create a cohesive story using fragmented narratives, line breaks, and separated stanzas mirror experiences of migration and loss. Her words, the tools she uses for her craft, catalyze a swollen, overwhelming, and unwieldy sort of weight, lurking with danger. Her poetry's current of language suffuses with precarity and the challenge of encapsulating memory and experience, continuity and change. Shire's poetry of ancestral memory, rooted in the generational experiences of Muslim women surveilled in Nairobi, exposes the deleterious effects of the internalized gaze of policing.

Shire's poems trace her matrilineal experiences with Muslim surveillance, foregrounding how this watchful gaze lingers in her body and continues to shape her psyche across time and space. Strangely,

Shire titles her poem, “Home,” demonstrating the elusive comfort this word evokes as an asymptote of unconditional ease that cannot be reached. In Shire’s poems, the familiar and the dangerous share the same space, conversing with one another. When Shire speaks of “know[ing] a shame that shrouds, totally engulfs,” a gaze of surveillance takes over, making her feel perpetually uneasy as though she is committing wrongdoing. This sentiment—the power of language both as a tool of beauty and of possible harm—echoes through Shire’s work, resounding off her poetic practice. As the daughter of Somali Muslim refugees born in Nairobi, who later moved to London, Shire grew up under conditions of social precarity that her poems reflect (Okeowo, 2022). Ultimately, the surveillance Shire internalizes emerges from a generational tradition of surveillance that her ancestors carry down to her (Shire and Mehri, 2022).

The societal authorities of Kenya pushed Muslim people to the margins, creating Christian-dominant political conditions rooted in policing and warfare. The late nineteenth-century colonial regime in Kenya, rife with undemocratic power structures, lacked representation of Muslims in the colonial government. Under such corrupt conditions, Muslim immigrants struggled to receive an education and citizenship (Prestholdt, 2011). The bone-deep history of the Muslim minority communities in Kenya resonates through the present, resulting in the socio-political targeting of these groups. In postcolonial Kenya, the history of marginalization for Muslim communities persists. Muslim political officials exist in the minority and continue to advocate for their rights in a staunchly religious nation (Prestholdt, 2011). In the 1990s, Kenyan government officials banned the Islamic Party of Kenya from participation in the national election, and this exclusion evinces how the ruling party instituted oppressive measures to exclude representation of Muslims (Truth, Justice, and Reconciliation Commission, 2008). The endemic exclusion of Muslims in Kenya magnified the systemic struggle for Muslims to obtain representation that takes place both in sociocultural contexts, like education, and political ones, like elections. Shire’s work illuminates the lasting effects of this policing across countries and geographies—she demonstrates how its impact stretches far beyond institutional discrimination. In the post-9/11 world, Shire reveals how the policing of Muslims creates a generational loss through surveillance and the internalized gaze surveillance imposes.

Shire’s poetry explores her experiences living with her mother, aunts and cousins in Kenya’s capital city, Nairobi. In her creative work, Shire describes acutely feeling the gaze that alienates her. Shire features Nairobi as one of the only locations named explicitly in her poems, while many unnamed others carry porous, more flexible geographic boundaries that mimic Shire’s complex personal relationship to a sense of place (Shire, 2011). Through her migratory, haunting poems, Shire narrates the stories of her people and her own experiences navigating conditions of surveillance, violence, and shame (Okeowo, 2022). Shire’s poems traverse both time and space, and they echo the language of her grandmother and her mother, steeped in generational warnings that a daughter hears from the older women around her. Through incorporating the shared voices of women close to her, Shire builds a body of work that is matrilineal in nature. Fellow British-Somali author Momtaza Mehri names this economy of language that relies on warning, calling on Shire’s work as embodying a “surveillance network of aunts” (Shire and Mehri, 2022). Shire’s work begs the question: What does a daughter of the Kenyan diaspora, living in the wake of systemic oppression, carry down? Her poetry examines this question, residing within and

reckoning with a surveillance network akin to that envisioned by one architect centuries ago.

In the 1800s, architect Jeremy Bentham conceived a model of prison surveillance that bears the intense, embodied weight of warning that lingers through Shire’s poetry. He called that architectural structure the panopticon (Fig. 1). Bentham’s panopticon economizes the gaze of surveillance. In the panopticon, guards occupy an opaque watchtower in the center of the prison. Prisoners surround the watchtower, and due to the watchtower’s opacity, they do not know when the guards watch them. Therefore, the prisoners remain vigilant in their actions, performing them as if the guards constantly surveil them. The panopticon limits the physical work guards would need to carry out to surveil the prisoners while increasing the efficacy of a prison by pushing prisoners to adopt an internalized gaze (Bentham, 2017).

In its nature, the panopticon mimics a hermetic system, a house in that its structure represents permanence, physicality, and centrality, encompassing an eternal space for both the prisoners and the guards. Shire evokes this structure in her poem, “Home”: “No one leaves home unless home is the mouth of a shark” (Shire, 2022). Shire introduces the question: what does it mean to discover home in a structure akin to a prison, made to be a place of shackling?

The model of the panopticon encapsulates what scholar Danielle Haque calls the “fraught futures” that Shire’s poems inhabit (Haque, 2002). Surveillance creates watchfulness that literally inhabits the space beside a shared conceptual future in this phrase. French theorist Michel Foucault deems this extension of surveillance “central in the history of repression: the transition from the inflicting of penalties to the imposition of surveillance” (Foucault, 2015). Shire echoes Foucault’s rendering of the panopticon’s immensity as the power of surveillance becomes invisible in the outside environment and hypervisible in the bodies of all surveilled people.

In Shire’s first home and her birthplace, the gaze of Muslim surveillance resonated through Nairobi, and it colored both her landscape and experience. Decades later this internalized gaze lingers in her creative work. Yet, Shire’s poetry confronts, interrogates, and investigates this panoptic surveillance that pulses throughout her generations, passed down matrilineally, a sort of

The post 9/11 world aggravated surveillance of Muslims in Kenya. The United States pushed Kenya to adopt stronger and more forceful antiterrorist measures in its home state, rooting out the threat of attack (Al-Bulushi, 2021). United States’s involvement in Muslim surveillance extended beyond its borders. Because of the allyship of

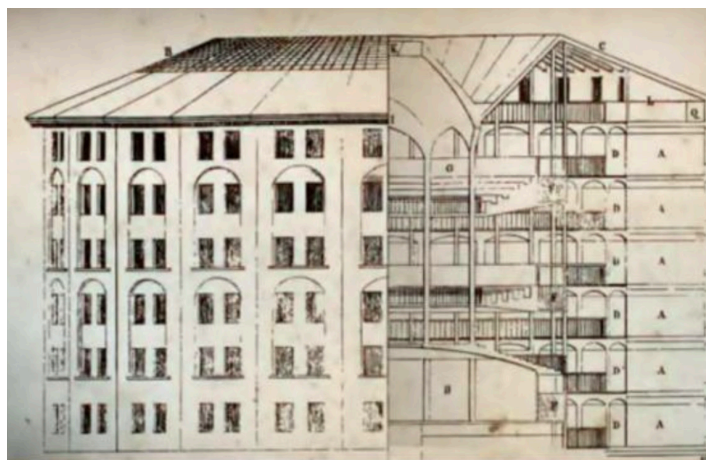


Fig. 1. Bentham, Jeremy. Panopticon: Or the Inspection House



the two countries, Kenya adopted some of the United States's surveillance measures to combat terrorism, including the stationing of additional troops targeted in specific communities. The United Kingdom government's 2019 travel advisory warning for Kenya, based on the violent terrorist attacks that the al-Shaabab terrorist group executed in the country the same year, demonstrates an international positioning on Kenya's national security: "you should be vigilant at this time" (United States Department of State Bureau of Counterterrorism, 2019). This call for vigilance, both for foreigners and Kenyan citizens, echoes Foucault's panopticon. The mirroring of both the citizen and the foreign outsider needing to be vigilant in the country illustrates the weaponization of social visibility. The beginning of a panopticon structure in Nairobi took root through increased surveillance of Muslims.

## I. Invisible Cities: Surveillance Beyond its Physical Borders

### "Ugly"

*Your daughter is ugly.  
She knows loss intimately,  
carries whole cities in her belly.  
As a child, relatives wouldn't hold her.  
She was splintered wood and sea water (Shire, 2022).*

Bentham envisioned the panopticon as a circular model covering an entire city, creating layers upon layers of surveillance surrounding a particular area (Furlong, 2015). This structure of the paragraph aligns with Nairobi, the largest city in Kenya, an all-encompassing space that functions as a microcosm replicated in other areas of the country. Cities generally represent a communal togetherness as the network of communities of the countryside coalesces into the comforting solidarity of a central body or territory. In Nairobi, Muslims lived in close communities that allowed them to practice their cultural traditions and bond over shared values. However, Nairobi's tightened security created a feeling of alienation in its Muslim population. Sociopolitical surveillance means residents never feel at ease in their geography. Their movements, interactions, or speech constricted them because of an external force. The alienation that surveillance induces mimics a key structure in the panopticon: the individual prison cell. The individual cells present in the panopticon, as depicted in Bentham's architectural sketch (Fig. 2), restrict the ability for community togetherness, heighten the feeling of aloneness in the surveilled population, and create estrangement from a greater world outside of the prison network.

In *Discipline and Punishment*, Foucault chronicles the nature of punishment in the modern sociocultural psyche, and he compares the prison cells in the panopticon to "so many cages, so many small theaters, in which each actor is alone, perfectly individualized and constantly visible" (Foucault, 2008). This node of hypervisibility means that this location, designed as a permanent lodging for the surveilled, can never truly embody the name home since it strips its inhabitants of comfort. Rather, it occupies a defensive network in which both the country and its citizens learn to be defensive by nature (Furlong, 2015).

In the panopticon of Kenya, the impact of Muslim surveillance resonates outwards—beyond its immediate community—in the same way the literal force of surveillance extends outwards—removing terrorist threats beyond its borders. The broadened scope of Kenyan

surveillance extends past its capital Nairobi into other cities of the county, such as the Coast Province and North East Province (International Crisis Group, 2012). Shire's hereditary Somalia possesses a high Muslim population which faced similar measures of surveillance and a similar history of discrimination long before the twenty-first century terrorist attacks (Lind, Mutahi, and Oosterom, 2015).

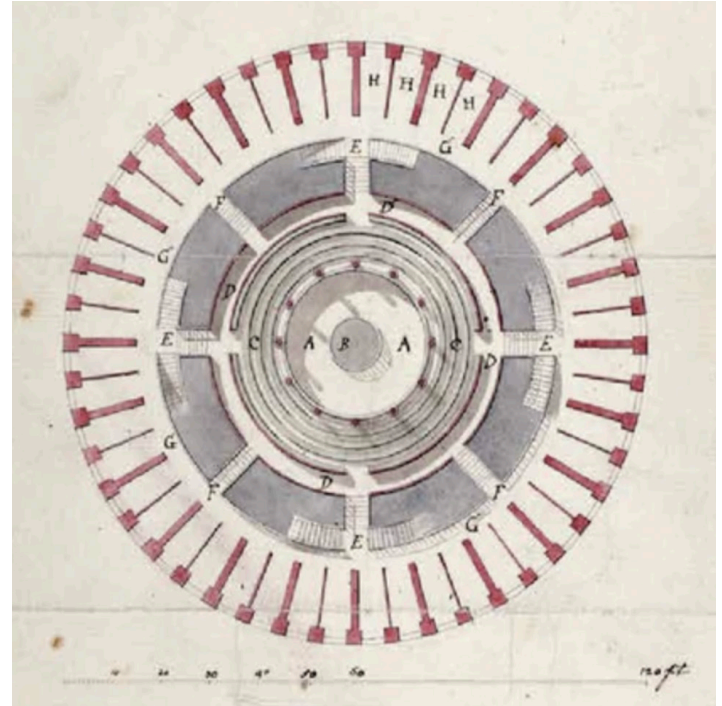


Fig.2. Furlong, Gillian. "Designs for a Panopticon Prison by Jeremy Bentham."

Jeremy Lind, a researcher investigating violence in livelihoods, discusses how this suppression "other[s]" an entire population as somehow threatening, providing the rationale for collective punishment measures" (Lind, Mutahi, and Oosterom, 2015). In Lind's interviews with generations of Muslim families, individuals consistently described the weaponized gaze of surveillance—a "blanket of suspicion"—as akin to the violent military expeditions during the colonial regime that rooted out entire populations of their people (Lind, Mutahi, and Oosterom, 2015). The statements of the interviewees evoke the idea that the only difference between colonial and postcolonial violence against Muslims feature the visibility of the violence struck among the people: the colonial government relied on external force while the postcolonial government relies on invisible surveillance (Lind, Mutahi, and Oosterom, 2015). As a result, generations of Muslim populations, like Shire's family, experienced and must reckon with the haunting effects of historic marginalization.

The feeling of historic marginalization lingers in Shire's creative work. In her poem, "Refugee," Shire reflects on the inheritance of loss:

*a daughter carries whole cities in her belly  
her hands are a civil war,  
a refugee camp behind each ear (Haque, 2002).*

Through the image of a city's violence and ruins, finding home in the body of a refugee like Shire, Shire illustrates how the aftermath of war remains a gestation of memory in the body, weighing her down with the aftershocks of conflict. Entrenched surveillance becomes a



generational trauma, passed down, a feeling that holds gravity and a feeling that the body remembers acutely. According to English professor and scholar Danielle Haque, navigating surveillance openly on the page allows Shire to build a space for herself and homeliness (Haque, 2002). Writing about the externalized gaze transforms surveillance from being opaque to being transparent, rendering this concept visible and dismantling its evasive power so it can finally be engaged with fully. In this space of engagement, Shire can both expose the lasting impacts of surveillance to a broader audience and find comfort in writing poetry that chronicles possible futures—what sort of homes might emerge after such a generational experience.

Shire's first full-length collection, *Bless the Daughter Raised by a Voice in Her Head*, remains preoccupied with honoring internalized surveillance and the remnants of ancestral stories. The collection invokes an explicit tie between the weaponized attention of surveillance, which turns surveillance into a violent yet invisible weapon used against the affected communities, and how it becomes internalized in the bodies of her people. (Shire and Mehri, 2022). Returning to the language in the title of her collection, Shire addresses her mother in a poem:

*Mama, I made it  
out of your home  
alive, raised by  
the voices  
in my head (Shire, 2022).*

The voices Shire evokes in the verses contain the gravity of ancestral warnings, and the urgency to act properly in case of an external gaze appearing. These voices mother her, shaping her and the way she walks in the world. The frequent line breaks create terse snippets of text, how Shire's generational teachings linger in her mind in fragmented form. Paradoxically, despite their fragmentary narrative, they together create a cohesive whole of how she must view the world and survive within it. Shire, in bringing in the image of internalized surveillance as a way in which her experiences of the panopticon reach beyond geographic barriers, evoking that, no matter where she travels, the feeling of being watched lingers.

## II. Guards in the Watchtower: The Tightening of Surveillance Measures in Nairobi and Surveillance Through Policing

*"Conversations about Home (at the Deportation Center)"*  
*"God, do you know how difficult it is to talk about the day your  
own city dragged you by the hair, past the old prison, past the  
school gates, past the burning torsos erected on poles like flags?  
When I meet others like me, I recognize the longing, the missing,  
the memory of ash on their faces" (Shire, 2014).*

The surveillance practices that took place in Kenya's capital Nairobi paradoxically represent the lack of openness even in a location with the greatest centrality. Anthropologist Zoltán Glück coined the term "security urbanism" to explain this presence in Nairobi. Even in prominent capital locations where city safety ought to be transparent, the state deployed an undercurrent of hidden national security practices unbeknownst to the citizens (Glück, 2017). These types of spatial practices relied on creating panopticon-style surveillance networks through the geography of the capital city, making surveillance into a cloaked routine (Glück, 2017).

One year after the 1988 Al-Qaeda attacks in Nairobi, Muslim communities reported how the Kenyan government banned their organizations and how they treated Muslims as threats in Kenyan national media that repeatedly broadcasted the presence of potential terrorist threats in Muslim-dominated areas (Al-Bulushi, 2018). Further, they discussed how suspicions cast over them on both the governmental scale and among their fellow citizens harmed Muslims. Samar Al-Bulushi, a professor in Anthropology, visited Nairobi in 2004 to investigate the effects of surveillance upon Muslim communities, coined the term "citizen-suspect" to discuss the nature of the treatment of Kenya's Muslim population. The social implications of the phrase indicate vigilance as inherently intertwined with what it means to be a Muslim citizen in the area of Kenya and that Kenya's Christian citizens alienated these citizens (Al-Bulushi, 2018).

Kenya's Anti-Terror Police Unit (ATPU), formed in 2003 in the wake of the 9/11 terrorist attacks and funded by the United States and United Kingdom governments, demonstrates the international positioning and pressure on Kenyan surveillance. Muslim communities in Nairobi suspected the ATPU carried out the abduction of a Muslim man, Hamisi, in 2010 (Al-Bulushi, 2018). Hamisi's abductors wore plain clothes and carried him into an unarmed vehicle outside of Nairobi's shopping center. They suspected that he colluded in the Kampala Bombings at the World Cup in Uganda. The officials who kidnapped Hamisi sent him to be questioned in Uganda, where he was detained and questioned regarding his involvement in the bombings. Hamisi's abduction followed a trend of Muslim citizens in Kenya being taken and questioned for crimes they did not commit.

Before Hamisi's kidnapping, he was among a group of Muslim activists studying and tracking these abductions, trying to find out more information about where they were held and by whom. According to Al-Bulushi, this could be a reason the government removed Hamisi from his community. When Hamisi's wife investigated what had happened to her husband, she came across similar cases of Muslim men disappearing from Nairobi, taken from their communities without their current whereabouts being shared, released years after their capture (Al-Bulushi, 2018). Hamisi's abduction represents a continuation of the undercover surveillance and repression that took place in Nairobi's Muslim community.

The sudden government intervention in a shopping mall without any previous knowledge of the surveillance tactics of this area demonstrates the all-encompassing, surrounding force of the panoptic gaze that the Muslim community in Nairobi became conditioned to (Al-Bulushi, 2018). Through events like Hamisi's abduction, Kenya blurs the distance between the guard who surveilled the community, the police forces, and the target who was surveilled, the Muslim community. Similar to the ATPU, the Kenya Defense Force worked with the international community to counter terrorism. Their mission of tamping down on external threats begs the question of what the Kenyan government considers as an internal threat versus an external one (Al-Bulushi, 2018). The positioning demonstrates a physical manifestation of Al-Bulushi's "citizen-suspect," creating an environment in which fear of surveillance alters the psyche of the community (Al-Bulushi, 2018).

### III. Conversation Tubes: Surveillance in Social Communities

#### *"Souvenir"*

*"You brought the war with you  
unknowingly, perhaps, on your skin  
in hurried suitcases  
in photographs  
plumes of it in your hair  
under your nails  
maybe it was in your blood" (Shire, 2022).*

Shire's poem "Souvenir" emphasizes the lasting effects of war upon the body, something that follows her and stays with her long after she has left the place of conquest. The poem emphasizes how these acts of warfare exhibit themselves beyond the political scope and into the social realm, permeating day-to-day acts like looking through suitcases and photographs—these activities become a vehicle for remembering pain. The prison-panopticon in Nairobi similarly exhibits itself not only through literal force but also through media, creating a sort of social repression that is difficult to escape. For example, the billboards in Nairobi that advocate for community security influences the social psyche of the community who consumes it. A digital mode of panoptic surveillance capitalizes upon what Foucault calls the "economy of power," choosing to surveil communities rather than outwardly punish them, creating an internal system of loss (Foucault, 2015). According to Foucault, the incorporation of surveillance as a running undercurrent affecting a community extends notions of power and control, increasing the different ways in which the state can both subjugate and subdue (Foucault, 2015). Specifically, surveillance technology in the digital era means that the citizen cannot separate themselves from the suspect, even when outside of a specific geographic territory.

Dr. Josh A. Hendrix, whose academic work specifically focuses on contemporary policing and its effects on modern communities, asserts that surveillance technology serves as a "physical embodiment of citizen distrust," reminding community members that they remain tracked like a threat (Hendrix et al., 2018). This sentiment reflects the targeting of Somali Muslims in Nairobi, a magnification of systems of oppression that mirrors Hendrix's analysis of surveillance for populations deemed high risk by the government. Consequently, implementation of surveillance targets specific communities, inherently rooted in an unequal distribution of policing resources (Hendrix et al., 2018). In Nairobi, this form of surveillance manifests itself through messages on billboards, displayed to the entire community. During Al-Bulushi's 2004 visit for her anthropological academic research on Muslim surveillance, Al-Bulushi highlights a billboard she saw emblazoned with the Swahili words: "Security begins with me; Security begins with you." These words urge citizens to turn in and watch over the Kenyans around them, creating a social policing effect that transcends the more detached, clinical structure of surveillance that a government holds the autonomy to enforce. The phrase emphasizes surveillance within intimate relationships through the pronouns me and you, highlighting hidden dangers in the closest networks among communities that can no longer be designated safe.

Through social surveillance, the government weaponized the citizens against one another and restricted the potential for community solidarity (Al-Bulushi, 2018). Ironically, these practices of pitting citizen populations against one another maximized the extremism they were created to prevent, causing populations to be increasingly

divisive and distrustful of one another. Additionally, they reduce the possibility for human kinship and resilience in a shared physical region (Metre, 2016). For example, Foucault, in his analysis of the panopticon effect, predicts this presence of surveillance dangerously flowing from governmental networks into social ones, breaking bonds among communities and regions. The panopticon's economy of power, according to Foucault, makes it "destined to spread throughout the social body," touching everything in its reach (Foucault, 2008).

The negative impact of surveillance Foucault alludes to reveals itself in Shire's work that chronicles the way in which the violence of the city permeates the body of a daughter of the diaspora. In her poem, "Assimilation," Shire describes this feeling of internalized violence, how she carries its threat with her wherever she goes. Growing up in London with her family, she recalls a family dynamic of watchfulness, in which she and her family members are "unable to excise the refugee from our hearts / unable to sleep through the night." Always anticipating danger, Shire describes needing to "bolt my body whenever I get the chance," protecting it from the possibility of harm. In her heart lies the remnants of surveillance, pulsing through her body's anatomy like an organ of its own. In the poem, her severed legs occupy the fourth chamber of her heart, as though transforming into a warning, reminding her to remain careful because danger looms. Even after leaving Nairobi, its social conditions and undercurrent of hidden danger remain entrenched in her mind and heart.

The manifestation of social surveillance in Nairobi radically contours the idea of the "citizen-suspect," introducing the idea of being a Muslim citizen in Nairobi as acutely tied to feeling suspected in both political and social contexts (Al-Bulushi, 2018). For coastal Muslim communities living on the outskirts of large urban areas like Nairobi, physical estrangement magnifies this othering of their citizenship. The citizens occupied what Al-Bulushi calls the "gray zone," a zone that straddles the line between peace and war (Al-Bulushi, 2018). As such, surveillance becomes a way in which a war against terrorism perpetuates itself. In Nairobi, communities remain unable to fully settle into a state of peace, yet the psychological war they endure hinges on internal surveillance rather than external aggression. According to a 2008 report from Kenyan Muslim populations representing the Truth, Justice, and Reconciliation Commission, citizens have difficulty pinpointing when and by whom they are being watched, facing various layers of surveillance and their own internalization of this gaze, which is why cases of surveillance are not brought up to the courts (Truth, Justice, and Reconciliation Commission, 2008). Al-Bulushi demonstrates how the experiences of Muslimhood become inherently shaped by the danger of surveillance forces in their homes, acting upon their identity and causing them to behave more cautiously (Al-Bulushi, 2018).

In ethnographic interviews conducted by Al-Bulushi, one such coastal community discussed the haunting disappearance of a Muslim man, Ahmed, removed from his Nairobi community in 2009 and taken to an unknown location. Others in the community were acutely affected by Ahmed's kidnapping, moving locations for safety. One woman, Maryam, found herself stuck between her hometown, Mombasa, and the more prominent city of Nairobi where she ended up choosing to stay because of its centrality, and relative transparency regarding policing. Her decision to reside in Nairobi made her "internalize and anticipate the unpredictability of state terror," becoming hyper aware of the locations in which the force of policing hurts members of her community (Al-Bulushi, 2018). For other Muslim people deemed suspects and later released by the police, custody

included questioning about their cultural dress, emphasizing their social and religious ties (Ndzovu 2014). Muslim citizens become a sort of watchtower themselves, forced to report on the actions of their community members. (Bredlid, 2021). These Muslim communities absorb the rhetoric of some Kenyan Christian citizens, who question their loyalty in Nairobi and even argue that they are “taking over the country” (International Crisis Group, 2012). This rhetoric renders Muslim communities hypervisible in Nairobi, deemed suspects by both the government and their fellow citizens.

Even after these communities migrate away from Kenya, surveillance lingers. F.B.I. agent Terry Albury remembered questioning Muslim citizens flying into the United States from Nairobi as a “standard drill,” asking them about their experiences in Kenya with extremism and radicalization (Reitman, 2021). These forms of pop-up surveillance permeate geographic boundaries, not restricting the feeling of being watched to Kenya’s clean-cut borders. The alienation of Muslim communities deemed citizen-suspects from the nexus of Kenya mimics the physical placement of the panopticon in which the cells of prisoners surround the center of the structure, which holds the guards and the watchtower (Fig. 2). Muslim communities inhabit the outskirts of Nairobi, attempting to create contemporary spaces of safety for themselves in the wake of the Christian-dominated regimes of the colonial period. At the center of the city lies police forces actively patrolling the area, inhabiting a watchful state over the surrounding Muslims. The site of the panopticon is the entire city of Nairobi, the territory encompassing a prison structurally (Furlong, 2015).

In a poem, “Midnight in the Foreign Food Aisle,” exploring midnights spent in the foreign food aisle of a convenience store, Warsan Shire explores the finding of shelter:

*You find yourself totally alone alone, in the foreign  
food aisle, beside the turmeric and saffron,  
Remembering your mother’s warm, dark hands,  
Prostrating in front of the halal meat, praying in a  
Language you haven’t used in years (Shire, 2022).*

In the aisle of the convenience store, Shire attempts to avert the gaze of surveillance, situating the poem hidden between the aisles of a commercial place, away from any external gaze watching her prayers. The foreign food aisle in which Shire sets the poem represents Shire’s alienation from a community who understands her as familiar rather than foreign, creating a tension between intimacy and isolation. However, through utilizing a second person point of view, Shire reaches towards an audience who understands and can intimately arrive at her diasporic experience without her needing to explain its deep-rooted intricacies. Choosing to pray among spices, including turmeric and saffron, reminiscent of her childhood in Nairobi, allows her to access her past, remembering her mother’s teachings and letting these teachings fill her with her first language. Her poem extends the yearning for home and safety, chronicling the presence of prayer as a measure of feeling comfort. Despite Shire’s adopted home of London, far from Kenya, Shire still feels the palpable threat of surveillance and the loneliness evoked by not having her female family members, who share her experience, close to her. The watchful presence of the guard transcends geographic boundaries, making her feel surveilled even in another country. However, in unveiling the depth of this gaze in her poem, Shire illustrates the way she finds cloistered, unseen and unsuspecting spaces to worship and engage

in ancestral memory. Through her poems, Shire can carve a safe space for herself, a node of familiarity and warmth. She immortalizes this small moment where she returns to her language and her mother’s teachings without shame or fear.

#### IV. Individual Prison Cells: Surveillance Creates Reification, “Othering”

##### “Tea With Our Grandmothers”

*I thought of my ayeeyo, the woman  
I was named after, Warsan Baraka,  
skin dark like tamarind flesh,  
who died grinding cardamom  
waiting for her sons to come home and  
raise the loneliness they’d left behind (Shire, 2011).*

From the War on Terror, the name given to the United States fight against terrorism starting in 2001 with the September 11 attacks, to the present, these orders of Muslim surveillance in Nairobi create a reification of the other, separating Muslim communities from a nationalist ideology. Through social surveillance, Nairobi compresses the distance between the citizen and guard figures first represented in the panopticon, linking the surveilled with the arbiters of surveillance and creating the foundation for citizen distrust and unease. When the government employs surveillance technology, layering on-the-ground police surveillance over social surveillance, they create the psychological feelings associated with war within the territory (Al-Bulushi, 2018). As Al-Bulushi describes in her analysis of her term, “gray zone,” carrying out military goals without physical military force still results in conditions of quasi-war (Al-Bulushi, 2018). In Nairobi, the state and its power are at the center of surveillance, targeting Muslim communities as a group in the name of security in a manner akin to “killing a mosquito with a hammer” (Lind, Mutahi, and Oosterom, 2015). The city becomes “not just the site, but the very medium of warfare,” manipulating geographic boundaries to restrict community freedoms and treat Muslims as threats (Al-Bulushi, 2018).

On Jan 15, 2019, the al-Shabaab terrorism group attacked the Dusit D2 hotel complex in Nairobi, aiming to incite violence against the wealthy Kenyans and visitors who stayed there and killing 21 people (United States Department of State Bureau of Counterterrorism, 2019). The worst attack in four years, the event sparked increased surveillance, and it foreshadowed the future of the panoptic gaze in Nairobi: only increasing as the violence and unrest increased in the area. Through attacks like al-Shaabaab’s violence, the intensity of surveillance heightens, making it urgent to act upon. The state continues to adopt surveillance as a “dominant weapon of warfare,” concealing its force to the Muslim communities acutely affected by its presence (Renton, 2018). Surveillance affects the political system so deeply that it becomes classified as its own political order, and its expansion resembles the imperialist desire of the colonial system, fighting for control of the psyche of a certain territory’s citizens. Al-Bulushi’s gray zone of surveillance-based war reflects a “permanent state of emergency,” a panopticon that neither the people nor the territory of the city can extricate itself from (Renton, 2018).



## V. Breaking Free from the Invisible City: Poetry as a Form of Liberation

### "Backwards"

*I'll rewrite this whole life and this time there'll be so much love,  
you won't be able to see beyond it (Shire, 2017).*

Surveillance remains an ongoing system of war between the government in Nairobi and Muslim communities, an extension of the war on terror that reaches globally and concentrates in Nairobi. In the same way that Bentham's architectural plan aimed to encompass an entire city, surveillance transcends boundaries and occupies immense space, becoming rooted even in the psyche of those whom the panopticon surveils. In Warsan Shire's poetry, she incorporates the voices of her people and family members into her book through interviews with them, creating a communal chorus through the body of her work (Okeowo, 2022). Her poem, "Backwards" meditates on the power of poetry to resist loss and invoke the care of her close family members, learning towards a life of abundance.

*The poem can start with him walking backwards into a room.  
He takes off his jacket and sits down for the rest of his life;  
that's how we bring Dad back.  
I can make the blood run back up my nose, ants rushing into a hole.  
We grow into smaller bodies, my breasts disappear,  
your cheeks soften, teeth sink back into gums.  
I can make us loved, just say the word.*

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Your cheeks soften, teeth sink back into gums  
we grow into smaller bodies, my breasts disappear.  
I can make the blood run back up my nose, ants rushing into  
a hole,  
that's how we bring Dad back.  
He takes off his jacket and sits down for the rest of his life.  
The poem can start with him walking backwards into a room  
(Shire, 2017).*

By invoking her father who passed away, the poem counters loss through bringing alive Shire's generational origins on the page. In addition, Shire resists other forms of deprivation, including growing older and being hurt. She investigates intensely intimate relationships to recast a world in which they are still soft, unhardened by the world and by cynicism. In this universe the poem imagines, Shire bridges together her own experience with that of those close to her, envisioning a world in which they all exist in the same space.

To do this, Shire adopts an extended palindromic structure where the second stanza mirrors the first, starting and ending with the father walking backwards into the room of the poem. In the room that the poem builds, the father can "sit down for the rest of his life," no longer needing to remain upright, to remain acutely watchful of his surroundings in case a threat appears. Through this mirroring that begins and ends with a legacy of restfulness, Shire highlights the power of reciprocal care and reaches toward a state of comfort where her bloodline no longer needs to occupy a vigilant state of internalized surveillance. Her work creates the project of seeing the panoptic gaze more clearly.

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# “My Favorite Labor is Child Labor”: Analyzing Children’s Work in Family Channels

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In the world of YouTube, family channels are timelessly popular both with audiences and advertisers. Chronicling the day-to-day lives of families, these channels heavily feature children of all ages, sometimes from the second they are born. Increasingly, questions have arisen as to the ethics of family vlogs. Are these videos memories or examples of child labor? In this paper I answer: Are children in family vlogs engaged in child labor? Using two popular YouTube families, the McKnights and the Shaytards, as case studies I show that children in family vlogs often meet the ILO’s definition of child labor. These children tend to be inextricably linked to the family channel’s success, stripped of any privacy, as their highs and lows are shared with millions of strangers for large sums of money. All the while, parents redefine internet safety, as it meets their needs.

The Idaho mountains seem like the backdrop of a fairytale. It is a sunny day and the Shaytard family, who many once called YouTube royalty, is trying to beat the heat by building a swimming pool in their backyard. At one point Shay Carl – the sarcastic father of five – points the camera at his children as they move their trampoline from one side of the yard to the other. He then sings, “[m]y favorite labor is child labor, make the kids lift heavy things,” (Butler 2015, 6:39-6:45). For something to be categorized as child labor, according to Shay Carl, it must involve a physically strenuous task, akin to children picking up fruits for hours under the harsh sun or working tirelessly at a factory. Child labor, in his mind, is worlds away from the thousands of hours his children have spent filming YouTube videos.

Family vlogging is one of YouTube’s most lucrative and popular video genres. It seems simple enough, mom and dad just filming a regular day in their life as cute kids go to school and visit the park. Oftentimes, this type of content is framed as a virtual diary. Imagine, these parents encourage viewers, daily videos going back to the day you were born! Yet, in addition to preserving family memories, these videos are also likely generating thousands if not millions of dollars for the parents (Perelli et al. 2023). Thus, childhood memories become intertwined with the family business.

In this paper I aim to answer the question: Are children in family vlogs engaging in child labor? For the purposes of this paper, I use the International Labor Organization’s (ILO’s) definition of child labor:

*“[The term child labor] refers to work that:*

- is mentally, physically, socially or morally dangerous and harmful to children; and/or*
- interferes with their schooling by: depriving them of the opportunity to attend school; obliging them to leave school prematurely; or requiring them to attempt to combine school attendance with excessively long and heavy work,”* (2023).

I argue that children in many family vlogs are engaged in child labor. The ILO establishes two conditions for work to constitute child labor: that it is harmful and/or that it impacts school time/ is very time consuming. The work of family channels can be very harmful to the children, as their identities and lives are used to maintain a successful family brand. Furthermore, the children’s free time is immensely infringed upon, as the children engage in large amounts of emotional

and other types of labor, always ready to perform for the cameras. To study this I conducted case studies and compared two of YouTube’s most popular family vloggers, the McKnights and the Shaytards. In the first part of the paper I discuss the importance of the children to curating an authentic family brand and provide examples of instances of child labor as defined by the ILO in family vlogs. I then explore how parents define internet safety to justify their actions. The case of family vloggers reveals how messy and unclear the boundaries between childhood and labor can be.

## Literature Review

### Social Media: Tailoring Content Towards Profitability

Social media platforms create unique interaction puzzles. Marwick and Boyd argue that the way we present ourselves shifts depending on our audience (2010). When we are having a conversation with one or two people, we will use shared lingo, avoid mentioning certain topics, and try our best to appeal to them. On social media, however, a person cannot know or appeal to all the people who could theoretically see their content. It is a new way of communicating, a person sending their message into a void that can hold anything from zero to millions of listeners. Kaplan compares the unique social dynamics of social media as to when a performer stands on a round stage. The performer, aka the poster, is going around performing their show, tailoring it to an audience they cannot see (2021). Along the way, however, some of those audience members can go on stage, interact by liking or commenting on the post, encouraging the performer to better tailor their content to them. Regardless of the social media audience void, Marwick and Boyd claim, in sharing things on social media people “need a more specific conception of audience than ‘anyone’ to choose the language, cultural referents, style, and so on that comprise online identity presentation,” (2010, 115). Put more simply, even if one cannot initially see who will read or hear their message, one will still try to tailor their post, to seem authentic, to a particular audience.

Authenticity, however, is not a universal concept. In their book, Taylor argues that authenticity is relative. What seems authentic to a group of football fans may not read as authentic to a book club and vice versa. Additionally, Taylor posits that, “authenticity needs to be thought of as a tool employed to achieve a certain aim and that has a performative effect for both the creator and the audience receiving the content,” (2022, 8). In other words, authenticity is not a quality, it is an action. People are making choices so that they may portray

themselves in a way they feel is authentic. Authenticity, then, is also a critical tool for making profitable online content. In filming family vlogs, channels are incentivized through views and comments to make seemingly authentic content for the greatest number of people, and thus, be more profitable.

### **Mommy Blogs: A Prequel to Family Vlogs**

The detection and analysis of proteins, nucleotides, and other anBefore YouTube existed, many women would relate stories of motherhood, parenting and life through blogs. Much of the literature on parents and children online focuses on these blogs, with a special emphasis on the ways they bonded readers and bloggers. In 2009, Kido López went so far as to claim that these blogs were radical. She argued that blogs on motherhood allowed women to connect as well as transform, “their personal narratives of struggle and challenge [...] are beginning to expand our notion of motherhood,” (2009, 744). As such, Kido López continued, women were using blogs to go against patriarchal narratives of motherhood as a loving act, revealing the ugly and difficult truths. As blogging became increasingly monetized, however, it seemed to lose some of its radical edge as many bloggers were accused of inauthenticity and lost their reader’s trust.

One case study examines the downfall of a 2000s popular mommy blog and argues that monetization is in tension with authenticity. Hunter claims that for mommy blogs, “[a]uthenticity is essential to building any sense of community,” (2015, 1317). Monetization, however, threatens that sense of authenticity, for it incentivizes bloggers to tailor their content to the advertisers over the readers. This, claims Hunter, leads to the blogs losing the radical honesty about motherhood that Kido López once described as radical. Sponsorships, if done wrong, can turn one’s fan base against them.

One big difference between mommy blogs and family vlogs is the children’s level of involvement. Whereas in a blog a child does not need to know that they are being written about, in vlogs, children often play a central, active role. In Abidin’s articles analyzing the first wave of second-generation influencers - the children of already established social media influencers - they posit that most family vlogging channels actually employ a filler and anchor content strategy to discourage accusations of child exploitation from their audience (2017; 2023). Anchor content is what is portrayed as the main talent of the family - hairstyling, baking, interior decorating tips, etcetera. Meanwhile, filler content is the behind-the-scenes, less “produced” side of the channel. It is the blooper reel at the end of the hairstyling video, the first-day of school vlog and the life-updates vlog. In creating that contrast between the highly produced anchor content and the “more spontaneous” filler content, Abidin argues that these families try to show viewers that the kids are not engaged in child labor. Rather, when they are at the center of the camera, they are showing their funnest, realest self. They are being authentic.

### **The Historically Blurry Lines of Child Labor**

Historically, what constitutes child labor, as well as when limits should be drawn is a highly contested subject. Throughout the 19th century and into the 20th century in the United States, many viewed children as valuable and indispensable earners for the working class family. Child labor, to large swaths of the population, was a non-issue (Zelizer 2021). As the movement against child labor gained traction, debates within it persisted. Though many agreed that children should not work in mines or factories, the boundaries were far less clear for family businesses or household chores. The first major national

child-labor law to successfully pass was the Fair Labors Standards Act of 1938 (FLSA). It was rather vague, however, as it urged for children to not be put under hazardous conditions. The act only included a definition of “oppressive child labor” after it was amended in 1949. Oppressive child labor was defined as when someone under the age of sixteen is employed by a non-parent or guardian, in a hazardous job to their health, their wellbeing and/or their schooling. It is important to note that even after the amendment, the act is vague in its definition of hazards to children, as well as carries the presumption that parents/guardians always have their child’s best interest in mind.

Child performers, whether dancers, singers or actors, are exempt from the FLSA. Acting has long been perceived as a fun job, more a form of play than actual work (Zelizer 2021). Furthermore, the entertainment industry fiercely advocated for child performers to not be included in child labor laws. One of the first attempts to protect child stars was the passage of the Coogan Act in California in 1938. This law made it so that entertainment contracts would be required to set aside a portion of the child’s earnings into an account they would only gain access to once they reached the age of majority (Gonzalez 2022). The law was then copied by various states, including New York. It, however, contained many loopholes and did not protect child stars while on the job. To present day, there are no federal regulations that protect child performers. Rather, protections of child performers in the United States are established on a state-by-state basis.

The boundaries between work and play for children in the present day are still highly debated. Qvortrup goes so far as to argue that schooling is a form of labor. The definition of labor, claims Qvortrup, should not be limited to instances of tasks done for immediate compensation. Being in school, insofar as it gives children skills necessary for the workforce, results in financial compensation in the long run and so, according to Qvortrup, should be considered a form of labor (1994). Levey extends this argument to children’s after school organized activities, specifically looking at beauty pageants. Many parents, explains Levey, spend large sums of money and time on their children participating in beauty pageants, motivated in part by a desire for their children to gain useful skills for their futures. Thus, argues Levey, organized activities like beauty pageants are also a form of child labor (2009).

### **Protections (or the lack thereof) for Children In “Real” Content**

For children on reality television shows, the precursor to child influencers, there are, for the most part, no protections, either on the job or financially. Reality shows are the newest Hollywood craze, as they are relatively cheap and easy to produce. Part of why they are easier to produce is that reality stars are not part of the Screen Actors Guild, the main labor union for television and film performers. There is a presumption made that, insofar as the content made using takes place in “real” life, people are not working (Levey 2022). Children in reality shows are especially vulnerable. Through a variety of loopholes, producers often categorize them as independent contractors and use the “realness” of reality television – though how real these shows are is up for debate – to argue that these children are not employees and do not fall under the FLSA protections (Greenberg 2015). In many cases, when the children’s parents are involved in the show, the children do not even have their own contracts – for instance, the kids in *19 Kids and Counting* or *The Real Housewives* (Telling 2023; Kale 2021). Thus, instead of being treated as employees whose images and lives play a key part in the show’s success, they are seen as bonus characters.

Child influencers, similar to reality stars, lack significant financial and labor protections. Whether or not their work is labor is questioned



both because the content is produced by the family, as well as because it is perceived as kids living their lives but with a camera. Child influencers are, usually, managed by their parents. In much child labor discourse, including the FLSA, the main national child labor protection act, there is a public and legal presumption that parents prioritize doing what is best for their children. Furthermore, because the content is perceived as taking place in “real” life, similar to reality stars, they are not viewed as employees deserving of protections (Levey 2022). In 2023, the state of Illinois made headlines when it passed the very first law in the United States protecting the earnings of child influencers (Walter 2023). The law, modeled after the Coogan law, makes it so that parents must start trust funds with earnings for their children if they are featured in more than thirty-percent of the parents’ content over a thirty day period and if that content earns ten cents or more per view. Other state legislatures have said they intend to pass similar legislation. Regardless, new laws still do not group child influencers as child laborers and they have yet to receive any substantial protections.

## Methods

Two families were selected as case studies. I chose to focus on just two families, both to establish patterns across two families, as well as because of time constraints. The first family is the McKnights. This family was chosen because they are one of the longest consistently running family channels on YouTube and have at times been some of the most popular. The second case study family is the Shaytards. This family was chosen because they are believed to be the creators of the family vlogging genre. Throughout the early 2010s and until their big scandal in 2017, they were easily the most popular family vloggers on YouTube. Furthermore, in contrast to the McKnight’s who upload family vlogs on a weekly basis, the Shaytards uploaded vlogs every single day for eight years.

Twenty videos were coded in total, ten for each family channel (see Appendices A, B, C and D for details). Ten of the videos were each channel’s most popular vlogs based on views. These were chosen to see what resonated most with their viewers. The other ten were randomly picked to see if there were any differences in the content between the most popular videos and the average videos. The coding process began inductively. Each video was viewed completely at least once. Then, they were rewinded to moments of interest and coded using NVivo. Through the process, a list of codes was developed. A few of the videos were rewatched once this list was established to ensure consistency with the codes across all of the videos.

## Who Are the McKnights?

The McKnights are a Texas-based family. Mindy McKnight, the mom, started to post vlogs on YouTube to a channel called Cute Girls Hairstyles (CGH) in the late 2000s. In the videos she would give hairstyle tutorials and she would use her kids as hair models. She is married to Shaun McKnight and together they have six children, from oldest to youngest, twins Brooklyn and Bailey, Kamri, Rylan, Daxton and Paisley. As time went on, people became increasingly curious about the kids. This led to some of the kids starting their own very successful YouTube channels. The main channel, CGH, also began to transition towards more family-vlog content. In 2016 they officially switched to making half hair content and half family vlogs. They would only post once a week, one week a hair related video and another week a family vlog. The family continues to post biweekly vlogs. The main channel has been renamed from CGH to Mindy McKnight. Nevertheless, to avoid confusion, throughout the paper I will refer to their channel as CGH.

## Who Are the Shaytards?

The Shaytards channel began in 2008 as a weight loss diary for father Shay Butler. Eventually his children, from oldest to youngest, Gavin, Avia, Emmi, Brock and Daxton, and his wife, Colette, began making appearances. In 2009 their channel catapulted to YouTube stardom after fellow content creator, Philip De Franco, shared one of their videos. From that point on the family committed to posting daily family vlogs. For a few years the Shaytards were easily YouTube’s most popular family vloggers with millions of subscribers and millions of daily views. Throughout this time they started multiple businesses, including a clothing venture. Nevertheless, their fame came crashing down in February 2017 when it was revealed that Shay Butler was cheating on his wife Colette (Schumman 2018). They were unable to recover from the controversy and since then their posts have been sporadic at best.

## Findings

### Children’s Roles in Family Channels

In most family vlogging channels, the parents hold the camera but are not the content. The parents function as a constant, knitting together the daily occurrences of the family, from showing the little one’s playdates to attending the older children’s sports events. In one CGH vlog titled “Brooklyn Gets Asked to Homecoming [...]” the various kids’ activities are shown as part of the parents’ carpool. Between shots at gymnastics and dinner prep, the mom sits in her car and gives explanations about her kids’ activities. Rarely does she talk about herself outside her status as a wife and a mother. At one point in the vlog, oldest child Brooklyn is asked to homecoming at a school pep rally. Just after that scene, mom Mindy points the camera at the boy who asked Brooklyn to the dance and asks, “were you nervous?” (McKnight 2016, 4:34-4:35). Though the mom is participating in the creation of the scene by asking the question, she is not the content. Rather, her question serves to further contextualize and explain what the kids are up to. This is a recurring pattern. In family vlogging, parents are often the directors and videographers while their children’s lives are the content.

Even moments that do not seem directly related to the children still revolve around them. For example, the Shaytards vlog, “Happy 9th Birthday Princessard,” starts with dad Shay and mom Colette entering a Target. They are dressed up for a late night Target visit so they quickly explain that they were just at their friend’s wedding. Given that they rely on interesting parts of their day to vlog, one would think a wedding would make exciting content. Yet, the wedding topic is soon brushed aside in favor of their daughter Avia’s 9th birthday. When they circle back to the wedding, it is quickly related back to their children. The dad says, “You know what that wedding tonight reminded me of? That we have two daughters and I think about the day that they get married?” (Butler 2014, 7:09-7:17). Their oldest daughter at this point is about to turn nine, so there is no real reason to be thinking about them getting married. Furthermore, a wedding is itself an exciting event. Regardless, they repeatedly mention their children while discussing seemingly unrelated topics like the wedding. Mom and dad’s Target adventures are exciting only if they connect back to the kids. Thus, children remain the focus of the content even when they are not on camera. This shows that the family’s brand is tightly wound around the children’s image and identity.

The importance of the children for the success of these family vlogs is further revealed by the editorial choices. Oftentimes, the parents will provide narration while the camera is pointed at the kids. At the beginning of the CGH vlog “Our Family Morning Routine” the dad Shaun shares his everyday tasks, some of which are unrelated to the

kids. The camera, however, is pointed at the children, acting as a decorative and engaging visual to his words. This is reinforced through title and thumbnail choices (McKnight 2016). For both CGH and the Shaytards the name of at least one of their children is in the title of three out of their five most popular vlogs. Similarly, for all five of the most popular videos for both CGH and the Shaytards, kids' faces are in the thumbnails. The title and thumbnail are crucial to garnering interest in the content. These, similar to filming choices, are decisions, instances where parents are calculating what part of their vlog they believe will garner the most clicks and engagement. In repeatedly using their children to market their videos, they are cementing the centrality of the children to the prosperity of their YouTube channel. Both in their filming and marketing choices, the children remain the central image of the channel.

### **The Harm: Sharing Children's Low Points for the Sake of Authenticity**

Children in family vlogs can have a camera on them at any time of day, regardless of the negative social, emotional and physical consequences. The ILS' emphasizes that for something to constitute child labor, it must cause emotional and/or physical harm to the child (2023). Family vlogs often cause emotional harm in that they strip the children of their right to privacy for the sake of content.

Kids in family vlogs do not have privacy. To enact the family's authentic and real brand, the children must share both their best and worst moments. For instance, in the Shaytards most popular vlog ever, Emmie, the middle child, is ill and in the hospital. The thumbnail of the video shows Emmie wearing a hospital gown and the title reads, "BABYTARD IS SICK!" Her illness is treated as a marketing strategy. When the video reaches the portion at the hospital, mom Colette films Emmie and asks, "What are we doing at the hospital?" (Butler 2014, 6:50-6:54). Emmie does not respond as she squirms. The mom then raises Emmie's blanket and explains, "Yeah, cover yourself up, she's not quite comfortable wearing a hospital gown," (Shaytards, "Babytard is sick!" 6:54-6:57). Despite acknowledging that Emmie is uncomfortable with the hospital gown, and presumably, with being filmed while wearing it, mom Colette continues to push past Emmie's boundaries. In a telling moment, the mom jokes, "You're probably wondering why she is in the hospital. We're not gonna tell you. Bye Guys!" (Butler 2014, 7:00-7:04). Just then the title cards start playing before coming to a screeching halt. Once more we see the mom's joking face as she says "Just kidding! That would be so mean," (Butler 2014, 7:07-7:10). The joke here is the implication that Emmie has a right to keep her illness private. Instead, mom Colette and dad Shay argue that their audience is entitled to know private details, such as illnesses, about their children. This particular instance works to further the family's authentic image, as it shows that, like any other family, sometimes their children are sick. Nevertheless, it is the result of an exploitative moment, where fitting with the ILO's definition of child labor, they seem to have caused their child emotional harm, pushing her boundaries and right to privacy in a moment of increased vulnerability.

CGH, similarly, often share private information about their children regardless of the social, emotional or physical costs. Paisley, the youngest McKnight child, was adopted into the family as a baby. Over the years, CGH has shared many details about Paisley's adoption story. In one instance, they show six-year-old Paisley excitedly receiving a happy birthday message from her birth siblings. She looks at the camera as she says, "those are my birth sister and birth brother," (McKnight 2017, 9:18-9:20). This is a vulnerable and personal moment for Paisley. Furthermore, as a six-year-old, she is not able to fully appreciate the

possible consequences, whether social or personal, of making this information accessible to anyone. Forever, regardless of what she desires in the future, people will have access to intimate details about her birth and upbringing. Her excitement and joy about family help construct CGH's wholesome authentic family image. Once more, however, it comes at an unquantifiable emotional cost to a child.

Sometimes, parents share seemingly embarrassing moments in the lives of their children, regardless of the emotional harm this may cause their children. In one Shaytards vlog, Avia, the second oldest Shaytard, is having a hard time at the beach. She then begins to cry and express distress. Rather than comfort his daughter, however, dad Shay laughs and continues filming, telling his daughter there is nothing to be afraid of (Butler 2010). While from an adult's perspective this may seem inoffensive, a relatable and authentic moment of a child having a tantrum, it is still an instance of a hyper-vulnerable moment in a child's life being used for content/profit, regardless of the potential harm to that child. Now, any of Avia's friends and/or classmates can go on YouTube and easily find a video of Avia in distress. Her distress is the price to pay for continuing to build her family's authentic image.

### **Overlap between Play and Sponsorship Time**

Even when children seem as if they are having fun on camera they are still engaging in child labor for their image is being used to generate a profit. Labor and fun, even for children, are not mutually exclusive. Both CGH and the Shaytards incorporate "fun" clips where their kids are promoting products. In these instances, the boundaries between down time and labor are blurred.

In a more overt example of child labor, in one Shaytards vlog, dad Shay and mom Colette use their kids to incentivize fans to buy their merchandise. They show their children, most of whom are under the age of ten, signing over two thousand calendars. It is part of their yearly calendar sale, explains dad Shay, encouraging fans to be one of the first two thousand people to pre-order a calendar so they receive one with all of their children's signatures. As the day progresses, Shay says, "We're still signing them guys. My hand, face, feet and feelings are sore," (Butler 2016, 7:38-7:44). Here he acknowledges that it is hard for him, an adult, to sign so many calendars. It is not far-flung to assume that the children, similarly, felt some exhaustion from the task. Thus, as the ILO definition of child labor establishes, this instance exemplifies how the children are potentially harmed emotionally, as their free time is taken away for the sake of the family business.

Oftentimes, however, the line between fun and labor is far blurrier. A few years ago, mom Mindy began a hair-product line that now sells across Walmart's across the United States. The children have always played a central role in advertising the products. In one particular video, they show the CGH children at a photoshoot for the products. Throughout the video they emphasize how much "fun" the kids are having, as their pictures are taken (McKnight 2022). They are getting their makeup done and sitting around the pool, all very fun and exciting. Nevertheless, the reason for the "fun" photoshoot is to create advertisements for Mindy's hair products. Regardless of how much the kids are enjoying themselves, ultimately, they are working as models. The children are engaging in labor, for they are producing images that are being used to sell products. This, however, is disguised under the illusion of the fun and glamor of a photoshoot.

In an even blurrier form of product promotion, family vloggers often incorporate ads into their videos. In one CGH video, mom Mindy and son Daxton are seen playing with Nintendo's in the back of their car. The mom explains that she and her son, "play together once in a

while when we're sittin in the car being bored," (McKnight 2016, 1:49-1:50). This moment of apparent leisure and joy, however, is a Nintendo sponsorship. At the beginning of the video, mom Mindy and dad Shaun thank Nintendo for "partnering with them" (McKnight 2016, 0:10-0:20). Similarly, in the McKnight's morning routine vlog, dad Shaun shows the little ones, Daxton and Paisley, using beddies - a type of sheet for young children. Dad Shaun touts the wonders of Beddies, claiming it makes their mornings much easier (McKnight 2016). He does not mention, however, that the CGH family has stakes in the company that makes Beddies. Instead, viewers are misled to believe that these are genuine, unbiased recommendations. Meanwhile, the kids are made to act out for the camera how easy it is to use the product. Their freetime is taken by the responsibility of generating content and financial profit for the family.

Thus, not only do children in family vlogs lack privacy, their lives are also made to revolve around the family's needs for advertisement, promotion and content. As such, they are spending large amounts of their freetime on camera and working for the family business. Consequently, they fit the ILO's standard of child labor that the child must spend large swaths of their afterschool time on the other activity.

### **At Least We Protect Them: The Language of Online Safety**

Both the CGH and Shaytard parents define online safety in a way that makes their choices for their children socially and ethically permissible. One way they did so was by, initially, not sharing the kids' legal names. In the CGH channel, they would refer to the children as CGH #1, CGH #2, CGH #3, etc. based on their birth order. Meanwhile, the Shaytard kids would be referred to by tard adjacent nicknames such as Babytard and Princesstard. As they used these nicknames, however, both families would still share the faces and experiences of the children. Eventually, both families stopped using nicknames for the kids. In choosing to hide their names but not their faces, these families created a definition of privacy that benefited the family business. Sharing a child's personal life events becomes fair game insofar as they are not sharing their legal identity.

These parents also used social media platforms policies to redefine safety. In the video, "Happy 9th Birthday Princesstard!" there is a part where the dad lets Princesstard, whose real name is Avia, know that she has received many happy birthday wishes via his Twitter account. Avia expresses a desire to receive the messages to her own account to which dad Shay replies, "when you're 13 you can get one," (Butler 2014, 12:03). Once more, family vloggers are redefining safe social media use for children. Dad Shay's comment suggests that it is dangerous for Avia to have her own account before she is thirteen, for that is the age at which one can officially (according to both X and Instagram) one can get a social media account. It is important to note, however, that thirteen is not a magical age at which point children gain the maturity to navigate social media, it is merely a policy used by various social media companies. Furthermore, it is dangerous to presume that social media is only bad for children when they are in charge of it. Sharing a child's image and identity online, whether they are five or thirteen, can be dangerous regardless of if they can log into the account. Nevertheless, these parents' redefinitions successfully present them as sensible and safe guardians who are taking all measures necessary to protect their children. The kids are not engaged in child labor according to these parent's efforts, for the parents are taking all necessary precautions to mitigate possible harm.

## **Discussion**

Children in many family vlogs are engaging in child labor, as defined by the ILO. The ILO stipulates two main ways in which paid tasks constitute child labor: when they harm children - whether that be emotionally or physically - and when they affect the child's schooling and/or result in a large commitment outside of school (2023).

The difficult work of maintaining an authentic brand tends to fall on the children, regardless of the consequences and pressure. Authenticity, as defined by Taylor (2022), is an action rather than a fixed term. Each content creator has their own definition of authenticity that they then attempt to represent to their viewers. If they stop being perceived as authentic they risk losing everything. For family vloggers, their relationship with authenticity is under constant tension. They tend to initially define authenticity as having an average working/middle income family. As they grow more famous and wealthy, however, it becomes more difficult to sustain that type of authenticity. There is a world's worth of distance between doing hairstyles on a bathroom counter and picking out your hairstyle to the Grammys (McKnight 2017). Instead, these channels lean on the children's relatable and universal experiences of childhood to craft an authentic brand. This comes at a cost, however, as children consequently lack the right to define what aspects of their life should remain private. Furthermore, it is a potential source of stress, as the people around them will forever have disproportionate access to information on their lives and upbringing.

Much of the harm caused in the search for authenticity is the result of placing a burden of emotional labor on the children. Children are a vulnerable population. They are dependent on their parents and, thus, it is hard to extricate what constitutes consent and what are parent's taken for granted assumptions as to what their children are comfortable sharing on camera. Furthermore, it is impossible to know for certain how much pressure children feel to perform for camera's and ensure the channel's success, as for families like CGH and the Shaytards, that has/is their main source of income. As Marwick and Boyd argue, what people post on social media is a performance (2010). Even if a child would have to get ready for school regardless of if they are being filmed, it is likely that the presence of the camera is a weight that adds a layer of performance, of labor, to these everyday tasks. Thus, when everything in one's life is open to the cameras, when it is nearly impossible for one to define the boundaries of their privacy against the power of their parents, children are thus engaging in large amounts of emotional labor. The weight of that emotional labor is a type of harm that does not necessarily have immediate consequences. Nevertheless, over the years, as the children of family vlogs navigate a world where friends and strangers alike know the intimate details of both their highest and lowest moments, that weight may become all too real and present.

In addition to the possible harm, as the ILO specifies in its definition, family vlogging can also consume much of these kids out of school time. Whether directly engaged in labor - such as, signing two thousand calendars for fans - or indirectly - such as, being filmed making your bed for an advertisement - the camera and the labor are never too far. Often framed as every day, fun life, they are made to incorporate product placements and create advertisements in their alleged freetime. Further increasing the stakes of harm, most family channels, including CGH and the Shaytards, do not share if and/or how the children are compensated for their work. Thus, not only are these children made to spend many hours producing content for their families, they may never be properly remunerated for it. Instead, parents try to assuage concerns of child labor by redefining online safety as when a child does not have control over a social media account and the public does not know their legal name.



## Policy Recommendation

Limits should be placed at the national level as to what and how children can participate in online content. As I demonstrate throughout this article, the presumption that parents always know and act in their child's best interest is incredibly challenged in the world of family vlogging. Parents may want to provide for their children while simultaneously benefiting financially from making their children the stars of their online content. Furthermore, there is no moral or ethical way that one can gain consent from a child to have their childhood shared with thousands if not millions of strangers. Thus, given the impossibility of true, informed consent, the clash of interests between parents seeking what is best for their children and what is best financially, and the various possible harms children in family vlogs are exposed to, children should not be in family vlogs. What I mean by this is not that parents should not be able to discuss their lives as parents. Rather, my suggestion is that, until a certain age, parents should not be able to post clearly identifiable content centering their children and generating a profit from it. All children deserve a childhood free of the emotional labor and harmful consequences attached to family channels.

## Conclusion

Family vlogging, with its competing tensions and large profits, is unlikely to disappear any time soon. Thus, it is all too important that the role of children in this type of content be closely examined and considered. Through this paper I sought to see if children in family vlogs fall into the ILO's definition of child labor. Through the case studies of CGH and the Shaytards, I demonstrated that family vlogging puts an undue emotional labor burden on children. Furthermore, it is harmful in so far as it violates children's right to privacy and can consume their freetime from school. All the while, it remains unclear if the children are receiving any financial compensation for participating in these vlogs. In an effort to address these kinds of critiques, the parents of these family channels have attempted to define internet safety in a vague manner that suits their needs. Regardless, I suggest that efforts should be made at the national level to protect children from being harmed for the sake of internet content.

There is still much to be researched and understood about children in family vlogs. This paper's major limitation was the limited sample size, both in videos coded and channels analyzed. It is possible that, by observing more videos and more channels, different patterns of the uses of children in these vlogs will emerge. There is also a time component. Both the Shaytards and CGH are early content creators, who set the ground for what family vloggers are like today. Thus, it is possible that there are differences in the work of children from older YouTube generations versus newer YouTube generations.

Furthermore, there are many interesting areas for future exploration. For instance, many of the most popular family vloggers, including the Shaytards and the McKnights, are members of the Latter Day Saints Church. This generates questions as to the relationship between religion, vlogging and children. Additionally, there is also a lot to be learned as to the families' marketing strategies. Due to time constraints, I was unable to conduct a deeper dive into the use of children in video titles and thumbnails. Nevertheless, there is much to be learned on the role children play by simply evaluating these families' advertisements. Another area

of interest that could answer many of the questions on possible harm is interviewing the children of family channels. Thus far, much of the research has centered around content analysis, with limited contact with the creator's investigated. As the children of family vloggers grow older, however, the opportunity opens up to understand how they interpret the ups and downs of their unique upbringing.

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## Appendix

## Appendix A

*5 Most Popular McKnight Family Blogs*

Video	Date Published	Views	Likes/Comments
Our Family Morning Routine   Behind the Braids Ep. 2 ( <a href="https://www.youtube.com/watch?v=ueFm5FCpw5I">https://www.youtube.com/watch?v=ueFm5FCpw5I</a> )	April 24th, 2016	14.54 million	143K Likes/ 15,460 Comments
Paisley Goes to First Daddy Daughter Dance   Behind the Braids Ep. 24 ( <a href="https://www.youtube.com/watch?v=mPYFacIQj6c">https://www.youtube.com/watch?v=mPYFacIQj6c</a> )	February 12th, 2017	13 million	69K Likes/ 5,468 Comments
Finding Our Summer Fun ( <a href="https://www.youtube.com/watch?v=jzES2BCRObk">https://www.youtube.com/watch?v=jzES2BCRObk</a> )	June 18th, 2014	10.46 million	44K Likes/ NA Comments
Paisley's First Day of School vs. Brooklyn and Bailey's   Behind the Braids Ep. 11 ( <a href="https://www.youtube.com/watch?v=SDBZSciCxec">https://www.youtube.com/watch?v=SDBZSciCxec</a> )	August 28th, 2016	7.07 million	75K Likes/ 7,081 Comments
Brooklyn Gets Asked to Homecoming in Front of School   Behind the Braids Ep. 12 ( <a href="https://www.youtube.com/watch?v=ELbDBq_LXf0&amp;t=2s">https://www.youtube.com/watch?v=ELbDBq_LXf0&amp;t=2s</a> )	September 11th, 2016	6.2 million	71K Likes/ 3,740 Comments

## Appendix B

*5 Most Popular Shaytard Family Blogs*

Video	Date Published	Views	Likes/Comments
BABYTARD IS SICK! ( <a href="https://www.youtube.com/watch?v=Os-SymeUFFU">https://www.youtube.com/watch?v=Os-SymeUFFU</a> )	August 14th, 2014	30.43 million	124K Likes/ 25,379 Comments
WE GOT A SWIMMING POOL! ( <a href="https://www.youtube.com/watch?v=nJ0mIqsSQEM">https://www.youtube.com/watch?v=nJ0mIqsSQEM</a> )	June 16th, 2015	26.45 million	96K Likes/ 9,434 Comments
A BABY IS BORN! ( <a href="https://www.youtube.com/watch?v=AEyfCz2CTH8">https://www.youtube.com/watch?v=AEyfCz2CTH8</a> )	October 16th, 2013	23.68 million	265K Likes/ 71,400 Comments
SHAYTARDS FAMILY CANNONBALL! ( <a href="https://www.youtube.com/watch?v=vaZ3ZRyMtb8">https://www.youtube.com/watch?v=vaZ3ZRyMtb8</a> )	December 3rd, 2014	23.45 million	79K Likes/ 13,557 Comments
HAPPY 9th BIRTHDAY PRINCESSTARD! ( <a href="https://www.youtube.com/watch?v=ueFm5FCpw5I">https://www.youtube.com/watch?v=ueFm5FCpw5I</a> )	May 5th, 2014	22.48 million	120K Likes/ 26,059 Comments

## Appendix C

*5 Randomly Selected McKnight Videos*

Video	Date Published	Views	Likes/Comments
Kamri Comes for a Visit, Snake Bites, and Family Photos!   Behind the Braids Ep. 128 ( <a href="https://www.youtube.com/watch?v=nkbCmpr0Dcg&amp;list=PPSV">https://www.youtube.com/watch?v=nkbCmpr0Dcg&amp;list=PPSV</a> )	September 28th, 2020	952K	14K Likes / 799 Comments
First Day of IN-PERSON School + Kamri at BYU   Behind the Braids Ep. 127 ( <a href="https://www.youtube.com/watch?v=ZuErYE3PPc&amp;list=PPSV">https://www.youtube.com/watch?v=ZuErYE3PPc&amp;list=PPSV</a> )	September 14th, 2020	589K	12K Likes / 852 Comments
First DAY of School   Rylan Gets Accepted to COLLEGE ( <a href="https://www.youtube.com/watch?v=FBSKOBjhpFE&amp;list=PPSV">https://www.youtube.com/watch?v=FBSKOBjhpFE&amp;list=PPSV</a> )	August 22nd, 2022	293K	5.7K Likes / 280 Comments
April Fool's Joke on Brooklyn and Bailey   Behind the Braids Ep. 1 ( <a href="https://www.youtube.com/watch?v=FYwu9eFeM74&amp;list=PPSV">https://www.youtube.com/watch?v=FYwu9eFeM74&amp;list=PPSV</a> )	April 11, 2016	4.9 million	58K Likes / 3,284 Comments
Tarantula Scare, Hairitage Family Photoshoot, Robotic Competition, and MORE! ( <a href="https://www.youtube.com/watch?v=RWgMLPJK5Zs&amp;t=124s">https://www.youtube.com/watch?v=RWgMLPJK5Zs&amp;t=124s</a> )	October 31st, 2022	170K	2.2K Likes / 120 Comments

## Appendix D

Video	Date Published	Views	Likes/Comments
OUR DREAM BEDROOM! ( <a href="https://www.youtube.com/watch?v=MPP12gaqwc&amp;list=PPSV">https://www.youtube.com/watch?v=MPP12gaqwc&amp;list=PPSV</a> )	October 24th, 2014	1.5 million	56K Likes / 4,905 Comments
I'M A GAY HUNGRY MAN! ( <a href="https://www.youtube.com/watch?v=Cd3N80Jn8A&amp;list=PPSV">https://www.youtube.com/watch?v=Cd3N80Jn8A&amp;list=PPSV</a> )	January 19th, 2011	607K	15K Likes / 4,593 Comments
HAPPY VALENTARDS DAY! ( <a href="https://www.youtube.com/watch?v=oYTDmWlfZXY&amp;list=PPSV">https://www.youtube.com/watch?v=oYTDmWlfZXY&amp;list=PPSV</a> )	February 15th, 2010	346K	16K Likes / 1,716 Comments
SHE'S CHOPPING IT OFF ( <a href="https://www.youtube.com/watch?v=9mbW7X0nlk8&amp;list=PPSV">https://www.youtube.com/watch?v=9mbW7X0nlk8&amp;list=PPSV</a> )	August 4th, 2016	1.4 million	26K Likes / 3,641 Comments
ALL DAY AT THE MALL! ( <a href="https://www.youtube.com/watch?v=fumTGXshSI4&amp;list=PPSV">https://www.youtube.com/watch?v=fumTGXshSI4&amp;list=PPSV</a> )	December 23rd, 2016	460K	11K Likes / 2,182 Comments

# Achieving Gender Parity: A Comprehensive Analysis of Women's Underrepresentation on the International Court of Justice and Strategies for Future Reforms

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The International Court of Justice (ICJ) is the highest judicial entity within the United Nations, resolving international conflicts to maintain global peace. The current judge selection process for the ICJ ensures diverse geographic representation with judges of varied nationalities, races, and cultures. However, female judges are underrepresented, comprising only 4.6% of judges in the court's history. This research article aims to examine the connection between this lack of female representation and the judge selection process, starting from the nomination phase and extending through the election process. It is argued that there are four primary drivers for female underrepresentation on the ICJ: almost exclusively focusing on geographical representation, a male-dominated nomination process, the preference of judicial qualities aligned with expertise in male-dominated professions, and re-elections allowing judges to serve multiple terms. A diverse ICJ bench is imperative to ensure impartial case outcomes because they have the potential to impact entire societies. Consequently, equitable representation of the global population at large is inevitable. This research article proposes strategic reforms focused on refining the nomination and election procedures to achieve gender parity on the ICJ.

## Introduction

The International Court of Justice (ICJ) is a powerful symbol of humanity's ongoing pursuit of peace during conflict. Located within The Hague's Peace Palace in the Netherlands, the ICJ was established in 1945 as the highest judicial body of the United Nations (UN). Its primary mission is to resolve disputes among countries through dialogue and the law, rather than resorting to violence. With jurisdiction over public international law disputes among the 193 UN Member States, the ICJ addresses issues such as conflict, war, and genocide, all in the pursuit of maintaining global peace and stability (List of All Cases, n.d.). Having handled 193 cases as of March 2024, the ICJ remains committed to upholding justice worldwide (Cases, n.d.).

Achieving justice in international courts is contingent upon a diverse bench of judges, each contributing unique perspectives and backgrounds to legal proceedings. This diversity is exemplified through the variety of interpretations of the law, stemming from differing legal philosophies, cultural viewpoints, and professional legal experiences. Such diversity guarantees a thorough examination of every aspect of a case, enabling judgments that authentically encapsulate the complexities of conflicts between countries while adhering to legal principles.

However, despite the ICJ's mission of advancing humanity's pursuit of world peace, it has encountered significant challenges in crafting a bench of judges that truly reflects the diverse perspective of the global societies it aims to serve. In other words, the court has never had more than four female judges at any given time, despite its bench consisting of 15 seats. These challenges contrast with the achievements of other institutions, such as the International Criminal Court (ICC), which successfully achieved gender parity back in 2018. Unfortunately, the ICJ has yet to make substantial progress in this

regard. In fact, the ICJ is still as diverse in 2023 as it was ten years ago, raising concerns about the court's ability to authentically represent the perspectives of the states it serves. Four out of the fifteen judges are currently women, the highest number in the history of the court. The court strives to include different nationalities and, therefore, different cultures, but, to this day, the ICJ does not yet have a well-balanced number of female and male judges. In a court that is representative of different countries, racial groups, and religions, why are female judges on the International Court of Justice still underrepresented?

The underrepresentation of female judges on the ICJ arises from four main factors: emphasis on geographical representation, a nomination process predominantly controlled by male decision-makers, the preference for traits commonly associated with professions primarily pursued by male ICJ candidates, and judge re-elections that keep current judges on the bench for multiple terms. These distinct issues reinforce the underrepresentation of women on the ICJ by creating a cycle in which male legal professionals set the bar for future judges who turn out to be like themselves. Increasing the number of women on the ICJ is crucial because only then can the general global population be represented truthfully, leading to case outcomes grounded in the law and more accurately reflecting the opinions of the global population.

In the process of answering the question of why female judges on the ICJ are still underrepresented, eight international experts from eight different countries were interviewed in December 2022 and January 2023 on their perspectives on gender parity in the context of international courts, the nomination process to the ICJ, and potential ways to increase the female representation on the ICJ bench, such as the elimination of judge re-elections and the introduction of a gender quota.



## I. The Importance of Gender Parity

Improving representation on the ICJ is a crucial step to take because it will allow for more diverse perspectives to contribute to court decisions. Not achieving gender parity on the judicial benches is problematic because the court's decisions impact entire societies. The ICJ should have both gender equality—achieved through policy changes to treat women and men equally—and gender parity, the demand for ‘an equal number of women and men,’ or in this case meaning seven or eight female and male judges each on the ICJ bench (Corsi, 2021). Decisions impacting the lives of both men and women are still, in the 21st century, predominantly being made by men in the highest jurisdiction sphere. This is especially, but not exclusively, important for cases involving women's rights: The case *Croatia v. Serbia* (1999–2015), which decided ‘on whether rape and sexual violence constitute acts of genocide,’ had only three female judges on the bench and therefore involved in the decision-making process (International Court of Justice, n.d.). This presents an issue because sexual violence during conflicts and genocides is primarily inflicted upon women, underscoring the importance of female judges' perspectives (Kelsey-Sugg et al., 2024). The ICJ ultimately decided that, while both countries committed acts of genocide, there was not enough evidence showing ‘genocidal intent’ (Milanovic, 2015). The ‘intent’ hereby includes both physically and mentally harming victims (Application of the Convention, 2015a). The three women, Judge Hanqin, Judge Donoghue, and Judge Sebutinde, submitted two individual declarations and one separate opinion. Judge Hanqin and Judge Donoghue submitted declarations and voted like the majority of the court but wished to express their individual concerns with the overall judgment. Judge Sebutinde submitted a separate opinion because she disagreed with the overturning of one of Serbia's preliminary objections to Croatia's claim against ‘violations of the Convention on the Prevention and Punishment of the Crime of Genocide’ during the Balkan War. In her opinion, upholding the objection could have led to a different court decision (Application of the Convention, 2015b). Out of the male judges, 58% submitted additional documents stating their individual opinions (Application of the Convention, n.d.). The more individual documents are submitted, the lower the legitimacy of the court decision. All female judges submitting additional documents after the court decisions had been made shows that they did not agree with the entirety of the decisions. The less diverse a court is, the more judging processes and results lack legitimacy (Kenney, 2013). Given that women are often disproportionately impacted by sexual violence compared to men, they are likely to offer a distinct perspective on the same matter. The outcome of the case might have been different had there been greater female representation on the bench.

As is customary in labor force studies, we limit our native and immigrant sample to male adults of working age (18 to 65). We also restrict our immigrant sample exclusively to males who immigrated to the U.S. after turning 18 to ensure the tracking of cohorts across censuses is unaffected by subsequent waves of immigrants who arrive as children. This accounts for the possibility that immigrant children likely assimilate faster than their adult counterparts due to their integration into the American education system.

Among experts, the consensus is that the legitimacy of court decisions can improve with an increased presence of female judges on the bench, even though it is generally difficult to isolate the exact factors that improve legitimacy. ICC judge Alapini-Gansou from Benin shared her opinion on whether more female judges on the ICC improved legitimacy upon achieving gender parity. She has been a judge on the ICC since March 11th, 2018. Prior to serving on the ICC bench, Judge Alapini-Gansou worked at the African Commission on Human and Peoples' Rights for 12 years, including three years as Chair of the Commission from 2009 to 2012. From 2012 to 2014, she was a judge on the Permanent Court of Arbitration (Judge Reine Alapini-Gansou, n.d.). When interviewed, she argued that she does not ‘want to pay tribute to women for that [increased legitimacy] because all of us [ICC judges] are here to improve legitimacy of the court’ (Judge Alapini-Gansou, 2023). However, according to another expert, Nathalia Contreras-Pardo from Colombia, who has taught human rights and constitutional law at the Universidad de Los Andes and the University of North Carolina, gender parity is crucial. She argues that achieving gender balance is essential for fostering broader societal trust in court decisions, thereby enhancing their legitimacy (Contreras-Pardo, 2022). Court legitimacy is important because, if judges do not reflect the global community, ‘then there will be more of a reluctance to resort to the legal system’ (Khalifa, 2022). Judges on the ICJ bench are entrusted with the task of interpreting international law and advocating for the interests of the citizens of the nations they represent. This responsibility cannot be adequately fulfilled by a bench consisting of only one gender. An anonymous informant added that, especially when issues involve gender, ‘like gender-based violence, women's voices are lacking and improving their representation probably does have an effect on [the] content [of the court's decisions]’ (Anonymous #1, 2022). Arriving at more well-balanced decisions can only happen if different parts of the population are equally represented. The world's population is made up of 49.6% women and 50.4% men, so 4.6% of judges in the history of the ICJ having been female clearly shows that there is a gender imbalance (Corsi, 2021). There are multiple causes for this misrepresentation, starting with the formulation of the Statute of the ICJ.

## II. The ICJ Statute and the Focus on Geography

The ICJ aims at representing the world's population on its bench. While its strategy of appointing a certain number of judges from predetermined regions has proven effective in generating a balance of different ethnicities, races, and nationalities, it has resulted in the exclusion of female judges. Article 9 in Chapter 1 of the Statute of the ICJ lies out the responsibilities of the ICJ to ensure a well-rounded constellation of the bench:

At every election the electors shall bear in mind not only that the persons to be elected should individually possess the qualifications required, but also that in the body as a whole the representation of the main forms of civilization and of the principal legal systems of the world should be assured (Statute of the International Court of Justice, 1945).

The word ‘shall’ renders the language of the Statute of the ICJ rather suggestive. To represent ‘the main forms of civilization,’ the ICJ mostly focuses on geographical representation (Statute of the International Court of Justice, 1945). To do so, the ICJ splits

the world map into five regional groups: Latin America and the Caribbean (two judges), Eastern Europe (two judges), Western Europe and other countries, including the United States (five judges), Africa (three judges), and Asia (three judges). This is an issue because female judges in certain regions, such as East Asia and the Pacific, as well as Sub-Saharan Africa, respectively only make up 17.78% and 23.95% of total judges (Constitutional Courts In Latin America And Sub-Saharan Africa, n.d.). Female judges are undervalued in these regions, resulting in less support on their way up the judicial ladder. Nathalia Contreras-Pardo argues that the ICJ ‘... was created in a different context’ where gender parity was not yet a policy goal ‘... and the question is why it [the ICJ Statute] has not been updated to the recent standards of equality’ to strive for gender parity (Contreras-Pardo, 2022). It follows that the outdated language of the Statute of the ICJ creates a barrier to success in the legal field for women and drastically limits the size of the nomination pool for female judges.

The scarcity of female judges on national courts is another factor that affects their presence in international courts. An expert on national courts, Amani Khalifa, participated in an interview on this topic. She is a lawyer at Freshfields Bruckhaus Deringer LLP, specifically engaged with cases in the Middle East and North Africa region. Her focus lies in the real estate as well as the oil and gas sectors, and she was called the ‘future star of arbitration’ by the Chambers Global legal rankings (Amani Khalifa, n.d.). Khalifa is the Co-Chair of the Africa Steering Sub-Committee for the Equal Representation in Arbitration (ERA) Pledge, advocating for female representatives on international arbitral tribunals (Committees, n.d.). Khalifa finds that if there are fewer women judges on national courts, there will be ‘fewer women on international courts as well’ because what might be perceived to be relevant experience to decide cases would not be found in many female candidates and ‘there is no substitute for experience’ (Khalifa, 2022). Since an all ‘male environment is taken for granted as being the default situation,’ it is difficult for women to work themselves up the judicial ladder in the same way (Anonymous #1, 2022). Khalifa describes this as a circular problem because female judges need experience to be nominated and later elected, but they are not provided the opportunity to work themselves up the judicial ladder. Even if potential female and male judges have equivalent credentials, the smaller pool of female judges lowers the chances of a woman being selected because male candidates outnumber female ones (Khalifa, 2022). Focusing on only geographical representation without accounting for low numbers of nominated female judges in some of the regions has therefore contributed to the exclusion of women on the ICJ. However, even if there are few female judges on national courts and therefore in the nomination pool of regions like East Asia and the Pacific or Sub-Saharan Africa, they technically only need one qualified woman to be nominated to have her elected and represent the region later. Therefore, geographical representation cannot be the sole reason for the underrepresentation of women on the ICJ.

### III. The Nomination Process

Fifteen judges serve on the court, usually for nine-year terms. The election process begins locally within the regional groups. Within these regional groups, there are national groups consisting of four individuals with judicial expertise and diverse

political affiliations who nominate judges to the ICJ. Article 6 in Chapter 1 within the Statute of the ICJ advises that, prior to formal nomination procedures, the national groups should seek input on potential nominees from reputable entities, including the highest court of justice in the respective country and faculty members from leading law institutions (Statute of the International Court of Justice, 1945). These institutions tend to be highly male dominated. For instance, the United States’ Supreme Court comprises four female judges alongside eight male judges (Current Members, n.d.). The United Kingdom’s Supreme Court features two female judges and ten male judges (Biographies of the Justices, n.d.). Likewise, within law schools, there is a disparity in the representation of female faculty members. Harvard Law School, for instance, has 28% full-time female faculty and 72% full-time male faculty members (Jenkins, 2018). Consulting predominantly male stakeholders during the domestic nomination process of ICJ judges could bias judge selection towards male candidates. Increasing the involvement of female stakeholders in the nomination process may enhance the chances of nominating female judges to the ICJ.

#### A. Psychological Influences on Judge Selection

According to the Oxford Handbook of Social and Political Trust, psychologically speaking, humans ‘place [their] highest levels of trust in people [they] interact with most closely and who are most like [themselves]’ (Uslaner, 2017). For the ICJ judge election process, this suggests that predominantly male decision-makers in the nomination process rather first think of male candidates and, if even, only of few female potential judges. However, this does not only have to be the subconscious favoring of people who are more like themselves, meaning men electing men, but also that fulfilling a high judicial role at the ICJ requires trust. People tend to trust candidates who are most like the nomination stakeholders and who are part of the same group, the male gender group in this case (Uslaner, 2017). These subconscious biases are difficult to measure or to eliminate.

#### B. Male Domination in the Nomination Process

By consulting primarily male organizations during the ICJ nomination process, institutional sexism—discrimination within institutional frameworks based on an individual’s gender, such as salary gaps in the workplace—contributes to the absence of female nominees (Capodilupo, 2017). Many presume that men are competent for positions in the government or the legal system, whereas women must demonstrate their extraordinary competency. Amy Cuddy, an American social psychologist, describes this as the ‘warmth and competence’ group stereotypes where ‘warm’ people are ‘good-natured, trustworthy, tolerant, friendly, and sincere’ and ‘competent’ people are ‘capable, skillful, intelligent, and confident.’ The combination of these characteristics varies across gender groups, where women fall into the ‘warm but not competent’ category unless they are wealthy and white (Cuddy et al., 2008). Cuddy mentions that feminists were even categorized as both low on warmth and competence. Potential male judge nominees are more likely to be seen as warm and competent opposed to female candidates because ‘... when groups tend to be concentrated in certain roles, they receive the stereotypes that follow from those roles’ (Cuddy et al., 2008). The international judicial roles are mostly filled by

men and therefore connected to the stereotypical character of themselves. This gender bias and the resulting constellation of the government, law schools, and courts reinforce the lack of female ICJ nominees through this institutional sexism. On America's highest court, the Supreme Court, there were three women in 2010 when the American female judge, Joan E. Donoghue, was appointed to the ICJ as the first American woman. This was also the first year when three female judges served on the Supreme Court instead of two in the years before (Cornell Law School Legal Information Institute, n.d.). This correlation suggests that, once women are involved in decision-making, the outcomes of judge election processes are different. Still, the numbers of women in high government and law positions are too low to achieve gender parity on the ICJ in this way.

### C. Vote Trading

The nomination process becomes increasingly complicated because countries leverage their international power and political relationships for vote trading, shaping the composition of the judge nomination pool. Luka Misetic, a partner at the international law firm Squire Patton Boggs, clarified that, at the end of the day, states, and not the national groups, have the last word in candidate nominations and elections (Miseti, 2023). As the youngest lawyer to defend a case in front of an international criminal tribunal, Misetic defended Croatian General Ante Gotovina before the International Criminal Tribunal for the former Yugoslavia in The Hague and was named one of the 100 most influential Croatians in the world (Bach, 2006; Luka S. Misetic, n.d.). According to Misetic, the reasons for why there are few female judges on international courts are 'systemic,' one of them being that many of the candidates are appointed in 'diplomatic trading' (Miseti, 2023). This diplomatic trading shows itself within a country through making deals with other countries to vote one way for a particular judicial candidate and in exchange agreeing on another unrelated vote at the UN. Misetic says he 'wished it were the case that they [national nominating groups] were getting excellent resumes from professional judges and then pick the best judicial candidate, but that is not how this process works.' For example, if Germany wants to present a candidate, they must look for other states willing to vote for that German candidate. A German male law professor who was interviewed and wished to remain anonymous explained that, in return, Germany makes promises to these states to vote for their candidate on a different occasion, such as for a Security Council membership (Anonymous #2, 2023). This candidate can therefore only be successful if the German government supports them and is willing to trade the German vote on a different occasion. Heavily involving a country's political interests outside the judicial appointment to the ICJ leads to the following problem:

Some societies are traditionally not viewing women in or advancing women to positions of authority, whether they be judges or whether they be diplomats. You [the nominating groups and governments] still have to make deals with those countries to get your [their] candidates on. So, you [they] might end up having to pick judges from the Middle East, from African countries or from Eastern Europe where they might have a societal legacy of not advancing women. You [they] still have to make deals with those countries, so that you [they] pick someone from their region or their country in order to get your candidates on board (Miseti, 2023).

Vote trading therefore strongly influences the nomination

pool beyond the direct control of regulators, driving down the number of female candidates that could potentially be elected. A recent example from the ICC is Zlata Đurđević from Croatia who received an endorsement from the UN committee for her candidacy, while her Italian opponent, Judge Rosario Salvatore Aitala, was not endorsed. Nevertheless, he won the election, most likely because 'Italy is a much more powerful country, especially at the time, than Croatia, and was able to cut more deals' (Miseti, 2023). More thought needs to be put into the landscape of nomination stakeholders, as well as into the nomination process, to create more opportunities for female judges to be nominated and later elected to the ICJ.

### IV. Independent Decision-Making: Good or Bad?

Based on the favored trait of region-dependent decision-making, the likelihood that a candidate will make independent decisions and not be sensitive to political factors is a major concern and decision factor during the nomination and election process (Creamer et al., 2017). Being known as a judge with independent opinions or as insensitive to policy considerations is known to reduce the expected vote share of the candidate in the relevant groups and organizations who seem to be looking for judges who do not tend to make independent decisions on their cases (Creamer et al., 2017). In this case, independent decisions refer to judges voting on cases based on their own beliefs, rather than on the standpoint of their home countries. The separation of independent and dependent decision-making in international law has a correlation with fewer women being nominated and later elected to the ICJ. According to psychological research, women typically make more independent legal decisions than men (Just, 2020). However, this does not necessarily have to mean that women disregard the standpoints of the country they are representing. This evidence suggests that women are less likely to be influenced by the other judges on the ICJ who are not only acting as individuals, but also representing different countries with diverging views.

The independence of female judges is evident as they exhibit lower susceptibility to the influence of other judges with opposing opinions. There are two studies relevant to establish this finding. First, Professor Sunstein from Harvard Law School found that in teams of three judges in America, three Republican judges vote one hundred percent according to their party's beliefs, and the same happens with another team of three Democratic judges (Sunstein, 2006). When the panels do not consist of three judges of the same political views, the outcomes differ slightly by the type of case, but in most cases, the voting pattern of judges changes when they are the political minority on a panel. One Democratic judge working on a team with two Republican judges tends to vote like a Republican judge. The same happens when a Republican judge joins a duo of Democratic judges: the decision of the Republican judge goes more toward the Democratic side. The decisions made by individual judges can therefore be influenced by the other judges on the relevant court (Sunstein, 2006). This evidence underscores the impact of the composition of judicial panels on decision-making processes, demonstrating that judges' voting patterns can change when they are the political minority on a panel.

Beyond the influence of judges with different beliefs on each other, gender also plays a significant role in court decisions.



Jennifer L. Peresie's research on three-judge federal appellate panels in Title VII Sexual Harassment and Sex Discrimination cases reveals a strong correlation between the composition of the panel and case outcomes. In the 311 examined cases where only male judges were present, plaintiffs, meaning the victims of sexual harassment and/or sex discrimination, won only 17% of the time. However, the addition of one female judge increased the plaintiffs' success rate to 34%, and with two female judges, it rose to 43% (Peresie, 2005). Female presence influenced both the decisions of Republican and Democratic male judges. For sexual harassment cases, the pro-plaintiff cases increased from 16% to 35%, and for discrimination cases, the number nearly tripled from 11% to 30% (Peresie, 2005). In total, male judges were influenced by the presence of one or two female judges on the panel, whereas the decisions of female judges were not impacted by the presence of one or two male judges. This study was about the rather sensitive topics of sexual harassment and sex discrimination where male judges may be more careful with their judicial reasoning and decision in the presence of women as equal members of the panel. Nevertheless, it is important to note that professionalism dictates that male judges should base their legal reasoning on the merits of the case rather than personal biases. While the addition of female judges to the panel seems to yield positive outcomes, it underscores the importance of diverse perspectives in achieving fair and impartial judgments.

These findings open new doors for the future of law-making as they do not only mean that men are more sensitive to making different decisions when women are involved in the decision-making process, but they also mean that this influence has a positive effect on the outcome of cases. This is, again, a sign to fight for gender parity on judicial courts, such as the ICJ. Now, for the nomination process of the ICJ, this means that women making more independent decisions might not even be undesirable for the countries that they represent. It does not necessarily mean that they put their own beliefs over the ones of their own countries, but it could rather mean that they will not let themselves be influenced by the opinions of judges who come from other countries and therefore represent different principles.

## V. Gender and Court Decisions

The reasons behind the exclusion of female judges advance considerations about the potential impact of gender representation on judicial outcomes and call for further exploration into diversifying judicial benches. In her book, *Can Three Women Really Change the Supreme Court?*, Dahlia Lithwick raised the question of what significance more women on a court could truly have on court decisions in the context of Elena Kagan being appointed to the United States Supreme Court as the third woman (Lithwick, 2010). Some people might interpret this question in the way that 'if women do not revolutionize judging or dramatically change outcomes, the achievement of representation and nondiscrimination by their participation does not offer a very compelling reason to mobilize, or even celebrate,' but one should ask why women need to have a revolutionary influence on court decisions in order to be included and what may justify their exclusion

(Kenney, 2013). It is sometimes assumed that when women enter institutions, they are only worthy of staying if they have a positive effect on the performance of said institution. Having no positive effect is automatically seen as having a negative impact on the performance. However, there is also no significant proof demonstrating the positive effect of men on institutional performance, as this is a question that fewer people are considering. Do women absolutely revolutionize judging? Probably not. Can they change how court decisions are made because they offer different views than their male colleagues? Yes, not always, but yes, as seen in the example of 100% of female ICJ judges submitting individual declarations and a separate opinion in the *Croatia v. Serbia* (1999–2015) ICJ case. Do female judges dramatically change case outcomes of current legal debates? Yes, they do change case outcomes, as seen in the example of sexual harassment and sex discrimination cases in the analysis of Peresie's research. Judges interpret the law through varied lenses, and it is worth looking more into how decisions may change in the future. Until then, one must first look at how the judge nomination pool for the ICJ is being formed and then think of ways to alter this system.

If the criteria for becoming a judge does not change in any way, then it is likely that elected female judges will have similar views to their male colleagues. This does not have to be true, as it currently is not the case with four women on the court, but it could be the case, and it therefore needs to be considered. If this was because women and men make, on average, similar decisions on all issues, then women voting like men would not be an issue. However, the analysis of sexual harassment and sexual discrimination cases as well as the *Croatia v. Serbia* (1999–2015) case have shown that this is not true. Gender parity may be achieved with the same nomination process, but the purpose of gender parity would not quite be achieved. Different selection criteria offer the opportunity to lead to judges on the ICJ bench with more diverse opinions and backgrounds than it currently is the case. We do not know what exact influence more female judges can have on ICJ decisions, but we do know that diverse opinions need to be considered and that female judges have the power to change court decisions.

## VI. Judge Qualifications

To fully understand the ICJ judge nomination process, it is essential to consider a candidate's qualifications as a determining factor in nominations. A successful candidate ought to be sufficiently intellectually equipped to fulfill their role. Both female and male judges at the ICJ are experts in international law and have equally earned their positions, which is why 'a candidate's level of expertise, education and personal reputation' are likely to not be critical points of comparison (Creamer et al., 2017). The full educational background of ICJ judges varies, but their degrees are very similar. All judges have their bachelor's degree. If they studied in a country where a law degree is not a bachelor's degree, such as in the United States, where it is a Graduate Degree, then they often first studied International Relations or Political Science. Joan E. Donoghue even studied Russian and Biology, which is a unique combination compared to other ICJ judges (President Joan E. Donoghue, n.d.). Every judge achieved their Juris Doctor (J.D.) and often also a Latin Legum

Magister (LLM) or a Doctor of Philosophy (PhD). Almost all judges have held professorships at prestigious universities, often in their home countries. All ICJ judges are lawyers and they have held a variety of different legal positions, but most of them had not been judges prior to serving on the ICJ. The educational background of the judges shows that they come from a variety of backgrounds, which, most likely, has a positive impact on court decisions, including a greater number of different experiences and opinions. The professional backgrounds of past elected ICJ judges reveal extensive expertise in the legal field, including various sub-focus areas.

Some experts argue that professors are particularly excellent candidates for serving on the ICJ bench. Vesna Crnić-Grotić, a professor of Law at the University of Rijeka in Croatia, argues that professors of law make excellent candidates ‘... because this is such a specialized field in international law, so in many countries it is really just for the professors to be dealing with these complex international issues that appear at the ICJ’ (Professor Crnić-Grotić, 2023). She was an agent for Croatia at the ICJ at the Convention for the Prevention and Punishment of the Crime of Genocide in Croatia v. Serbia and can therefore offer both expertise from the perspective of a professor as well as of an experienced professional involved with the ICJ (Vesna Crnić-Grotić, n.d.). She also acknowledges that the work of professors is often rather theoretical, suggesting that lawyers and ambassadors with a law degree, particularly specializing in international law, might make better equipped candidates for the ICJ. The takeaway is that there should be a great variety of former professions on the ICJ if they have extensive knowledge in international law affairs (Professor Crnić-Grotić, 2023). However, in some way, the professions are also limited because ‘judges have to know how to apply the law and not only how to achieve a fair outcome’ (Khalifa, 2022). Instead of rethinking the criteria for professions that ICJ judges should be working in or should have worked in, one therefore needs to further investigate how the pool of qualified candidates within these professions can be diversified.

### A. The Path to the ICJ Bench

To further investigate the core barriers and potential avenues for female judges to be considered for ICJ nomination, the anonymous German law professor explained common ‘springboards’ that provide aspiring candidates with required background knowledge and exposure to the national decision-makers. He identifies four key professions serving as common pathways to the ICJ: high-ranking public officials, such as government legal advisors (e.g., Judge Donoghue); permanent representatives at the UN (e.g., Judge Salam); international law professors (e.g., Judge Nolte); or high-ranking judges within their respective national courts (e.g., Judge Bhandari, former Indian Supreme Court Judge).

Given the male dominance in governmental and high-ranking judicial positions within national courts, female candidates may encounter barriers in accessing these essential springboards to the ICJ nomination pool (European judicial systems, 2016; Press release: Women in politics, 2021). Consequently, especially developing countries must actively seek out female candidates who would ‘... formally have the same qualifications as male candidates from other countries, leading to the number of women [with these professional experiences] being very limited’ (Anonymous #2).

However, careers within the UN and academia can serve as effective springboards for female judges. The UN system has made significant strides towards gender balance, achieving nearly equal participation of both female and male delegates (Improvement in the status of women in the United Nations system, 2023). While top-ranking law schools in the United States currently exhibit a lower presence of female law professors, there is a gradual increase in the representation of female law professors across law school in general (Katz, 2023). This upward trajectory suggests that careers in academia could increasingly provide realistic springboards for female judges to enter the ICJ nomination pool.

### B. The Relevance of Political Involvement in Judicial Nominations

An additional selection criterion—the role of interstate politics—creates another barrier to the successful nomination of women. The combination of political involvement and walking on or towards one or more of the four mentioned springboards can give candidates an even greater competitive advantage. However, preferring judges who not only make judicial decisions based on politics, but who are also heavily involved in them, excludes many potential female candidates because they tend to be less involved in interstate politics. Judges ought to be deeply connected to the political landscape in their home country (Creamer et al., 2017). 74.5% of members of global national parliaments are men and only 25.5% are women. Even though these percentages do not entirely represent the share of female and male judges involved in politics, they show that women are overwhelmingly less represented in high government positions, implying that the percentage of female judges in politics is lower than the one of male judges (Press release: Women in politics, 2021). The lack of political involvement of female judges lowers their chances of being nominated by a national group. Even the four women who have been elected to the ICJ do not show as much political involvement compared to their male colleagues. Xue Hanqin held governmental positions in the field of international relations (Judge Xue Hanqin, n.d.). Joan E. Donoghue held a variety of political positions, such as a legal advisory position in international law for U.S. president Obama (President Joan E. Donoghue, n.d.). Specifically, Joan E. Donoghue was therefore largely involved with politics in her home country, while Xue Hanqin worked on a more international scale. Hilary Charlesworth was not involved in politics before her appointment to the ICJ (Judge Hilary Charlesworth, n.d.). Similarly, Julia Sebutinde did not fulfill political roles in her home country (Judge Julia Sebutinde, n.d.). Both were elected in later years than Judge Hanqin and President Donoghue. Politics cannot be ignored in the domestic nomination process as the ICJ needs to allow for a variety of geographical origins and political affiliations to make well-balanced decisions on its cases. However, this political nomination process is currently constructed in a way that largely prevents women from being nominated and later elected.

An area of improvement could be to define multiple backgrounds that can make a respected judge on the ICJ. Having been involved in interstate politics can be one of them,

but it certainly should not be the focus. The two latest female judges elected to the ICJ do not show a history of political involvement. This marks a step toward considering political involvement less intensively, but, proactively, more qualities that make a good judge on the ICJ should be defined to allow for greater representation of women throughout the election process.

### C. Expertise versus Politics

It could also be possible that the true driver of political involvement was the inclusion in and familiarity with the political elite who ends up being the decision-making group during the nomination process. Judge Samba from the ICC offered her point of view. She is from Sierra Leone and joined the ICC bench on March 11th, 2021. Beforehand, she held high judicial positions in her home country, including serving as Justice of the Supreme Court of Sierra Leone in 2021 and Judge of the High Court from 2015 to 2019 (Judge Miatta Maria Samba, n.d.). Samba explained that she did not feel like she had to be politically involved to be nominated and later elected. Rather, she was chosen based on her merits, based on the work that she did at the national level in Sierra Leone, especially having prosecuted in a national court. She was 'known as an expert in criminal law in Sierra Leone and therefore equipped to serve on the court' (Judge Samba, 2023). Similarly, Judge Alapini-Gansou from the ICC '... worked hard in a judicial way and I am [she is] an expert in what I [she] applied for [ICC], but without being a member of a political party, it is important that a candidate is well-known by the political actors in their home country' (Judge Alapini-Gansou, 2023). She therefore suggests that political involvement is a helpful recognition enhancement, but that the true key to a successful nomination is being a well-known expert in international law. Being an international judge is a position that requires technical knowledge, suggesting that the best judges cannot be an expert in international law and a politician at the same time (Anonymous #2, 2023). Nathalia Contreras builds upon this thought, saying that 'the judges still need political skills. If you [they] want to get to an international body, you [they] have to be known by the politicians. They might not have to be politicians themselves, but they should be connected in their home country, or even in their region [defined by the Statute of the ICJ]' (Contreras-Pardo, 2022). Aligned with this reasoning, prioritizing the advancement of female experts into roles where they can gain judicial expertise and recognition holds the potential to enhance female representation in the ICJ nomination pool, addressing the existing disparity between female and male ICJ candidates.

## VII. Interlocking Factors Contributing to Female Underrepresentation

The focus on geographical representation, the underrepresentation of women in key roles during the nomination process, along with the preference for qualities typically linked to male-dominated professions all mutually reinforce one another. The status quo in some of the regional groups, such as Africa and Asia, leads to fewer women entering the field of law or politics. For example, Saudi Arabia allowed women to practice law only in the year 2013 (Zoepf, 2016). These preexisting conditions then lead to

fewer women being at the top of the legal and political landscape, becoming members of high-ranked law school faculty, and being appointed to the highest court of the individual countries. These male-dominated entities are consulted by the national groups who determine the qualities that a future judge on the ICJ should have. The promoted ideal qualities, such as involvement in politics and political decision-making, then start the cycle again by providing an example of what the ideal legal practitioners look like. This encourages the support for aspiring judges who align with this stereotype, predominantly consisting of male candidates.

The seemingly never-ending cycle can be broken with measures to promote gender parity, which is a unique problem to tackle because allowing for the voices of both genders to be heard increases the credibility of the ICJ and leads to well-balanced decision-making. It is difficult to change whether more women than currently are making it to the nomination and election decisions, partly because the work of the nominating groups is non-transparent and partly because gender diversity in high government positions, law school faculties, and the highest national courts worldwide are all separate topics that would need to be individually explored and largely depend on individual countries. Nevertheless, there is room for modification in the nomination and election process for ICJ judges.

## VIII. Nudging Gender Parity

Experts agree that changes to the nomination process need to be made and that advocacy for gender parity for the domestic nomination process is important. The most crucial change to be made is that the UN needs to communicate to the political actors on the national and international level that gender parity must be achieved. One way to do so could be 'for electing bodies, such as the General Assembly and the Security Council to say that they will only elect a state party if they nominate at least one female candidate' (Judge Alapini-Gansou, 2023). This has been done before by other courts, such as the African Court of Human and People's Rights, to achieve gender parity. Another example is the Parliamentary Assembly of the Council of Europe rejecting Malta's all-male candidate list when at least one female candidate was required (Anonymous #2, 2023). The Parliamentary Assembly of the Council of Europe limited the power of domestic national elites and made clear demands about what the list of candidates should look like. This is a productive way to create a more diverse pool of candidates because countries who might truly not have a qualified female candidate are then inclined to invest in more opportunities to help women climb up the judicial ladder. Judge Alapini-Gansou makes it very clear that 'we need to keep gender parity in mind and make them [the nominating and electing parties] realize that it is the time of women now' (Judge Alapini-Gansou, 2023).

The fastest, but also the most aggressive measure to ensure gender parity would be a requirement to include at least seven women on the ICJ bench. Such a quota would be effective immediately at the next judge elections and it would be the fastest and the most guaranteed way to achieve an almost equal number of female and male judges on the court. This quota would keep geographical representation in the focus during



the election process and it could eliminate the consequences of having predominantly male groups select the judges because there would be a limited number of male judges who could be chosen. However, individuals should not be denied their seat based on their gender and a gender quota might therefore not be the right choice of action. What is truly needed in the nomination process to the ICJ are nudges to naturally achieve gender parity. With a quota, gender parity would be achieved through a shortcut and not through rethinking and rebuilding the nomination process as part of the election process. A quota also 'stigmatizes the marginalized people that you [one] are [is] seeking to bring in and destigmatize because to some it might seem like they [female judges] are having spots reserved for them' (Anonymous #1, 2022). It is also difficult to say at which exact number a quota should lie if it were to be implemented or if there should only be a minimum number of female judges, which shows that there are too many uncertainties surrounding a gender quota. Overall, a forced gender quota on the ICJ would be a very abrupt intervention and it is unlikely to be put into place. Instead of imposing a quota on the judicial bench directly, a quota 'at the beginning of the nomination process with a minimum requirement of female and male nominees makes sense because it might otherwise influence election results too much' (Professor Crnić-Grotić, 2023). Gender parity and electing the most qualified ICJ judges should not be mutually exclusive. This can be achieved by strictly diversifying the nomination pool from the start of the judge selection process.

## IX. Gender Parity at the ICC

Within the ICC, the pursuit of gender parity is not only a central topic of discussion but, more importantly, a focal point of action. This underscores the ICC's commitment to gender equity on its bench. The ICC has not only set the goal of achieving gender parity but also implemented specific measures to actualize it, setting an exceptional standard for international courts. Judge Alapini-Gansou describes gender parity as 'a normal process' and 'we [the ICC] cannot say that this success story about gender parity within the ICC is coming from nowhere. It was hard work by all the stakeholders, saying that we [the ICC] need more women at every stage of the election process' (Judge Alapini-Gansou, 2023). She mentions that the court opened a gender committee to work toward preserving gender parity at the ICC through written statements and specific plans to achieve and maintain gender parity.

The term of six male judges will terminate next, which means that there will be six seats to be filled at the next election. The current nine female judges will stay on the bench until their terms are fulfilled. Judge Samba argues that there will most likely be a female domination of the ICC after the next election if even only one new female judge will be elected. Therefore, 'there might not be gender parity as time progresses,' but in future election rounds this phenomenon will balance out so that gender parity persists and neither gender outnumbers the other one on the ICC bench (Judge Samba, 2023). Considering future elections, the ICC's gender committee's efforts towards upholding gender parity hold

significant importance. As subsequent elections unfold, on average, the domination of either gender is unlikely, and a balance is to be expected. This would ensure the continuity of gender parity on the ICC bench.

### A. Changing the Legal Language

To naturally achieve gender parity at the ICJ, an additional statement in Section 9 of the ICJ Statute could be included to advocate for the nomination and subsequent election of additional female judges. Such a statement might not seem powerful enough at first, but the ICC successfully achieving gender parity proves otherwise. The court achieved gender parity in 2018. The language of the Rome Statute for the ICC, practically the equivalent to the Statute of the ICJ, clearly states that 'the states parties shall, in the selection of judges, take into account the need, within the membership of the Court for a fair representation of female and male judges' (United Nations Diplomatic Conference, 1998). The Rome Statute outlines two additional requirements for the nomination and election of judges: accurately representing the principal legal systems of the world as well as ensuring geographical representation. These two requirements closely mirror those articulated in the Statute of the ICJ. The phrasing of the Rome Statute 1998 Article 36(8a) does not suggest a fixed quota for judge elections, but it makes gender parity an official goal of the court. This is something that the ICJ is missing in its Statute. The ICC consists of 18 judges on nine-year terms with nine female and nine male judges on the court. For comparison and as a reminder, the ICJ consists of 15 judges, four of them currently being women. In recent years, the ICC has published statements on gender parity and took part in gender parity efforts of other organizations. Without having to force gender parity, the ICC achieved their goal through showing the benefits of gender parity and creating more opportunities for female judges, one of them being a greater likelihood of being nominated and later elected to the ICC. This is not a one-time effort, but a long-term commitment to ensuring continuous gender parity on international courts. The ICC did not need a forced gender quota for judges on the court to achieve gender parity. For some, statements about the importance of including women in major decision-making processes might almost seem too easy to be the solution to gender issues. However, it worked for this international court, and it can work again. Words may not immediately promote the desired movement toward gender parity, but words will create personal beliefs and values in decision-makers who may then change their behavior. The question remains why the ICJ has not used words in the same way.

[Note: This section was finalized prior to the 2023 ICC election. As of March 2024, there are eleven female judges and seven male judges on the ICC (Current Judges, n.d.).]

### B. Persisting Challenges to Gender Parity at the ICJ

Although the ICC sets an example of how gender parity can be achieved at an international court, the same exact strategy may not be successful at the ICJ due to the differences between the two courts. The ICC and the ICJ are two different international courts not only in the sense that they handle different kinds of legal issues and prosecute individuals rather than settling disputes between states, but also in the sense that their nomination processes are different. Currently,

two primary differences between the ICC and ICJ hinder the ICJ from directly adopting the ICC's strategies to achieve gender parity, emphasizing the importance of thoughtful deliberation when crafting gender parity solutions.

The first difference is that the ICC formalizes in its statute that achieving gender parity is a necessity for elections. Furthermore, the ICC requires their nomination groups, the Assembly of States Parties, to justify their nomination choice. The ICJ lacks such formal mandates. Even though the Assembly of State Parties can only nominate one candidate, justifying their opinion helps nominate qualified judges, no matter their gender (Electing the best ICC & ASP leaders, n.d.). The State Parties write a detailed note on how their candidate fulfills the judicial requirements to be on the court. These requirements are very similar to the ones of the ICJ, such as candidates being of high moral character and having relevant experience in international law. However, the difference is that the States Parties are also asked to justify their decision regarding the Statute's Article 36(8a) (iii), which argues for the fair representation of women and men on the court (United Nations Diplomatic Conference, 1998; The Prosecutor and the Deputy Prosecutors, n.d.). The positive effect of this can be proven with the fact that the representatives of the States Parties at the ICC (from African States, Asia-Pacific States, Eastern European States, Latin American and Caribbean States as well as from Western European and other States) are proposed by the Head of State or the Minister of Foreign Affairs of the individual countries (ICC, n.d.; The States Parties, n.d.). These two positions are predominantly filled by men. However, this did not turn out to be a barrier to gender parity on the ICC, which suggests that the same could be true for the male-dominated decision-making groups of ICJ nominations. Again, the goal is to change how nomination decisions are made and justified. It is a must to pay more attention to gender parity at the ICJ as gender homogenous court benches only offer limited perspectives on relevant issues. The gender parity success story of the ICC suggests that there might not even need to be any big changes in the composition of the national groups, but that having nominators thoroughly explain their choices can lead to a well-balanced court while still choosing the most qualified candidates.

## X. Judge Re-elections at the ICJ

The second relevant difference between the ICC and ICJ lies in the renewable terms at the ICJ. ICC judges have non-renewable nine-year terms. This is likely a reason for the slow gender parity movement at the ICJ. Members who have performed well during their terms are likely to be re-elected. Most of the members, especially before 2010, are men, meaning that not only new male judges are elected, but former judges are also re-elected. Since 1995, 19 judges were re-elected, and 17 judges were not re-elected. Since 2010, four out of five judges were re-elected, not counting James Richard Crawford, who passed away before his term ended, and newly elected judges since 2015, because their first term has not ended yet (Chesterman, 2021). Achieving gender parity, especially at a faster rate, is more realistic without the option

to re-elect judges.

Among the interviewed experts, there is consensus that re-elections not only slow down the gender parity process, but that they also do not leave enough room for new talents in general, no matter the gender. A recent example was the candidacy of Professor Maja Seršić from Croatia. Peter Tomka, a current ICJ judge from Slovakia, has been occupying one of the two Eastern European seats on the bench for about 20 years. This made him the rival of the new candidate Maja Seršić. 'Peter Tomka is an excellent judge, and he has been on the bench for a long time, she could only lose' (Anonymous #2, 2023). This suggests that 'his [Peter Tomka's] connections and his reputation were two things too strong to beat for Maja Seršić' (Professor Crnić-Grotić, 2023). Without re-elections, the two Eastern European seats could have been occupied by new judges, offering a more diverse range of opinions over the years. Judge Samba agrees, saying that after her nine-year term she feels that it is right to give the seat to 'younger and more vibrant judges' instead of having re-elections as an option. She also raises an important point of taking back her newly acquired knowledge to her home country and further helping in her judiciary as a way of giving back to the country that trusted her with representing it on the ICC (Judge Samba, 2023). Similarly, Judge Alapini-Gansou argues that seats on the ICC bench should be 'left for the next generation' (Judge Alapini-Gansou, 2023). Striking a balance between a diverse constellation of court benches by allowing new candidates to become judges on international courts, while also recognizing the acquired wisdom of long-serving judges, therefore remains a crucial consideration for international courts.

There is value both in denying re-elections, but also in having experienced judges on the court for a longer time than their initial terms. Luka Misetic agrees that 'being able to run again limits the number of opportunities' for female judges to be elected, but generally speaking, he is not in favor of term limits because, in his experience, it is hard to find high-quality judges for international courts, male or female, that he wants to see continue being on the bench, 'because many of them have little or no experience trialing cases' (Misetić, 2023). He argues that a large percentage of potential candidates are not used to 'running trials efficiently to reach the right decisions quickly.' While this is a valid point, there is also a balance to be struck between having judges with a lot of experience and 'also having judges that have a fresh perspective to make sure that the law is evolving as it should as society changes. As women, we can bring this different perspective' (Khalifa, 2022). Even if a popular and highly knowledgeable Judge, such as Peter Tomka, does remarkable work at the ICJ, the overall population is not well represented as time goes on because the diversity on the ICJ bench is also influenced by different generations of thinkers bringing different experiences to the decision-making processes.

To address the issue of re-elections, the European Court of Human Rights decided to allow no re-elections. The reasoning, however, uncovers that there was not only a lack of gender parity at the court due to repeated re-elections, but 'candidates were actually found to not be independent anymore because they want to please their country to be nominated again'

(Professor Crnić-Grotić, 2023). Countries may not prefer independent judges, but, in the eyes of the European Court of Human Rights, being an independent thinker is a preferred quality of a judge. Professor Crnić-Grotić further explained that judges who make ‘too independent’ court decisions have low chances of re-elections. She mentions that this inclines judges to vote in a way so that their government will support their re-election, leading to ‘the re-election possibility actually playing a role in the quality of [court] decisions,’ and potentially granting the respective countries an advantage during judgments. Having identified the reasons for why the ICJ could benefit from terminating any form of re-elections, it is now worth summarizing which exact changes can be made to the nomination and election processes of ICJ judges to then evaluate which modifications can be put into place.

## XI. Action Items to Achieve Gender Parity

I believe that geographical representation and gender parity should be the primary concern during the election process of ICJ judges. As previously discussed, the geographical representation is given by having no more than one judge from a country serve on the court. Geographical representation ensures national diversity and, in some cases, also racial and religious diversity on the ICJ, which is why it needs to be kept as a selection criterion. Still, solely geographical representation does not lead to gender parity on the court, which is why new selection criteria need to be added that can be combined with geographical diversity. Gender parity should not be forced but could be promoted through the following suggested three changes in the overall election process. First, eliminating the opportunity to be re-elected could increase the pace at which gender parity is being achieved at the ICJ. A greater frequency of new judges on the court gives a greater number of qualified candidates the chance to be elected, many of whom could be female judges. Second, new language in the Statute of the ICJ is essential to communicate the importance and the responsibility of national groups to include gender parity considerations when making their nomination decisions. Like the ICC, the third change that the ICJ would benefit from is continuously participating in the conversation on gender balance in international law and publicizing their goal for gender parity regularly. Adding a section to the Statute on gender parity and publishing written statements about the goal of the ICJ to reach gender parity are high-impact options to work towards achieving gender parity on the ICJ bench.

## XII. Feasibility of ICJ Statute Adjustments

Having identified core inhibitors of gender parity in the ICJ, one must realistically evaluate how feasible significant changes made to the Statute of the ICJ would be. Three interviewed experts commented on this analysis and concluded that making formal changes to the Statute of the ICJ is not an option. ‘Big countries realize the power of having a judge on the bench,’ so they are likely to be against nomination quotas, as they might not see any of their potentially qualified female nominees as successful candidates, and against the elimination of re-elections because

it increases their chances of losing their current seat on the ICJ bench quicker than they might do now (Professor Crnić-Grotić, 2023). ‘There is no chance to amend the Statute of the ICJ because it is very formalistic. It would be like changing the Charter of the UN. It will not happen,’ mainly because there would need to be a ⅔ majority within the General Assembly and Security Council, including the five permanent members voting for the changes to the Statute of the ICJ. ‘You would open a Pandora’s Box’ and many other change requests to the ICJ Statute could come up (Anonymous #2, 2023).

On the related issue of judge criteria rather being tailored towards traits seen in male judges based on their prior professions, Contreras-Pardo says that ‘the ideal[istic] person in me [her] says that we should change the criteria after which judges are nominated, so that it is written down and it has the force of the law. However, the process to reform the ICJ Statute is complex, and it is more efficient through interpretation. We need to make sure that it is interpreted according to the current times’ (Contreras-Pardo, 2022). Formal changes to the ICJ Statute might not be an option unless the UN would strictly agree that there will only be changes made to sections whose improvement could lead to gender parity. This may not lie in the interest of most countries, leading to no formal changes being made in the next few years. However, regional groups can make informal political agreements to increase the pressure amongst each other to work towards gender parity on the ICJ bench.

## XIII. Representation Beyond Gender Parity

The suggestions for changes that could be made to the nomination and election process of ICJ judges were created with the goal to have an almost equal number of women and men on the bench of the court. However, this is only one step toward the accurate representation of human society at the ICJ. Even within the two groups of female and male judges there is more diversity needed in the future. For example, an increased number of female judges should not only mean more white women on the court, but women from diverse racial backgrounds. Additionally, splitting the world’s population into the female and male genders leaves out the representation of other genders, such as transgender and genderqueer, as well as people with different sexual orientations in the LGBTQIA+ community. Enhancing awareness of diverse identities is important because it fosters inclusion of varied backgrounds and life experiences that can significantly shape case outcomes. Diversifying the bench of the ICJ could promote constructive critique among judges, potentially leading to even more comprehensive decisions.

Nevertheless, achieving gender parity between the female and male gender on the ICJ makes sense as the first step to represent the world’s population more accurately because there is a great number of qualified women that can be nominated. There is no exclusive proof that starting out with more female judges on the court is the best first step toward a more diverse bench, but it is a step. The ongoing struggle for female representation reflects the need for additional time to incorporate genders beyond the binary and individuals with diverse sexual orientations, considering their persistent underrepresentation in the pool of potential ICJ candidates.



## XIV. Recent Developments

The most recent ICJ elections, held in November 2023, resulted in the appointment of five judges to the court. As of February 6, 2024, the composition of the ICJ remains unchanged, with four female judges out of a total of 15 judges. Former ICJ President Judge Joan Donoghue's term concluded, and she has been succeeded by Judge Sarah H. Cleveland from the United States of America (Current Members, n.d.). Three new male judges were elected, filling vacancies left by their three male predecessors, while Judge Hilary Charlesworth from Australia was re-elected (Five judges elected, 2023).

This election marked a departure from previous trends in terms of the number of re-elections, but there was no change in the number of female judges on the ICJ bench. Despite the reduction in overall re-elections compared to the 2020 election, where four out of five judges were re-elected, the potential negative impact of re-elections on achieving a diverse bench remains significant (Security Council Elects 5 Judges, 2020). Eliminating re-elections could also offer a chance for a broader representation of countries over time, thus mitigating the concentration of power in certain nations.

[Note: This section was added after finalizing the article to incorporate the latest information regarding the 2023 ICJ elections. While the article primarily reflects data preceding November 2023, the conclusions remain relevant given the sustained lack of increase in female representation on the ICJ bench.]

## Conclusion

The ICJ stands as a beacon of justice that gives nations hope for global peace. The court's decisions influence the trajectories of nations and protect citizens' human rights. Yet, the absence of gender parity on its bench casts a shadow upon the very principles of equality and fairness it strives to uphold. It is imperative that achieving gender parity on the ICJ becomes a primary goal of the court during the next election cycle.

While diversity is important, pursuing it should not keep the court from appointing the most qualified judges. In my opinion, there should be long-term efforts to increase the number of qualified female judges, but also to allow more genders and individuals with various sexual orientations to enter the legal field through university scholarships and other educational opportunities. It is difficult to say when these efforts would create successful outcomes, but, in the long run, they will change the landscape of global leaders in law, which is necessary to ensure the most diverse and, at the same time, qualified bench of the ICJ. Gender parity would not only be a milestone for female judges; it can be a catalyst for amplifying the voices of several underrepresented identities. By achieving gender parity, we will take the first step toward a more inclusive bench, paving the way for greater diversity in the future.

ICJ court cases are not only about which country wins or loses, but the importance often lies in the content of the decisions. The current lack of diversity within the ICJ

bench hinders its ability to deliver fully nuanced judgments. Embracing representation across various identities – gender, sexual orientation, geography, race, and religion – not only enriches case outcomes but enhances the court's legitimacy in the eyes of the public affected by its decisions.

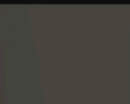
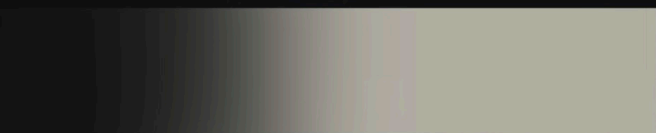
Nevertheless, there is hope for gender parity in the future. Rather than overhauling the stakeholders in the nomination and election process, the focus should be on tangible actions to achieve gender parity. In parallel with the ICC, the ICJ should actively engage in discussions on gender parity, consistently reaffirming its commitment to fostering a diverse bench through both written and public statements. If gender parity remains unattained after the next two election cycles, by 2029, I propose the implementation of term limits that eliminate re-elections, thus preventing judges from serving consecutive terms on the bench. This approach not only expands the pool of potential candidates, many of whom could be female judges, but also ensures that no countries maintain automatic prolonged representation on the ICJ bench.

Ultimately, international cooperation is essential to enact these changes. Enhanced diversity on the ICJ can serve as a model for the composition of legal decision-making bodies, ensuring judgments rooted in the law, crafted by judges with varied cultural perspectives and professional backgrounds. Over time, the representation of diversity within the legal field can extend its positive influence on other legal institutions and international as well as national courts to further inspire a collective drive for unity in the global pursuit of peace during conflict.

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# Features

# FEATURES

## Unveiling the Puppet Master: Parasitic Behavioral Hijacking in the Zombie Fruit Fly System

Cabbage flies killed by parasitic fungus *Entomophthora muscae*. Courtesy of Tomasz Klejdysz.

Andrés Muedano Sosa '27

It unfolds like a scene from a horror movie. A hungry fruit fly (*Drosophila melanogaster*) wanders in search of food, unaware of the fungal spore that has landed on its back. Over the next few days, the fungus (*Entomophthora muscae*) will infiltrate the fly's body, breach its blood-brain barrier, and penetrate its brain tissue, eliciting dramatic behavioral changes. Finally, at dusk on its last day of life, the now zombified fly will climb to a high point along a vertical surface (a behavior known as summiting), secure itself to the surface via its proboscis, raise its wings so as to expose its dorsal abdomen, and die. In the following hours, the fungus will create canon-like structures along the fly's exposed back—structures from which new fungal spores will be ejected. These spores will land on other unsuspecting flies, thereby initiating another cycle of infection.

Unraveling the mysteries of the *E. muscae*–*D. melanogaster* zombie fruit fly system remains an ongoing effort, with many lingering questions. How did the

parasitic relationship between the fungus and fly first evolve? What molecules drive the fly to start climbing, specifically at sunset? And, perhaps most importantly, how is a parasite able to control the behavior of its host? The newly opened Elya Lab in the Department of Molecular and Cellular Biology, led by Assistant Professor Carolyn Elya, Ph.D., is committed to finding the answers to these questions.



Assistant Professor Carolyn Elya, Ph.D. Photo courtesy of Carolyn Elya.



## From the Backyard to the Bench

Elya first encountered zombie flies as a graduate student in the laboratory of Michael Eisen, Ph.D., at the University of California, Berkeley. At the time, she was conducting research on the relationship between a fly's microbiome and behavior. To obtain data from wild flies, she would frequently set traps in her backyard and screen for infected samples. One day, she found odd-looking flies with fungal spores accumulating along their backs. Intrigued, she collected them, sequenced their genetic material, and subsequently confirmed them to be infected with *E. muscae*.

Scientists have long known about the ability of *E. muscae* to infect and manipulate flies, with the first description of the fungus dating back to 1855 (Elya et al., 2021). However, the specific biological processes underlying fly infection and behavioral manipulation remain elusive. Seeking to address this, Elya changed trajectories for her doctoral research and focused on the development of a laboratory system to study the parasitic relationship between *E. muscae* and *D. melanogaster*. At Berkeley, she characterized the fly's transcriptional response to the fungus and provided evidence that the fungus infects the fly's brain, thus paving the way for the research she would subsequently conduct as a postdoctoral fellow and, now, assistant professor at Harvard. With a multidisciplinary approach integrating genetics, biochemistry, neuroscience, and microbiology, Elya and her team are now working to understand *E. muscae*'s pathogenic and behavior-manipulating abilities, guided by the following questions.

### *E. Muscae* invades the brain. But does it have to?

Imaging experiments have demonstrated that *E. muscae* infiltrates *D. melanogaster*'s central nervous system 48 hours after exposure—perhaps an unsurprising finding given the observed behavioral effects of the infection (Elya et al., 2018). To infiltrate the brain, *E. muscae* disrupts the permeability of *D. melanogaster*'s blood–brain barrier—the membrane controlling which substances can pass from the fly's “bloodstream” into the brain (Elya et al., 2018). In this sense, brain invasion appears to be a hallmark sign of fruit fly infection by *E. muscae*. But is this brain invasion necessary to trigger summing behavior? Initially, it might seem self-evident that, without access to the brain, the fungus would not be able to affect fly neurons and thereby manipulate behavior. However, the recent discovery that transfusing

hemolymph (the invertebrate equivalent of blood) from summing flies to uninfected flies induces summing-like behaviors suggests the possibility of a mechanism other than brain invasion (Elya et al., 2023). It is plausible that summing is prompted by a metabolite present in the fly's hemolymph, either secreted by the fungus or synthesized as part of the fly's immune response. Such a metabolite could traverse the blood–brain barrier, triggering summing without the fungus needing to invade the brain directly. To test this hypothesis, research assistant Charlie Heacock is currently investigating whether transgenic fruit flies bearing a mutation that fortifies the blood–brain barrier are less prone to summit. As such, Heacock's research holds the potential to elucidate the mechanisms underlying summing initiation, shedding light on the fascinating interplay between parasitic manipulation and host physiology.



Dead zombie found in the wild. Photo courtesy of Carolyn Elya.

### Zombie flies will summit. What prompts them to?

The observation that summing can be induced solely through hemolymph transfusions suggests that certain substances in the hemolymph trigger this behavior (Elya et al., 2023). While the identity of these factors remains



unknown, Elya and her team have pinpointed the specific neurons they affect. Through imaging experiments, they found that fungal cells specifically accumulate in the pars intercerebralis (PI), a brain region that projects to the corpus allata (CA), an endocrine gland in the brain. Following this observation, they theorized that summing might be driven by the release of juvenile hormone (JH), a locomotion-inducing molecule synthesized in the CA. Elya and collaborators tested this hypothesis by inhibiting the production of JH, observing that this treatment greatly reduced summing behavior in infected flies (Elya et al., 2023). Next, they performed an experiment through which they disrupted candidate neurons using a potent neurotoxin and found that silencing PI neurons resulted in summing inhibition. Together, these findings led to the theory that CA-mediated release of JH, driven by the activation of PI neurons, is what drives summing behavior.

Based on these results, summing factors likely induce changes in behavior by activating PI neurons, ultimately leading to increased locomotion. To determine the identity of these factors, Harvard GSAS student Julius Tabin is currently conducting assays to find what molecules in summing fly hemolymph appear to activate PI neurons. Identifying these factors will lead to a better understanding of the neural mechanisms behind summing behavior. Furthermore, studying how the sequences coding for these factors have changed over evolutionary time might shed light on how the relationship between *E. muscae* and *D. melanogaster* first emerged.



Fresh cadavers under a microscope. Photo courtesy of Carolyn Elya.

## *E. muscae* is itself infected by a virus. What is the virus doing?

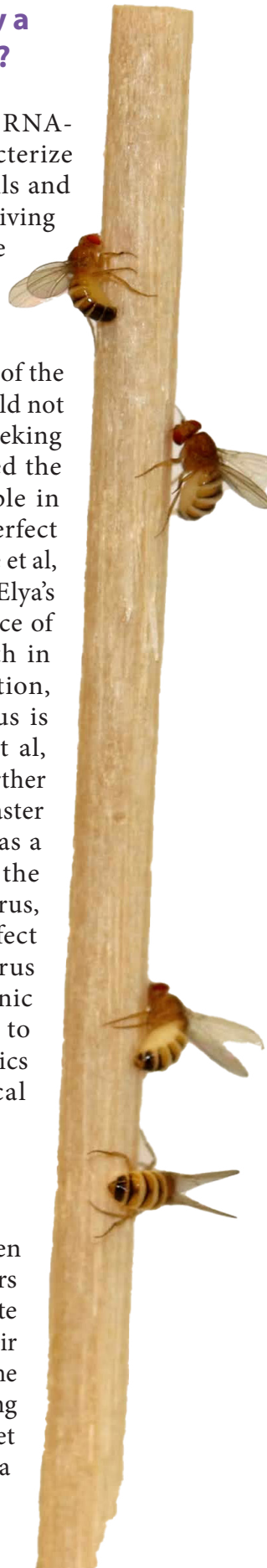
Elya previously conducted RNA-sequencing experiments to characterize the transcriptome of *E. muscae* cells and pinpoint the genetic mechanisms driving the infection process. However, the findings of these experiments proved to be startling: many of the identified RNA sequences could not be mapped to the genome of the fungus, meaning that the fungus could not have possibly synthesized them. Seeking to trace their origin, Elya compared the sequences to those readily available in online databases, soon finding a perfect and surprising match—a virus (Coyle et al., 2018). In a subsequent experiment, Elya's collaborators confirmed the presence of viral RNA in *E. muscae* cells, both in culture and during fruit fly infection, providing evidence that the fungus is itself infected by a virus (Coyle et al., 2018). These findings only lead to further questions. Is the virus the puppet master of the infection, using the fungus as a mere carrier? Or, alternatively, is the fungus somehow weaponizing the virus, making use of it to successfully infect the flies? By studying how this virus contributes to *E. muscae*'s pathogenic abilities, Elya and her team aim to unravel the mechanisms and dynamics of a possibly tripartite biological interaction.

## Zombiologists at Large

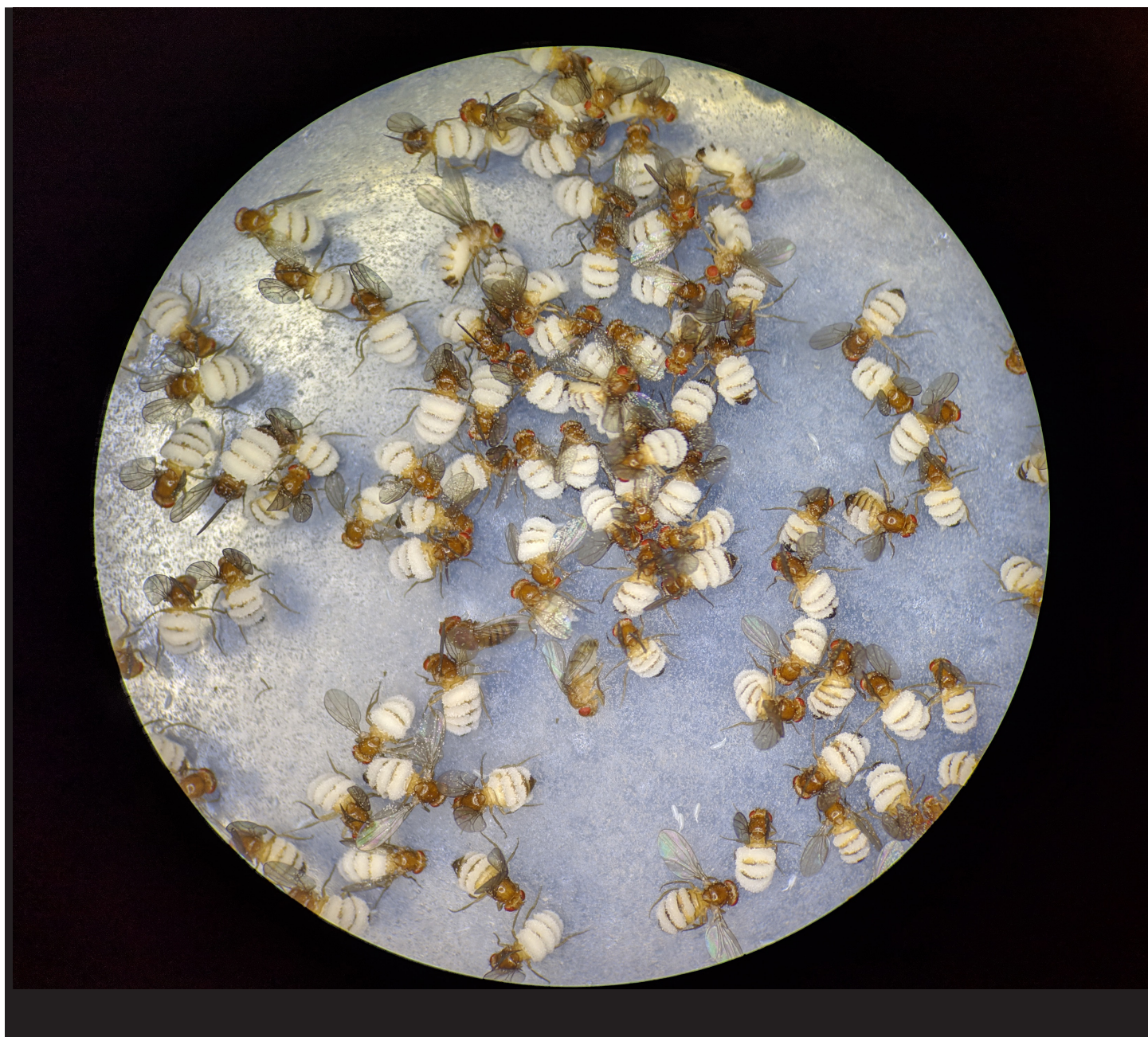
Studying the relationship between *E. muscae* and *D. melanogaster* offers a captivating glimpse into the intricate interactions between pathogens and their hosts. From the initial infiltration into the fly's body to the induction of summing behavior, each step of this macabre yet fascinating biological system presents a

Infected flies will summit along a vertical surface.

Photo courtesy of Carolyn Elya.







Zombie flies under a microscope. Photo courtesy of Carolyn Elya.

new layer of complexity begging to be unraveled. Through innovative research and interdisciplinary approaches, the Elya Lab is working hard to elucidate this complex symbiotic relationship, characterizing the relationship between host physiology and infection, identifying key molecules underlying observed behavioral alterations, and studying the involvement of additional biological agents in the infectious process. Through these concerted efforts, the Elya Lab's research holds the potential to illuminate fundamental biological processes driving parasitic behavioral hijacking.

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Scientific advocacy. Courtesy of Project Brain Light.

Olivia Oh '27

## Introduction

Currently, only 40% of graduate students and 17% of postdoctoral fellows report regularly engaging in advocacy and outreach work. They cite lack of time, funding, and awareness of opportunities that fit within their time and budget constraints as the biggest barriers to their participation (Rouzer et al., 2023).

Advocacy in scientific research can take on a variety of forms; most generally, advocacy in scientific research consists of using data and verifiable facts in order to influence decision-making or policy change. From publicizing original research to actively reaching out to community members through STEM education events, scientific advocacy holds the power to exert meaningful change in both local communities and government policy-making (Cockrell, n.d.).

However, despite the current lack of scientific advocacy

among up-and-coming researchers, there is still hope that there can be a culture shift among scientists and a movement toward greater activism. In June 2023, hundreds of scientists in India protested government efforts to restrict educational access to Western scientific theories. Similarly, in May 2023, scientists in Mexico participated in a strike against the creation of a centralized government agency to oversee research and control funding, while scientists in Norway protested the nation's slow-moving climate policy (Frickel & Tormos-Aponte, 2023). These scientists' displays of public activism and demands for policy change can inspire other researchers to also engage in greater advocacy and community outreach efforts.

At Harvard, one of the leading advocates for outreach in scientific research is Professor Nadine Gaab. An Associate Professor at the Harvard Graduate School of Education, Professor Gaab's work focuses on typical and atypical learning trajectories from infancy to adolescence with an emphasis on language, reading and literacy development, and the role of environment in shaping learning trajectories. Beyond academic research, Professor Gaab is deeply



involved in community outreach and uses her findings to advocate for change in educational practice and policy. Professor Gaab regularly leads panels for parents and families, in addition to leading efforts to bring STEM learning to underresourced schools in the Boston area. She is the founder of an EdTech company and has worked with educational non-profit organizations to author papers on the importance of integrating grassroots advocacy and scientific research in the development of public policy (Gaab, n.d.).



**Fig. 1.** Professor Nadine Gaab. Photo courtesy of Harvard Graduate School of Education.

## Deficiencies in Scientific Research Advocacy

Despite the efforts of investigators like Professor Gaab, the majority of researchers are still hesitant to immerse themselves in advocacy. One resounding question seems to echo through the doubts of these scientists: Can science and policy mix?

The answer is an unequivocal yes.

As constituents, scientists are stakeholders in the process of creating public policy, and government officials need the information and data generated and verified by scientists in order to make decisions. Additionally, much of the funding for scientific research comes from government bodies, making it necessary that scientists collaborate with government officials on their research agenda. Scientific research already exists within the framework of institutional politics; the only way to try to overcome bias is to acknowledge the inevitable complexities of the processes that drive decisions about funding and dissemination of research findings (Robbins, 2021).

Many scientists believe that there could be a conflict of interest if they were to engage in advocacy—would they be trying to inform public policy based solely on the desire to provide reliable information, or would they be advocating for decisions based on their own interests? However, much of scientific research is built upon a mutual understanding of transparency, where scientists hold each other to the standard of reporting results honestly, as shown by the requirement by many major institutions and universities that researchers disclose any conflicts of interest. These practices could inform similar behaviors in the realm of advocacy and public policy. As long as scientists are clear about their motives, there should be no conflict of interest (Kone, 2019).

Beyond the realm of the institutional bodies and the scientific research community, engaging in advocacy generally does not detract from the credibility of a scientist in the eye of the public, making fears of career detriment unfounded (Kotcher et al., 2017). Rather, according to Professor Gaab, there should be an effort to “break down the barrier of scientists in the ivory tower [...] and really [engage] the community” (Gaab, 2024). Effectively communicating scientific research in a way that is approachable and easily understandable by community members can help build greater awareness for important advancements and the need for continued change, thereby creating opportunities for valuable collaborations between researchers and advocacy groups (Gaab, 2024). Professor Gaab’s own work has exemplified the possibility of these important partnerships; through work with the grassroots organization Decoding Dyslexia, a national network of parents advocating for effective interventions for dyslexia in the public education system, Professor Gaab has co-authored a paper pushing for system-level change and learning disability policy development, providing an example of the possibilities for intersection between research and community action (Gaab & Duggab, 2024).

## Importance of Advocacy

In the often murky ecosystem of policymaking, scientific advocacy can hold a hugely beneficial effect, making it necessary that researchers be aware of the exact areas of advocacy in which they can make an impact. Researchers hold the power to protect and increase funding for science, to advance the process of scientific discovery, and to apply scientific evidence to public policy and thus improve the quality of life for their community. By presenting their data to government agencies, researchers can advocate for funding for their projects, creating the opportunity for

continued innovation. Scientists are also often called upon by government officials for guidance when deciding how to shape public policy; by sharing certain pieces of information, researchers can influence government officials into advocating for legislation that can benefit community members (Baron & Hoeksema, 2021). However, unless researchers make their voices heard, these key decisions in how research is funded and how information is shared will be left solely to policymakers, who only have an indirect stake in science.

While advocacy is important for anyone involved in scientific research, encouraging outreach and community engagement is especially pertinent for trainees and researchers who are just embarking on their careers. For early-career scientists, being involved in activities outside the laboratory or clinic can feel intimidating, and advocacy work is often undervalued as a professional activity that is not rewarded or incentivized under traditional academic structures. These scientists, who have just begun their careers, tend to prioritize their research rather than

outreach due to their doubt that these activities will foster their career goals and their lack of confidence that they have adequate knowledge to promote science in the public arena (Rouzer et al., 2023).

However, engaging in scientific outreach is beneficial to establishing a career in science, as it provides early-career researchers with the opportunity to develop management and communication skills that can be translated into laboratory or clinic settings. Adaptive communication and leadership are necessary when collaborating with other scientists or when working with government bodies for funding. Outreach work can also foster a sense of belonging for trainees; seeing their research have direct impacts on public policy and receiving trust from government officials and the general public can make early-career scientists feel more confident in their knowledge and abilities. Creating a sense of belonging is necessary for recruiting and maintaining a diverse scientific research community, especially as women and historically underrepresented

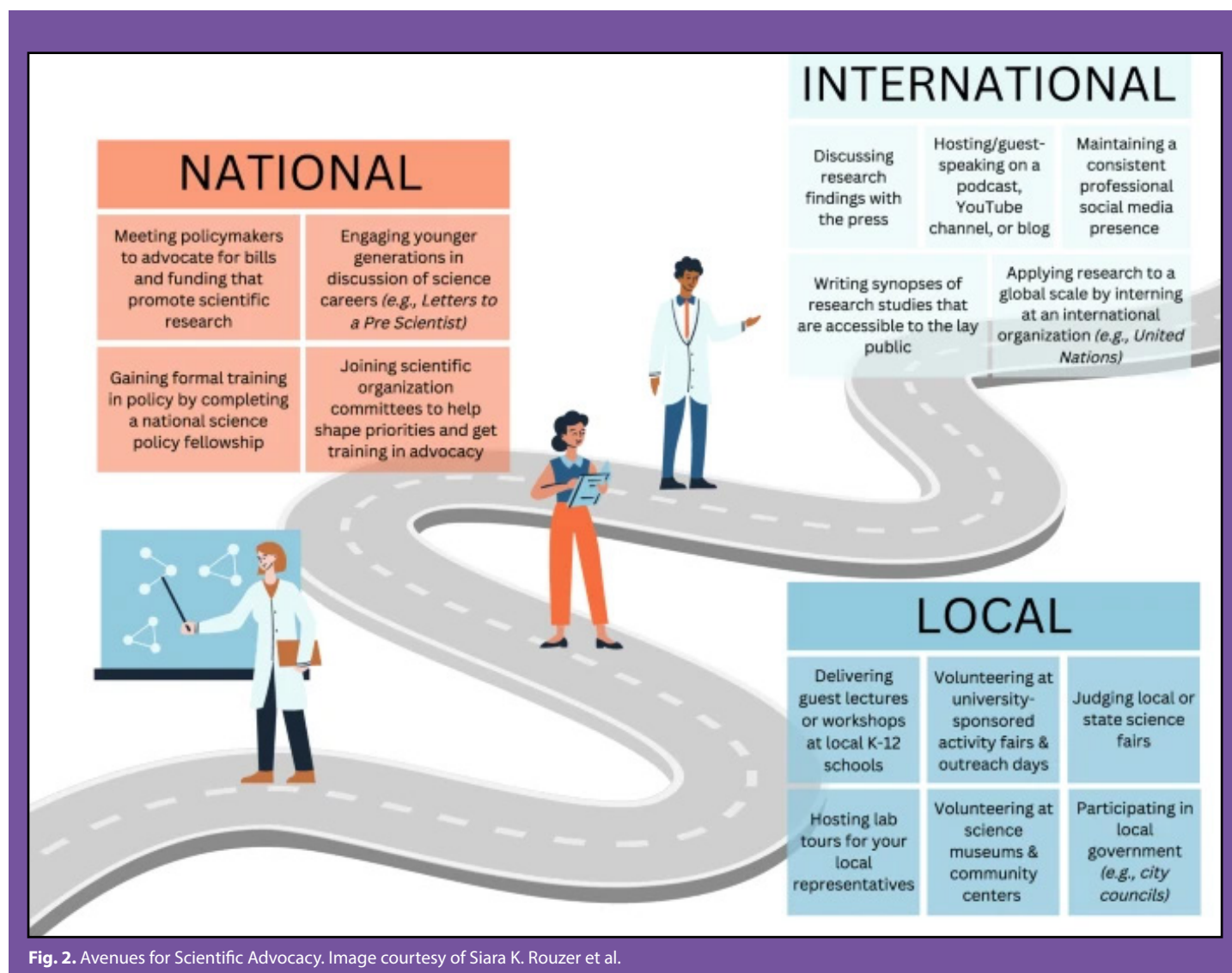


Fig. 2. Avenues for Scientific Advocacy. Image courtesy of Siara K. Rouzer et al.

individuals often cite lack of confidence and a sense of belonging as driving forces behind their decisions to leave scientific research (Rouzer et al., 2023).

## How Can We Increase Advocacy?

There is no one-size-fits-all solution to increasing advocacy—rather, the beauty of outreach and community engagement work is that there is a great range of ways to get involved (Fig. 2). From hosting webinars and seminars to working directly with community members and government officials, there is a method of advocacy for everyone. With the rise of the Internet and social media, it is no longer even necessary to leave the laboratory or the home in order to connect with the world and be involved in meaningful change (Hentchel, 2017).

Researchers who are already involved in scientific advocacy have been sharing their stories online, showing other scientists how their decisions to be involved in policy-making and community engagement have resulted in important real-world changes. As the Dutch scientist Niklas Hohne shared in his interview, “science covers the questions at the heart of society’s problems” (Woolston, 2016). The purpose of research is to find objective information that can be shared and used to make an impact on the world; scientists must understand that, without advocacy, their research may never have the opportunity to make it beyond the setting of a laboratory or scientific journal.

Professor Gaab herself has outlined various avenues to engage in community outreach and public policy, employing both top-down and bottom-up models. Through ideas that range from posting on social media about speaking engagements and upcoming studies to working with grassroots organizations and federal agencies, such as the National Institute of Health, Professor Gaab demonstrates that advocacy can take on a myriad of forms, with the only requirement being the willingness and the open spirit to dive into a field that is currently underrepresented in academic research (Gaab, 2024).

## Conclusion

Advocacy and community outreach are necessary to advance scientific research beyond the vacuum of the laboratory. Research is meaningful only when data is being used to create real-world change and respond to the needs of the community; by taking a multifaceted approach to advocacy and working with

both community members and institutional agencies, researchers hold the power to make a lasting impact. Change does not always have to come in grand sweeping gestures or major policy developments. Rather, the continued devotion to spreading knowledge and making science relevant to the community is the key to cultivating a new approach to research, where advocacy and outreach are integrated into everyday practice.

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Dalevyon Knight '27

### **An overview of Covid-19 and its Consequences**

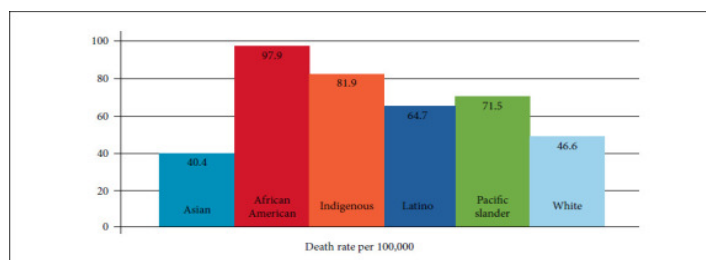
The COVID-19 pandemic is commonly regarded as one of the most catastrophic disasters of the 21st century, as it resulted in the death of millions worldwide and brought the globe to a halt. The “lockdown” era that followed the first wave of COVID-19 infections came with detrimental consequences on several aspects of society including our food systems, our health, and our livelihoods. Even today, while approximately 1,500 people continue to die from COVID-19 each week, leaving many families without their loved ones, people across the United States struggle with the social and personal ramifications of the pandemic (*Symptoms of New COVID Variant JN.1, Latest Studies on Paxlovid Rebound and Hydroxychloroquine*, 2024).

Although children and middle-aged adults often have the lowest mortality rates for COVID-19, they are still affected by

the disease. One of the earliest effects of the pandemic was the period of quarantine, or a period of self-isolation, required to contain the disease after exposure or infection. These periods of self-isolation caused child, teen, and adult mental health to decline. For example, many students throughout the world experienced sudden changes to their social lives and daily routines, such as the inability to access education, food insecurity, and potentially unsafe home environments (*Mental Health & COVID-19: What Parents and Caregivers Should Know*, n.d.). Similarly, four in ten adults reported symptoms consistent with anxiety and depression by 2021, a two-fold increase from 2019 (Panchal & Saunders, 2023). In addition, reports of substance abuse have increased dramatically since the beginning of the pandemic—largely constituted by fentanyl abuse—as have suicide rates (Panchal & Saunders, 2023). Overall, the COVID-19 pandemic has uprooted civilian life and changed the world as we know it, leaving lasting impacts on mental health and wellbeing.

## Systemic Healthcare Barriers Affecting the Black American Community

While COVID-19 has affected all communities, the virus has had a widespread impact on communities of color, specifically Black American communities. Black Americans have always faced systemic barriers to quality healthcare in the United States, and COVID-19 only worsened these hindrances. For example, many Black Americans were not able to afford or access quality healthcare during the pandemic, and—as a result—Black Americans had the highest mortality rates among all racial groups in 2020, with 97.9 deaths per 100,000 people (**Fig. 1**) (Vasquez Reyes, 2020). This high death rate reveals that the systemic barriers to healthcare greatly disadvantaged Black Americans during the COVID-19 pandemic. Numerous Black Americans are often uninsured or underinsured, leaving many unable to afford the quality healthcare they need. According to a brief by The Office of Health Policy, the uninsured rate for Black Americans is 12% compared to White Americans at 9% (ASPE, 2022). The disproportionate rate of uninsurance between Black Americans and White Americans had detrimental effects in a pandemic context. For those individuals who had moderate to severe cases of COVID-19, going to a hospital and obtaining treatment was a barrier few chose or were able to endure, and the prevalent lack of insurance within the Black American community, therefore, drastically affected their physical health, leading to an even bigger impact on their mental and emotional health.



**Fig. 1.** COVID-19 mortality rates by race in 2020 (figure courtesy of Vasquez Reyes)

Not only did healthcare barriers exacerbate the COVID-19 pandemic for Black Americans, but economic and societal pressures played a role as well. A significant number of Black Americans worked in essential businesses during the pandemic, making it difficult for them to adhere to stay-at-home orders and thereby increasing their risk of contracting COVID-19. According to data released by the U.S. Department of Labor, in 2020, only 31% of Black Americans had jobs that required telework compared to 41% and 51% for White Americans and Asian Americans, respectively (Asfaw, 2022). The sacrifices Black Americans had to make in order to provide for their loved ones throughout the pandemic meant that their health was in an extremely compromised position. This daily battle between the danger of the workplace and the needs of the home led to major internal struggles in Black American communities during the pandemic.

Black Americans' living situations also provided a barrier to healthcare. Black Americans are more likely to live in close proximity to one another, which often leads to a lack of social distancing and a higher risk of COVID-19 contraction. Furthermore, these areas typically lacked the social and infrastructural stability that other predominantly White suburbs tended to have, including locations to receive medical care (Norwood, 2021). Moreover, these areas tended to be ignored by lawmakers on a local and national scale, and the residents of these areas suffered physically and mentally. Beyond these ghettos, however, Black Americans' lives and demands continued to be ignored. Black Americans were and continue to be more likely to be found in the prison system where the disease could spread rapidly. Black Americans were incarcerated in state prisons at nearly 5 times the rate of White Americans in 2020, and thus, a direct correlation was established between Black American incarceration rate and COVID-19 contraction rate (Nellis, 2021).

## Link Between COVID-19 and Black American Mental and Emotional Health

There is an inextricable link between the COVID-19 pandemic and Black American mental and emotional health that is further complicated by external stressors, trauma, and even cultural stigmas. Like many other demographic groups, the fear of potentially losing loved ones took a significant toll on Black Americans. As Black Americans were already disadvantaged through systemic healthcare barriers, for many families, this fear became a reality. Nationwide, Black Americans died at 1.4 times the rate of White Americans, a staggering inequity that caused many Black Americans to experience difficulty adjusting to normal life post-pandemic. In addition, the unresolved trauma that Black Americans faced due to the pandemic often affected their career and relationships with others, with psychology researchers Maarten Eisma, Paul Boelen, and Lonneke Lenferik referring to this trauma as prolonged grief disorder (PGD). There were higher rates of PGD in Black populations during the pandemic, as characterized by a distressing yearning for deceased loved ones that lasts over 6 months (Eisma et al., 2020). This prolonged grief caused Black Americans to mourn their loved ones rather than focus on other important aspects of their livelihood.

Subtly, pre-existing cultural stigmas also impacted Black Americans during the COVID-19 pandemic. The fear of judgment and criticism by others led and continues to lead many Black Americans to believe that they did not have a mental health problem post-pandemic. Thus, Black Americans were less likely than others to obtain mental health counseling from a licensed professional, worsening their readjustment to everyday life. Data released by the American Psychiatric Association revealed that while Black Americans are just as likely as the general population to have a mental illness, only a third will receive mental health care (Leary, n.d.). There are a variety of factors that contribute to this statistic. Historically, Black Americans have been misdiagnosed with mental and physical disorders at a higher rate than other races



and have been exploited by the United States government and medical community in the name of “advancement.” One such example is the 1932–1972 Tuskegee Syphilis Study where hundreds of Black men were brutally mistreated and denied treatment for the sake of supposed medical advancement (Centers for Disease Control and Prevention, 2022). Black Americans’ overall lack of trust in medical professionals is therefore known as the “Tuskegee Effect,” and provides a great hindrance to Black American mental and emotional healthcare today. In fact, this distrust extended beyond the healthcare sphere. The numerous killings of Black Americans such as George Floyd, Breonna Taylor, and Ahmaud Arbery at the hands of White police officers and vigilantes led to intense protests and general distrust of police officers, only heightening Black American stress during the COVID-19 pandemic. The link between systemic barriers, external stressors, and Black American mental and emotional health led to a disastrous outcome for the Black American community, the effects of which are still evident now.



**Fig. 2.** Student taking an exam (rawpixel)

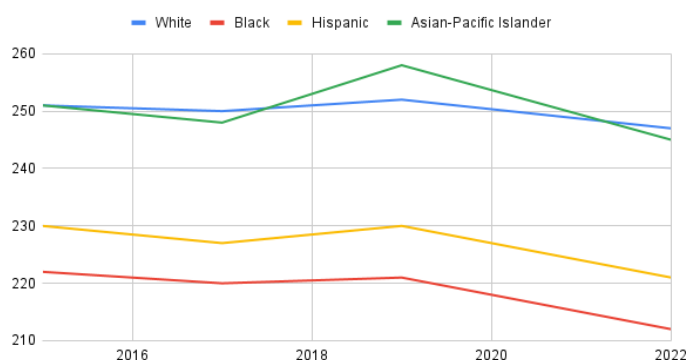
## The Impact of Covid-19 on Black American Children and Teens

Another aspect of COVID-19 affecting Black American mental and emotional health is reflected in educational hindrances or obstacles to education. Online platforms such as Zoom deprived children and teens of face-to-face social interaction and in-person teaching. With Black American students already disadvantaged through the public school system, the pandemic only exacerbated these issues. In 2023, the average composite ACT score for all students across the United States was 19.5 out of 36, but the score was 16 out of 36 for Black students—the lowest score since 2019 (Foster, 2023). While this statistic alone cannot be directly attributed to the pandemic, it does raise questions about post-pandemic learning and the efficacy of the transition from a previously online school experience to an in-person learning experience. Elementary school students also reflect this point. The U.S. Department of Education found that Black American scores dropped a considerable eight points from 2019 to 2022 compared

to a four-point drop by White fourth-grade students (**Fig. 2**). While this data does support the fact that the pandemic prevented students from all racial backgrounds from learning effectively, the data shows the relatively drastic effects of online learning on Black students. The Assistant Secretary of Education for Civil Rights, Catherine E. Lhamon stated that the new data about the impacts of COVID-19 in schools reflects the “troubling differences” experienced by Black American (Siid, 2023). Among the top of these differences were racial harassment, disproportionate discipline rates for Black American boys, and lack of access to educators and technology. These differences affected Black American children’s ability to perform, further leading to a feeling of inadequacy within the Black American student population (Siid, 2023).

Beyond test scores, online learning led to deprived social interaction within student populations. Heightened relationships over phone calls, video calls, and social media led to the redefinition of friendship and intimacy for many young students. Often, students felt as if they were compelled to socialize online in order to maintain their social status within their friendship circles. Over time, however, increased time on social media and complete reliance on these virtual friendships led to a high risk of depression in adolescents (Mayo Clinic Staff, 2024). The anonymity aspect of social media also posed a challenge. Many students of all demographics were subjected to intense cyberbullying and harassment that they might not have encountered in an in-person environment. According to the American Adolescent Psychiatric Association, stress and mental health conditions may be exacerbated by cyberbullying, particularly among those who have experienced emotional abuse (*Cyberbullying during COVID-19*, n.d.). Thus, during the pandemic, the impact of cyberbullying and harassment was paramount. Early research in 2020 suggested that students who spent more than three hours on their devices were 55% more likely to be victims of bullying (Rech et al., 2013). As a result, many Black American students still have not recovered, and their academics, mental health, emotional health, and even physical health are still at a low today.

**Average fourth-grade math scores, all public schools**



**Fig. 3.** National Average Fourth Grade Math Scores Across Demographics (figure courtesy of Iris Sung, data from U.S. Department of Education, National Assessment of Educational Progress)



## What now?

Black American mental health should not be ignored or forgotten in the context of the long-term effect of COVID-19 on our world. The systemic barriers and the medical data have revealed that there is a cultural cycle that needs to be broken in order for mental health progress to be made for Black Americans. Medical professionals and researchers are just now starting to recognize the effect of COVID-19 on Black American mental health, but this recognition is only the start. While tips from these professions to promote wellbeing—such as integrating prayer and meditation into daily life—can help Black Americans temporarily improve their mental health, they continuously have to face a world filled with barriers that seek to hinder their progress. Only time will tell how further research on this issue and strong attempts to close the mental health gap will fare in a post-COVID world as it becomes more necessary than ever to tackle Black American mental health.

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# FEATURES

## Breaking the Barrier: Exploring the Blood–Brain Barrier's Connection to Depression

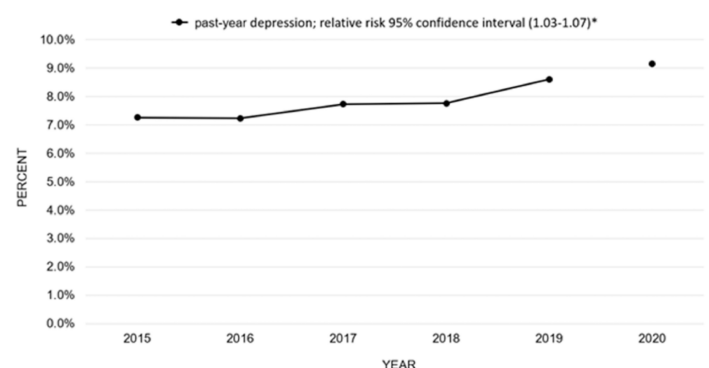
Alyssa Cai '27

### The Depression Epidemic

Today, mental health difficulties are more prevalent than ever, with approximately 300 million people suffering from depression worldwide. Moreover, the World Health Organization predicts that depression will surpass ischemic heart disease—the most common cardiovascular disease that restricts blood flow—to become the most prevalent disease by 2030 (Moukaddam & Tucci, 2017).

Depression is a multifaceted disease, and it is evident that unipolar depression, the most common form of depression, is not the only psychiatric condition reaching epidemic proportions. Unipolar depression occurs when an individual solely experiences depressive episodes; by comparison, bipolar depression occurs when an individual experiences both manic (characterized by elated and energized behavior) and depressive (characterized by sad and hopeless behavior) episodes ("Bipolar Disorder," n.d.). An estimated 60 million

people worldwide suffer from bipolar depression, and an additional 21 million people suffer from schizophrenia. The mental health epidemic has had significant consequences, as hospitals, outpatient care, and community outreach centers are unable to accommodate the high patient demand for psychiatric care. Medical centers have overstretched services, underfunded patient care, and overwhelmed staff members



**Fig. 1.** Past-year depression trends in Americans from 2015–2020 (Goodwin et al., 2022)



due to an influx of patients in need of mental health support. The impact on the healthcare sector is only a portion of the problem; the economic costs of mental health have drastically risen over the years, indicating that mental health issues are on the rise and are more costly than ever. Unipolar depression and related conditions in the United States cost around \$83.1 billion in 2000 and \$280 billion in 2020 (Moukaddam & Tucci, 2017; "Reducing the Economic Burden of Unmet Mental Health Needs," 2022). The toll of depression has also induced high rates of burnout amongst both patients and healthcare providers alike, resulting in losses of enthusiasm, overall cynicism, and low senses of accomplishment (Moukaddam & Tucci, 2017).

Beyond their direct impacts on individuals worldwide, depression and similar psychiatric disorders are associated with a slew of other physical ailments. Depression, especially in people of older ages, can result from other serious medical illnesses such as diabetes, cancer, heart disease, and Parkinson's disease ("Depression," n.d.). Depression is also predictive of subsequent myocardial infarction (heart attack), exacerbates existing cardiovascular disease, and increases mortality following myocardial infarction ("Depression," n.d.).

Because of the physical, economic, and social impacts of depression, as well as the urgency that results from the rising depression diagnoses, there is a paramount need to understand more about depression and mental health. Between 2004 and 2019, nearly 36,500 depression-related research papers were included in the Web of Science Core Collection database, and a total of 157 countries and territories conducted research on depression (Wang et al., 2021). This breadth of research indicates that depression is receiving attention from many regions around the world, a recognition of the issue's severity. However, depression is a complicated disease that requires a nuanced understanding of behavioral, social, physical, and biological phenomena, making it challenging to characterize from any one perspective. Many people attribute depression to a primarily social problem, with the cognitive theory of depression positing that people's negative appraisal of their life events makes them more susceptible to the development and recurrence of depressive episodes (Joormann & Gotlib, 2010). By comparison, the hopelessness theory of depression suggests that combinations of negative cognitive styles and negative life events create a sense of hopelessness in patients and is thereby sufficient by itself to bring about the disease (Cheek et al., 2015). Recently, more research into the physiological components of depression revealed that the blood-brain barrier (BBB), an important structure in the brain, could play a prominent role in depressive disorders, dispelling theories that focus solely on the psycho-social components of depression.

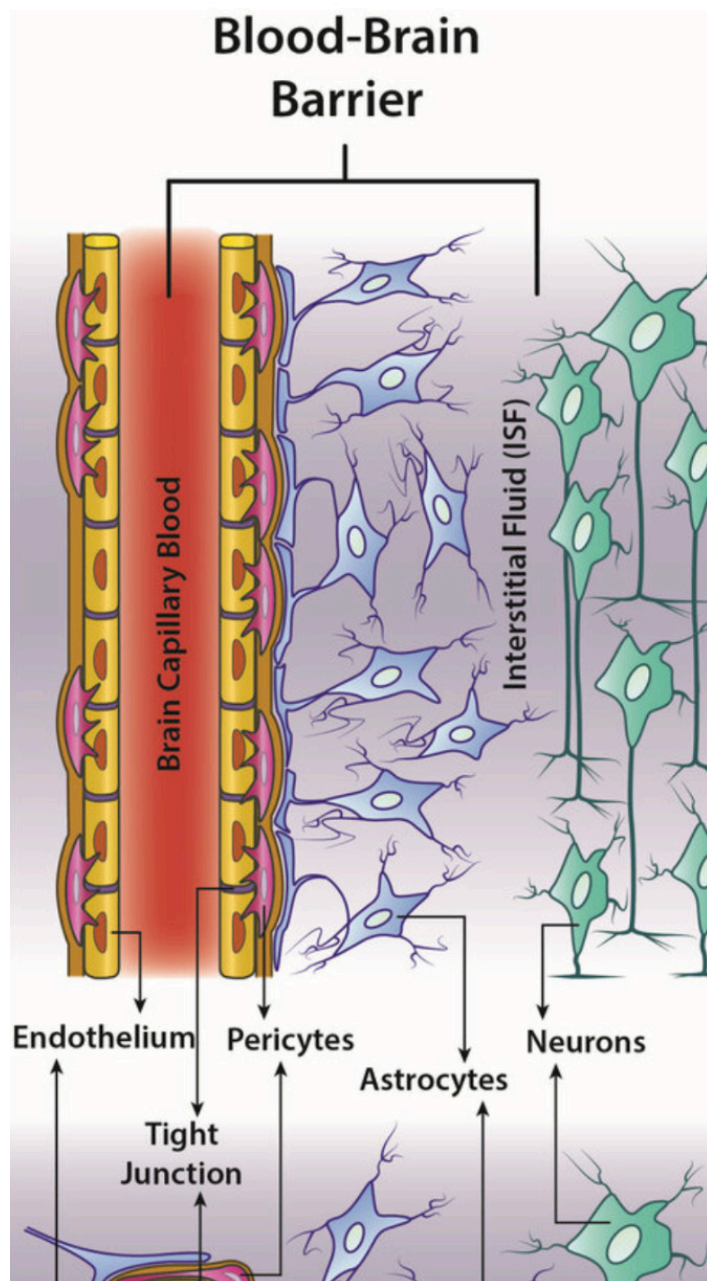


Fig. 2. A diagram of the components and layers of the BBB (D'Agata et al., 2017)

## What is the Blood-Brain Barrier?

The BBB is a semipermeable membrane that allows cerebral blood vessels to regulate the passage of molecules into the brain, which is critical for maintaining the brain's healthy function. To create the strongest defense against outside forces, the BBB is composed of endothelial cells, pericytes, capillary basement membrane, and astrocyte end-feet. (Dotiwala et al., 2023). Endothelial cells form the innermost layer of blood vessels in the brain and play a central role in the BBB. Peripheral endothelial cells, which are found outside of the brain, are transcellularly permeable, resulting in "high rates of caveolin-mediated

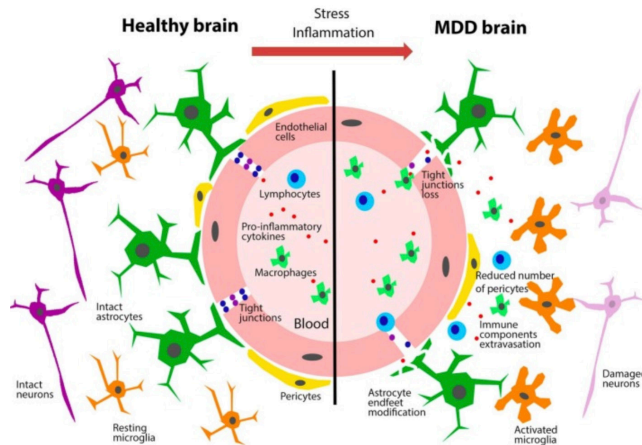


transcytosis, diaphragm-containing pores termed fenestrae, or large discontinuities or gaps in the endothelial layer” (Aird, 2007). By comparison, the endothelial cells lining blood vessels in the brain are particularly tightly packed together, preventing the free movement of molecules past the cells. These cerebral endothelial cells lack fenestrations and exhibit low rates of transcytosis—properties that greatly limit transcellular

nonspecific leakage of molecules to and from the brain, often leading to detrimental effects (Horowitz et al., 1992; Cornford et al., 1998).

## Depression’s Link to the Blood–Brain Barrier

As more investigation is conducted on the BBB and its connection to various neurological conditions, novel information about its relationship with depression has emerged. Recent research has shown that disruption of the BBB is associated with Major Depressive Disorder (MDD). Using dynamic nuclear imaging, investigators measured the functionality of endothelial cells in MDD patients using the relative uptake ratio (RUR) of blood flow in the brachial artery after hyperemic challenge (Medina-Rodriguez & Beurel, 2022). They found that MDD patients exhibit lower RUR than healthy controls, with a low RUR indicating poorer endothelial functioning. Interestingly, the serum—the non-clotting liquid component of the blood—of MDD patients has also been found to promote apoptosis of endothelial cells in vitro when compared to the serum of patients without depression. Together, these results indicate that reduced endothelial function in MDD patients may be partially due to factors in their blood reducing the function or inducing apoptosis of endothelial cells (Politi et al., 2007). To further elucidate the relationship between the BBB and depression, researchers have investigated mouse models of MDD. Mice subjected to chronic social defeat stress—intended to simulate the effects of MDD—were found to have reduced expression of Claudin-5, a highly enriched tight junction protein vital to the physical barrier properties of the BBB (Green et al., 2019). Stress-susceptible mice also exhibited abnormal blood vessel morphology in the nucleus accumbens—the part of the brain that controls motivation and action—and suffered cerebrovascular microbleeds, both of which are indicative of vascular pathology after stress (Menard et al., 2017; Lehmann et al., 2020). Finally, vascular endothelial growth factor (VEGF) was implicated in promoting paracellular (the passage of molecules between adjacent epithelial cells) and transcellular (the translocation of molecules through the cells—barrier function (Park-Windhol & D’Amore, 2016). Unsurprisingly, increased VEGF levels were associated with BBB disruption, and this disruption was linked to depressive-like behaviors, thus demonstrating another potential link between BBB and MDD (Matsuno et al., 2022).



**Fig. 3.** Image of compromised BBB in cases of depression (Medina-Rodriguez & Beurel, 2022)

permeability—which is critical for their barrier function. Additionally, the endothelial cells found in the brain have tight junctions between them, which are protein complexes that connect adjacent cells and create a seal that further restricts the passage of substances (Sandoval & Witt, 2008). These junctions act as molecular gates, selectively permitting the entry of necessary nutrients like glucose and amino acids to the brain while simultaneously blocking the passage of potentially harmful substances such as pathogens and toxins. Astrocytes—star-shaped cells that surround blood vessels in the brain—contribute to BBB function by releasing signaling molecules that help regulate endothelial cells and maintain the integrity of tight junctions. (Kubotera et al., 2019). Together, these components result in the cohesive structure of the BBB, united to provide the brain with a strong defense against any potentially harmful molecules or pathogens. Because of the BBB’s important role in regulating the ions and molecules that enter the brain, the breakdown or disruption of function in the BBB results in a multitude of health issues BBB breakdown contributes to the pathology of neurological conditions such as multiple sclerosis and has also been associated with neurodegenerative disorders such as Alzheimer’s (Profaci et al., 2020). For example, the dysfunction of just one transporter in the BBB, the MCT8 thyroid hormone transport, can result in psychomotor retardation syndromes (Vatine et al., 2017). Additionally, the degradation or dysfunction of the BBB can lead to

## Implications of Research and Future Applications

It may seem evident that, given the association between BBB disruption and depression, novel depression therapies should seek to restore BBB function. However, targeting BBB permeability for therapeutic interventions presents a significant paradox. On one side, there has been a longstanding pursuit of increasing BBB permeability as a key goal to combat brain-related diseases, thereby allowing drugs to penetrate the brain. Thus, it has been hypothesized that increasing BBB permeability could enhance conventional antidepressant effects for MDD patients. However, the restoration of BBB integrity through the reduction of harmful inflammation alone has also shown efficacy in producing antidepressant effects. For example, blocking inflammatory molecules such as tumor necrosis factors or IL-6 results in a restoration of BBB integrity and the reversal of depressive-like behaviors in mice (Cheng et al., 2017; Menard et al., 2017; Li et al., 2019). Understanding this phenomenon of BBB permeability complicates the therapeutic realm, providing two opposing paths forward in the treatment of diseases such as MDD. However, this understanding also provides broader insight into why current therapies lack the efficacy patients need, motivating future research seeking to understand and harness the BBB. By doing so, investigators can produce therapeutics and treatment methods that may improve the psychiatric conditions of people currently suffering from depression worldwide.

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# FEATURES



## Recent Advancements in Tissue Engineering: The Organ-on-a-Chip

Wafiqah Zubair '26

From pipetting biological solutions within a vented biosafety cabinet to collecting epidemiology data on the ground at a disease hotspot, medical research is a fast-growing and extremely expensive industry. The National Institutes of Health (NIH), a federally funded organization for “all things health” in the U.S., spends almost \$48 billion annually on healthcare-related research and clinical trials, dispersed among universities, medical schools, hospitals, professional laboratories, and NIH’s own labs (National Institute of Health, 2023). Along with these foundational labs, private research facilities, large pharmaceutical companies, and biotech startups all compete within the biological innovation and medical therapeutics space. As a result, some biomedical researchers, many within the subfield of clinical medicine, publish more than 60 papers a year, or once about every 6 days (Ioannidis et al., 2023).

### The Drawbacks of Traditional Biomedical Research

As the field undergoes rapid advancements, limitations of traditional

biomedical research models are brought to the forefront: (1) it is hard to find a balance between the application-based drawbacks of in vitro studies and ethically challenging in vivo studies; (2) animal studies do not always translate well to human physiology; and (3) animal experimentation is monetarily and temporally expensive.

In vitro research, which mimics biological processes outside living organisms, often fails to capture the complex mechanisms involved within the original species. For example, many cells grown in the lab adhere to the bottom of Petri dishes and grow in a single layer, while cells in the human body grow in multiple layers and are found in a 3D extracellular matrix. Thus, in vitro research is commonly used in preliminary studies of a therapeutic to test initial effects and to ensure its safety for use in living organisms. On the other hand, in vivo experimentation is conducted on non-human animals, including mice, rats, dogs, monkeys, and pigs. More than 110 million animals are sacrificed each year in American laboratories, and even more are intentionally induced with debilitating diseases, caged in small spaces, and exposed to harmful side effects of potential drug candidates (PETA Staff, n.d.). Moreover, a systematic review found that animal experimentation for human

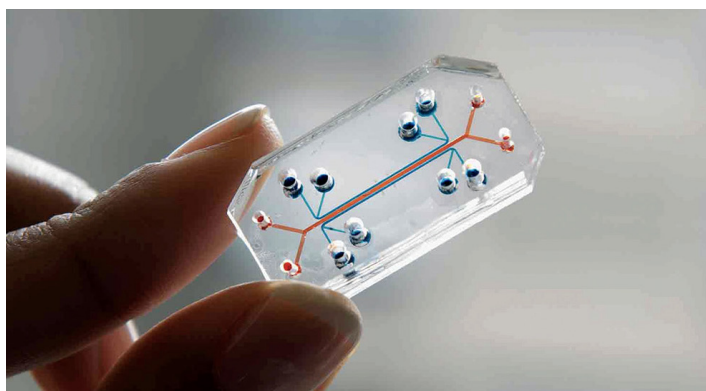


application has historically led to many cases of misleading data and human harm due to a combination of laboratory-specific variables, variance between humans and other species, and differences in disease-related effects on humans versus animals (Akhtar, 2015). Furthermore, animal experimentation is time-consuming and expensive: a single cancer therapy study using rodents costs about \$2 to \$4 million and spans 4 to 5 years. Compared to “petri dish” in vitro testing, in vivo experiments are between 50% and 3000% more expensive (Van Norman, 2019).

If in vitro testing is not fully effective and in vivo testing is both detrimental to animals and costly, then what is the solution? Many researchers are working to mitigate these concerns using different methods. Some are turning to artificial intelligence to narrow down drug compounds from millions of potential candidates, effectively saving a considerable amount of time and resources. Others are seeking to develop novel solutions by leveraging the benefits of both in vitro and in vivo models while minimizing each’s drawbacks.

## The Organ-on-a-Chip

One particularly robust solution is the organ-on-a-chip (OoC), a small chip that contains lab-grown tissues, natural tissues, or clusters of cells immersed in a controlled environment of nutrients, fluids, and essential molecules (Leung et al., 2022). They can be used to mimic microenvironments within the human body, test cell-cell interactions, and assess the impact of drugs. OoCs—a culmination of advances in tissue engineering, microfabrication, 3D bioprinting, microsystems, and microfluidics (the study of fluid flow through micro-sized channels)—bridge the gap between in vivo and in vitro studies by more accurately mimicking complex human physiolog while decreasing experimental costs and animal harm (Leung et al., 2022). In one of its original forms as a lung-on-a-chip, lung airway cells are grown in fluid-filled nanosized channels (colored lines) and separated by porous membranes within a PDMS chip (made of a clear, semi-flexible rubber material). This unassuming device was used to study the effects of respiratory diseases like pulmonary edema and COVID-19, guiding further research and therapeutic development (Fig. 1) (Folch, 2022).

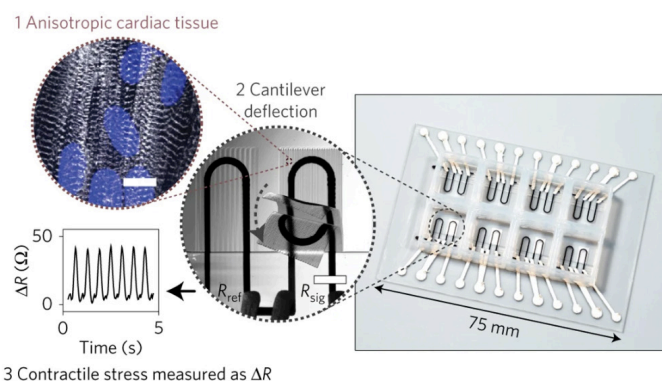


**Fig. 1.** Lung-on-a-chip (Folch, 2022).

## The Heart-on-a-Chip

One famous example of the use of the OoC concept is the 3D-printed cardiac devices with fully integrated sensors from the Disease Biophysics Group at Harvard University. In the human body, cardiac muscle cells contract to pump blood into and out of the heart. The force these cells exert when they contract is called tissue contractile stress and can vary in response to different stimuli (e.g., minerals, hormones, neural signals, disease, drugs) (Burrows, 2016).

In 2016, Lind et al. improved existing methods to measure this useful contractile stress parameter with the development of a heart muscle organ-on-a-chip, only 75 millimeters wide and made of eight individual wells (Fig. 2). The device is printed in a continuous process and utilizes four individual printing nozzles and six different ink materials (determined via optimization testing to better mimic cardiac tissue stress and contractility). It includes grooved microstructures so that when rat heart muscle cells, or neonatal rat ventricular myocytes, are introduced into the device, these cells are guided to assemble into self-organized tissue (Lind et al., 2016).



**Fig. 2.** Device to measure contractile stress of cardiac tissue (Lind et al, 2016).

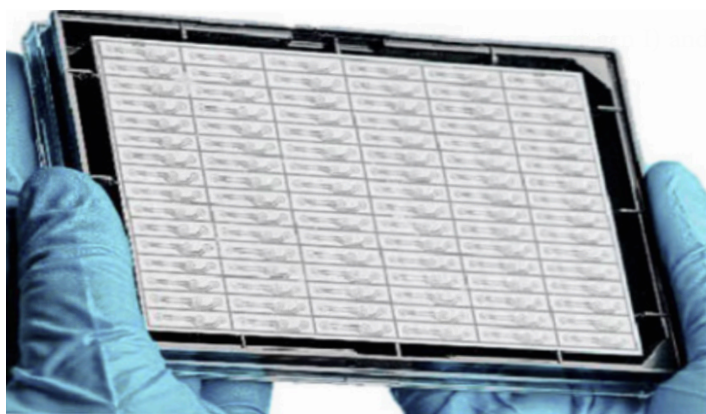
This device is superior to previous measurement methods because embedded OoC sensors are direct, noninvasive, and enable electronic data collection (rather than optical collection via a microscope). As a result, scientists can store the device in a cell incubator—a closed box kept at about 99 ° and constant humidity levels—to better mimic the human body temperature. This enabled researchers in the Disease Biophysics Group to study the impact of common hypertension drugs, thicker cardiac tissue models, and even time on tissue contractile stress (Lind et al., 2016).

## The Tumor-on-a-Chip

OoCs can do more than just mimic normal human body microenvironments—they can also mimic pathological states, including cancer. Cancer cells can proliferate rapidly, which is detrimental inside the human body but makes it much easier to keep tumors alive for in vitro studies. This benefit was evident when a biotechnology company in the Netherlands suspended

breast cancer cells in their company's high throughput organ-on-a-chip platform. Each device featured up to 96 iterations of a microfluidic chamber (**Fig. 3**), allowing them to simultaneously test multiple conditions across multiple trials (Lanz et al., 2017).

This approach differs from a 2D Petri dish or well-plate culture, as it involves suspending cancer cells in a liquid medium (e.g., collagen I) and inserting them into a chamber of the OoC device. Changes in both pH and time facilitate the gelation of collagen, successfully creating a 3D extracellular matrix (ECM) for the cancer cells to grow and proliferate in. This ECM environment, along with constant perfusion of cell nutrients, improves cell health and more closely mimics the *in vivo* tumor microenvironment, allowing researchers to observe distinct cellular functions and properties that cannot be observed in 2D cultures (Lanz et al., 2017). Thus, chemotherapy drug screening in 3D OoC cultures is more useful and applicable than screening in 2D cultures.



**Fig. 3.** Device with wells to hold ECM-embedded cancer tissue (Lanz et al., 2017).

## The Human-on-a-Chip

The human-on-a-chip or body-on-a-chip boasts several tissue types within one device. At an industrial lab in Florida, a team of researchers has constructed a multi-organ system—that includes the liver, the spleen, the endothelium, and circulating red blood cells (RBCs)—to examine the pathological effects of malaria, particularly the effects caused by the protozoan parasite *P. falciparum*. Corresponding cell types are seeded within the liver, spleen, and endothelium compartments (**Fig. 4**), while RBCs and nutrients follow a gravity-driven flow between these compartments with sinusoidal rocking. Once the protozoa strains are introduced into the RBC culture in the device, various parameters of each cell type are tested along with the effects of chloroquine, an antimalarial medication (Rupar et al., 2023).

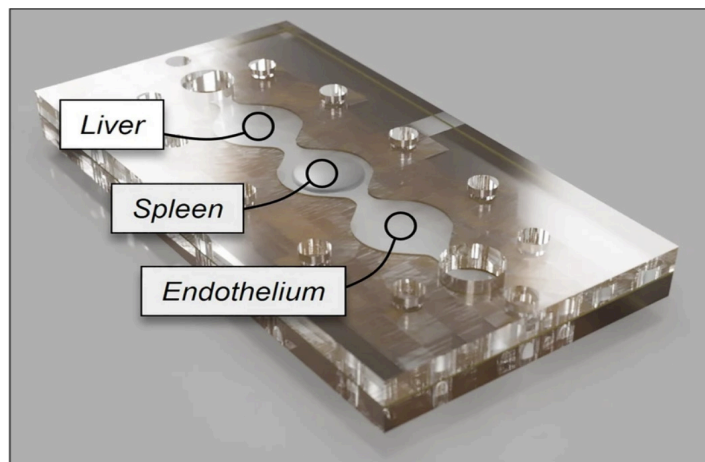
The body-on-a-chip can be a meaningful approach for many reasons. Conditions like malaria systematically affect more than one organ or area of the body (via infected RBC circulation), which is often hard to recapitulate with traditional *in vitro* methods. This OoC construct is a close replica of the

infected RBCs' interactions, focusing on organs related to the fundamental properties of malarial infection: the spleen assists the immune system in clearing the parasite, endothelial cells contain receptors to which infected RBCs bind, and the liver is responsible for drug metabolism. As a result, Rupar et al. were able to create a controlled, yet connected environment to study their pathology of choice (2023).

## Organ-on-a-Chip Limitations

While OoCs offer promising advantages and opportunities, the organ-on-a-chip system is not flawless. Although their small size allows for the design of cheaper and easier-to-recapitulate experiments, it also presents disadvantages, as the simulated microenvironment often cannot completely replicate the full complexity of the environment within an organ. For example, a liver tissue microenvironment may not be able to establish sinusoids, which are tiny blood vessels found in an actual liver (Reif, 2014). This omits essential organ functions and may lead to discrepancies in experimental results in comparison to actual clinical trials, but it generally results in fewer discrepancies than conventional *in vitro* studies. Still, many labs are working to overcome this gap by leveraging strategies from adjacent fields (i.e. novel 3D bioprinting techniques and digitally controlled dynamic environments to induce vascularization). There are also technical challenges—since the quantity of fluid flow is very small, unwanted properties may appear due to surface tension and improper mixing of fluids (Danku et al. 2022).

Moreover, OoCs are a relatively new technology, lacking standardization of design between various labs and applications. Thus, even if the design of an OoC is well-elaborated within research papers, its many moving parts may lead to less reproducible results between different experiments. Ethical concerns include the process of gaining permission to use a person's cells once OoCs are personalized to patient groups or



**Fig. 4.** Body-on-a-chip combining liver, spleen, and endothelium 3D cell cultures (Rupar et al., 2023). 2017).

even individual patients. As the field grows rapidly, question emerge: what protections would a fetus-on-a-chip deserve? What if a brain-on-a-chip develops some measurable consciousness property (Thakar, 2023)? At present, the state of OoC design means these questions are not yet pressing, yet considering rapid advancement of the biomedical research community, they stand none the less.

## Conclusion

Regardless of the current limitations surrounding organ-on-a-chip technology, this field of biomedical research is here to stay. Many biotech companies from the Netherlands-based Mimetas to the Texas-based Systemic Bio are working to streamline and industrially manufacture these microfluidic chips. Additionally, OoC systems are being more broadly integrated into the biomedical research enterprise. For example, the incorporation of deep learning, an area of artificial intelligence, enables the instant screening of massive databases to narrow down experimental groups and facilitates rapid analysis of the large amounts of data generated by high-throughput OoC systems (Li et al., 2022). The organ-on-a-chip provides a platform for seemingly endless possibilities and will undoubtedly continue to change the face of conventional biomedical research, one recapitulated tissue at a time.

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# FEATURES



## Nature's Evolving Assassins: How Antibiotic Resistance is Threatening Our Ability to Fight Disease – And What We Can Do to Stop It

Image Courtesy of Adobe Stock

Ambika Grover '27

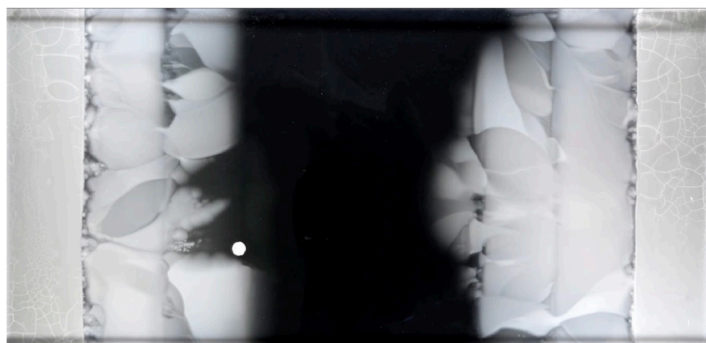
Combating disease remains the tireless goal of the research community, as biomedical innovations undoubtedly lead to longer, happier, and more fulfilling lives. In the clinical context, this has propelled humanity to seek solutions for many prevalent diseases. Today, a growing challenge in engineering a modern medical defense system lies in resolving a challenge of our own creation: growing resistance to the powerful antibiotics used in the treatment of infectious diseases (Muteeb et al., 2023). Our attempts to ensure health have thus revealed themselves as double-edged swords, requiring caution and moderation.

Understanding the duality of antibiotics starts with an unusually large petri dish inside the Baym Lab, nested in Harvard Medical School's Department of Biomedical Informatics and Microbiology. For the Baym lab, their "Mega-Plate Petri Dish" is a revealing glimpse into the capacity of antibiotic resistance. This experiment begins with a 2-foot by 4-foot petri dish divided into nine segments and covered in thick agar (a cooled gel-like substance that provides nutrients

for bacteria). Different amounts of antibiotics are added to the gel, starting from the corners of the dish. At the furthest corners, there is 0 antibiotic concentration. With each  $n$  integer step from the corners, the researchers add  $10^n$  units of antibiotic. If introduced immediately, there is no chance of bacteria survival at the innermost layer, which consists of 1000 units of antibiotics.

The setup of the Baym lab's mega-plate Petri dish remains incomplete. Now loaded with antibiotics, the bacteria is introduced: the researchers prepare *Escherichia coli*, more commonly known as *E. coli*. (often recognized for its role in foodborne diseases). A variety of antibiotic and bacterial candidates could be substituted for this experiment. These include penicillin, commonly used to treat *Streptococcal pharyngitis* (the bacteria that causes strep throat); ampicillin, a medication used to treat meningitis (inflammation of the brain and spinal cord membranes); and tetracycline, a broad-spectrum antibiotic intended to treat infections affecting the skin (NHS, 2024).

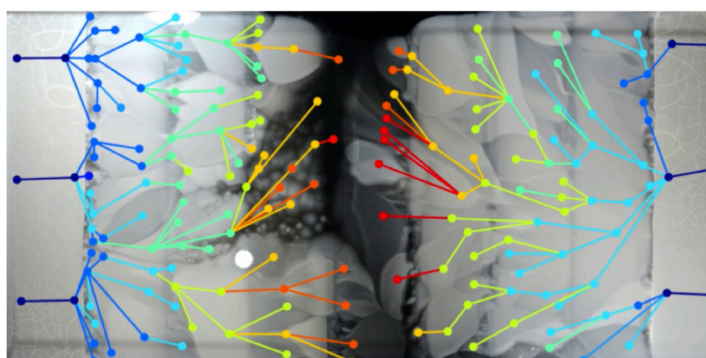
*E. coli* spreads quickly to the portion of the plate with no antibiotic, as expected. It additionally survives



**Fig. 1.** The bacteria make their way toward the innermost portion of the petri dish, developing antibiotic resistance in response to antibiotic exposure. Courtesy of the Baym lab.

the layer consisting of one antibiotic dose. To survive, *E. coli* is required to adapt, resorting to its natural adaptation mechanisms. As the bacteria travels inwards, mutants gradually appear as white clusters; these mutant bacteria resist the antibiotic. After a slight pause when the bacteria reach 10-unit barrier, another new mutant is formed (**Fig. 1**). Over 11 days, bacteria crawl to the 1000-unit innermost part of the Petri dish, surviving in an environment where they would have died just days previously (**Fig. 2**).

What are the implications of the evolving mutations of *E. coli* and other bacteria in the real world? In clinical settings, bacteria can evolve quickly and threaten already immunocompromised patients with little warning. Antibiotic



**Fig. 2.** Over 11 days, bacteria have reached the 1000-unit innermost part of the Petri dish due to numerous mutations that made it more resistant. Courtesy of the Baym lab.

resistance erodes physicians' ability to combat infectious diseases including tuberculosis, tetanus, cholera, and UTIs, among many others. This resistance also impacts the health of animals and plants, thereby diminishing productivity and endangering food security. Most importantly, the development of resistant bacteria is a direct consequence of our reliance on antibiotics to defend against disease (WHO, 2022).

## An Overview of Antimicrobial Resistance

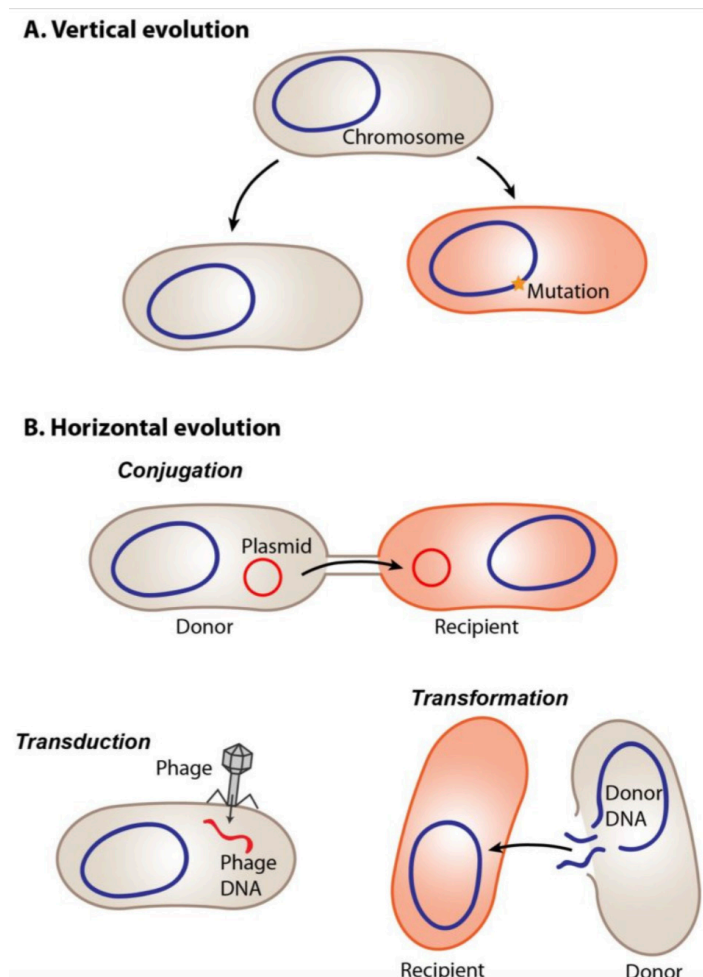
The broader category of antimicrobial resistant (AMR) microbes—occurring when viruses, bacteria, and other organisms evolve mechanisms to protect themselves from human therapies—result in the deaths of least 1.27 million people annually. Moreover, the specialized antibiotics used to treat already multidrug-resistant microbes costs the United States alone \$4.6 billion every year (CDC, 2021). These challenges are relatively normal: AMR was first observed in the 1940s and 1950s in the form antibiotic resistance—AMR applied to specifically to bacteria. The first hint of the danger of antibiotic resistance came in Alexander Fleming's 1945 Nobel Prize acceptance speech, in which he suggested that it “would not be difficult” to make microbes resistant to penicillin in the laboratory (ReAct, 2020). These observed effects quickly escalated. For example, *Staphylococcus aureus*, the cause of staph infections, is a bacteria that affects the skin and spreads through contact. Identified as resistant to penicillin by Mary Barber in Britain in the early 1960s, *S. aureus* rapidly spread worldwide, undeterred by antibiotics intended to treat it (Podolsky, 2018).

Bacteria use two primary mechanisms to withstand the effects of antibiotics (Habboush, 2023). Often, bacteria can acquire resistance via a new genetic mutation that helps them survive when exposed to antibiotics. Alternatively, bacteria may obtain DNA from another already resistant bacterium via multiple potential mechanisms. The former is known as intrinsic resistance; for example, an antibiotic designed to target the wall of a bacterium cannot do so if a strain of *S. aureus* lacks a cell wall due to mutation. This is an example of an advantageous mutation likely to be passed down from generation to generation through vertical mutation (**Fig. 3**). The second mechanism—horizontal gene transfer—happens through transformation, transduction, or conjugation (**Fig. 3**). In transformation, a bacterium engulfs a piece of ambient DNA. In transduction, DNA is transferred from one

**“Bacteria can develop unique traits that enable their survival despite exposure to antibiotics.”**

bacterium to another via a virus. In conjugation, DNA passes through an intercellular tube-like structure (Cecchetelli, 2019). Together, these evolutionary systems can defeat our ability to fight and cure disease. Resistant *E. coli* and *S. aureus* remains a concern in nearly 80 countries, where 42% and 35% of strains resist the best available antibiotics to treat them.





**Fig. 3.** An overview of vertical (passing down mutations) and horizontal evolution (conjugation, transduction, and transformation) in bacteria, which help to make them more resistant (FutureLearn, n.d.).

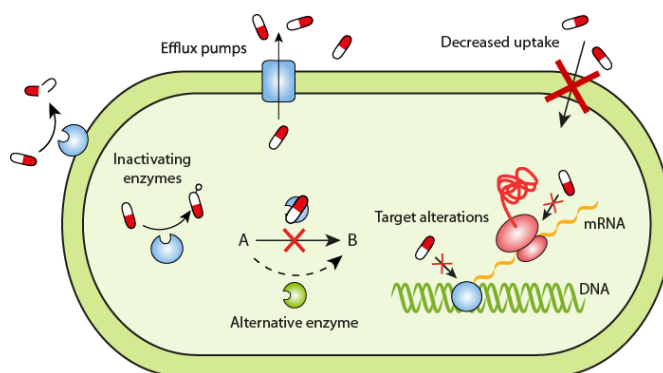
## Molecular Mechanisms of Antibiotic Resistance

Antibiotics can be either synthetic or naturally derived therapeutics; they often interact with bacterial receptors to gain entry into the cell, provoking specific cell responses and mechanisms of resistance in the organisms they target. In addition to their role in treating infectious diseases, advancements in antibiotic development have propelled breakthroughs in the context of cardiovascular disease, in immunosuppression (helpful in bone marrow or organ transplant contexts), and in cancer treatment.

As discussed, bacteria can develop unique traits that enable their survival despite exposure to antibiotics. For example, chemotaxis is the process of directed cell mobility that enables bacterial “swimming” in response to a given stimulus (ScienceDirect, n.d.). The pathogen *Pseudomonas aeruginosa* (primarily associated with pneumonia) exhibits chemotaxis in a surprising manner; counterintuitively, these bacteria swim toward

antibiotics. In doing so, the bacteria move as if they are responding to a competing bacterial colony and are preparing to become suicidal, releasing molecules to defend against the competing colony in the process. In reality, they are lured to their deaths by antibiotics. This self-induced destruction explains just one situation in which clinical antibiotics help eliminate pathogens (Oliveira, et al).

With this framing in mind—the high levels of fluidity that bacteria possess and their ability to rapidly adapt—how do bacteria develop an affinity for resistance? Two primary mechanisms of antibiotic resistance are (1) the creation of efflux pumps that can push antibiotics out of the bacteria and (2) the use of deactivating enzymes (known as transferases) that prevent adequate binding of the antibiotic to its intended target (**Fig. 4**). First, efflux pumps serve as transporters that remove harmful substances from the internal environment of bacteria to the outside. This is important given that most antibiotics that interact with a specific target accumulate within bacterial cells. Efflux pumps are located at the membrane of bacterial cells. When a bacteria develops a pump that recognizes the characteristic profiles of an antibiotic (through mechanisms of vertical and horizontal transfer), it becomes substantially easier for these bacteria to resist antibiotic-induced death. Notably, these efflux pumps do more than assist bacteria in antibiotic resistance: the *E. coli* AcrAB efflux system, for example, pumps out bile acids and fatty acids to lower bacterial toxicity (Okusu et al., 1996). Second, transferases within bacteria seek to modify the antibiotic, attempting to bind and modify it, eliminating its functionality. Often, transferase enzymes chemically substitute a functional group situated at the exterior-most position of the antibiotic, preventing binding (Das et al., 2017). These enzymes, known as antibiotic-modifying enzymes, are the largest group of enzymes that play a direct role in antibiotic resistance.



**Fig. 4.** An illustration of various antibiotic resistance strategies of bacteria (Win-stred-Yuen et al., 2018).



## Implications of Antibiotic Resistance

After all other antibiotics have tried and failed, treatment of bacterial infections in a clinical setting can require a drug of last resort (DoLR), which is utilized after all other drug options have been exhausted. The antibiotics falling under this classification are broadband, attempting to eliminate harmful bacteria through any means necessary. Unfortunately, due to historical usage, there is already a very high level of resistance to many last-resort antibiotics, limiting their effectivity. As such, DoLRs are primarily regarded as a patient's last chance when they suffer a multi-drug resistant infection (Li, et al, 2022).

There is much to consider with respect to how to approach fighting antibiotic resistance. At Harvard and affiliate institutions, labs such as the Baym and Kahne labs are engaged on this front. However, these labs face a significant, growing challenge. There are 2.8 million infections per year in the United States attributed to antibiotic resistance. The aftermath of COVID slowed our ability to fight AMR. In the first year of the pandemic, more than 29,400 people died from AMR infections; 40% were infected at the hospital. Furthermore, funding for research investigating antimicrobial-resistant infections has decreased by 18% in recent years (CDC, 2024).

There are also underlying social concerns associated with how bacterial infections are treated. There remains a widespread crisis of antibiotic abuse. As Abhijit Banerjee outlines in his book *Poor Economics*, part of this crisis stems from the fact that many individuals with a lack of medical knowledge feel more “comfortable” being handed a pill—such as an antibiotic—to remedy their illnesses as opposed to leaving the doctor's office empty-handed. Additionally, some individuals refuse treatment altogether, while others take over-the-counter general antibiotics without considering whether their social costs are worth the individual benefits.

Given this diversity of behavior and belief in using antimicrobial drugs, significant work needs to be done to motivate a careful balance between antibiotic use and appropriate caution. Science must play a dual role: helping to inform the public about the necessity of treatment while ensuring this care is handled with proper diligence and caution. Without action, antibiotic resistance may quickly become one of the largest challenges of the 21st century, and the solution to this pressing issue remains as much of a question of biomedical research as of public health. Thus, only the evaluation of antimicrobial resistance at the intersection of these fields has the potential to sustain the innovations necessary to treat infectious diseases for decades to come.

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# FEATURES

## Frontiers of Microbially-Informed Medicine

Leah Lourenco '26

### Introduction

Pharmacomicrobiomics is an emerging field at the intersection of pharmaceutical science and the microbiome. In this rapidly developing discipline, research investigates the interactions between current therapeutics and the patient microbiome, often focusing on the gut microbiome. The gut microbiome is a community of trillions of microorganisms that reside in the human gut—namely the stomach, small intestine, and large intestine. These microbes are constantly changing in accordance with patient diet and lifestyle, and recent research has shown that many diseases can be linked to certain microbiome compositions (Blackmer-Raynolds and Sampson, 2023). In the past, most microbiome research has been on metabolic interactions with antibiotics and plant-derived therapies, but pharmaceuticals are the focus in this new frontier of research (Saad et al., 2012).

Current research in pharmacomicrobiomics specifically explores pharmaceutical–microbiome interactions and aims to understand how pharmaceuticals can be most effective for patients. In some cases, this may be attempting to regulate the microbiome composition through the use of probiotics or dietary changes (Arga et al., 2024). In other cases, researchers are now considering the efficacy of personalized pharmaceuticals. These pharmaceuticals are engineered to work better in conjunction with the patient-specific microbiome. This new approach holds great potential in several disease-specific cases including irritable bowel disease, cancer, Parkinson's, and mental illness, yet the field of pharmacomicrobiomics has the potential to revolutionize the treatment of many other diseases with continued research.

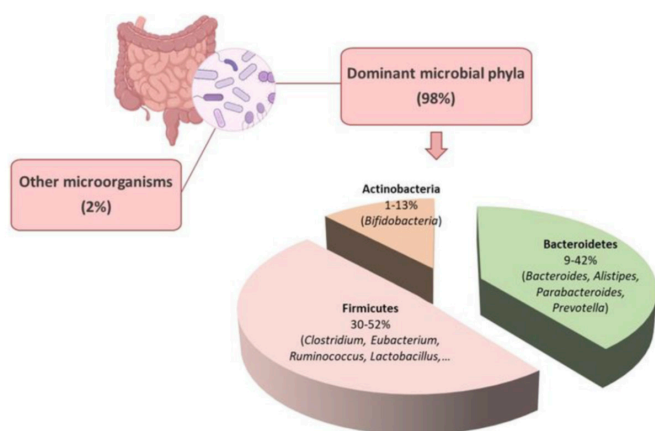
In order to illustrate fully the potential of the pharmacomicrobiomics field, it is important to have a comprehensive understanding of the key microbes in the human microbiome and the ways in which they interact with drugs. By studying individual cases where microbes and pharmaceuticals have worked in conjunction as a more efficient treatment or where microbes have attenuated

the effects of other pharmaceuticals, exploration and understanding of the frontiers of pharmacomicrobiomics can begin.

## Profile of Human Gut Microbiome: Who are the main microbes?

Studies have found that each individual has a microbiome that is completely unique and is influenced both by early development in childhood and day-to-day lifestyle. The more diverse the gut microbiome is, the healthier the individual is, with the most diverse microbiomes even decreasing the individual's chance of developing a number of diseases, both gastrointestinal-related and non-gastrointestinal-related (Rinninella et al., 2019).

The human gut microbiome's vast diversity makes it nearly impossible to detail every unique microorganism that plays a role in our gut. **Figure 1** shows the typical composition of the human microbiome. A broader perspective allows us to gain a deeper understanding of the three most important groups of microbes at the phylum level of order: Firmicutes, Bacteroidetes, and Actinobacteria.



**Fig. 1.** The typical composition of microbes found in the human gut microbiome (Conz et al., 2023).

## Firmicutes

In the Firmicutes phylum, there are five main genera of microorganisms including *Lactobacillus*, *Bacillus*, *Clostridium*, *Enterococcus*, and *Ruminococcus*. Increased presence of Firmicutes is linked to consumption of high-fiber carbohydrates during early childhood development. The primary function of Firmicutes in the microbiome is carbohydrate digestion (Ottman et al., 2012). The different genera of the Firmicutes respond varying to high animal protein versus high fiber diets. Firmicutes play a large role in the adult microbiome as they are one of the most dominant

phyla next to Bacteroidetes and Actinobacteria (Rinninella et al., 2019).

## Bacteroidetes

The most important organisms of the Bacteroidetes phylum are *Bacteroides* and *Prevotella*. These microbes are experts at digesting protein and carbohydrates, a mechanism they perform often in the large intestine (Thomas et al., 2011). Bacteroidetes increase when animal proteins are introduced into the childhood diet. High levels of *Bacteroides* are linked to diets that include more animal protein, which is similar to the standard Western diet. A high-fiber diet is linked to a decreased level of *Bacteroides* (Rinninella et al., 2019).

## Actinobacteria

Actinobacteria are not as prominent as the other two phyla of microorganisms found in the human gut. Similar to Bacteroidetes, Actinobacteria aid in the digestion of proteins and carbohydrates, mostly in the large intestine (Binda et al., 2018). There is primarily one genus of Actinobacteria of relevance to the gut microbiome, *Bifidobacterium*. Infants who were breastfed tend to have more diverse *Bifidobacterium* microbiota than formula-fed infants. Actinobacteria are also increased by a high animal protein diet (Rinninella et al., 2019).

Within this diverse microbial community, microbes work together to keep us healthy. Different compositions of these key microorganisms have a notable impact on human health. For example, the Bacteroidetes-to-Firmicutes axis is a ratio of the two phyla in the gastrointestinal composition that is being studied as a potential biomarker for obesity among other diseases (Magne et al., 2020). The Bacteroidetes-to-Firmicutes axis is a strong indicator of the level of an individual's microbiome diversity. On average, diversity is maximized when Firmicutes make up ~80% and *bacteroidetes* make up ~15% of the microbial population (Manor et al., 2020).

Naturally, relative microbial diversity is variable, making some individuals more likely to develop certain chronic diseases and conditions. For example, children with obesity have been linked to increased levels of Firmicutes and decreased Bacteroidetes. Furthermore, irritable bowel syndrome patients have been identified with elevated Firmicutes and depleted Bacteroidetes and Actinobacteria (Rinninella et al., 2019). The microbiome has been shown to be indicative of conditions beyond the bowel, including type 2 diabetes, Alzheimer's, Parkinson's, autism, and even stress.



## Research Areas at the Forefront

The main focus of the field of pharmacomicrobiomics is the interactions between these microorganisms and pharmaceuticals. There are a plethora of routes that researchers are taking in an attempt to tackle this project that spans multiple disciplines of medicine. These cases range from oncology to psychiatry, and each brings exciting new approaches to their respective fields.

### Oncology

The gut microbiome has been linked to interactions with traditional cancer therapeutics. In some cases, the drugs begin to accumulate in the microorganisms, and, in other cases, the microbes directly metabolize the drugs into a less effective alternative. Sometimes, however, the microbes benefit the patient. In most cases, the specifics of the mechanisms of drug-microbe interactions are unknown and are currently under investigation (Conti et al., 2022).

Traditional chemotherapy pharmaceuticals take an untargeted approach in their attacks, simply hoping to have a meaningful efficacy against cancer cells. Research has suggested that *Bifidobacterium* strains may be able to work in conjunction with platinum-based drugs—such as cisplatin and carboplatin—to reduce tumor growth. The bacteria and platinum-based drug work together to boost T cell levels in the body, effectively raising attacks on cancer cells. There are also cases where microbes cause drugs to become reactivated. Drug reactivation can lead to increased microbiome disruption, and even further internal injury (Conti et al., 2022).

In oncology, researchers are currently applying prebiotic, probiotic, antibiotic, and fecal microbiota transplants in an attempt to boost the efficacy and safety of cancer therapies. These approaches are all meant to alter the gut microbiome composition in order to make it more compatible with therapy (Conti et al., 2022). Attempts to personalize oncology using pharmacomicrobiomics represent another exciting frontier. One group was able to develop a method for mapping drug-microbe interactions within an individual (Javdan et al., 2020). This approach, shown in **Figure 2**, illustrates how further mapping would allow for individualized patient predictions of drug efficacy.

### Parkinson's

Parkinson's disease is characterized by the loss of dopaminergic neurons, which leads to a deficiency of dopamine in the brain and prevents the brain from executing smooth movements. This loss of fine motor control causes patients to suffer from shaking, stiffness, and instability, significantly impacting their quality of life (National Institute of Neurological Disorders and Stroke, n.d.). The primary

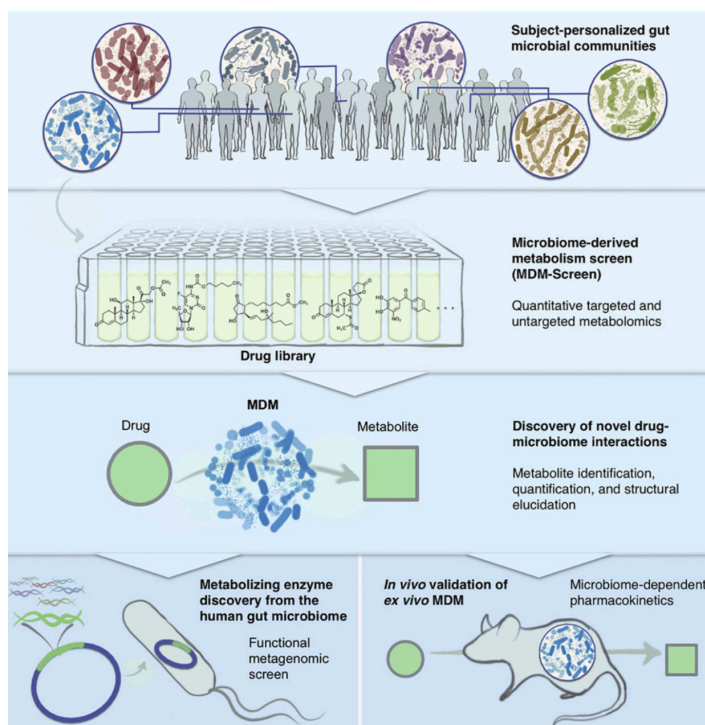


Fig. 2. Possibilities for personalized medicine (Javdan et al., 2020).

drug currently used for Parkinson's patients is levodopa (L-dopa). Levodopa works against Parkinson's disease by crossing the blood-brain barrier and becoming dopamine, serving as a replacement for naturally-produced dopamine in patients with Parkinson's. Often, levodopa is metabolized in the bowel before it can reach the brain, where it is useful. When metabolized outside of the blood-brain barrier, it can no longer cross through to the brain. Even when administered with drugs that are supposed to counteract the metabolism of levodopa, efficacy is still low (Maini Rekdal et al., 2019).

With the rise of pharmacomicrobiomics, a new solution to levodopa metabolism has also become apparent. One study investigated the drug-microbe interactions present during levodopa metabolism. The study found that *Enterococcus faecalis* is likely the primary metabolizer of levodopa, even in the complex



Fig. 3. Levodopa-microbe interaction pathway (Maini Rekdal et al., 2019).

microbiome. The levodopa can be even further metabolized by *Enterococcus lenta* (Maini Rekdal et al., 2019). This metabolic process is shown in **Figure 3**. Knowing that these interactions occur will allow

researchers to consider more advanced solutions for preventing the metabolism of levodopa.

### Irritable Bowel Disease

Irritable bowel disease (IBD) is another medical condition commonly treated by medications that can have their efficacies impacted by drug-microbe interactions. IBD is characterized by increased immune activity within the gastrointestinal tract that leads to extreme inflammation, scar tissue buildup, narrowing, and other complications. IBD treatment can be approached using five different classes of therapeutics: aminosalicylates, corticosteroids, immunomodulators, anti-TNF biologics, and small molecule inhibitors. Sometimes, intestinal microbes can activate therapeutics, but gut microbes can often render these drugs completely useless (Becker et al., 2023).

The immunomodulator class of therapeutics works primarily by repressing the immune system in order to prevent the immune system from attacking the bowel. Thiopurines, a group of immunomodulators, have been connected to microbe interactions that increase the efficacy of the drug and open up a pathway to making thiopurines more localized (Becker et al., 2023). In individuals with IBD, *C. concisus*, *E. coli*, and *B. fragilis* are more common in the microbiome. These strains together are capable of converting the thiopurines into a more active form of the drug (Fig. 4). These microbes could eventually allow the anti-inflammatory effects of thiopurines to be more targeted and their adverse effects to be minimized (Becker et al., 2023).

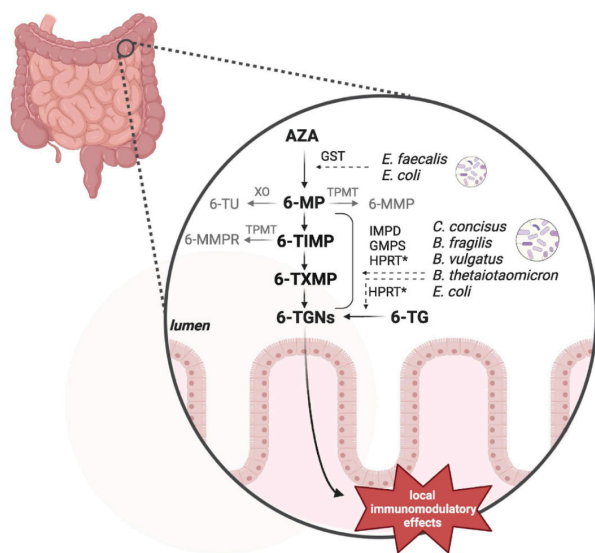


Fig. 4. Thiopurine-microbe interaction pathway (Becker et al., 2023).

Biologics—drugs produced by biological mechanisms—are very popular in the IBD treatment space. These therapeutics work to prevent inflammation in IBD patients. In order to do this, they primarily block messages from the immune system. TNF- $\alpha$  inhibitors are a group of therapeutics that both promote healing and block an essential protein in the inflammatory cycle (Biologics and Inflammatory Bowel Disease (IBD), n.d.). Patients often gain antibodies against the medications and must switch. Notably, some microbes may be able to degrade these antibodies naturally (Becker et al., 2023). Furthermore, if doctors had a clear understanding of the microbiome-biologic interactions, it may be easier to predict the most effective treatment.

### Psychiatry

Studies have shown that the gut microbiome even has an impact on mental health and mood. For example, the microbiome has been shown as relevant in patients with psychotic disorders. Increased gut microbiome diversity has been linked to healthy patients, while decreased diversity is generally linked to patients with mental health disorders. Patients who take antipsychotic and antidepressant medications experience an increase in *Bifidobacteria* and *Lactobacillus* strains and an overall improved gut microbiome diversity in comparison to before treatment (Minichino et al., 2024).

There is a strong correlation between postpartum depression and gut microbiome disruptions. After birth, it is common for patients to experience fluctuations in microbiome composition, mainly related to Firmicutes and Bacteroides. This can cause changes to the processing of molecules such as estrogen, progesterone, and serotonin. One enzyme,  $\beta$ -glucuronidase, is known for its role in metabolizing estrogen to an overactive form. Research suggests that the microbiome disruption that occurs postpartum may also interfere with this enzyme—and potentially others—causing a decrease in hormones like estrogen and progesterone. This lack of hormone balance may be one contributor to the development of postpartum depression (Zhang et al., 2023).

Further research must be conducted at the intersection of psychiatry and medicine. At this point, correlations between prescriptions and microbiome diversity have been made, but there is little known about the mechanisms involved. An emphasis on the mechanisms in further studies may illuminate better solutions for patients.

## Discussion

The field of pharmacomicrobiomics promises to provide a novel approach to the treatment of a large variety of medical problems. As this new field emerges, there are some limitations to current solutions. With such a new field, there is a necessity for more specific research on mechanistic interactions, and, unfortunately, there are many drugs and microbes to be documented. It will take a large amount of time to completely understand every interaction. There is a necessity for more clinical *in vivo* and *in vitro* experimentation.

The cases presented here are at the forefront of innovation. As researchers continue to realize the importance of these microbe–medicine interactions, research may be able to illuminate further interactions. The efficacy of old drugs and new drugs alike may be optimized by these studies. It seems as though the field is quickly moving towards precision medicine, which would allow practitioners to present solutions that take patient biology and lifestyle into account in order to best treat ailments (Zhao et al., 2023). By gaining a better understanding of the molecular mechanisms involved in complex interactions, researchers become closer to identifying improved solutions for patients across many disciplines. Studying pharmacomicrobiomics allows for more informed engineering and application of pharmaceuticals.

Pharmacomicrobiomics studies create exciting possibilities for medicine in the future. Focusing on drug–microbe interactions in the gut has the potential to greatly improve clinical outcomes of therapeutics. In all fields of medicine, if doctors could compare a patient's individual microbiota profile with potential drug interactions, patients would be able to avoid wasting time finding the proper treatment. Prescriptions could be optimized for patients, avoiding unnecessary side effects. If there was a greater understanding of drug–microbe interactions, doctors and researchers would also have a better understanding of how pharmaceuticals behave within our bodies. This expansion of understanding would altogether improve healthcare efficiency and societal health.

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# FEATURES



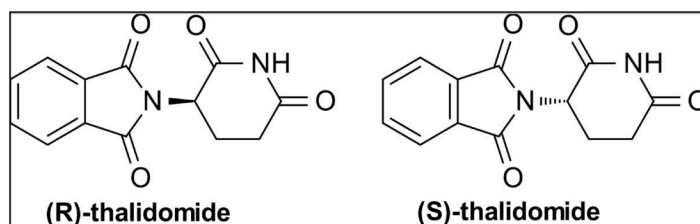
## The Vindication of Thalidomide

How modern advances in chemistry and molecular biology have unveiled the therapeutic properties of a birth-defect-inducing sedative.

Image Courtesy of I, Research


Héctor Andrés Martínez Luna '27

Teratogens are chemical species that can affect fetal development—not quite what the German pharmaceutical company *Grünenthal* had in mind when they synthesized and introduced thalidomide to the market in 1954 as an over-the-counter sedative. Unfortunately, thalidomide became an instant hit among pregnant women suffering from morning sickness, leading to the sale of 14.6 tons of the drug by 1960 in Germany alone (Rajkumar, 2004). It wasn't until 1961, when doctors first reported a link between thalidomide and congenital malformations, that the popular drug was discontinued. Often referred to as the *Thalidomide tragedy*, an estimated 10,000 infants were affected with limb malformations and organ failure worldwide, out of which 40% died within one year of birth (Franks et al., 2004). Decades of clinical research since, however, have resulted in thalidomide becoming a common drug to treat advanced leprosy and even multiple myeloma, a type of blood cancer (Rehman et al., 2011). Moreover,



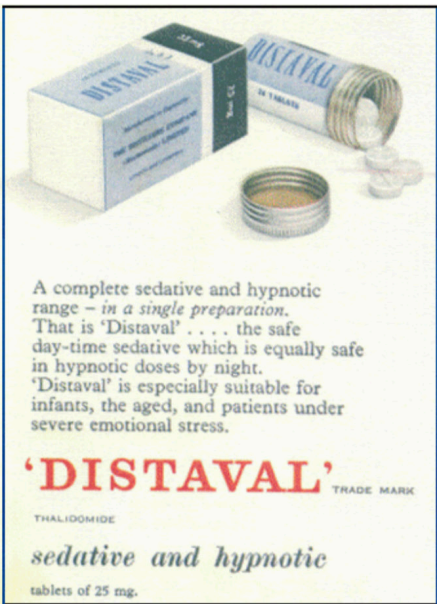
**Fig. 1.** Thalidomide is a derivative of glutamic acid and it has two distinct stereoisomers: S(-) is the teratogen whereas R(+) functions as a sedative. These variants can interconvert to one another under physiological pH, leading to the double-faced nature of thalidomide (Oxbridge Applications, 2015).

the recent discovery that thalidomide binds to the cereblon protein (CRBN) is paving the way for a new generation of promising small-molecule drugs known as molecular glue degraders. From “one of the worst manmade medical disasters in history” (Robson-Mainwaring, 2019) to a “powerful cancer therapeutic” (Oleinikovas et al., 2023), thalidomide’s medical ‘vindication’ is unprecedented. **How did this happen? What makes it such a promising drug? And what does “vindication” mean for medicine?** This article seeks to introduce the history and science behind these questions.



**a)**

Distaval thalidomide advertisement, 1961.



**b)**

Distaval thalidomide advertisement, circa 1961.

**Fig. 2. a, b)** Thalidomide adverts from 1961 under the commercial name 'Distaval'. They emphasize how thalidomide is safe and non-toxic even when accidentally ingested by children (British Medical Journal, 1961).

## Serendipitous Discoveries Paved the Way

Despite thalidomide being effectively banned from European markets in 1961, it continued to be available in countries elsewhere. In 1964, Dr. Jacob Sheskin from the Hadassah Medical Center in Israel reported that a patient's leprosy improved after being administered the sedative (Rehman et al., 2011). This serendipitous discovery reignited Western interest in thalidomide. In the following decades, the use of thalidomide in the U.S. on a controlled experimental basis was approved by the Food and Drug

Administration (FDA) for inflammatory skin disorders and graft-versus-host disease, among other conditions (Rehman et al., 2011).

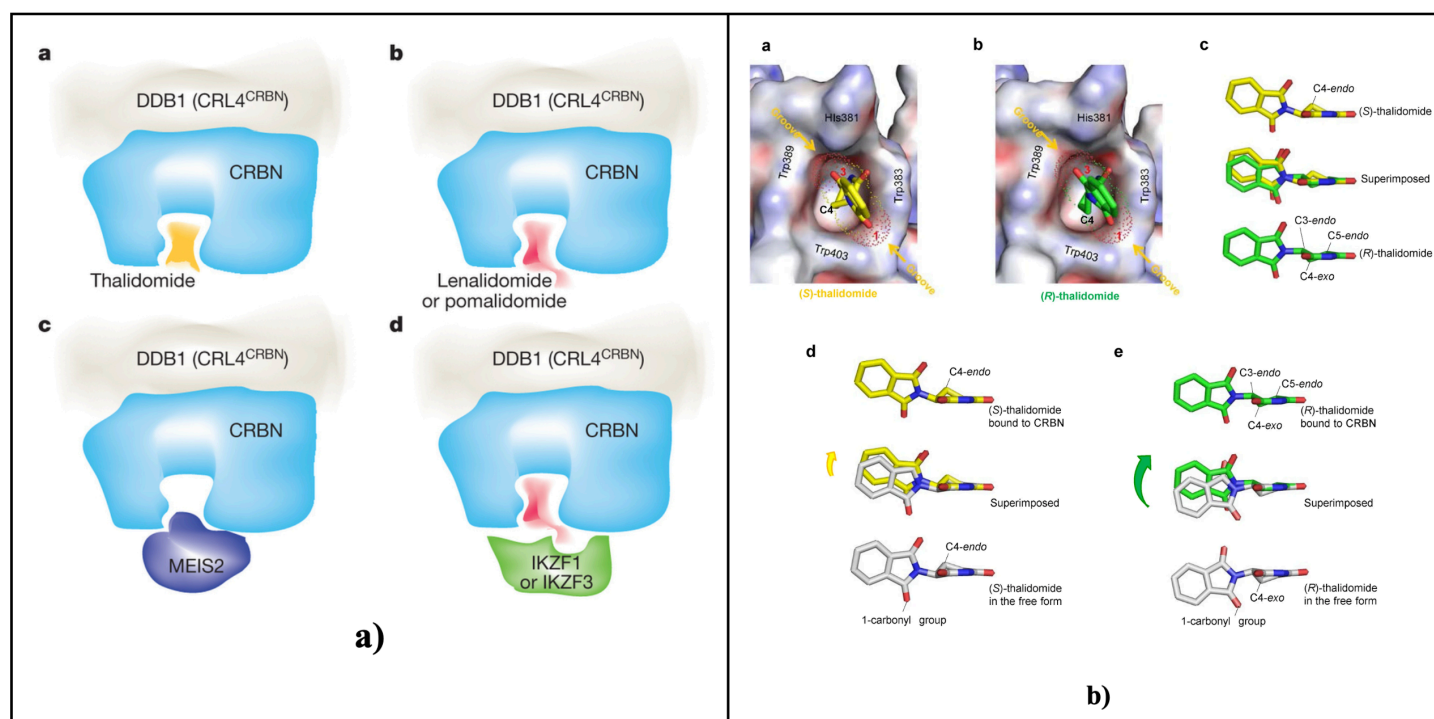
Renewed interest in thalidomide yielded important insights into the structure and properties of the drug. While the molecular pathways of how the drug acts on leprosy patients are not yet fully understood, it is known that thalidomide has anti-inflammatory and anti-angiogenic properties (Rajkumar, 2004). Experts have demonstrated that this inhibition of angiogenesis, or the creation of new blood vessels, is a primary cause of thalidomide-induced birth defects (Therapontos et al., 2009). This property, however, can also be harnessed for good in cancer medicine—as tumors expand, they require a growing supply of nutrients that can only be acquired by creating new capillaries that divert blood flow from organs to the cancer cells. If thalidomide's inhibition of angiogenesis can be targeted toward tumors, the drug becomes a potential new cancer treatment. This realization in the late 1990s kept thalidomide in the spotlight of Western medicine and further incentivized research (Rehman et al., 2011).

In 2010, Dr. Hiroshi Handa from the Tokyo Medical University in Japan serendipitously discovered that thalidomide and its derivatives—now referred to as Immunomodulatory Imide Drugs (IMiDs)—act as



**Fig. 3.** A thalidomide survivor in therapy at Chailey Heritage in East Sussex. Photograph: Jane Bown





**Fig. 4.** Binding of thalidomide to CRBN protein. a) Showcases a schematic of different substrates or small molecules that bind to the active site of CRBN, including the molecular glue mechanism of lenalidomide and pomalidomide that binds transcription factors IKZF1/IKZF3 to CRBN (Fischer et al., 2014). b) pyMOL three-dimensional visualization (Mori et al., 2018).

molecular glues that bind to CRBN (**Fig. 4**) (Rehman et al., 2011). This discovery was a scientific breakthrough, as it enabled scientists to interrogate the specific pathways by which thalidomide inhibits angiogenesis. Consequently, the mechanisms under the sought-after functionality of thalidomide—inhibition of angiogenesis—grew less abstract and more accessible to experimental research.

### Cellular and Molecular Mechanisms

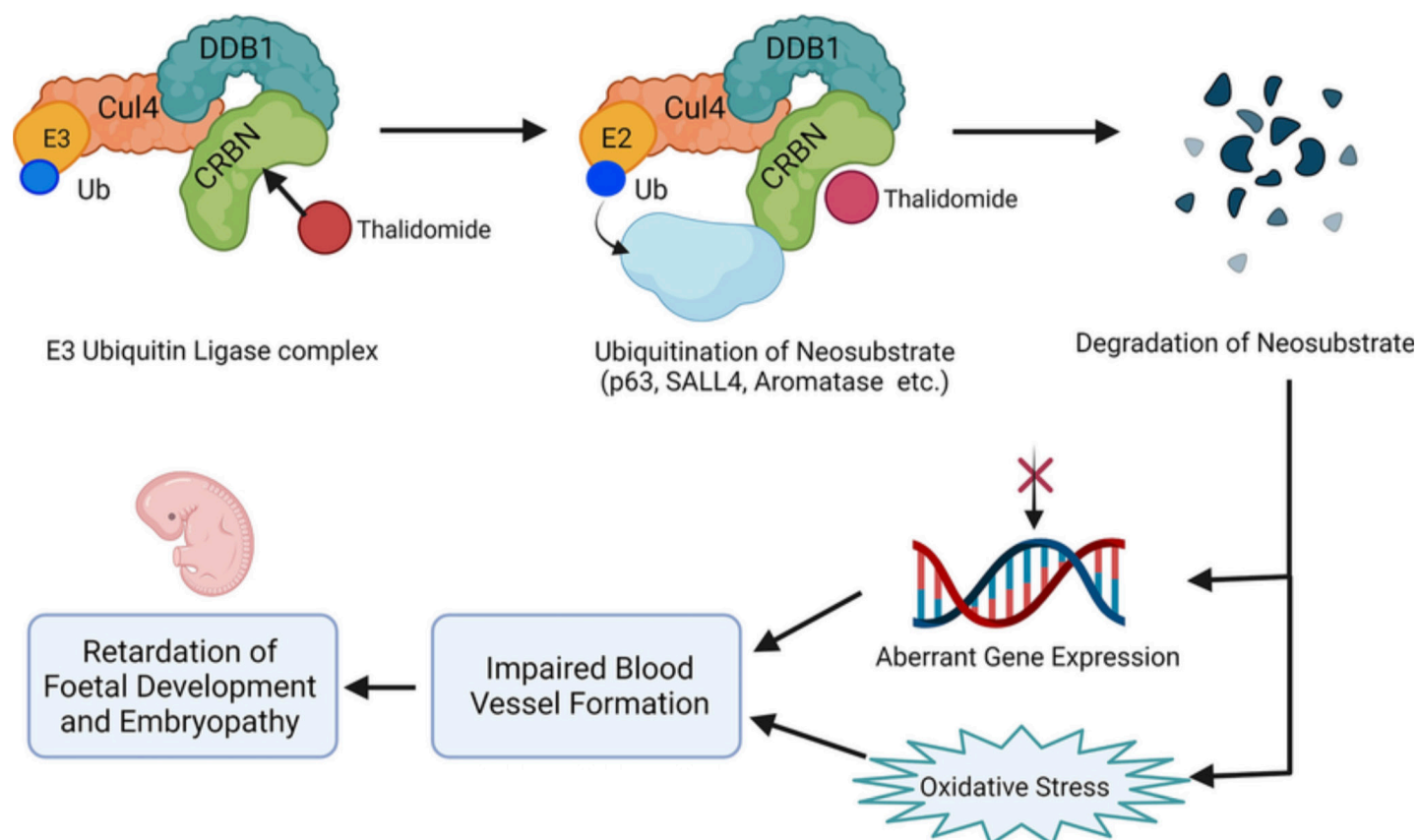
IMiDs such as lenalidomide bind to the CRBN protein which forms part of a larger E3 ligase complex (Oleinikovas et al., 2023). E3 ligases are enzymes that influence the addition of ubiquitin molecules to specific proteins, essentially flagging them for degradation. The resulting IMiD-E3 complex then binds to different protein targets (**Fig. 4**), initiating the ubiquitination of a class of proteins called transcription factors, which can regulate the expression of cancer genes (Oleinikovas et al., 2023). To summarize, when an IMiD binds to CRBN, the resulting IMiD-E3 complex triggers the degradation of transcription factors (**Fig. 5**). The IMiD essentially acts as a “glue” that when bound to CRBN changes the functionality of the larger E3 protein complex.

Molecular glues bind proteins that do not usually interact (Dong et al., 2021). In biology, proteins are complexes of amino acids with distinct shapes that enable them to perform distinct functions within cells. Responsible for a range of varied functions from metabolism to immune reactions,

proteins enable the molecular mechanisms necessary for life. Given the complexity of protein-protein interactions in the human body, even molecular changes to the structure of one protein can have cascading effects on its functions and bonds with other proteins. Molecular glues are therefore extremely significant in medicine—if one sticks two proteins together that do not normally interact, they create a protein complex with new and potentially clinically relevant functions.

The binding of thalidomide to CRBN inhibits the proliferation of plasma cells—a type of immune cell—which is extremely useful when trying to inhibit the unregulated proliferation of cancerous plasma cells (Licht et al., 2014). When dealing with cancer cells, aggressive and non-specific treatments like chemotherapy that compromise both cancerous and healthy cells may do more harm than good. Instead, non-aggressive, specific agents have the potential to disrupt the tumors at critical points, thereby setting off a chain of reactions resulting in the death of the cancerous cells. Angiogenesis is often a critical point to be disrupted in the treatment of myeloma, the cancer of plasma cells, given that bone marrow angiogenesis is essential for the progression of this disease (Shu et al., 2022). By restricting angiogenesis through the formation of the IMiD-E3 complex, thalidomide discriminates against cancer without the added toxicity of damaging healthy cells (**Fig. 5**) (Dong et al., 2021).





**Fig. 5.** IMiD-E3 molecular glue degrader mechanism as initiated by the binding of thalidomide to the active site of the CRBN protein. In this context, 'neosubstrate' refers to targets such as transcription factors IKZF1 and IKZF3. Those two factors regulate genes crucial to plasma cell development, hence why their degradation can impair blood vessel formation (angiogenesis) (Gao and Song, 2020).

## Applications in Modern Medicine

Thalidomide and its variants can have clinical applications based on their anti-angiogenic properties. If thalidomide's disruption of angiogenesis can be both therapeutic and poisonous, as in the case of thalidomide-induced birth defects, how can we reconcile these differences? How can we make a treatment out of a teratogen? One approach to this problem is to look for other IMiDs that, like thalidomide, possess the elementary features necessary for the restriction of angiogenesis but are not teratogenic. In 2013, experts including Dr. Hiroshi Handa reported that pomalidomide can bind to CRBN stronger than thalidomide and lacks teratogenic effects, making for a much more efficient and safe cancer drug than thalidomide (Mahony et al., 2013).

The steps taken to synthesize thalidomide and unearth its properties represent the trial and error of scientific rationality. Today, scientists have the potential to critically analyze small molecules and devise protocols to turn them into effective drugs. The world has entered the era of rational drug design, where the progression of diseases like cancer can be pinpointed to exploitable molecular targets. The concept is simple: if one knows how the molecular structure of a disease relates to its function, one also can

determine what type of small molecule drug might inhibit it. It is an elegant principle that, much like how thalidomide derivatives bind to CRBN and restrict the expression of transcription factors critical for myeloma, focuses on eliminating diseases through specific targeting. If structure begets function in biology, then mutations in structure can beget disease, and inhibitions of said mutations may restore the health of patients without the need to cause off-target damage in non-mutated cells.



**Fig. 6.** Pomalidomide capsules under the commercial name 'Pomalyst'. Photograph taken by multiple myeloma patient Phillip Jeffrey (2015).

Today, decades of research on thalidomide have yielded important advances in rational medicine. Thalidomide, lenalidomide, and pomalidomide are the three IMiDs that are now globally distributed and routinely used for treating leprosy, multiple myeloma, and lenalidomide-resistant multiple myeloma, respectively. In the U.S. alone, an estimated 35,000 people are affected with multiple myeloma every year (NIH, 2018). Despite the Thalidomide tragedy of the 1960s, the drug continues to impact the lives of thousands of people—this time for the better.

Throughout the article, the history and science of thalidomide were introduced to answer questions about how the drug has resurfaced in the twenty-first century as a cancer therapeutic. It is tempting to envision a transformation of thalidomide from poisonous to therapeutic, but thalidomide's chemical composition is constant. If anything, it is the perception of thalidomide that has been transformed. Serendipitous discoveries, such as those of Dr. Sheskin and Dr. Handa, introduced evidence that challenged experts' perceptions of thalidomide as a toxic, non-therapeutic chemical. The perception of thalidomide has been vindicated; our relationship with chemistry is not static. As scientific advances sharpen our understanding of nature, we learn to vindicate that which we didn't fully understand and exploit it to lead better lives.

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# FEATURES

## “Rationality”: The Role of Hot Executive Functions in ADHD

Photo from ravil\_s on depositphotos.com.

Jae Dahin Ji '27

(figures courtesy of Natalie Zhang '27)

### Introduction

Attention-deficit/hyperactivity disorder (ADHD) has long been associated with executive dysfunction, a theory that dominates modern research in cognitive neuroscience and clinical-developmental psychology. In recent years, the concept of executive functions (EFs)—modes of higher-order cognition that are essential for adaptive, goal-directed behaviors—has been categorized by experts into two categories: hot EFs, which involve “processing of information related to reward, emotion, and motivation,” and cold (also known as cool) EFs, which concern “purely cognitive information processing” (Salehinejad et al., 2021). The field has historically neglected the role of these hot factors and focused on cognitive skills such as academic achievement, school readiness, and social

behavior (Brock et al., 2009; Peterson and Welsh, 2014). Because ADHD’s most prominent symptoms manifest in impaired time management, mental programming, and working memory, the study of hot EFs in ADHD patients is too often viewed as trivial.

In ADHD research, scientists often conduct analyses using functional MRI (fMRI), which measures brain activity by detecting changes in blood flow and thereby provides insights into brain regions involved in specific cognitive tasks or emotional responses. Evidence from the striato-limbic area, the key neuroanatomical player in regulating emotional processing and motivation, has provided new insights into the impact of hot EFs on ADHD. By weighing reward and emotion processing as major implications of the affective EF system, researchers have found that abnormalities in hot EFs are as relevant as those in cold EFs in individuals with ADHD. The importance of hot EFs in patients with ADHD has been elucidated through experiments investigating numerous neurological processes including reward



anticipation, reward delivery, delay discounting, orbitofrontal cortex activation, and emotional regulation.

## Reward Anticipation

The ventral striatum (VS) plays a crucial role in reward processing, motivation, and reinforcement learning in the brain, and reduced VS activation during reward anticipation is one of the most consistent findings regarding motivation in ADHD patients. Plichta and Scheres (2014) reiterated this in their meta-analysis of eight fMRI studies, and in this review, they discussed the monetary incentive

### 0. Pre-task: Participant learns cue — monetary value associations

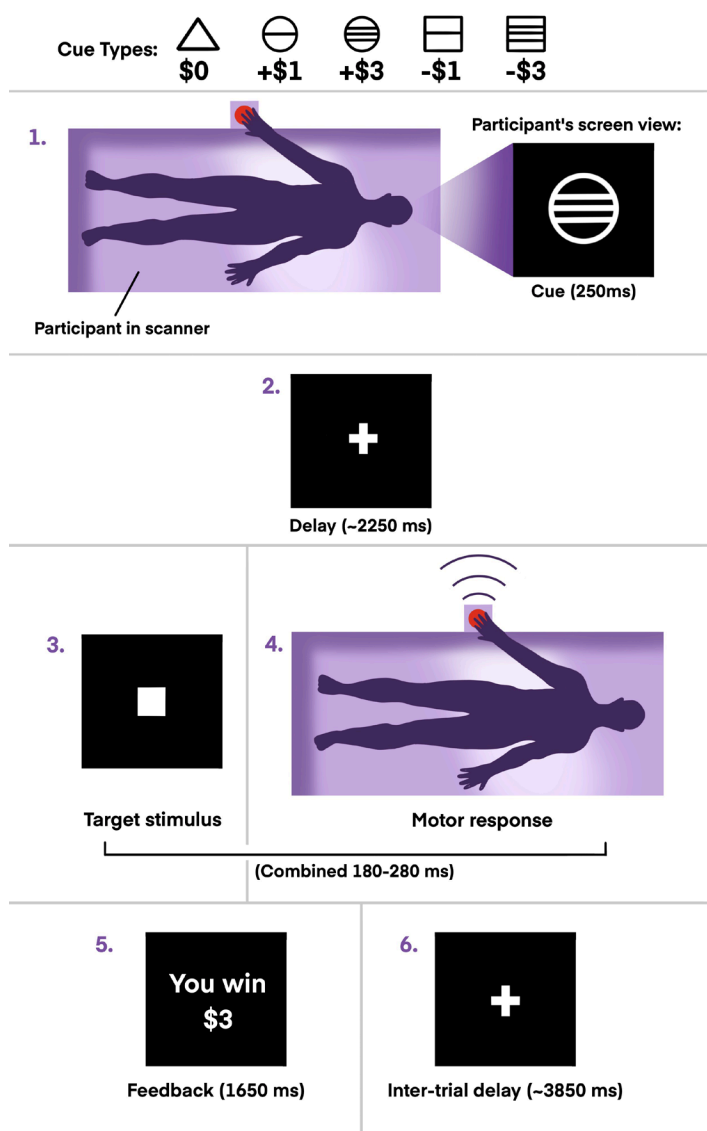


Fig. 1. Diagram of a MID task (courtesy of Natalie Zhang '27)

delay (MID) task, a test utilized to examine the brain activity associated with reward anticipation. A typical MID task might involve five phases: (1) presenting a cue; (2) delaying with a crosshair display for a random period of time; (3) flashing a brief target stimulus signaling the opportunity to win money; (4) executing a simple motor response (for example, pressing a button); and (5) providing feedback on the participant's performance via the shortening or lengthening of the response time window (**Fig. 1**). This methodology effectively allows for the examination of both reward (a monetary prize) anticipation and feedback processing (changes in response time). Scheres et al. (2007) found a VS hypoactivation during these two processes in adolescents with ADHD, compared to matched controls through a blood-oxygen-level-dependent (BOLD) fMRI investigation. This may be due to diminished temporal foresight, a hot executive dysfunction typical of ADHD patients (Weissenberger et al., 2021).

The fact that the symptom domain of hyperactivity-impulsivity—which is highly associated with hot factors—was negatively correlated with VS response, while that of inattention—which is a primarily cold factor—showed a much more minimal pattern lends further support to a significant relationship between hot EFs and ADHD. Indeed, Ströhle et al. (2008) confirmed that reduced activation of the left VS during reward anticipation “was associated with impulsivity and total ADHD symptom severity” in adult males, a phenomenon that Plichta and Scheres (2014) observed in all ADHD patients.

## Reward Delivery

Not only do individuals with ADHD display decreased VS activity when rewards are anticipated, but they also display increased VS activity when rewards are actually delivered. A 2014 fMRI study using an altered MID task maintained that BOLD responses in the VS increased in the controls but not in the ADHD group during reward anticipation; moreover, upon reward delivery, ADHD patients demonstrated significantly greater BOLD responses in the VS and left dorsal striatum (Furukawa et al., 2014; **Fig. 2**). This provides evidence for the role of hot EFs in ADHD because it is consistent with established findings detailing an ADHD-associated impairment in predictive dopamine signaling. With more research, this could be used as proof that

the transfer of dopamine release from established reinforcers (i.e., rewards) themselves to the predictive cues after repeated pairings is deficient in ADHD patients, a phenomenon that has been observed in non-human primates and rats (Ljungberg et al., 1992; Pan et al., 2005).

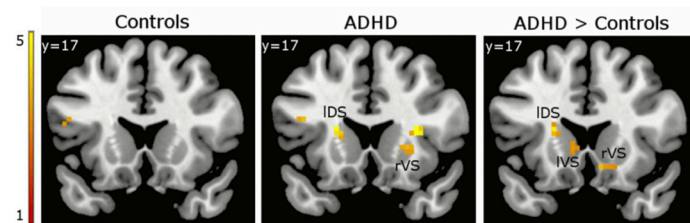


Fig. 2. "Striatal responses to reward delivery in ADHD and Control groups" (Furukawa et al., 2014)

Similarly, increased reward signaling within the superior frontal gyrus and VS was seen in adolescents with ADHD relative to matched controls even when evaluating interference control—a traditionally cold EF—via the Stroop color-word task, which measures the interference between naming the color of a word and reading the word itself and is often used to assess cognitive flexibility and selective attention (Ma et al., 2016). Functional connectivity analyses revealed a hyperconnectivity between the VS and motor regions; the association of connectivity with performance improvement in the controls but not in the ADHD group provides insight into the reduced activation of the VS during feedback processing in the aforementioned MID task studies.

## Delay Discounting

Another small sector of current ADHD research focuses on the deficits to delay discounting in ADHD patients. Odum (2011) defines delay discounting as “the decline in the present value of a reward with delay to its receipt,” and making the conventionally wiser choice between impulsive (smaller but sooner) and self-controlled (larger but later) options is especially challenging for those with the hyperactivity-impulsivity subtype. Although delay discounting tasks measure both cold and hot EFs, they provide explicit evidence for the gravity of the latter in ADHD, as the disorder alters three hot EFs: impaired motivational restraint, decreased tolerance to delays, and poor temporal foresight. Reduced neural activation in ADHD patients lies mostly in

the ventrolateral and dorsolateral prefrontal cortex (PFC), which are involved in both hot and cold EFs such as decision-making, planning, problem-solving, and cognitive control (Ortiz et al., 2015; Rubia et al., 2009). Therefore, there is also a cause to study responses from the hot EF system to delays in rewards among ADHD groups.

## Orbitofrontal Cortex (OFC) Activation

Findings on the altered reward processing networks in ADHD patients are more inconsistent when considering OFC activation. The OFC is involved in decision-making, reward processing, and social behavior, and it integrates sensory information to guide appropriate responses and evaluate the value of stimuli. Several studies found enhanced OFC activation: for example, Ströhl et al. (2008) saw that compared to healthy controls, adult male ADHD patients showed increased activity in the right OFC upon experiencing an experimental “gain” via another MID task. Conversely, other discoveries highlight a distinctly reduced OFC activation during reward delivery. Notably, OFC underactivation was evident in a study of ADHD patients and controls who performed a modified Go/NoGo task, a cognitive test that traditionally evaluates response inhibition, requiring participants to respond to certain stimuli (Go trials) while withholding responses to others (NoGo trials) (Dibbets et al., 2009). Although

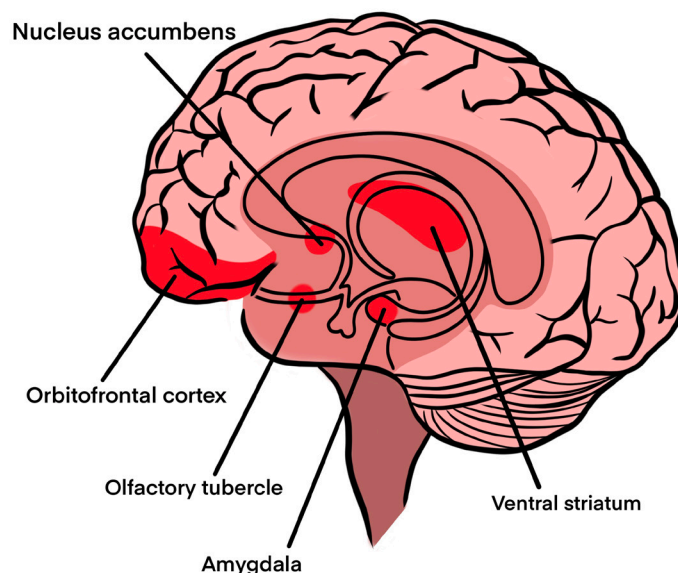


Fig. 3. Neuroanatomical locations of relevant striato-limbic areas (courtesy of Natalie Zhang '27)

researchers did not detect any behavioral signals that would imply feedback-related differences between the two, the ADHD group displayed an undeniable underactivation of the OFC during positive feedback.

In another case, Cubillo et al. (2012) gathered medication-naïve subjects—individuals who had not received any medication for a specific condition or disorder prior to assessment or treatment—with a childhood diagnosis and persistent symptoms of ADHD in adulthood, and Cubillo et al. commented that it is possible to attribute this decreased OFC activation to conduct disorder comorbidity because children with conduct disorder already suffer from an OFC underactivation. However, this hypothesis is still ongoing, and there is no extensive evidence to either support or refute it. These inconsistencies with regard to the OFC also align with its typical irregularity (compared to the VS's relative lack thereof) in reward processing, so the OFC provides no noticeably discernable or valid contribution to this discussion.

## Emotion Regulation

In parallel, emotion regulation, a newer topic of interest in 21st-century ADHD research, is another major factor worth investigating to prove the magnitude of hot EFs in afflicted individuals. Upon concluding a longitudinal study with the discovery that individuals whose ADHD persists into adulthood report higher symptoms of emotional impulsivity, Barkley and Fischer (2010) reasoned that emotional impulsivity “[arises] from deficits in the ‘hot’ executive frontal network.” This may be related to insufficient top-down (guided by higher-level factors such as beliefs, expectations, and prior knowledge, influencing perception, attention, and interpretation of information) control over increased bottom-up (guided by processing where information is analyzed based on incoming sensory input, influencing perception and cognition without higher-level guidance) emotional reactivity. This is in accordance with the significant role of the cold executive system in an ADHD brain. Given this, one may predict that ADHD patients will display reduced striato-limbic activation when encountering negatively valenced (having an emotional or evaluative quality) distractors and enhanced activation for positively valenced stimuli.

However, in 2011, Posner et al. examined neural activity in adolescents with and without ADHD

while they performed a working memory task in which fearful faces would be subliminally presented in the midst of other cues. They found that the ADHD patients had a more activated right amygdala (which plays a central role in processing emotions, particularly fear, and in modulating emotional responses and memory consolidation) and greater connectivity between the amygdala and lateral PFC (lPFC) than the control subjects did. These results suggest that amygdala activation during tasks that mimic monetary loss is also abnormally high (Wilbertz et al., 2017), so ADHD patients are at a distinct functional disadvantage in terms of controlling their exaggerated responses to such stimuli even when reward processing and emotion regulation collide.

## Conclusion

Research presents that hot EFs are indispensable to individuals with ADHD, especially when assessing reward processing and emotion regulation in the striato-limbic region. As Cubillo et al. (2012) mention, a caveat is that “very few fMRI studies have tested for neurofunctional deficits during emotion processing in ADHD,” and even fewer have been conducted in adult ADHD. Findings are also more inconsistent as subjects' ages increase due to limitations that become more pronounced with time, such as “small sample sizes, high rates of comorbidity, long-term medication history, and the need for a retrospective diagnosis of ADHD in childhood.”

Moreover, nearly all of the neuroimaging described was obtained in a region of interest (ROI), so there is a critical lack of whole-brain studies. This is due to several reasons: (1) while whole-brain studies provide a comprehensive view, targeted scans can offer detailed insights into the neural mechanisms underlying ADHD symptoms; (2) whole-brain studies imply several technical and methodological challenges, such as standardizing protocols and gaining access to sophisticated resources; and (3) the heterogeneity of ADHD makes it difficult to pinpoint specific brain regions or networks that are consistently affected across all individuals with ADHD. This calls for an immediate movement toward comprehensive and replicable early intervention studies in younger patients. Furthermore, it may be integral to include those who only experience certain symptoms of ADHD—as opposed to holding a formal diagnosis—in



ADHD studies, as it is important to recognize both the inflexibility of psychological diagnostic criteria and barriers to accessible healthcare. Ultimately, although there are some conflicting judgments in the current literature, the fMRI evidence delineated here—and the surplus that exists outside of it—demonstrates that there is, at the very least, enough of an impetus to warrant more thorough investigations of the dynamic between hot EFs and ADHD.

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