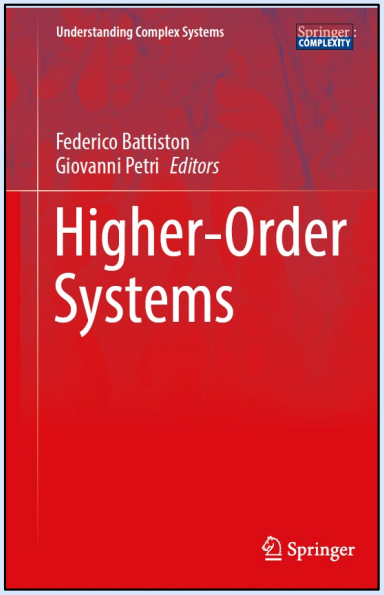
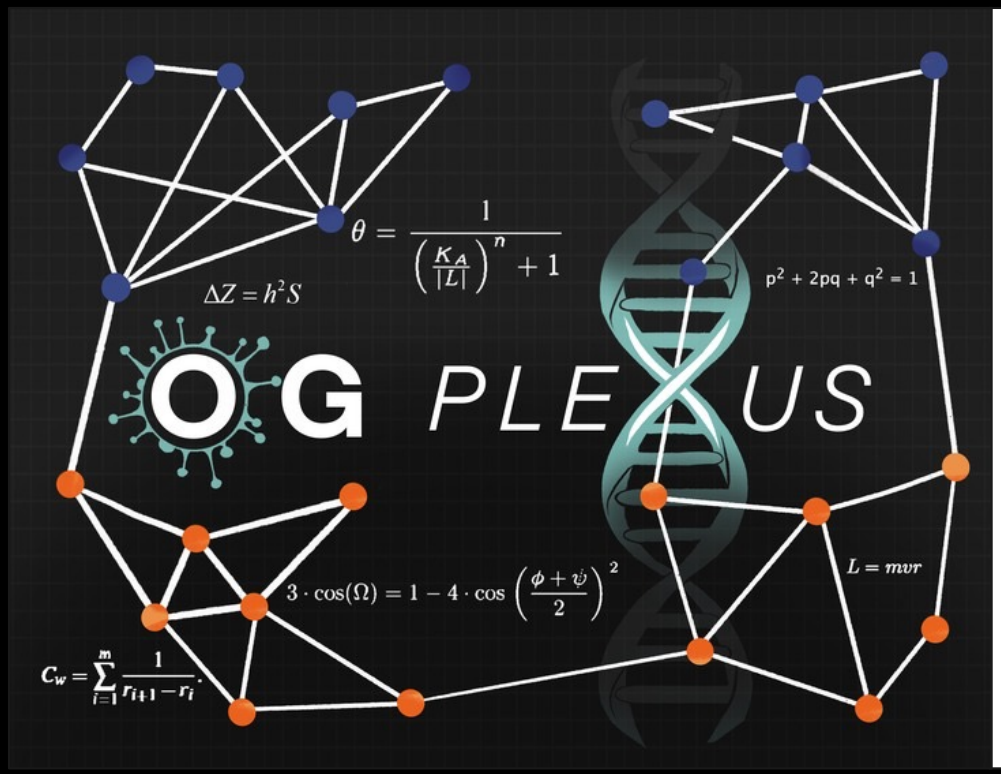
“Biological information…is now surrounded by other parcels of information, that all interact in surprising ways, creating a biosphere that is both more corporeal and capricious than scientists and naturalists have appreciated.”

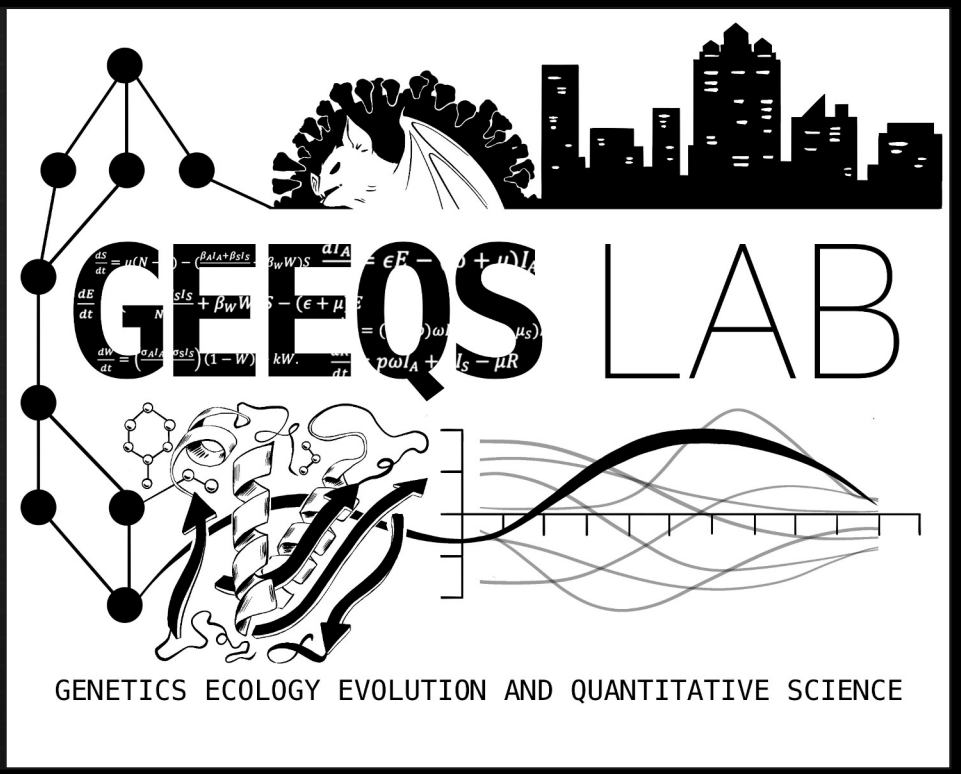
Samuel V. Scarpino



Chapter 18
Higher-Order Interactions in Biology: The Curious Case of Epistasis

C. Brandon Ogbunugafor and Samuel V. Scarpino





Medium.com/ogplexus
@big_data_kane

Context Crafts Complex (Biological) Systems:

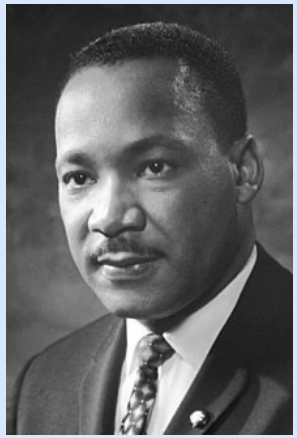
Parcels, Pandemics, Perspectives, and People

A talk by:

C. Brandon Ogbunu(gafor)
Assistant Professor of Ecology and Evolutionary Biology, Yale University
External Professor, The Santa Fe Institute
MLK Visiting Assistant Professor, Department of Chemistry, MIT

Massachusetts
Institute of
Technology

Martin Luther King Jr Visiting Scholars Program @ MIT

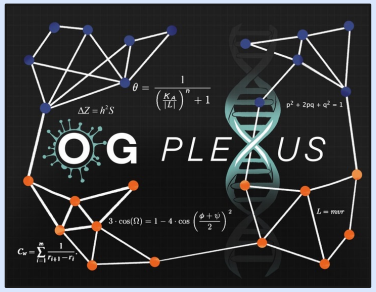


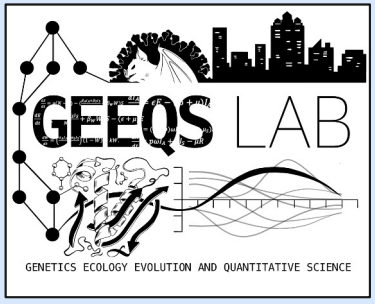
Massachusetts Institute of Technology

- Department of Chemistry
  - **Prof. Matthew Shoulders**
  - Shoulders Lab
  - Prof. Troy Van Voorhis
  - Administrative staff
- Nominators & supporters
  - Prof. Ed Boyden (BE/McGovern)
  - Dir. Eboney Hearn (OEOP)
  - Prof. Stefan Helmreich (Anthropology)
  - Prof. Tami Lieberman (CEE/IMES)
  - Prof. Fox Harrell (CSAIL)
- Administrators and other fellows
  - Beatriz Cantada
  - John Dozier
  - Lupe Fiasco

Gratitude

- Ogbunu Lab, Yale University
- GEEQs Lab @ Yale
  - Dr. Andrea Ayala
  - Dr. Carolina Diaz
  - Dr. Sudam Surasinghe
  - Dr. Sarah Rene Phillips
  - Ketty Munyenyembe
  - Swathi Manivannan
  - T.J. Johnson





Gratitude

Anarina Murillo

Rafael Guerrero

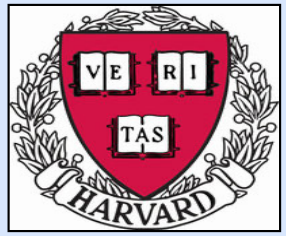
- Salvador Almagro-Moreno
- Stephon Alexander
- C. Malik Boykin
- Maggie Eppstein
- Christopher Rose
- Rafael Guerrero
- Randall Harp
- Daniel Hartl
- Rori Rohlfs
- Sohini Ramchandran
- Lorin Crawford
- Ben Kerr
- Susan Remold
- Carl Bergstrom
- Vaughn Cooper
- Doc Edge
- Fatimah Jackson
- Christopher Marx
- S. James Gates
- Pleuni Pennings
- Joao Rodrigues
- Samuel Scarpino
- Eugene Shakhnovich
- Paul Turner
- Daniel Weinreich
- Senay Yitbarek
- Wendy Turner
- Martha Munoz
- Luis Zaman
- Carl Bergstrom
- Alvaro Sanchez
- Nina Jablonski
- Henry Louis Gates
- Joseph Graves
- Ibrahim Diakite
- Tina Lasisi
- Jenny Pham
- Lourdes Gomez
- Ketty Munyenyembe
- Victor Meszaros
- Miles Miller-Dickson
- Andrea Ayala
- Anarina Murillo
- Taiwo Togun
- Mohammed Toure
- Tandin Dorjii
- Francis Awuah-Baffour Jr.
- Joseph Graves
- Fatimah Jackson
- Carlos Castillo-Chavez
- Jeremy Draghi
- Joshua Weitz

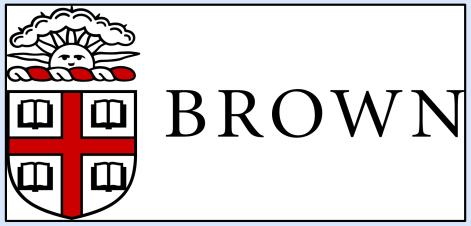
Ibrahim Diakite

Maggie Eppstein

Financial and administrative support

- Brown University
- National Science Foundation
- National Institutes of Health
- Yale University
- University of Vermont
- Harvard University
- UNCF/Merck
- Ford Foundation
- The Broad Institute
- Robert Wood Johnson Foundation
- Kavli Institute for Theoretical Physics, UCSB
- The Foundations Institute, UCSB
- More!



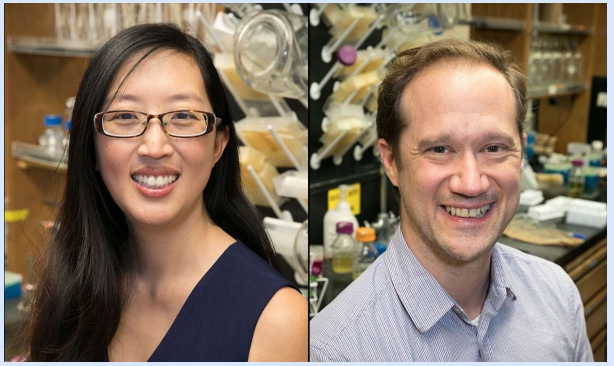


Gratitude

- **Vermont Complex Systems Center**
  - Maggie Eppstein
  - Peter Dodds
  - Chris Danforth
  - Randall Harp
  - Laurent Hebert-Dusfresne

Gratitude

- **Santa Fe Institute**
  - Carrie Cowan
  - Carla Shedivy
  - Sachi Pena
  - Samuel Scarpino
  - Michael Garfield
  - Chris Kempes
  - Cristopher Moore
  - Michael Lachmann
  - Travis Holmes
  - Renee Tursi
  - David Krakauer



Context Crafts Complex (Biological) Systems:

Parcels, Pandemics, Perspectives, and People

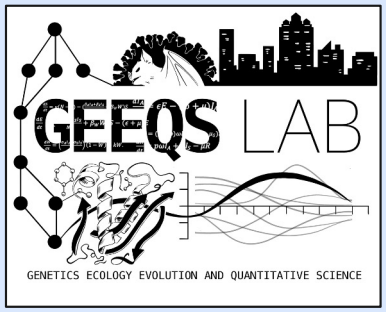
A talk by:

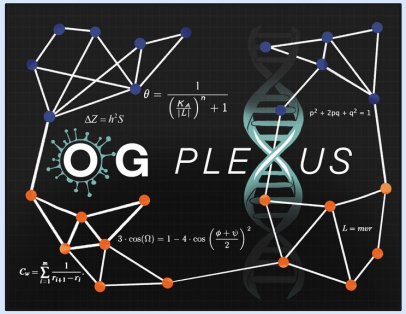
C. Brandon Ogbunu(gafor)
Assistant Professor of Ecology and Evolutionary Biology, Yale University
External Professor, The Santa Fe Institute
MLK Visiting Assistant Professor, Department of Chemistry, MIT

Massachusetts
Institute of
Technology

Agenda/Argument

- Today I will demonstrate a perspective on the study of complex systems that emphasizes the role of context and environment.
- Example: the intersection between epidemiology and the study of the criminal legal system.
- More broadly, I argue that engagement with culture and society can unlock new directions, and applications of existing methods.

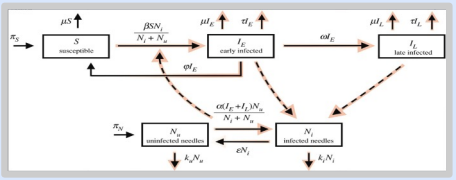




Who am I, exactly?

About me: “By Day…”

- **“(Professor) C. Brandon Ogbunu”**
- Computational Biology, Systems Biology, Evolutionary biology, Complex systems….
- We use **diseases** as systems to ask questions about evolution, information, ecology, behavior and culture

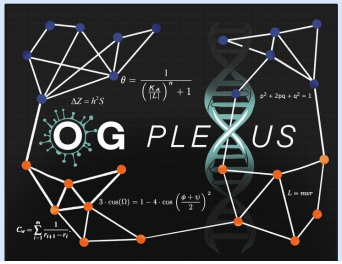


```
# probability of establishment|colonization attempt
Pcol <- array(dim=c(A, N))
for (i in 1:A){
  for (j in 1:N){
    Pcol[i, j] <- Z[j] * exp(-((E[i] - mu.i[j]) ^ 2) / (2*sigma[j] ^ 2))
  }
}
```

VOL. 181, NO. 5 THE AMERICAN NATURALIST MAY 2013

Evolution of Increased Survival in RNA Viruses Specialized on Cancer-Derived Cells

C. Brandon Ogbunugafor,[1,2,*] Barry W. Alto,[1,3] Thomas M. Overton,[1,4] Ambika Bhushan,[1,5] Nadya M. Morales,[1] and Paul E. Turner[1]



Yale

Massachusetts Institute of Technology

About me: “By Night…”

- **“Big Data Kane”**
- A computational scientist who studies the intersection between science, data & culture
- Technical papers, outreach, activism, writing & media
  - Contributor to *The Atlantic*, *Andscape*, *WIRED*, *Undark,* others
  - Featured on the Emmy-Award Winning *Finding Your Roots: The Seedlings*
  - Contributing editor at *Radio Lab*

RADIOLAB

WIRED

NBA

One year after the bubble, the NBA’s COVID-19 response is helping the world understand the pandemic

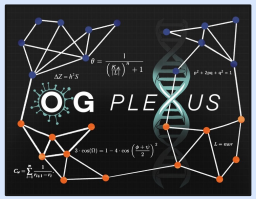
Scientists are using the league’s data to understand the delta variant and other topics

The Great Fusion of 2023 (Day + Night)

- **Interactions** shape biological systems (mostly in the setting of disease)
- These interactions shape **how molecular evolution happens**
- These interactions shape **how epidemics manifest**
- These interactions shape **science, and the world** in which it is all embedded

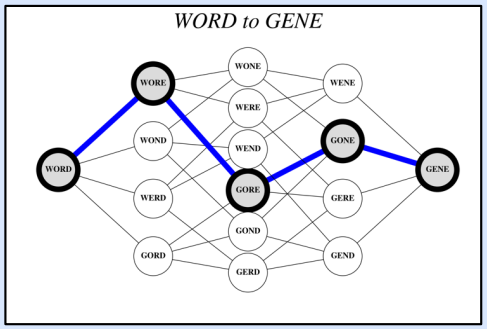
What is complexity?

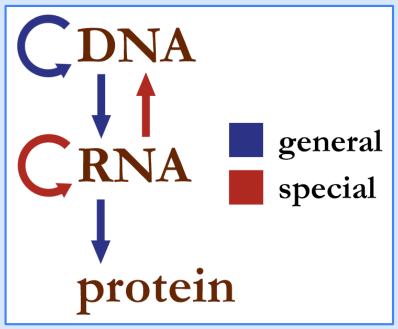
- Fun conversation with Michael Lachman
- “You seem more interested in the science of interactions within fields than you do the application across them.”

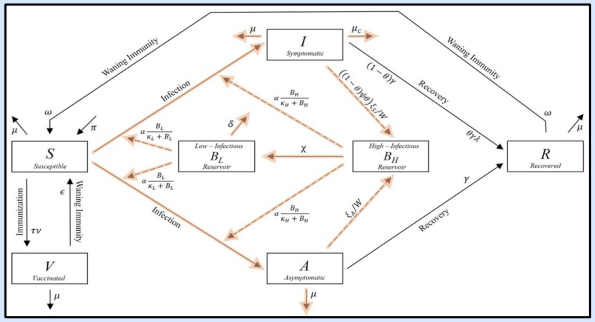


The Ogbunu **complex systems** creed

- What are the **actors** that drive complex biological systems?
- What is the nature of the **interactions** between them?
- What **contexts** modulate these interactions?







What is context?

What is context?

This has been the best play I've seen all year!

https://www.thoughtco.com/quoting-out-of-context-fallacy-250332

What is context?

This has been the best play I've seen all year! Of course, it is the only play I've seen all year.

https://www.thoughtco.com/quoting-out-of-context-fallacy-250332

What is context?

This was a fantastic movie

https://www.thoughtco.com/quoting-out-of-context-fallacy-250332

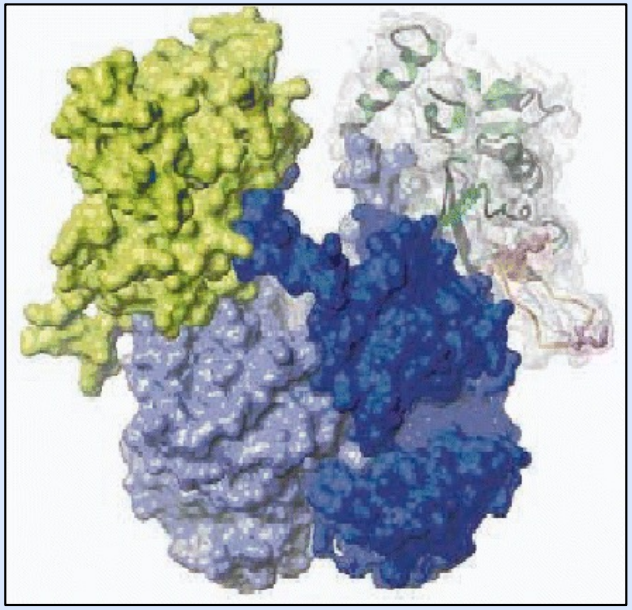
What is context?

This was a fantastic movie, as long as you aren't looking for plot or character development.

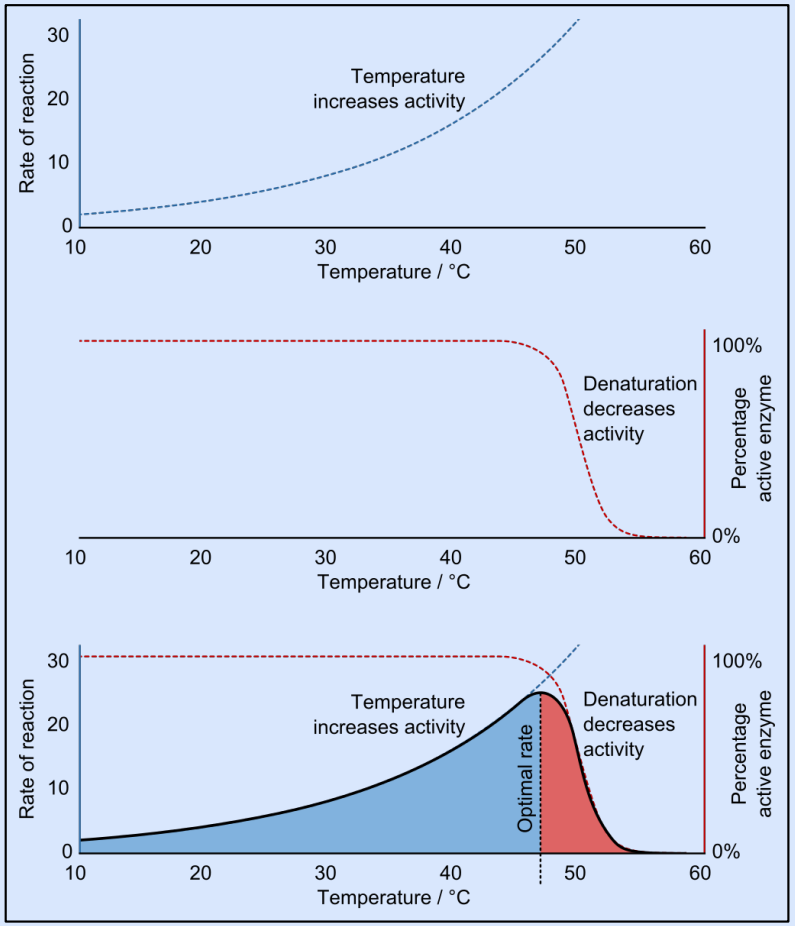
https://www.thoughtco.com/quoting-out-of-context-fallacy-250332

What is context?

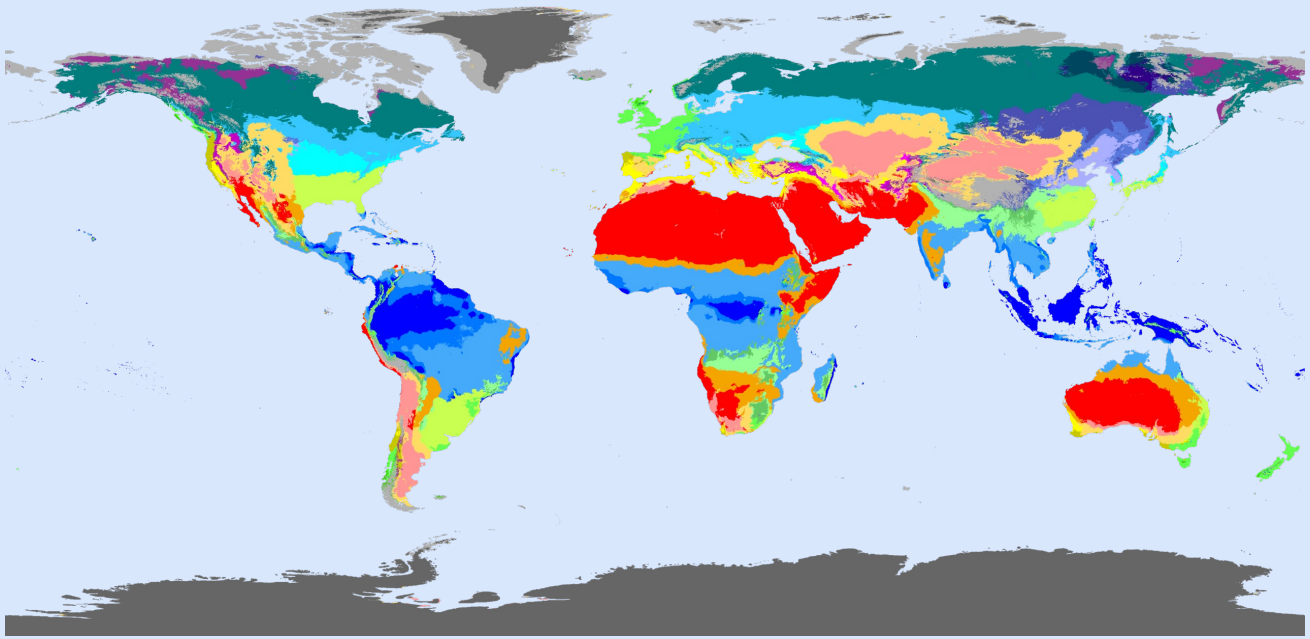
What is context?



Dihydrofolate reductase



What is context?

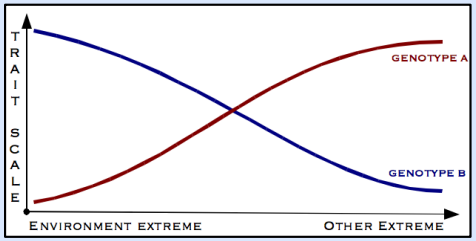


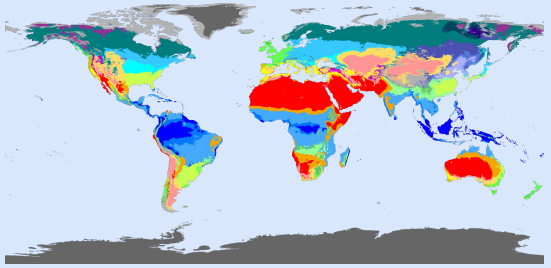
What is context?

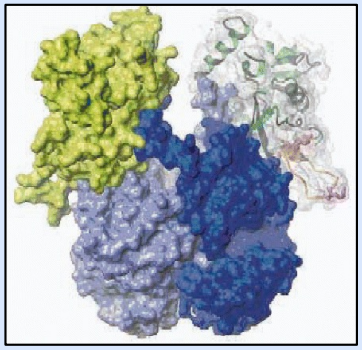
What is context?

What is context?

- Quantitative genetics
- Physiology
- Climactic, ecological
- Local, lived, daily, corporeal
- Historical, structural, and psychological

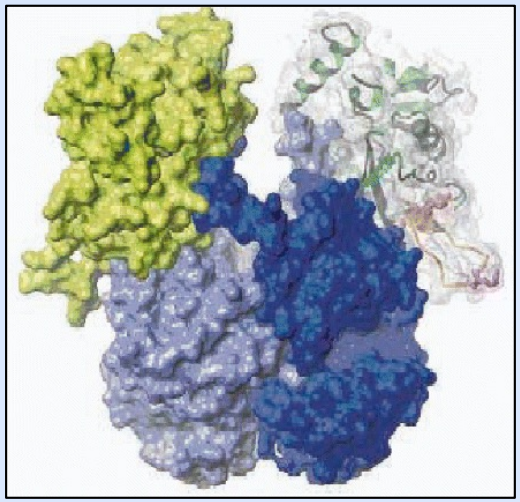




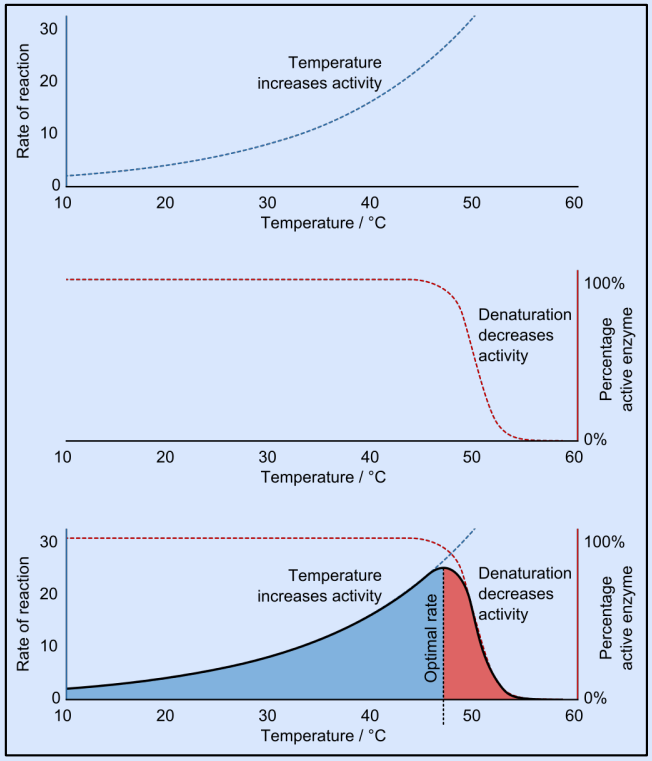


Pillar I: Disease evolution program

We'll use **protein evolution** as a model for questions about how to think about the importance of gene-by-**environment** interactions

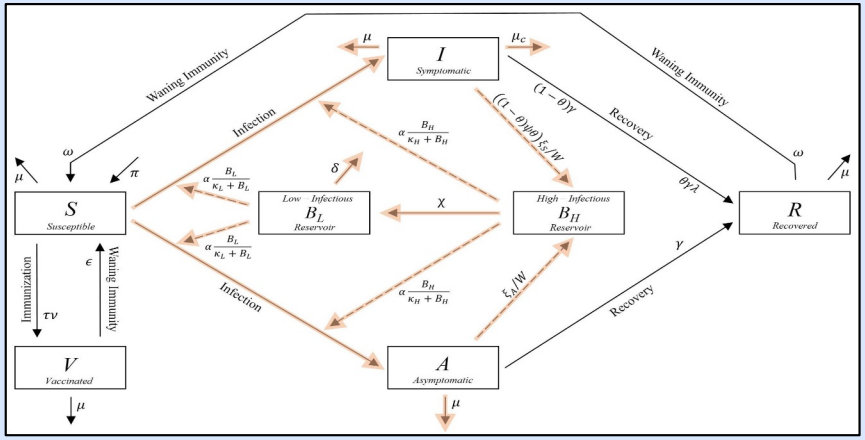


Dihydrofolate reductase



Pillar II: Ecology of disease program

We use **epidemics** as a model for how to think about the interaction between **environments** and disease



https://en.wikipedia.org/wiki/Hemoglobin#/media/File:1GZX_Haemoglobin.png

Pillar III: Science, data, and culture program

NBA

One year after the bubble, the NBA's COVID-19 response is helping the world understand the pandemic

Scientists are using the league's data to understand the delta variant and other topics

Brandon Ogbunu is a radical collaborator

MLK Visiting Professor tries to "maximize connection time" while studying protein evolution.

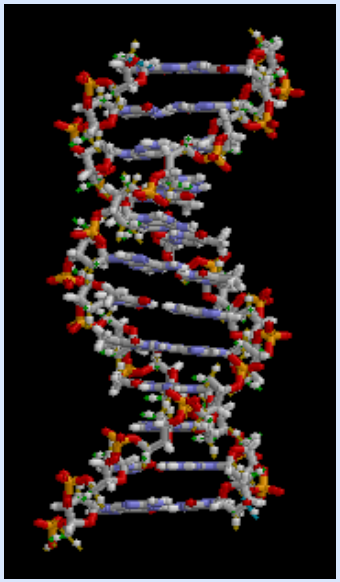
Phie Jacobs | School of Science

January 9, 2023

Zeitgeist (2018 – 2023)

Scientific ambitions and controversies

Genomic prediction



Genetic engineering

Scientific ambitions and controversies

SARAH ZHANG SCIENCE 02.01.16 7:00 AM

DNA GOT A KID KICKED OUT OF SCHOOL—AND IT'LL HAPPEN AGAIN

Why White Supremacists Are Chugging Milk (and Why Geneticists Are Alarmed)

Are We Being Misled About Precision Medicine?

Doctors and hospitals love to talk about the cancer patients they've saved, and reporters love to write about them. But deaths still vastly outnumber the rare successes.

By Liz Szabo
Ms. Szabo is a health reporter for Kaiser Health News.

Sept. 11, 2018

The Genetics of Type 2 Diabetes Is a Mess

A recent study shows why genetic advances in medicine are so challenging.

Scientific ambitions and controversies

- Race science extremism is on the rise
- Related to a global rise in fascism
- Already led to several instances of mass violence

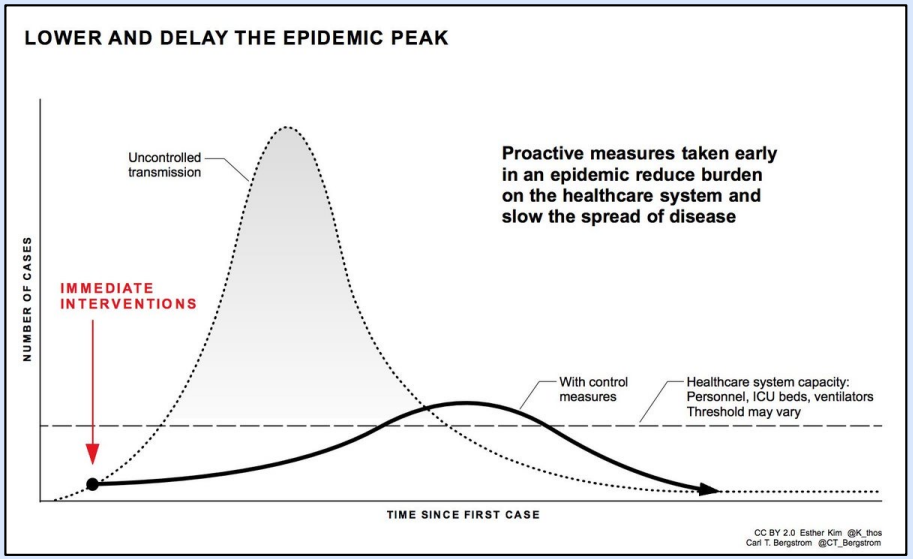
C. BRANDON OGBUNU IDEAS MAY 27, 2022 8:00 AM

Quashing Racist Pseudoscience Is Science's Responsibility

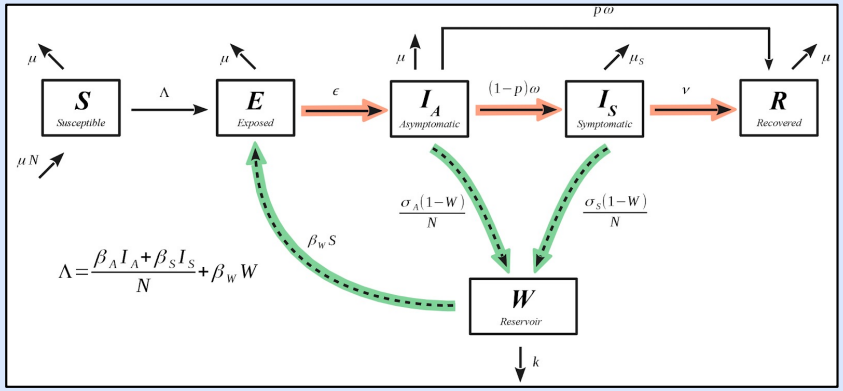
The recent act of racist terrorism in Buffalo has raised the stakes on how science is communicated and sold.

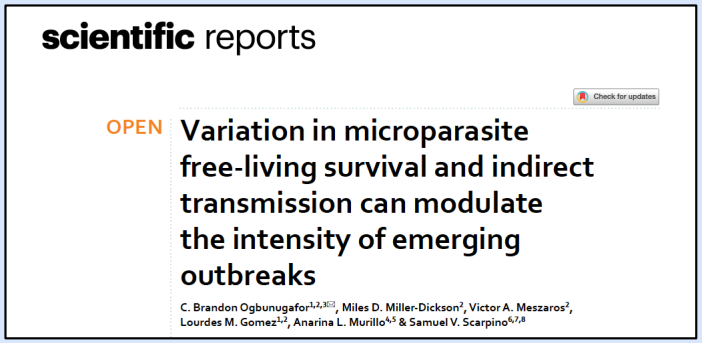
Why White Supremacists Are Chugging Milk (and Why Geneticists Are Alarmed)

SARS-CoV-2

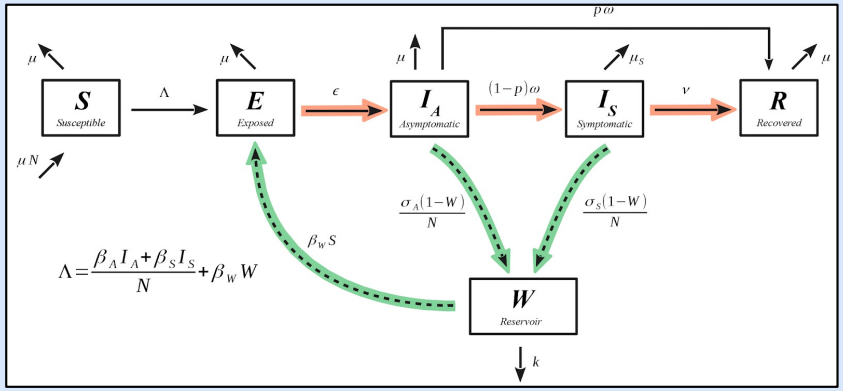

LOWER AND DELAY THE EPIDEMIC PEAK
Uncontrolled transmission
Proactive measures taken early in an epidemic reduce burden on the healthcare system and slow the spread of disease
IMMEDIATE INTERVENTIONS
NUMBER OF CASES
With control measures
Healthcare system capacity: Personnel, ICU beds, ventilators Threshold may vary
TIME SINCE FIRST CASE
CC BY 2.0 Esther Kim @K_thos
Carl T. Bergstrom @CT_Bergstrom

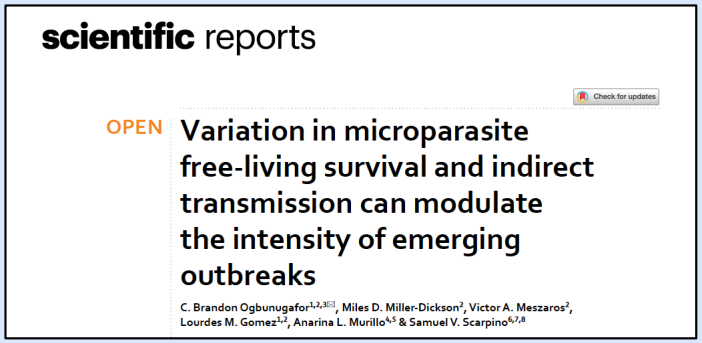
Basic Science





Basic Science

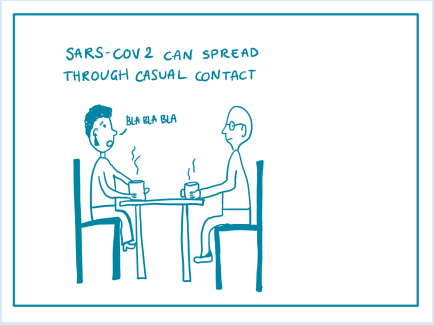




Public engagement

Senay Yitbarek
(UNC Chapel Hill)

Pleuni Pennings
(SFSU)



https://vimeo.com/400477097

COVID-19 public engagement

IDEAS

Go Ahead, Joke About the Pandemic

The public-health power of humor on Black Twitter

By C. Brandon Ogbunu

C. BRANDON OGBUNU IDEAS 08.02.2020 09:00 AM

The Flagrant Hypocrisy of Bungled College Reopenings

Higher education has ignored its main mission: to teach critical thinking. It's time to take the adults back to school.

C. BRANDON OGBUNU IDEAS 04.05.2020 12:00 PM

Don't Be Fooled by Covid-19 Carpetbaggers

Coronavirus credentialism is rampant and dangerous. Knowing who's legit and who's an opportunist can save lives.

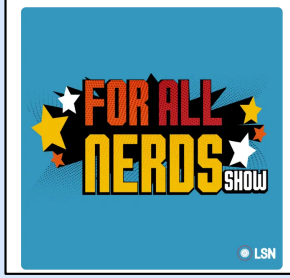
C. BRANDON OGBUNU IDEAS 03.18.2020 09:00 AM

How Social Distancing Became Social Justice

Like Me Too and Black Lives Matter, the Flatten the Curve movement has fomented a profound reckoning with privilege and inequality.

Black Doctors Work Overtime to Combat Clubhouse Covid Myths

- Conspiracies flourish on app including about vaccines and 5G
- 'Hey, I was skeptical too, but here's where I am now'



A Dat Rona Special Report Featuring Professor Brandon Ogbunu

For All Nerds Show

Society & Culture

Listen on Apple Podcasts ↗

It's a very special episode this week, as Tatiana and Benhameen welcome back Professor Brandon Ogbunu to speak about everything that has happened since we last spoke with our esteemed Coronavirus expert.
We hope you are all enjoying your Thanksgiving, and staying safe while you are doing so! Thank you for listening and supporting the ForAllNerds throughout this tumultuous time.

NBA

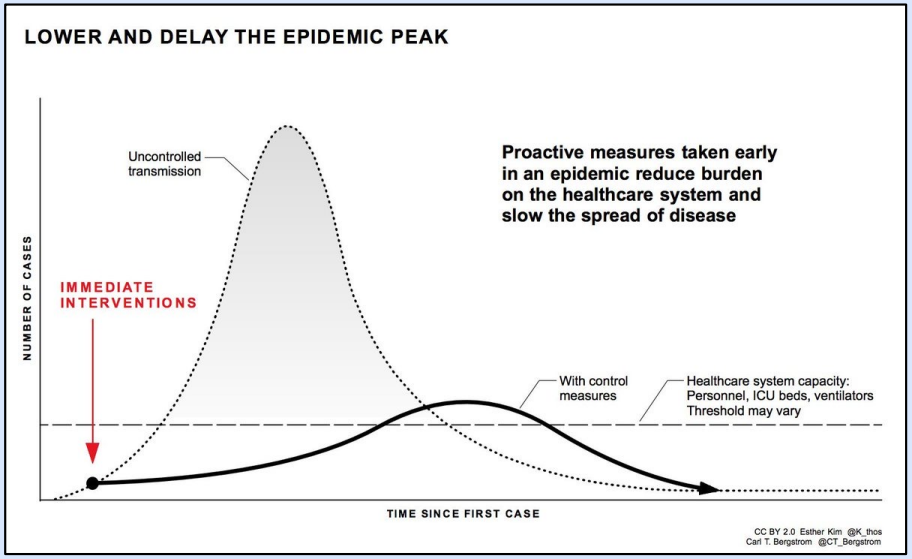
The NBA bubble is a grand experiment in epidemiology

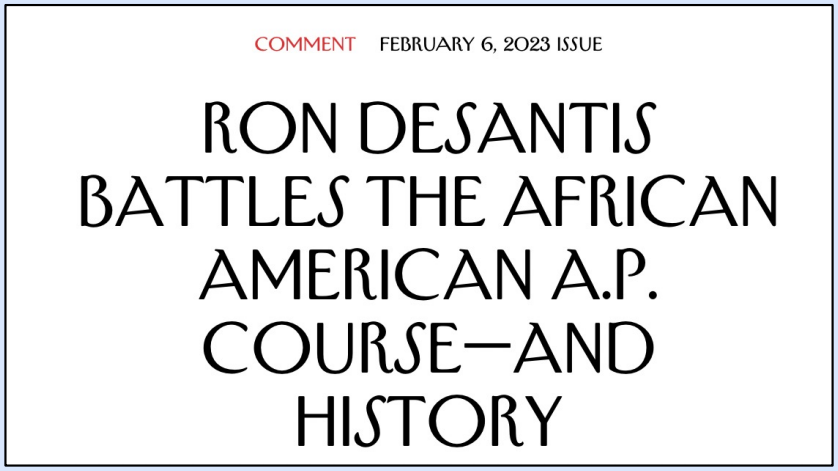
We'll see how technology, policy and human behavior influence an epidemic – and what we can do to stop it

Summary – Science is in trouble

- Trust in science is low
- Misinformation runs rampant
- Scientific and ethical issues abound
- The rise of authoritarianism

- **Solution?**
- **Think about the intersection between science and culture**





What is the role of a scientist in society?

THE STORY COLLIDER
STORIES ABOUT SCIENCE

RADIOLAB

How do we address this?

- **New conceptual instruments**
  - New model systems
  - New thought experiments
  - Pedagogical instruments
  - Art, fiction, cultural relics

GENETICS, 2022, iyac142
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Perspectives

OXFORD GENETICS

Gattaca as a lens on contemporary genetics: marking 25 years into the film's "not-too-distant" future

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†These authors contributed equally to this work.

- **Strategies**
  - Communications experts
  - Connectors and generalists

Lorin Crawford
(Microsoft Research)

Lupe Fiasco
(MIT)

Culture can serve as a great model for biological questions.

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[†]These authors contributed equally to this work.

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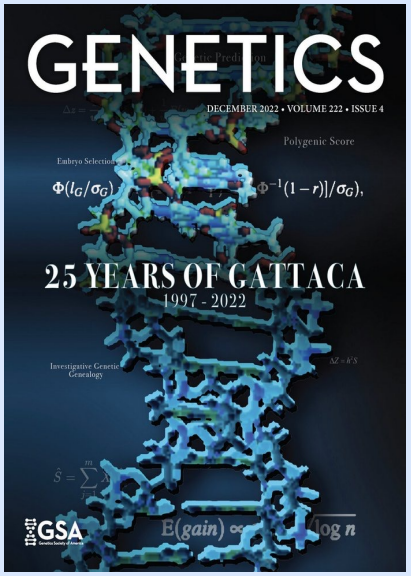
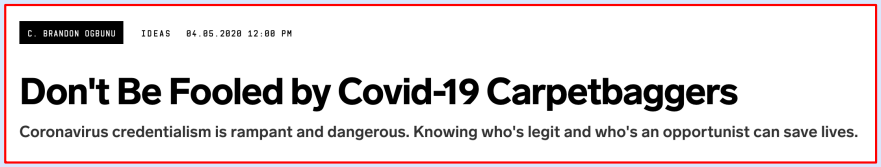
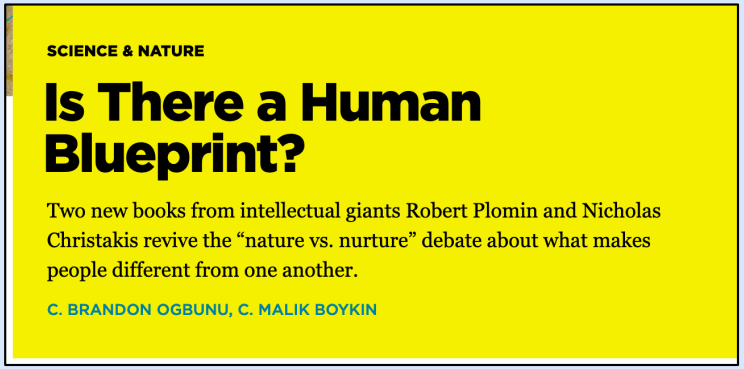


What is the role of a scientist in society?



The Boston Review



Scientific American

Culture can serve as a great model for biological questions.

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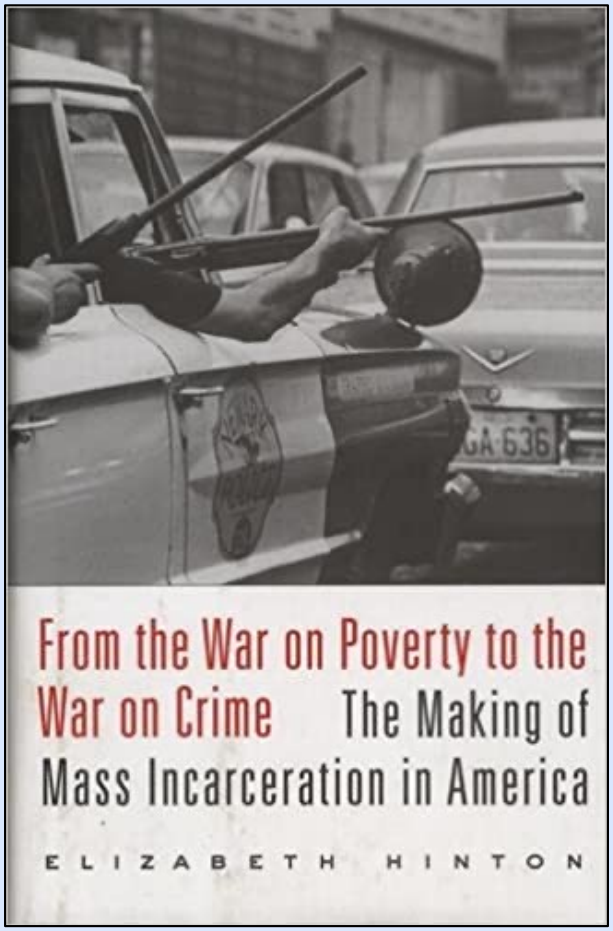
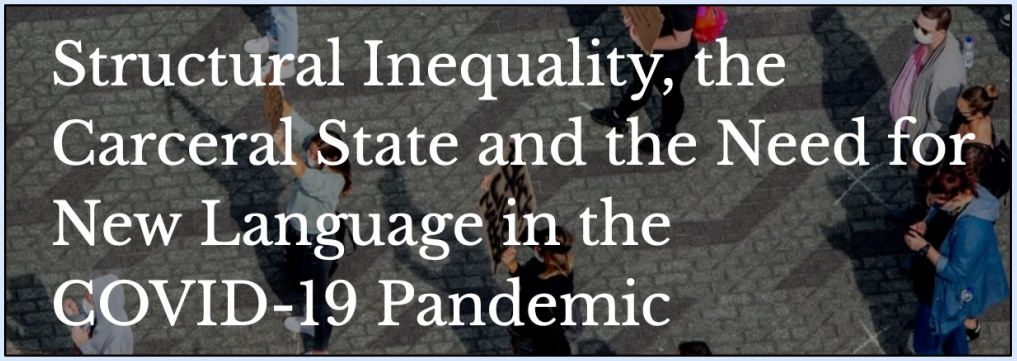
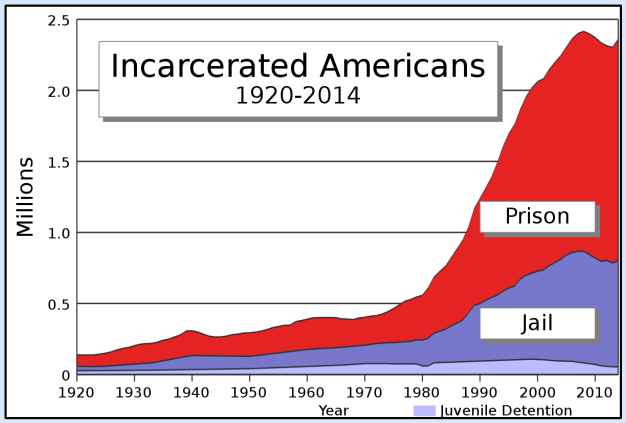
Cultural and social systems can benefit from methods and perspectives from quantitative systems

Cultural drivers of disease: Mass Incarceration





Ogbunugafor C.B., Structural Inequality, the Carceral State and the Need for New Language in the COVID-19 Pandemic, *Synapsis: a Health Humanities Journal*, 2021



We know that social forces can create conditions for infectious disease.

But how do infectious diseases influence social phenomena?

Cultural drivers of disease: Mass Incarceration




Klein B, Ogbunugafor CB, Schafer BJ, Bhadricha Z, Kori P, Sheldon J, Kaza N, Sharma A, Wang EA, Eliassi-Rad T, Scarpino SV. COVID-19 amplified racial disparities in the US criminal legal system. Nature. 2023 Apr 19:1-7.

Article

COVID-19 amplified racial disparities in the US criminal legal system

The COVID-19 pandemic amplified long-standing racial biases in the U.S. criminal justice system

NEWS AND VIEWS | 19 April 2023

COVID pandemic increased racial disparities in US prison populations

A public data set on the size and racial composition of US prison populations has been generated. Its analysis indicates how biases in sentencing lengths shape prisons' racial make-up in the United States.

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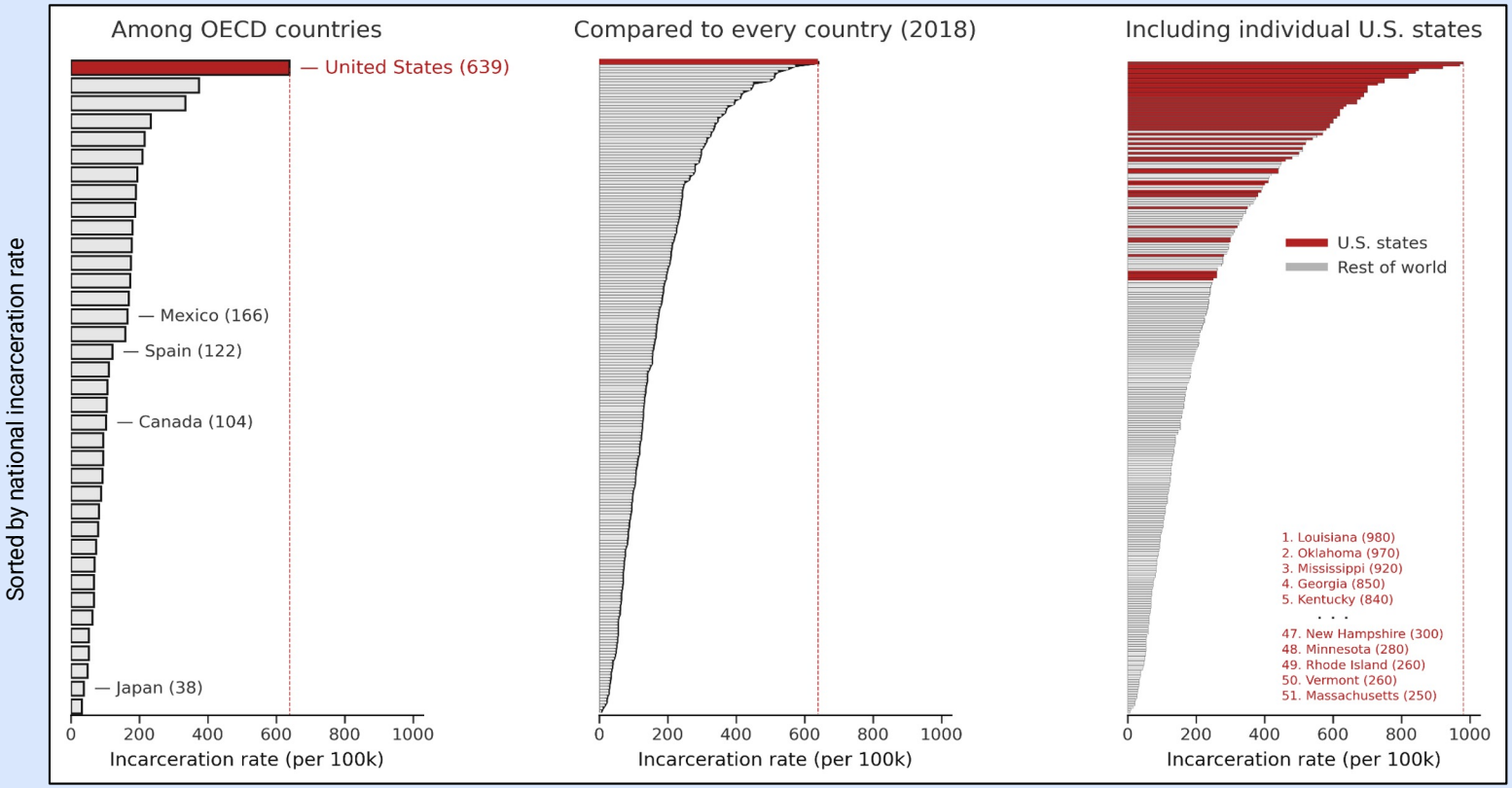
Sam Scarpino 
Elizabeth Hinton 

Pandemic mass incarceration:

The COVID-19 pandemic amplified long-standing racial biases in the U.S. criminal justice system

A complex (biological) systems problem!

The scale of mass incarceration in the US



20% of the world's **incarcerated** population

5% of the world's **total** population

Data from World Prison Brief

Mass incarceration and race: Pervasive inequity

- Black people make up 13% of the total U.S. population.
  - But comprise over 38% of the total incarcerated population.
- Incarceration rate of Black vs. white people in the U.S.
  - 2,306 vs. 450 per 100k.
- Incarcerated Black people serve 19.1% longer sentences on average.
  - After controlling for past offences and severity, this increases to 20.4%.

Sentencing data from the U.S. Sentencing Commission's "Booker Report" (2017)
https://www.ussc.gov/research/research-reports/demographic-differences-sentencing

Demographic numbers from Prison Policy Institute:
https://www.prisonpolicy.org/research/race_and_ethnicity/

The COVID-19 pandemic amplified long-standing racial biases in the U.S. criminal justice system

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The data science pipeline

Brennan Klein

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A public data set on the size and racial composition of US prison populations has been generated. Its analysis indicates how biases in sentencing lengths shape prisons' racial make-up in the United States.

- "We manually assembled and validated a dataset covering all 50 U.S. states, the District of Columbia to both quantify the widening racial disparity observed during the first year of the COVID-19 pandemic and uncover its plausible causes."
- "Comprising over **7,000 records across more than 20 years**—is an unprecedented view into the dynamics of prison populations before, during, and after the pandemic."
- Use of FOIA requests, calling of justice departments, combing through literature

This is a **complex** story, based on 2 key observations

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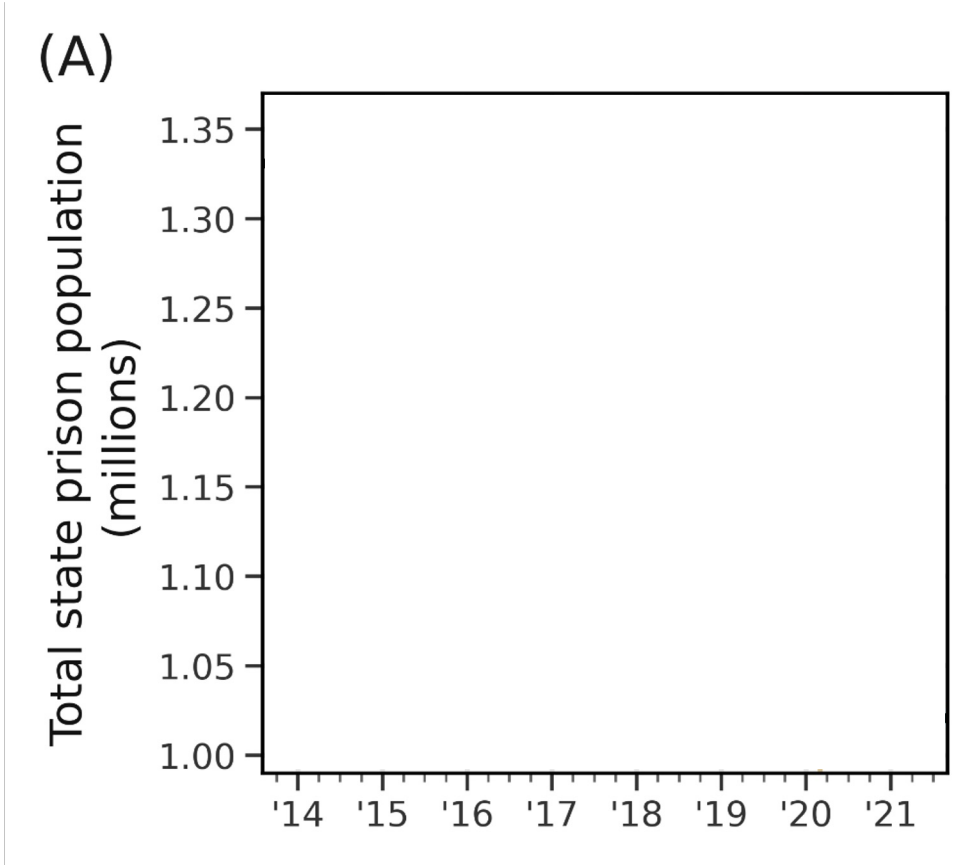

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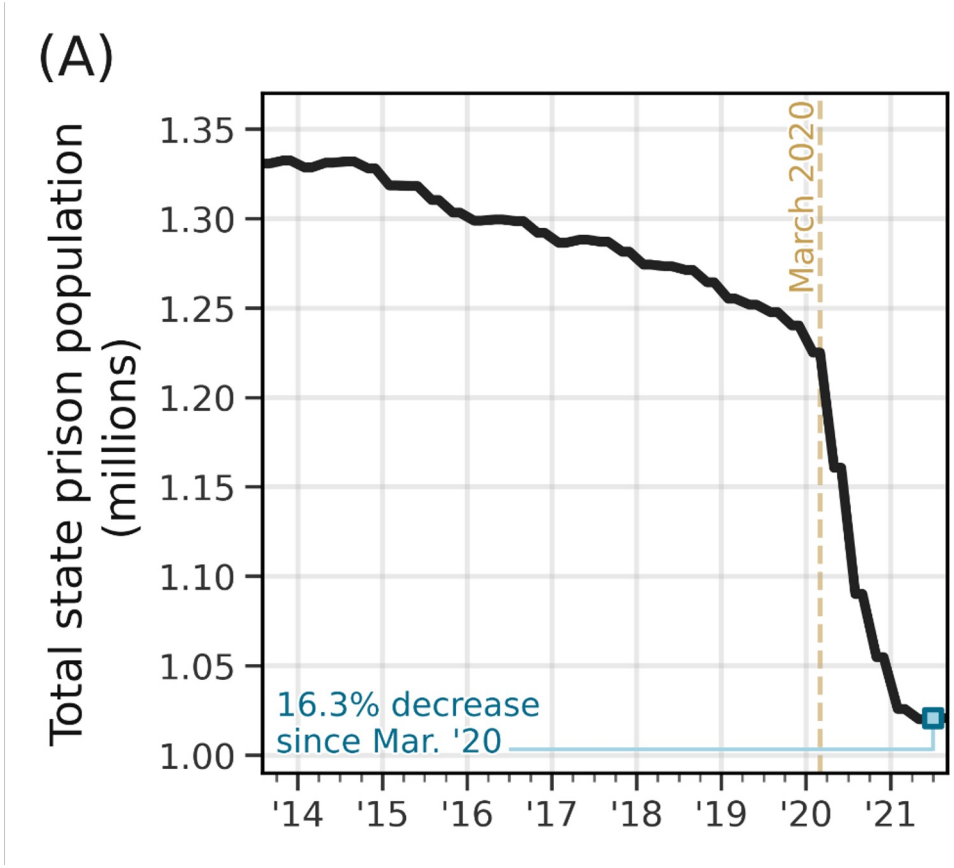

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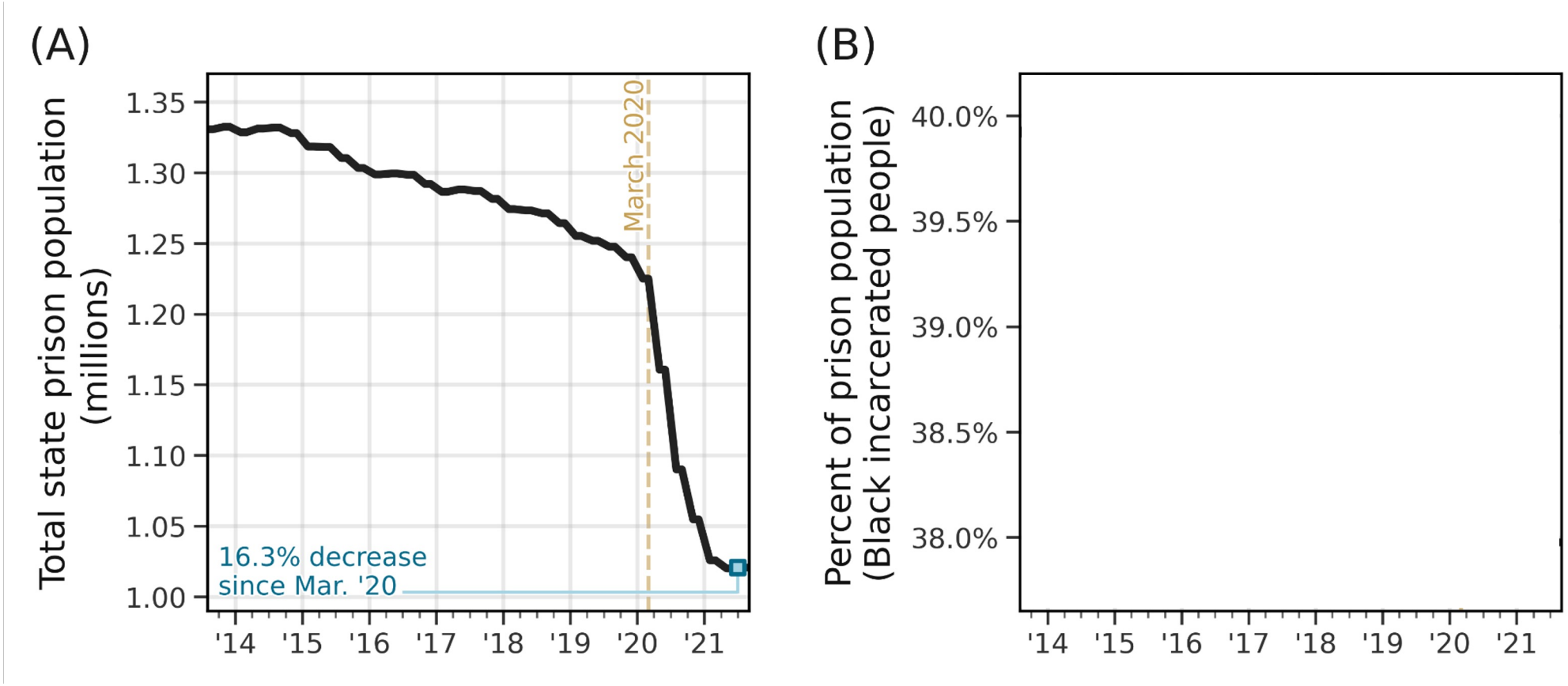

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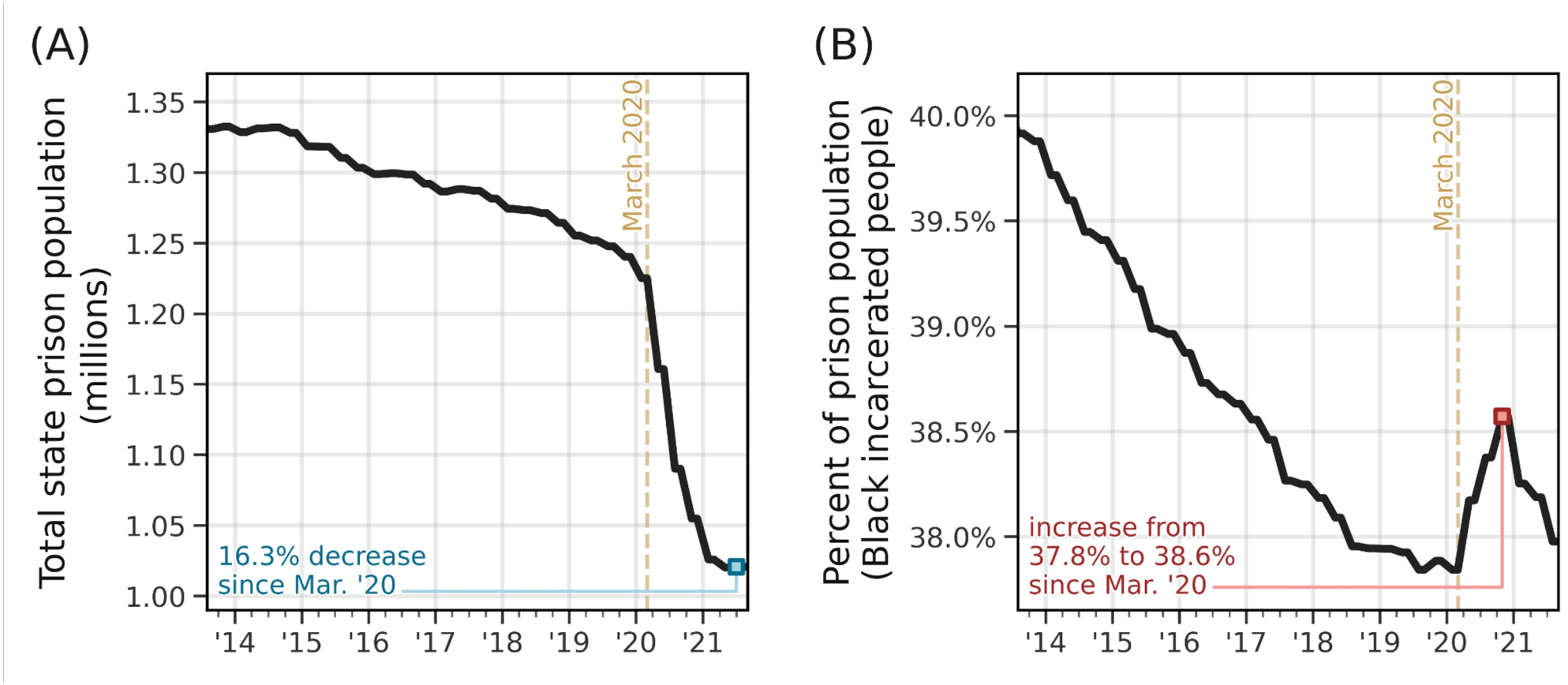

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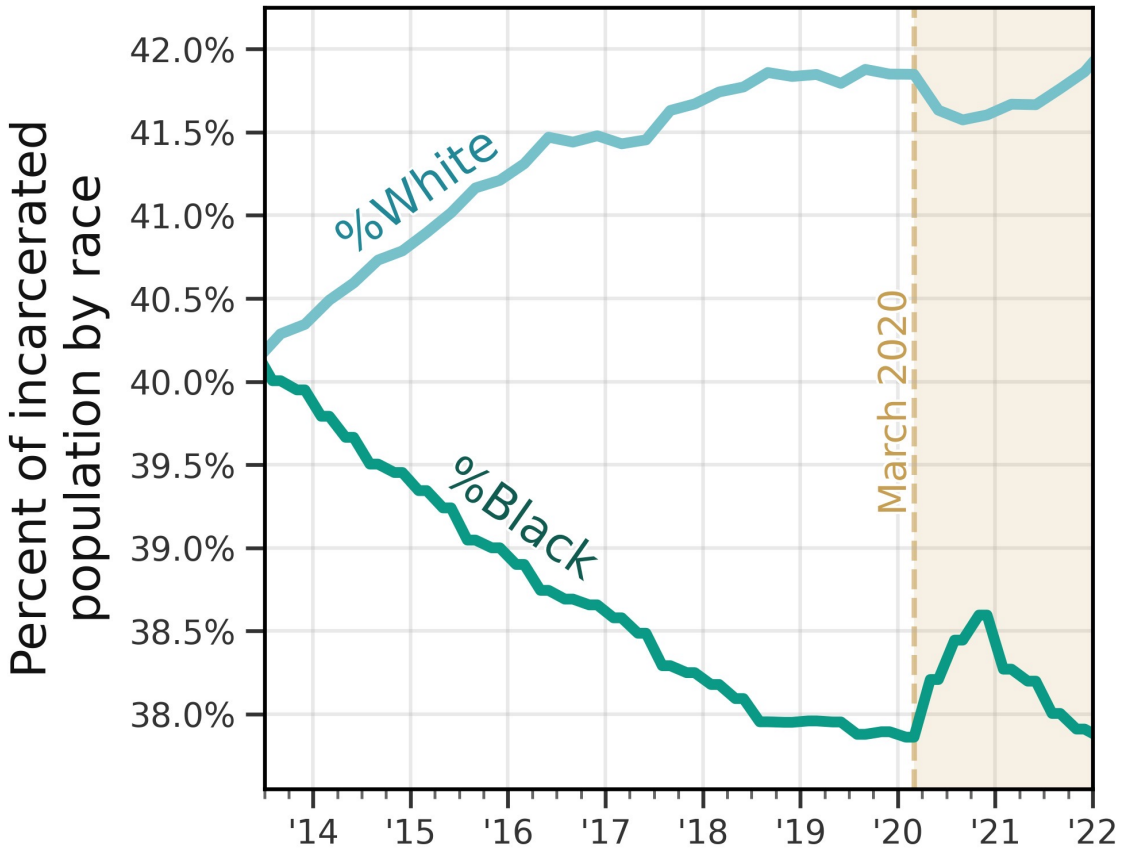
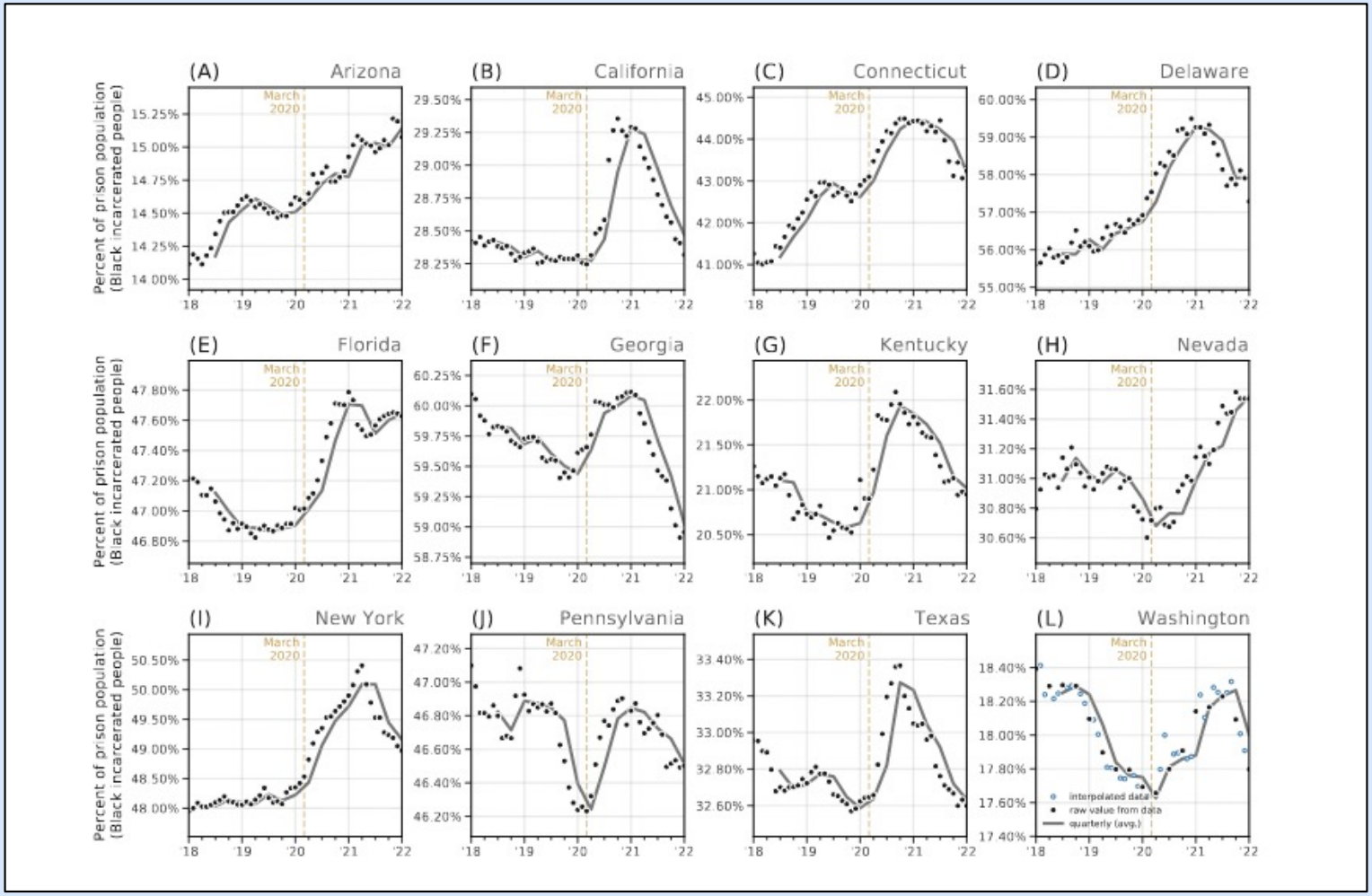
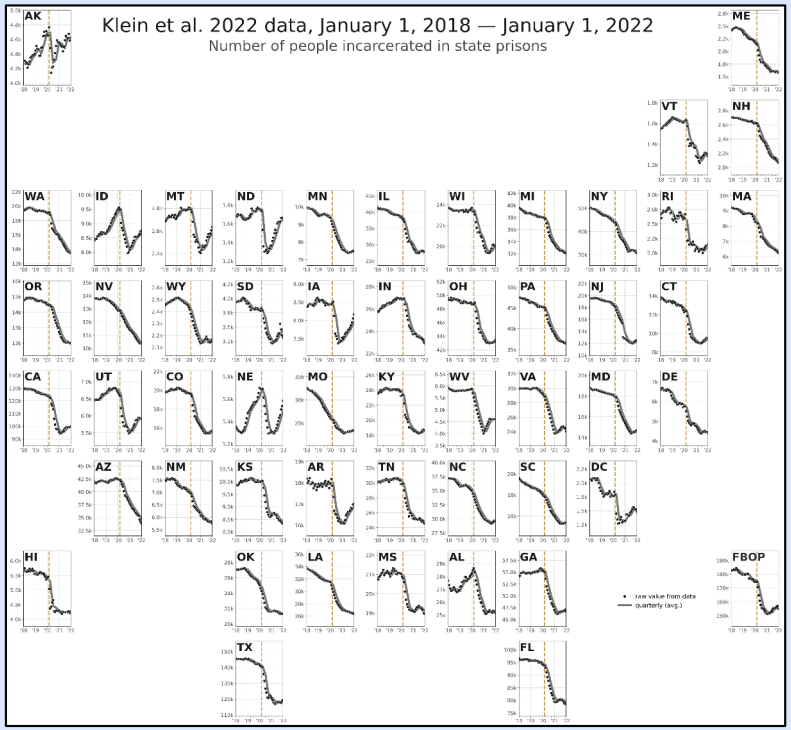
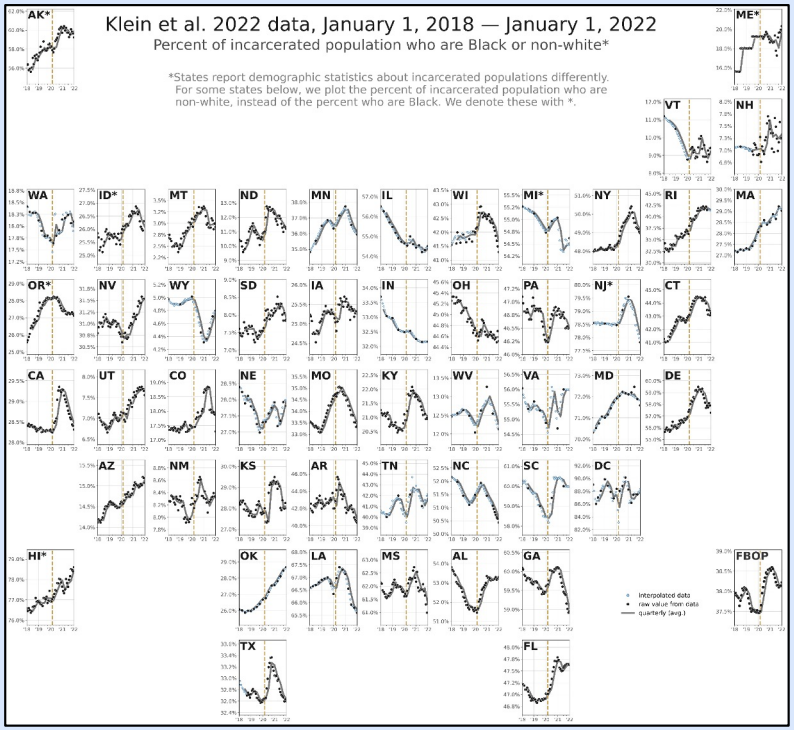



(A) Arizona
(B) California
(C) Connecticut
(D) Delaware
(E) Florida
(F) Georgia
(G) Kentucky
(H) Nevada
(I) New York
(J) Pennsylvania
(K) Texas
(L) Washington
Percent of prison population (Black incarcerated people)
March 2020
'18
'19
'20
'21
'22
interpolated data
raw value from data
quarterly (avg.)

Main observation: Also observed in nearly every state



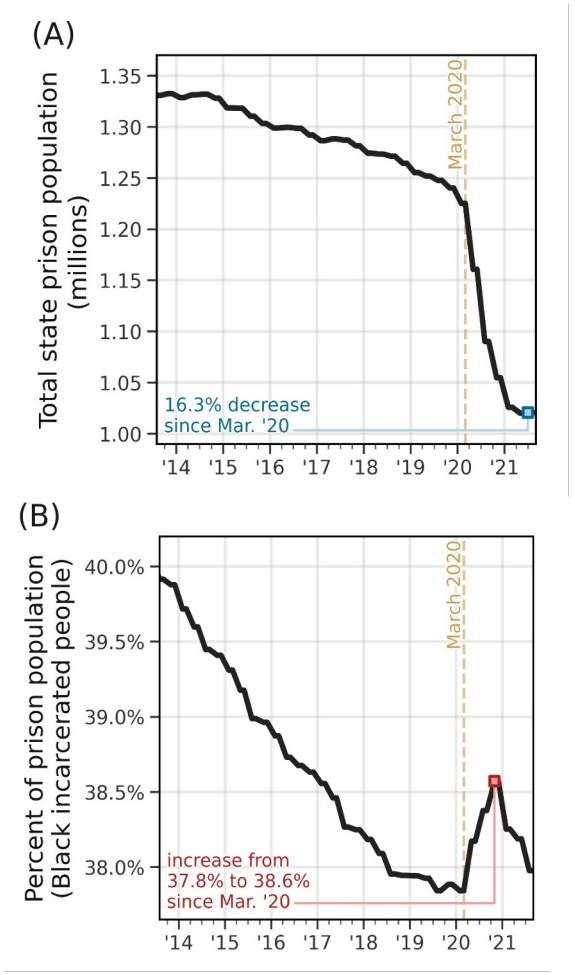


Graphic from Klein, Ogbunugafor et al., (2023)
Nature, doi: 10.1038/s41586-023-05980-2

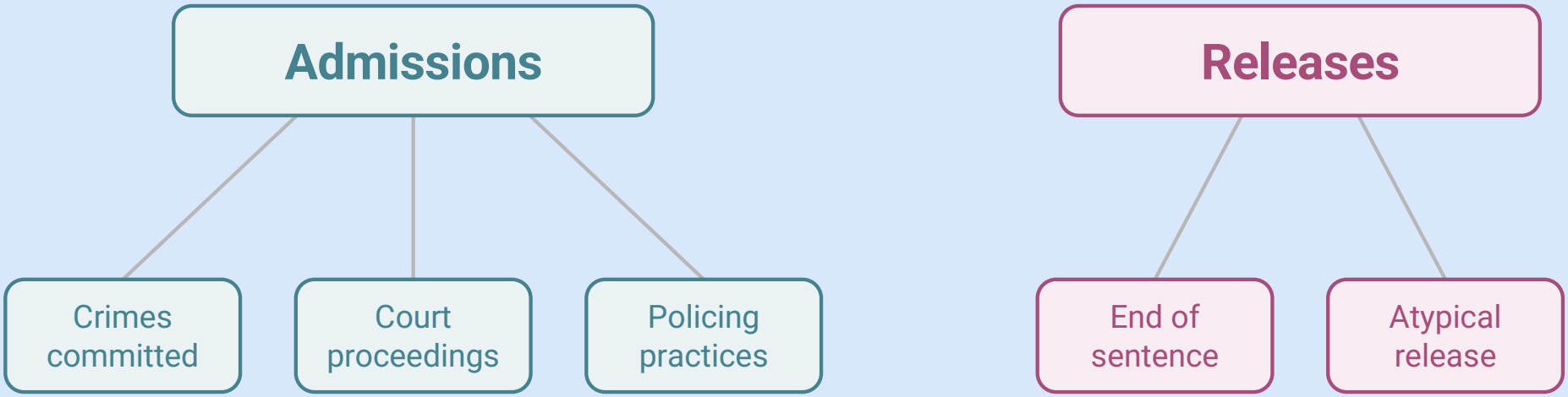
This is a **complex** story, based on 2 key observations

1. Why do we observe the trend in (A)?
2. Why do we observe the trend in (B)?
   a. If we think we know an answer, how would we show it?
   b. What data would we need?

3. What (if anything) does this work tell us about mass incarceration in the U.S.? Does it inform action?



Potential mechanisms



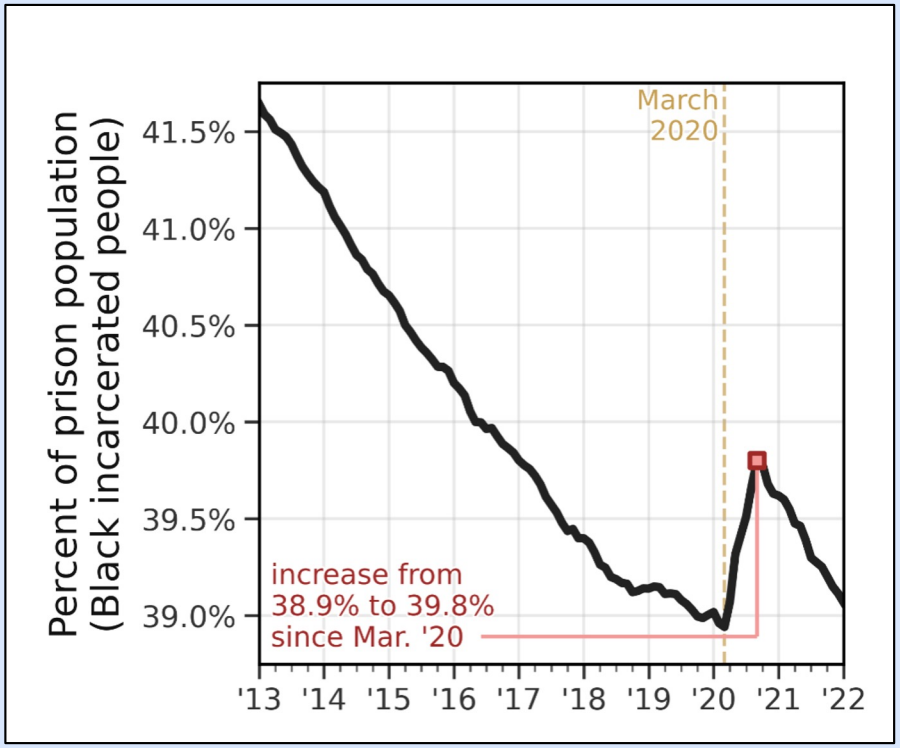
Potential mechanisms

The abrupt spike in the % Black incarcerated population likely varies by state.

Universally, though, every possible mechanism falls into two possible types:

Bias in **admissions**

Bias in **releases**



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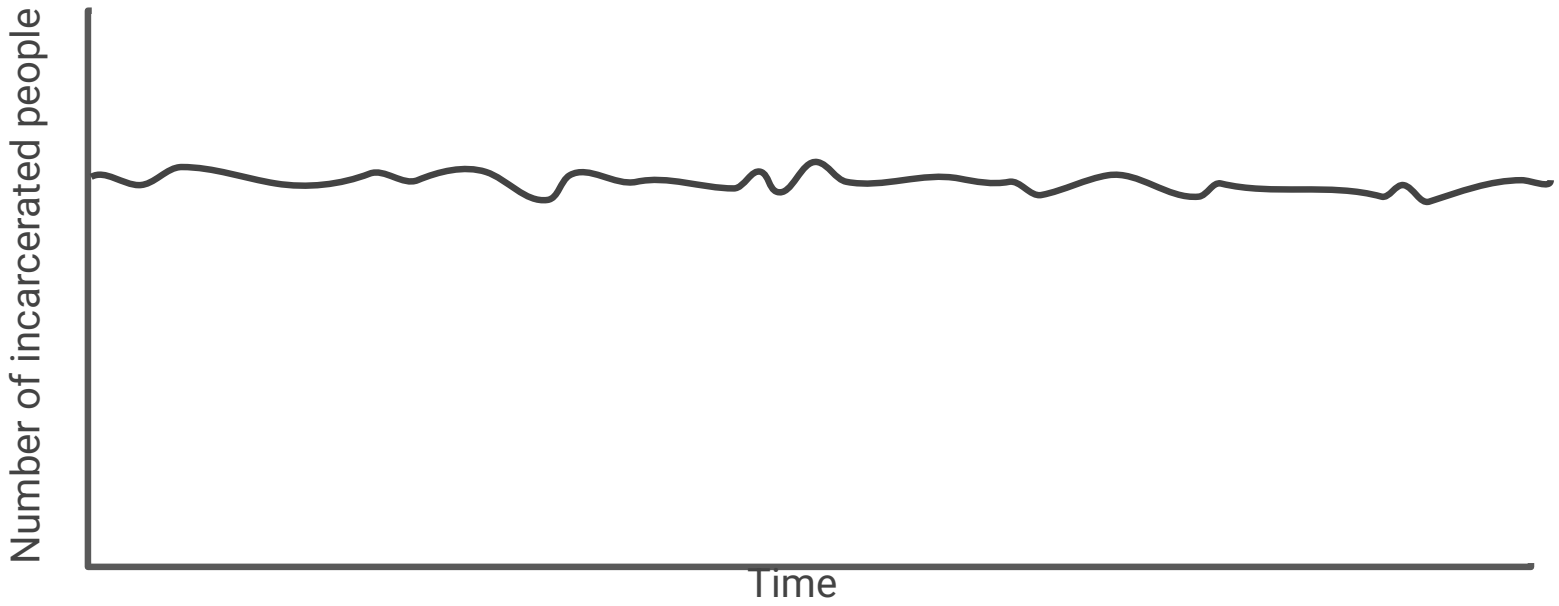
Potential mechanisms

Consider an example time series data of a prison population



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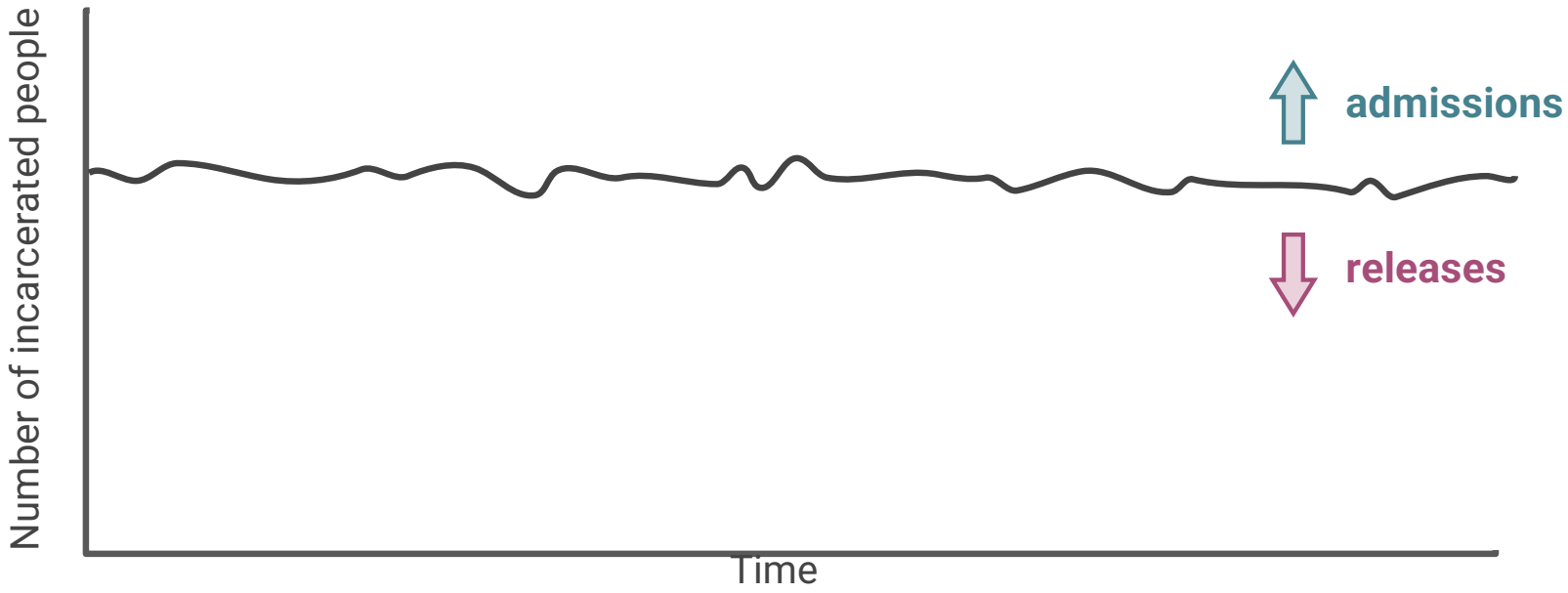

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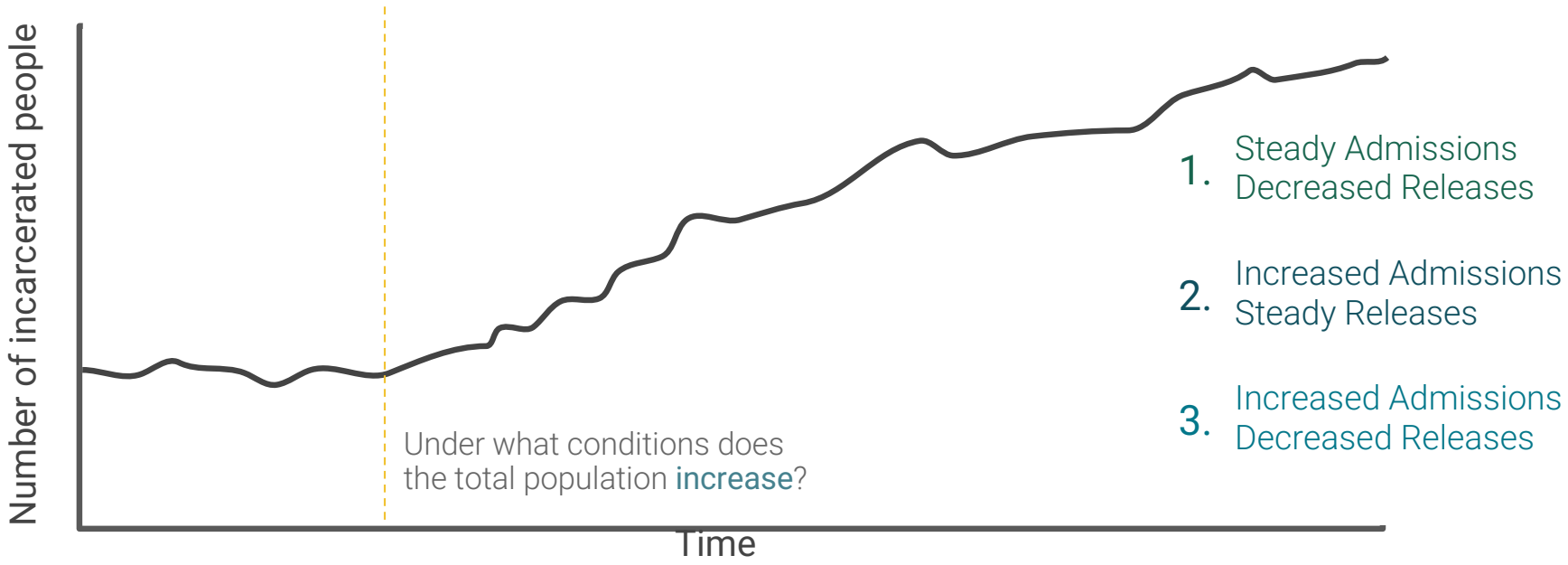

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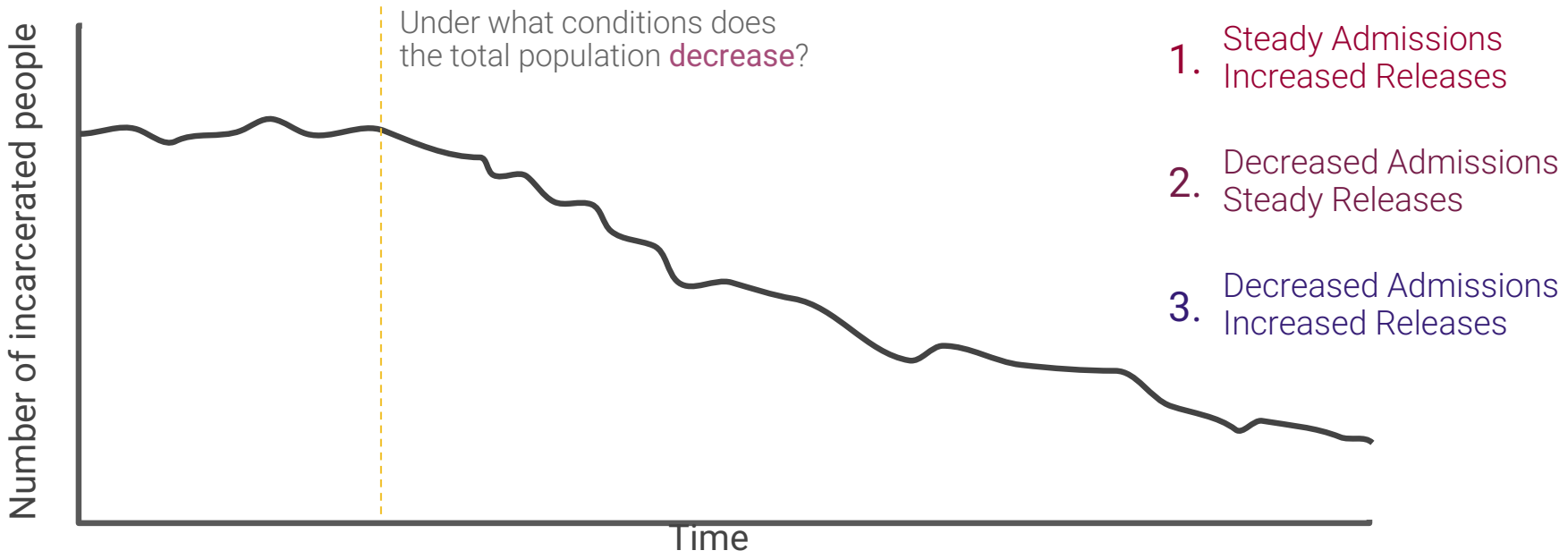

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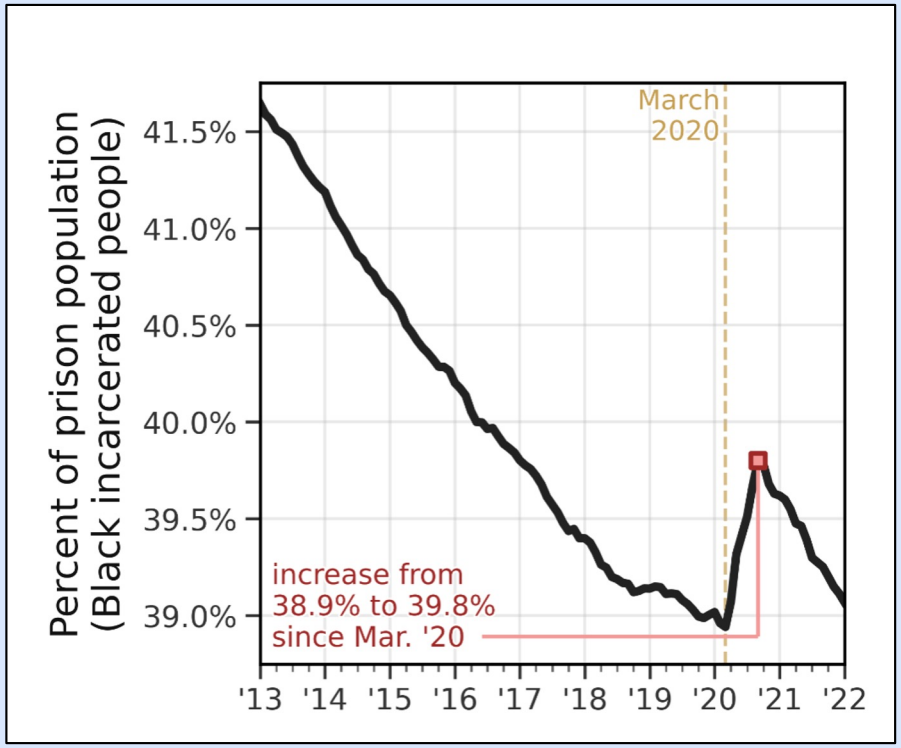


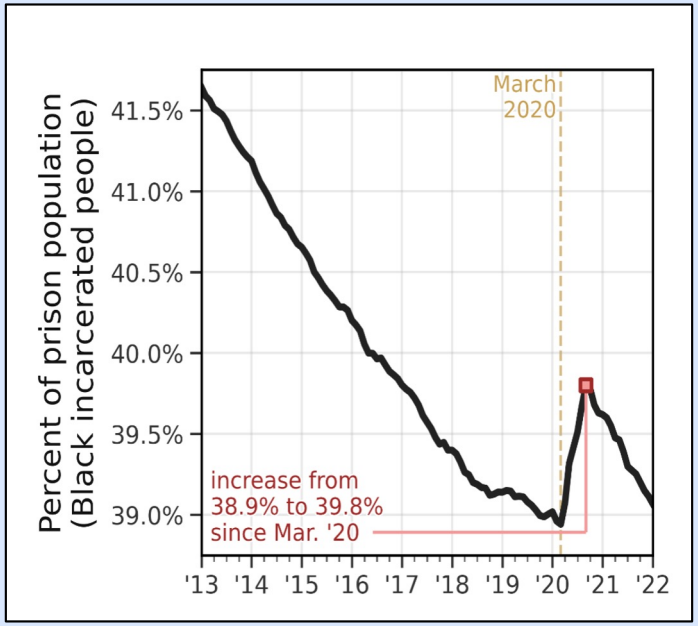
Graphic from Klein, Ogbunugafor et al., (2023) *Nature*, doi: 10.1038/s41586-023-05980-2

General mechanism, next steps, discussion

Stepping back: There's reason to believe *we should have expected* to see this kind of pattern in the data.

If a prison has differences in :

1) The average time spent in prison based on race
2) a sudden decline in prison admissions, we will see some variant of this trend. Why?



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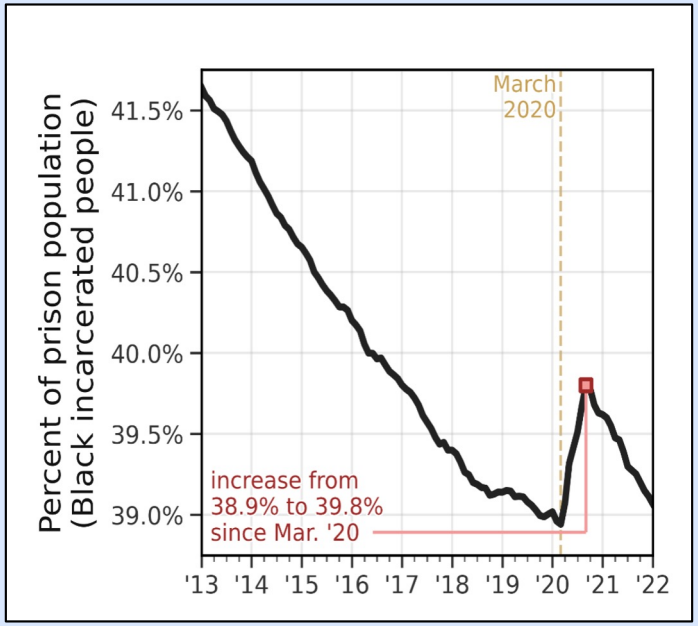
General mechanism, next steps, discussion

Recall from before: Incarcerated Black people serve ~20% longer sentences than white people, on average.

Knowing state-specific sentencing disparities allows us to make highly accurate predictions for the magnitude and duration of the spikes.

(and whether we expect them to occur at all)



Sentencing data from the U.S. Sentencing Commission's "Booker Report" (2017)
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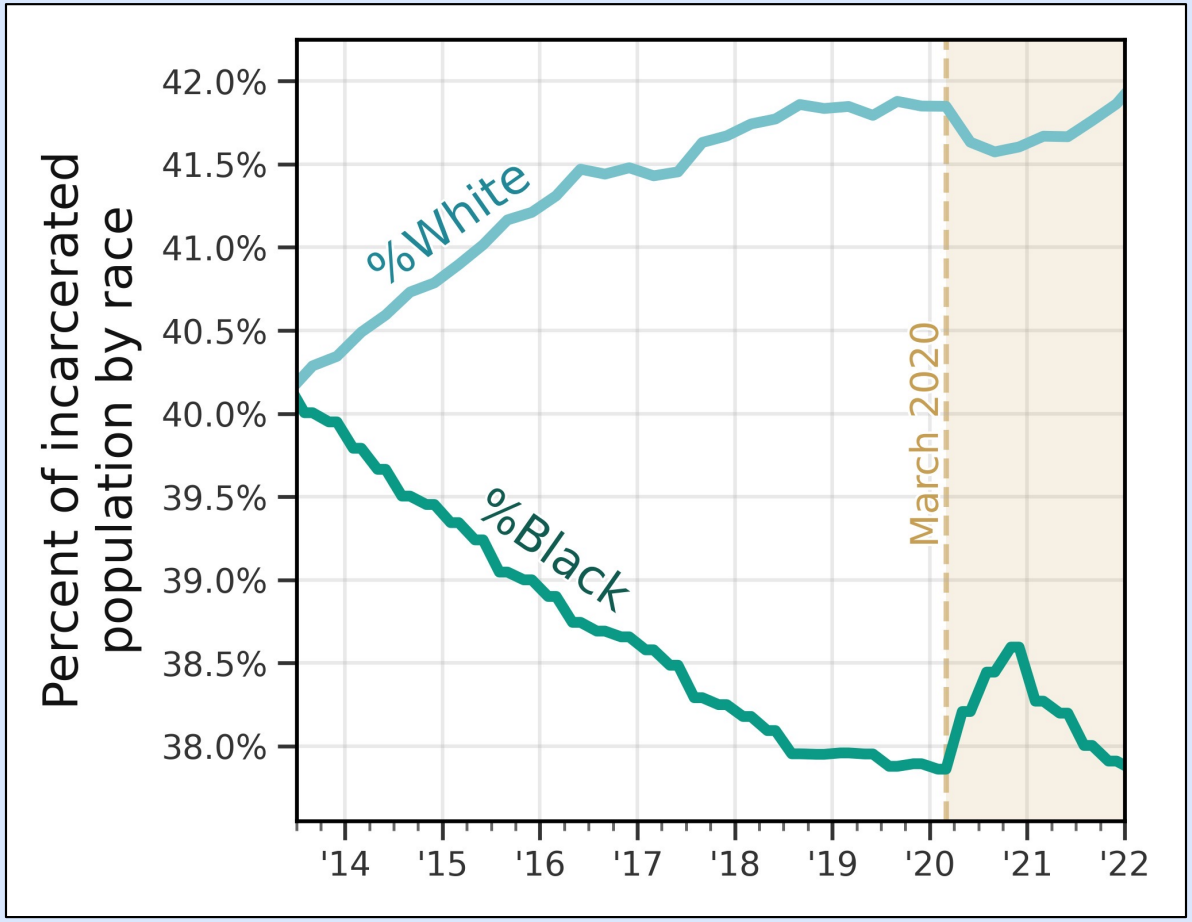
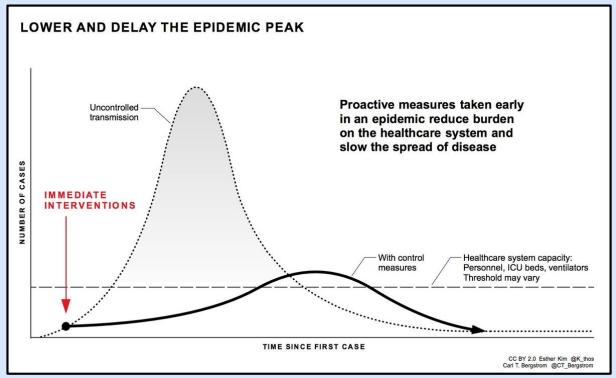


Stress test analogy



"Taken together, our findings reveal that the **pandemic provided a 'stress test' for the criminal legal system**. In engineering, stress tests involve exposing a system to extreme conditions in order to reveal its fragilities. **Using a range of data sources, we have argued that COVID-19 amplified underlying racial disparities in the carceral state.**"

The COVID-19 pandemic amplified long-standing racial biases in the U.S. criminal justice system

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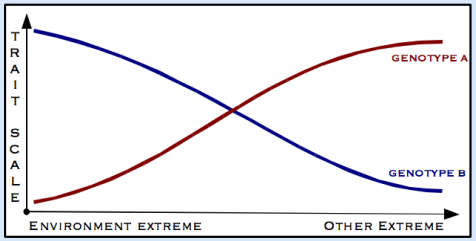
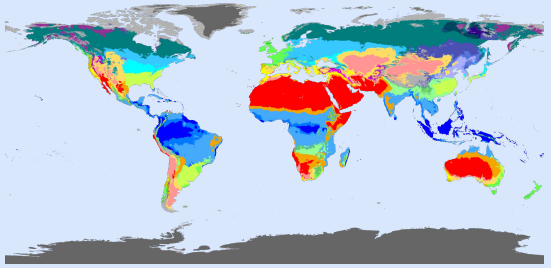
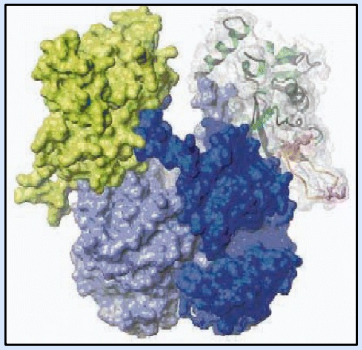
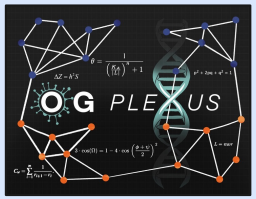
What is a context?

- Quantitative genetics
- Physiology
- Climactic, ecological
- Local, lived, daily, corporeal
- Historical, structural, and psychological



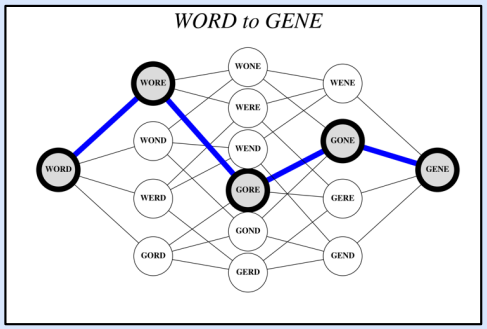


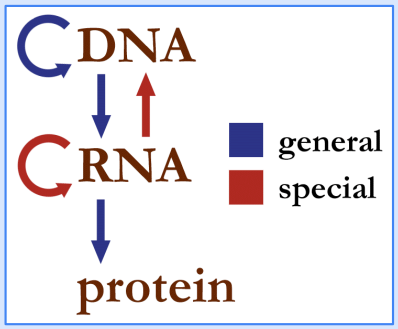


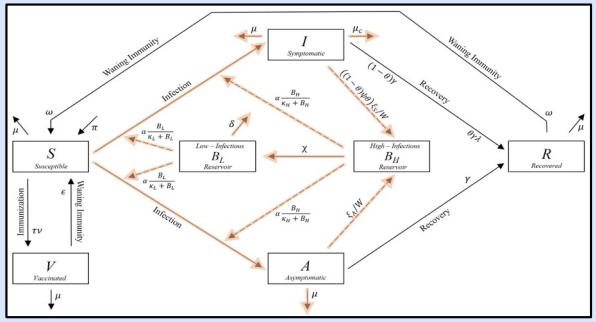


The Ogbunu **complex systems** creed

- What are the **actors** that drive complex biological systems?
- What is the nature of the **interactions** between them?
- What contextual details **modulate** these interactions?

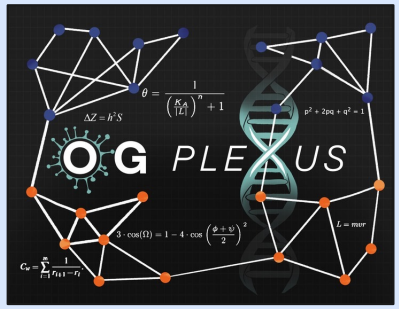






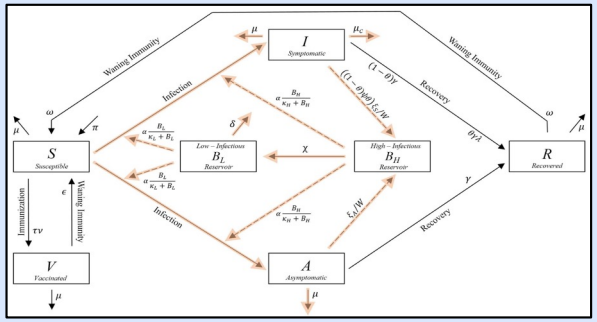
A guide to the study of complex systems

1. Should focus something that you care about.
2. Suspect that the system is driven by nonlinear interactions between actors.
3. Must *identify* (at least) and collect/measure the data necessary to understand the system.
4. Open-minded with regards to your method.
5. *Radical* cross-disciplinarity.



Culture:

The personal story should be a central part of science.



Thank you!