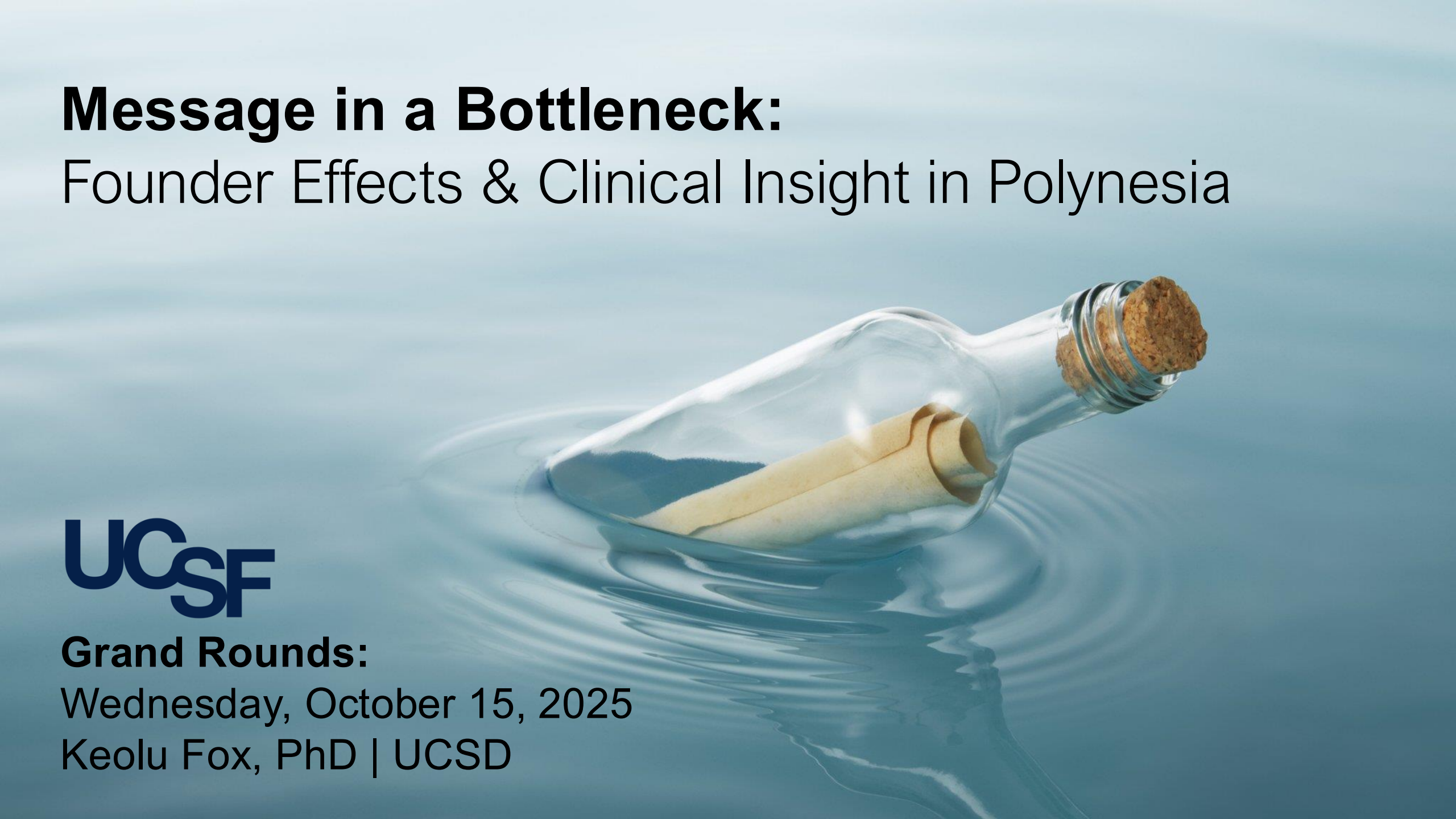
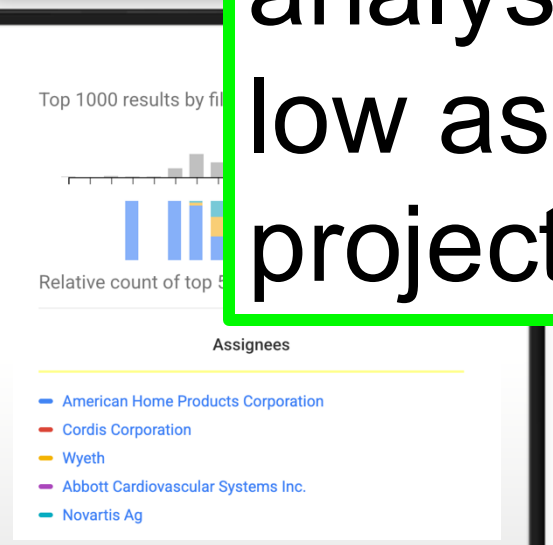
Message in a Bottleneck:
Founder Effects & Clinical Insight in Polynesia

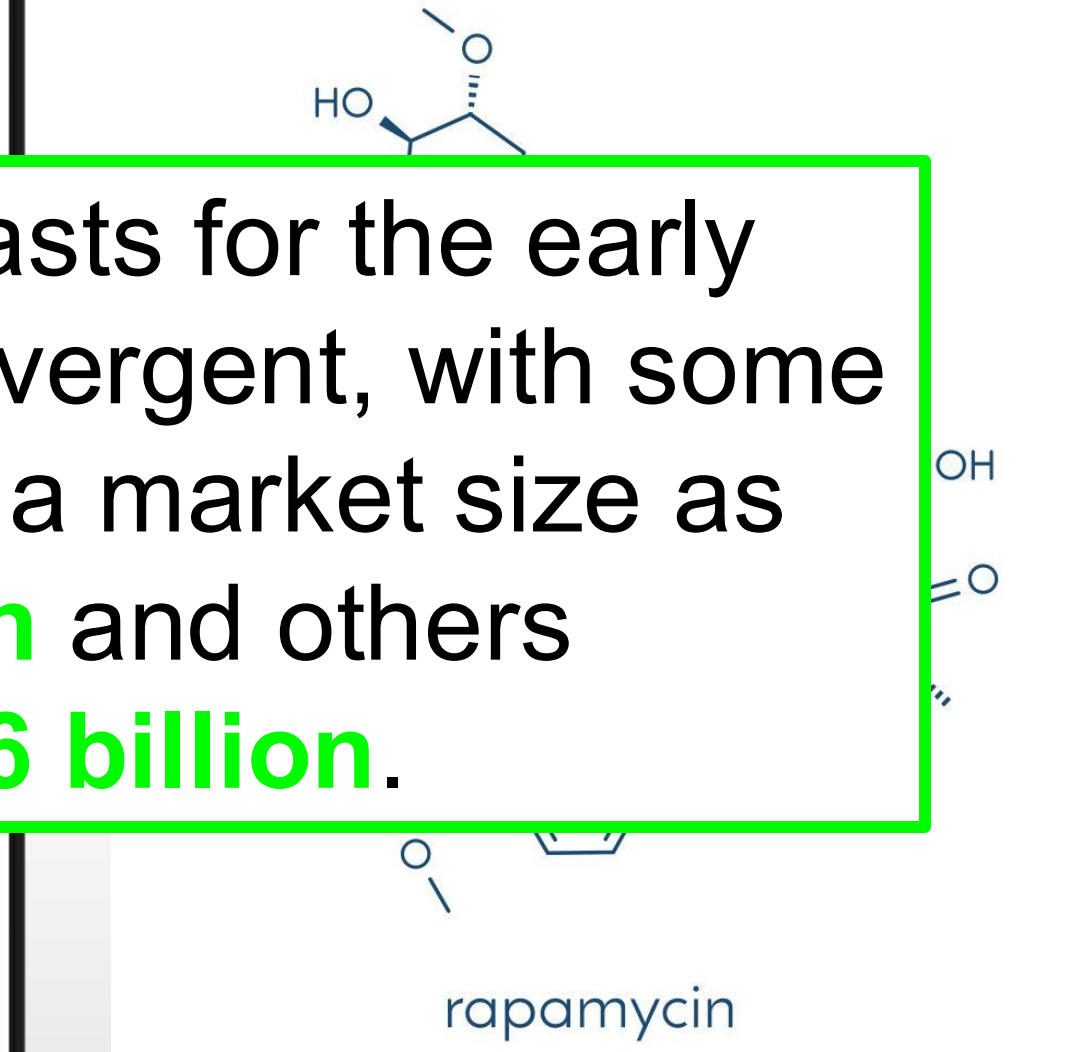


UCSF

Grand Rounds:
Wednesday, October 15, 2025
Keolu Fox, PhD | UCSD

2030–2033: Forecasts for the early 2030s are highly divergent, with some analysts predicting a market size as low as **$370 million** and others projecting over **$2.6 billion**.





Comment

https://doi.org/10.1038/s41467-025-57935-y

Partnerships with Indigenous Peoples for an ethical bioeconomy

Maria C. T. Astolfi, WarīNkwī Flores, Rolando Perez, Ulises J. Espinoza, Teal B. Zimring, Jay D. Keasling & Keolu Fox

Biotechnology offers a sustainable route to manufacturing, but closing the loop towards safeguarding biodiversity remains challenging. Here, we explore how partnerships with Indigenous Peoples and Local Communities (IP&LC) can promote an ethical and circular bioeconomy.

Recently, scientists reported in *Nature* how biomanufacturing provides a sustainable route to an essential pharmaceutical. Liu et al. engineered yeast to produce QS-21, a potent adjuvant in FDA-approved vaccine formulations administered to millions globally[1]. Today, the commercialization of QS-21 relies on laborious extraction from *Quillaja saponaria* trees in South America, leading to ecological damage, shortages, and rising costs. Notably, the medicinal use of the tree is Traditional Ecological Knowledge (TEK) of the Mapuche Peoples[2]. With various similar products approaching the market, QS-21 can provide a model for commercializing biodiversity-derived products. But will a biotechnology-based supply chain lead to a sustainable and ethical bioeconomy? What are the emerging practices to achieve such a goal?

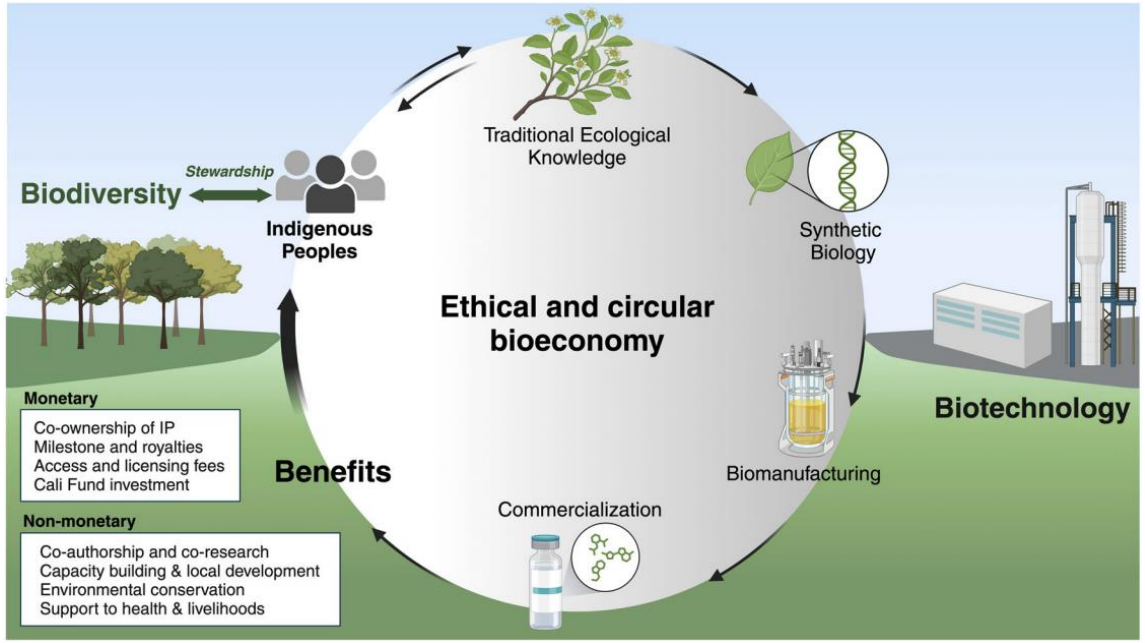
The World Health Organization (WHO) reports that approximately 40% of the commercial drugs today derive from plants and Traditional Medicine[3]. As biotechnology provides new supply chains to these medicines, Indigenous Peoples and Local Communities (IP&LC) raise critical considerations regarding the fair and equitable use of their TEK and the potential of synthetic biology to disrupt the local production that sustains their ways of living. This topic has historically divided biotechnologists and IP&LC. However, safeguarding the biodiversity that provides these life-saving medicines is a shared responsibility and is of interest to all parties.

circularizing bioprocesses[4]. Economic and ethical frameworks can drive circularity in the bioeconomy to meet these sustainability goals. Through such frameworks, products derived from biodiversity and Traditional Ecological Knowledge (TEK) would return a percentage of the proceeds to their stewards and custodians (Fig. 1). Investing in IP&LC directly supports conservation and regenerative efforts, as they safeguard 40% of the world's remaining protected areas and ecologically intact landscapes[5].

The Nagoya Protocol closes the loop from biotechnology to IP&LC. It is a landmark legal framework for fair and equitable access and benefit-sharing (ABS) from using Indigenous genetic resources, establishing a global instrument to execute the mission of the United Nations Convention on Biological Diversity (CBD)[6]. Recent genomics and synthetic biology advancements have significantly expanded its scope to protect Indigenous Peoples' rights on Digital Sequence Information (DSI)[7]. These resolutions have substantial implications for biotechnologists. A perspective shift to include key considerations (Box 1) regarding the land and peoples our research relies on is crucial for a fair and ethical practice.

Data frameworks are also advancing with extensive discussion in the field of genomics but remain limited in biotech[8,9]. Emerging advancements based upon the UN Declaration on the Rights of Indigenous Peoples (UNDRIP) affirms Indigenous Data Sovereignty (IDSov) and Governance (IDGov) as integral to self-determination, establishing Indigenous Peoples' authority over data collection, ownership, and use[10]. As guidelines for practitioners, the Global Indigenous Data Alliance (GIDA) has created the C.A.R.E. principles (Collective Benefit, Authority to Control, Responsibility, and Ethics) for data protection[11].

To drive innovation forward to meet the global challenges ahead, upholding these frameworks will enable biotechnologists and Indigenous Peoples to access biodiversity and benefit from a growing bioeconomy. This commitment fairly credits the contributions of Indigenous TEK and fosters trust between IP&LC and biotechnologists (Fig. 1).



BOX 1

Key considerations for biotechnologists working with biodiversity, Indigenous Peoples and Local Communities, and Traditional Ecological Knowledge-derived technologies

Land: Where do the knowledge or genetic resources (e.g., physical samples, digital sequence information) I am working with originate?

Peoples: Do any peoples or communities steward or rely on these natural/genetic resources, knowledge systems, or practices?

Data collection and disaggregation*: How were the samples collected, and did these communities consent** to their collection?

Data storage*: How is the data stored, and who may access and benefit from it?

Engagement and collaboration: Are there foundations, institutes, representing organizations, or individuals from these communities with whom I can engage?

Equitable and fair benefit-sharing: If the resulting discovery is deployed for profit or not, are there monetary or non-monetary benefits (Fig. 1) that can be shared with the communities?

*Part of Indigenous rights to Data Sovereignty (IDSov) and Governance (IDGov)

**Part of Free, Prior, and Informed Consent (or FPIC) of Indigenous self-determination rights


Welcome to
INDIGENOUS FUTURES INSTITUTE
IFI
UC San Diego


Kohala
Big Island


Diversity


Soil


Extinction


Invasion

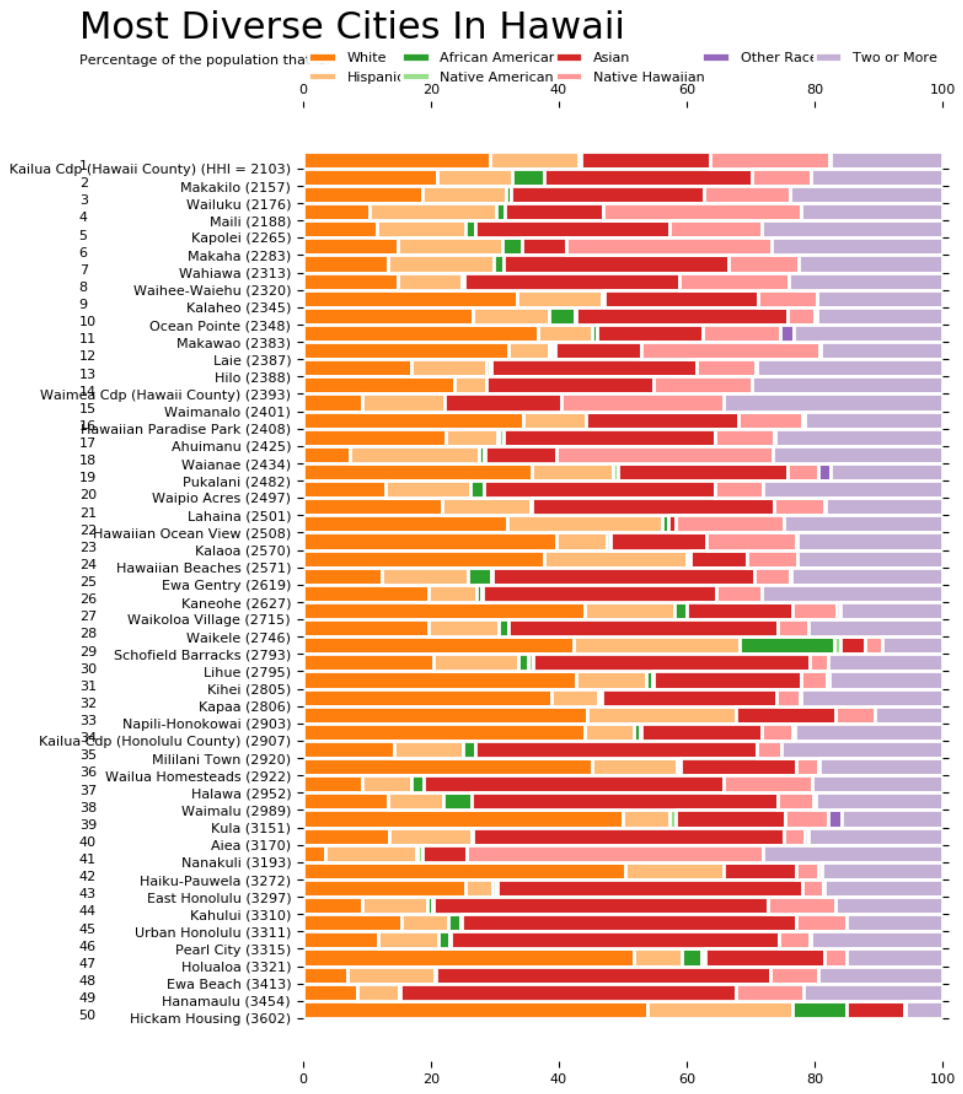
Four of Hawaii's counties ranked among the top 15 most diverse counties in the Nation

Hawaii County, Hawaii (#1)

Maui County, Hawaii (#2)

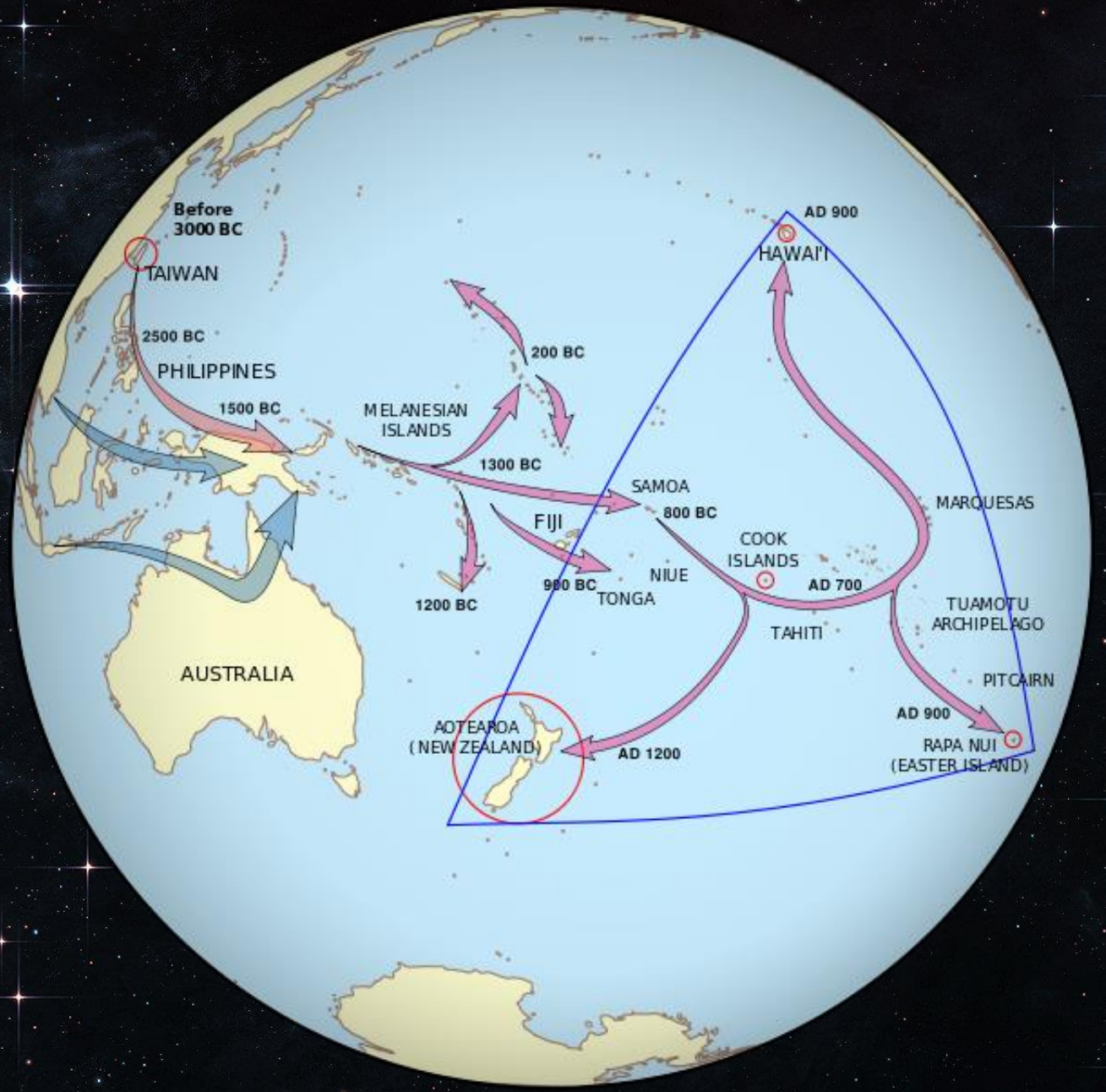
Kauai County, Hawaii (#4)

Honolulu County, Hawaii (#11)

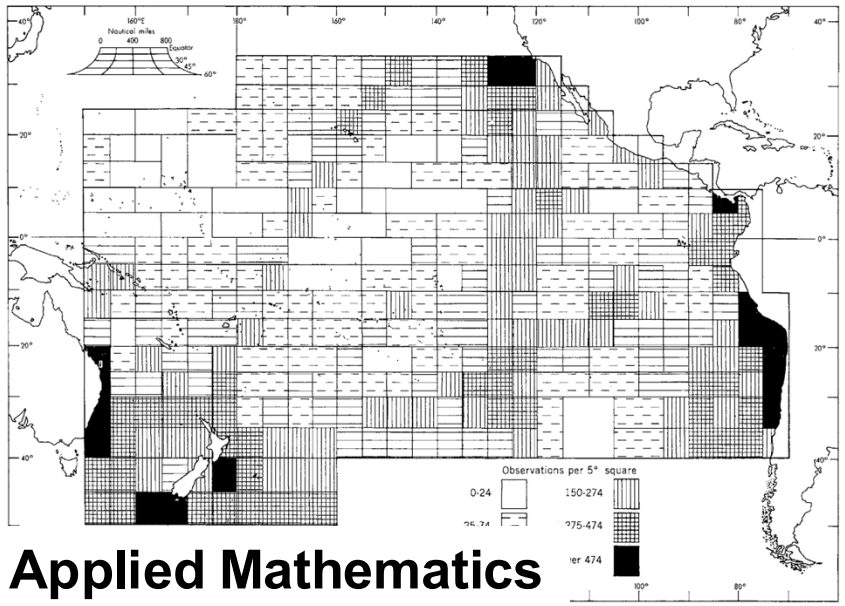


https://www.census.gov/library/visualizations/interactive/racial-and-ethnic-diversity-in-the-united-states-2010-and-2020-census.html

Where did these time estimates come from?

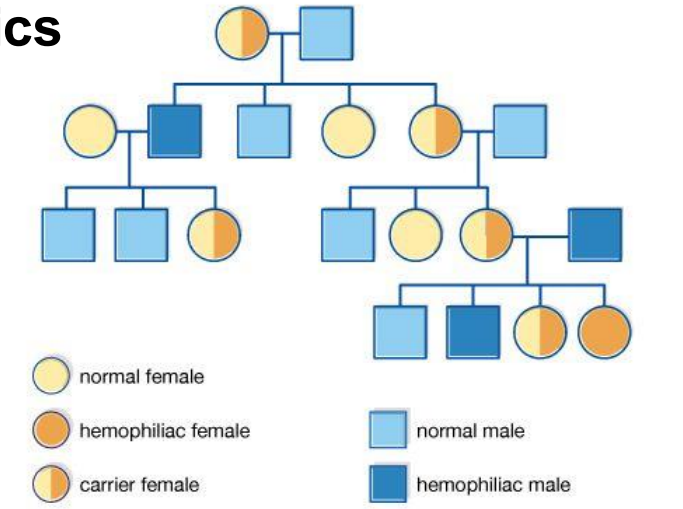


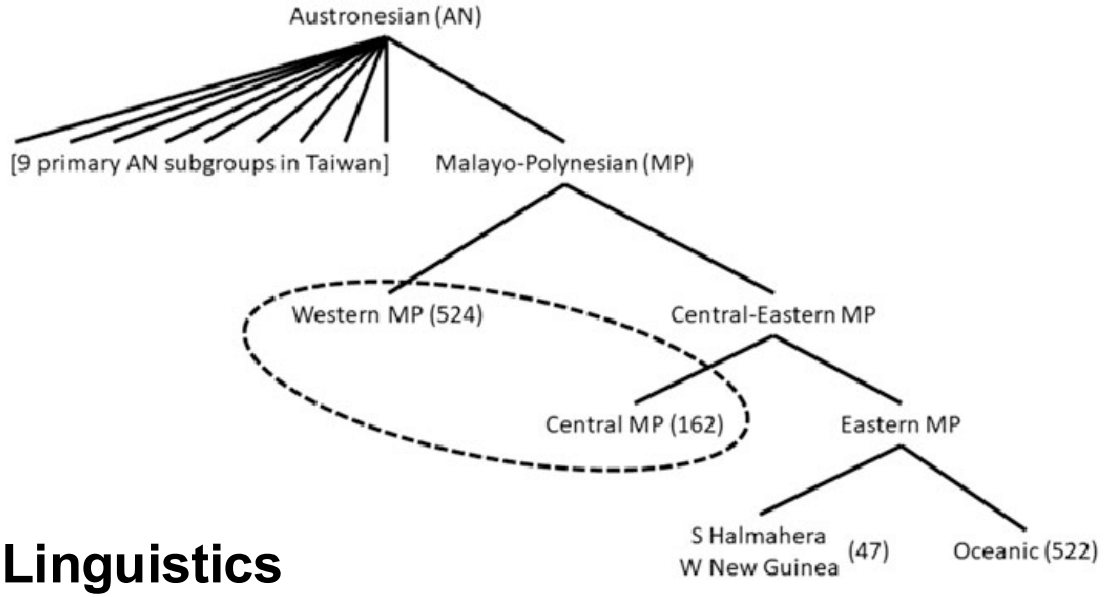
Archeology



Applied Mathematics

Genetics

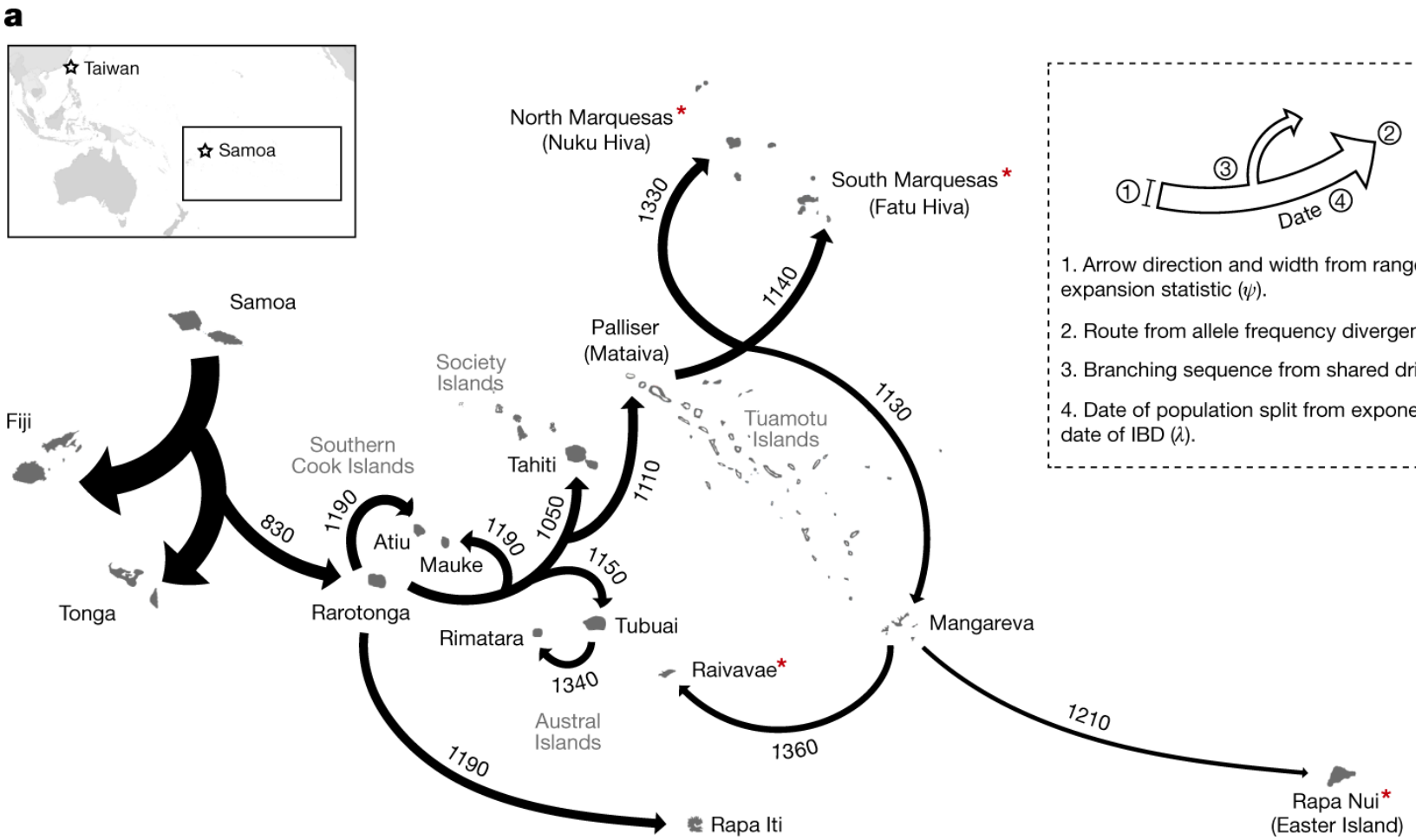


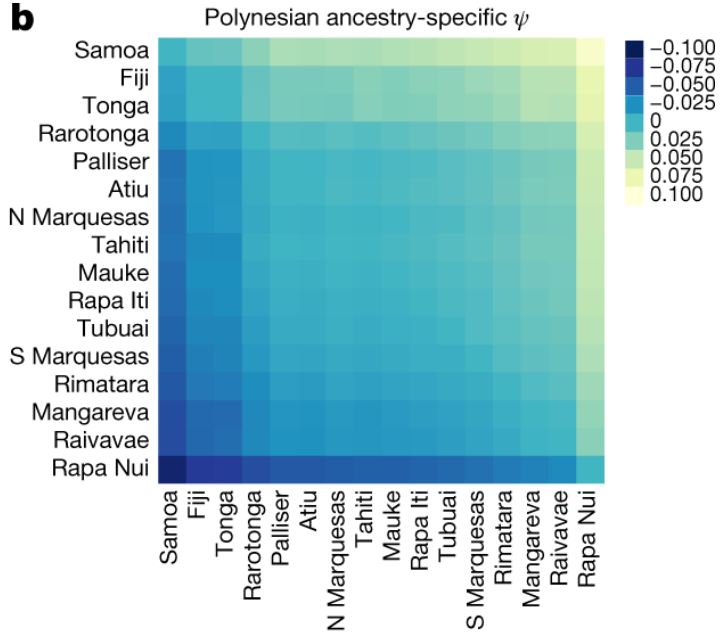


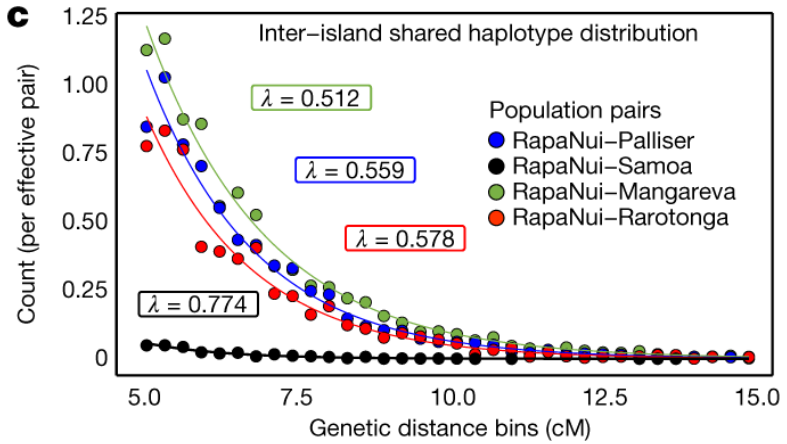
Linguistics

Paths and timings of the peopling of Polynesia inferred from genomic networks

nature

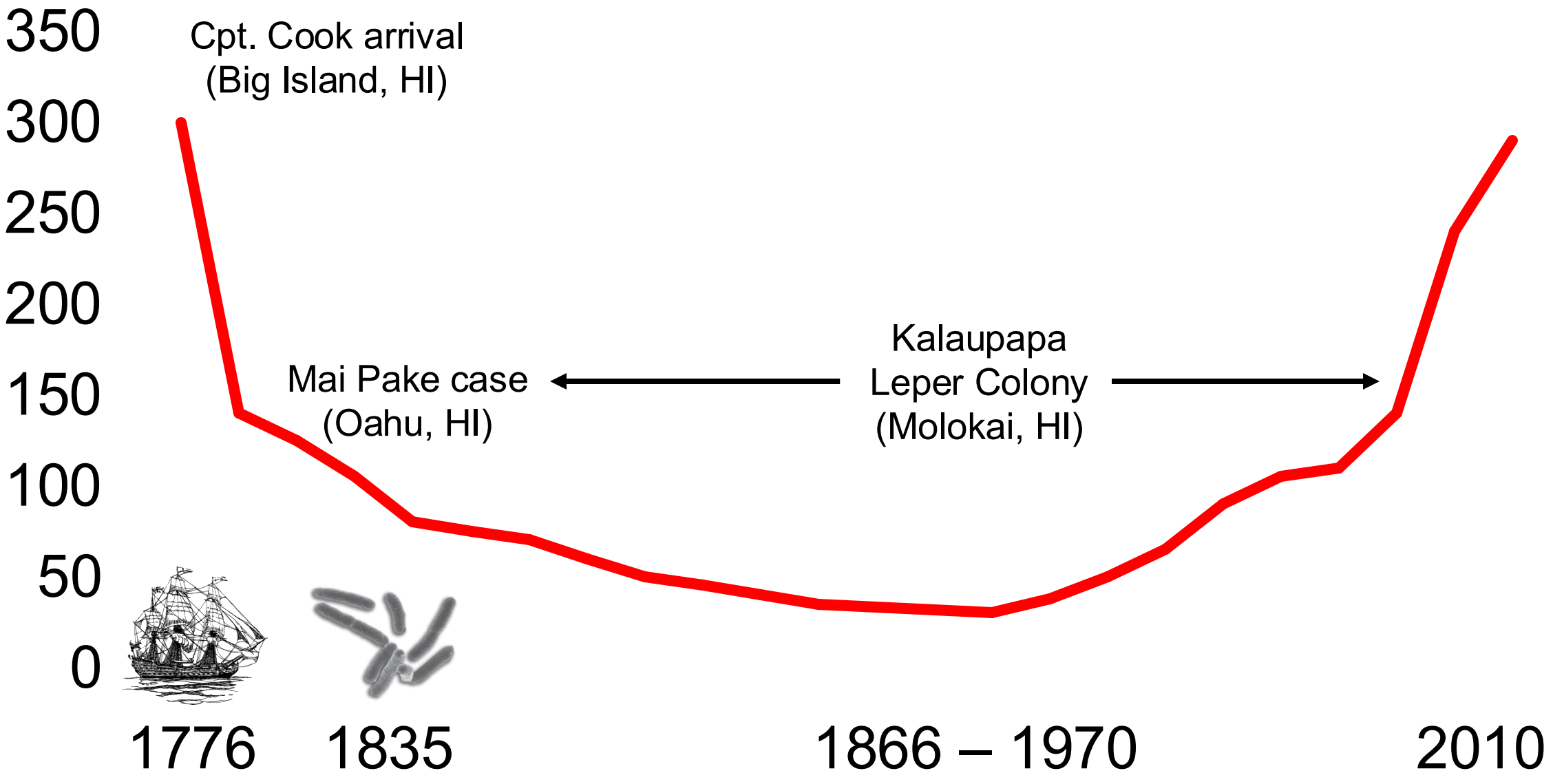






UH Archives

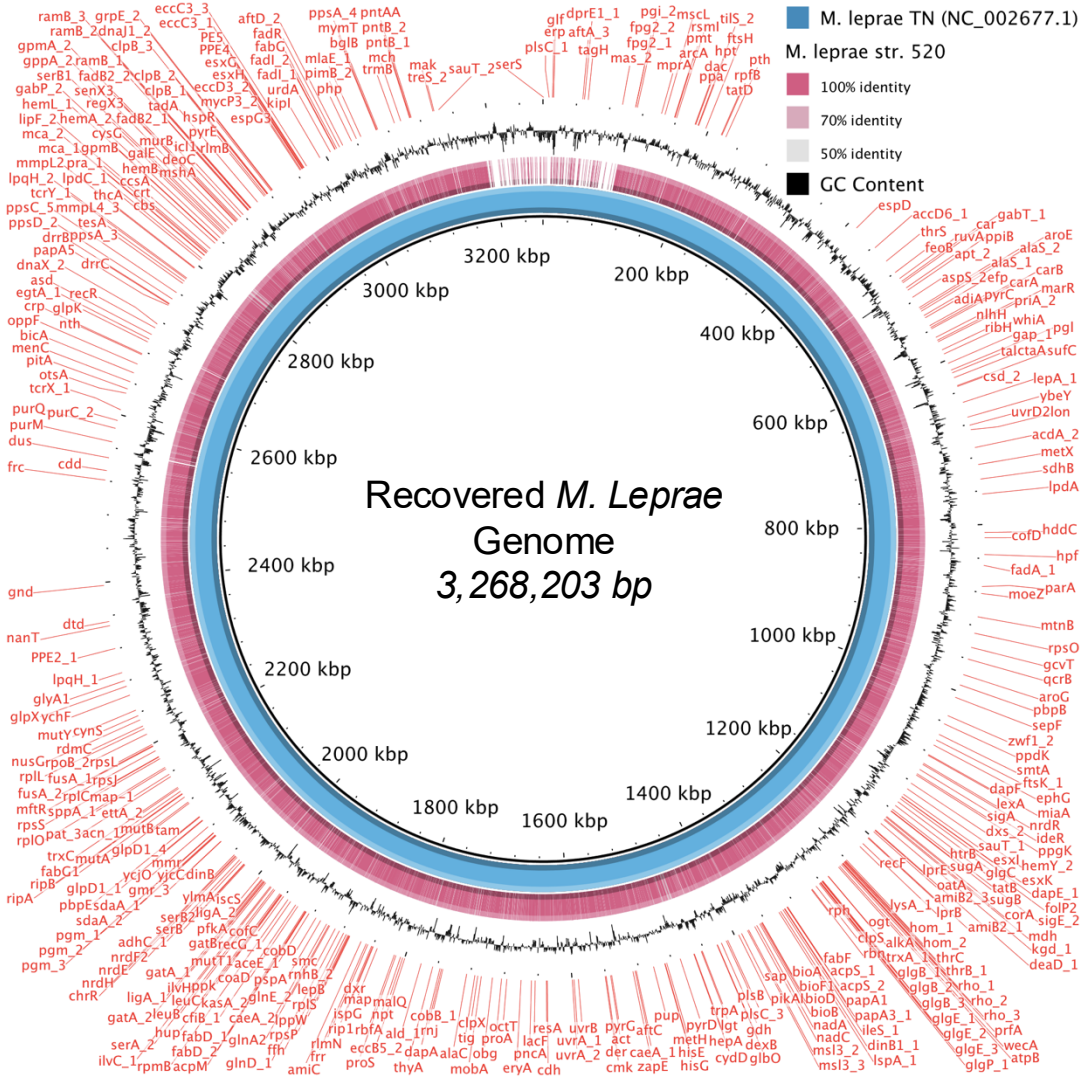
Native Hawaiian Population (in thousands)



Pew Research Center & Kamehameha schools (2015)

Sequencing ancient *ma'i pa'ke* bacteria from Polynesia

Processing ancient leprosy samples
(Stone aDNA Lab, Arizona State University)



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Research

Cite this article: Blevins KE, Crane A, Lum C, Furuta K, Fox K, Stone AC. 2020 Evolutionary history of *Mycobacterium leprae* in the Pacific Islands. *Phil. Trans. R. Soc. B* 20190582. http://dx.doi.org/10.1098/rstb.2019.0582

Accepted: 16 May 2020

One contribution of 14 to a theme issue 'Insights into health and disease from ancient biomolecules'.

Subject Areas:
evolution, health and disease and epidemiology, genomics

Keywords:
Mycobacterium leprae, whole genome, leprosy, Hansen's disease, Pacific Islands, FFPE

Evolutionary history of *Mycobacterium leprae* in the Pacific Islands

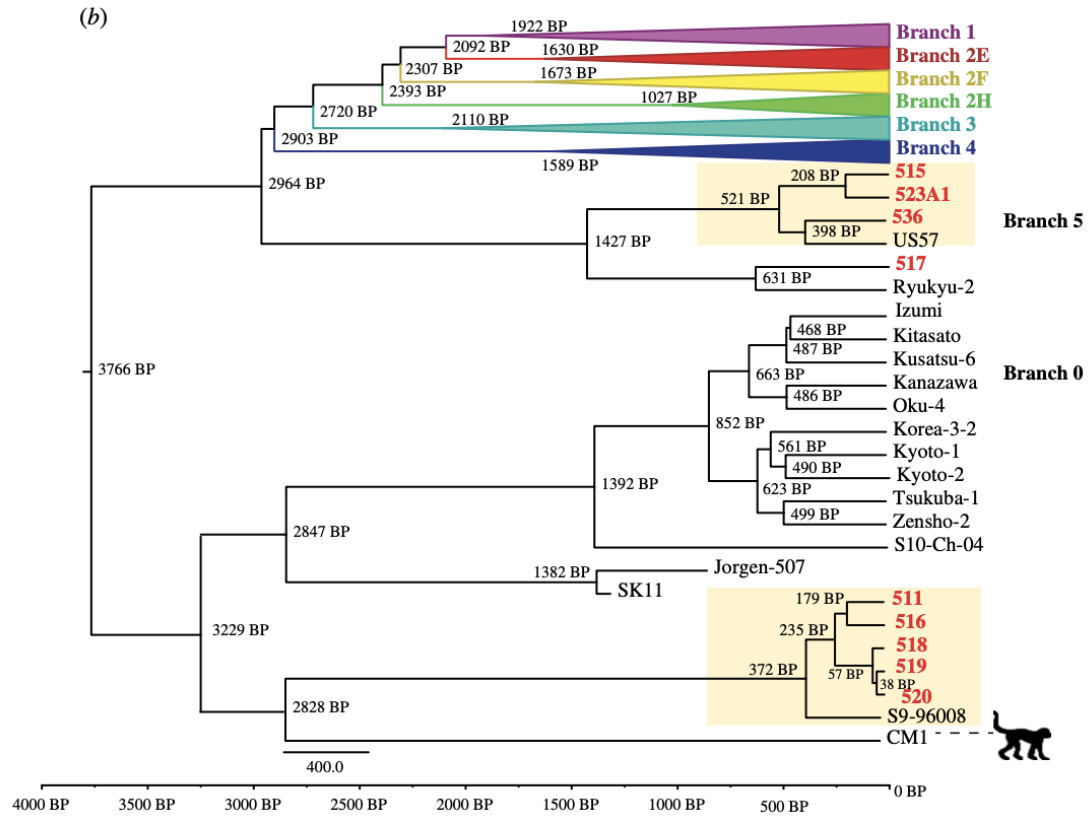
Kelly E. Blevins[1,2,†], Adele Crane[3,4,†], Christopher Lum[5], Kanako Furuta[6], Keolu Fox[7,‡] and Anne C. Stone[1,3,4,‡]

[1]School of Human Evolution and Social Change, [2]Center for Bioarchaeological Research, [3]School of Life Sciences, and [4]Center for Evolution and Medicine, Arizona State University, Tempe, AZ, USA
[5]Department of Pathology, John A Burns School of Medicine, University of Hawaii, Honolulu, HI, USA
[6]Hawaii Pathologists Laboratory, Honolulu, HI 96813, USA
[7]Departments of Anthropology & Global Health, University of California, San Diego, CA, USA

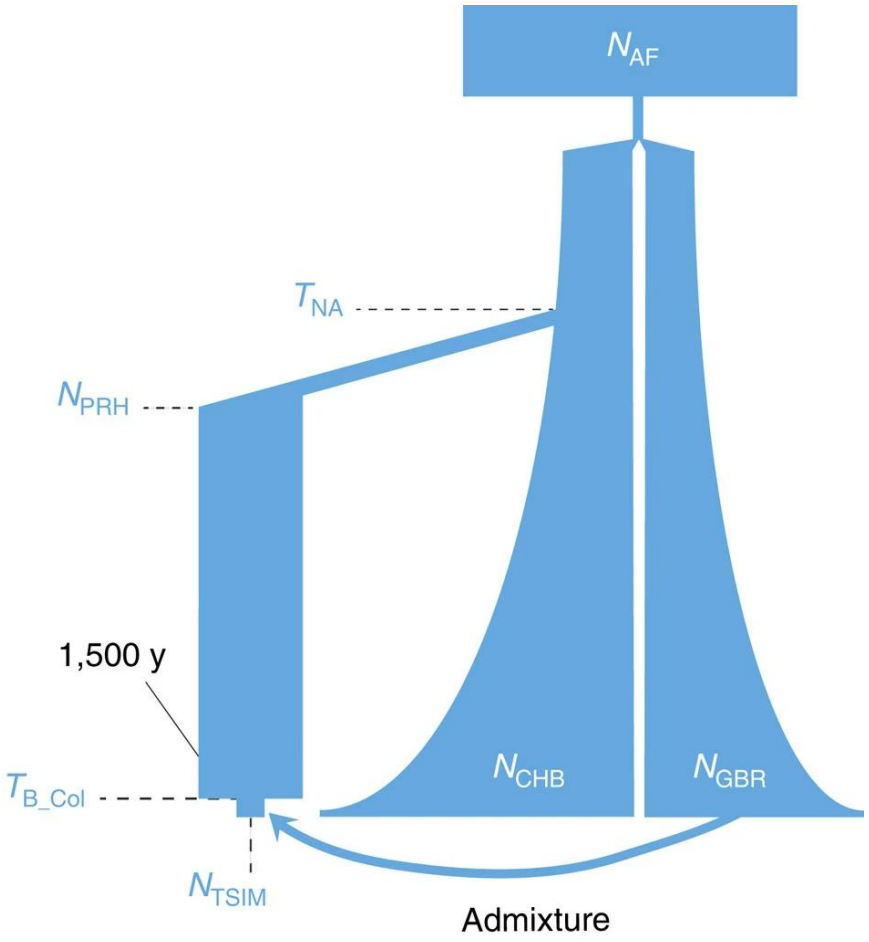
KEB, 0000-0002-5740-639X; AC, 0000-0001-5761-4271; ACS, 0000-0001-8021-8314

As one of the oldest known human diseases, leprosy or Hansen's disease remains a public health concern around the world with over 200 000 new cases in 2018. Most human leprosy cases are caused by *Mycobacterium leprae*, but a small number of cases are now known to be caused by *M. lepromatosis*, a sister taxon of *M. leprae*. The global pattern of genomic variation in *M. leprae* is not well defined. Particularly, in the Pacific Islands, the origins of leprosy are disputed. Historically, it has been argued that leprosy arrived on the islands during nineteenth century colonialism, but some oral traditions and palaeopathological evidence suggest an older introduction. To address this, as well as investigate patterns of pathogen exchange across the Pacific Islands, we extracted DNA from 39 formalin-fixed paraffin-embedded biopsy blocks dating to 1992–2016. Using whole-genome enrichment and next-generation sequencing, we produced nine *M. leprae* genomes dating to 1998–2015 and ranging from 4-63× depth of coverage. Phylogenetic analyses indicate that these strains belong to basal lineages within the *M. leprae* phylogeny, specifically falling in branches 0 and 5. The phylogeographic patterning and evolutionary dating analysis of these strains support a pre-modern introduction of *M. leprae* into the Pacific Islands.

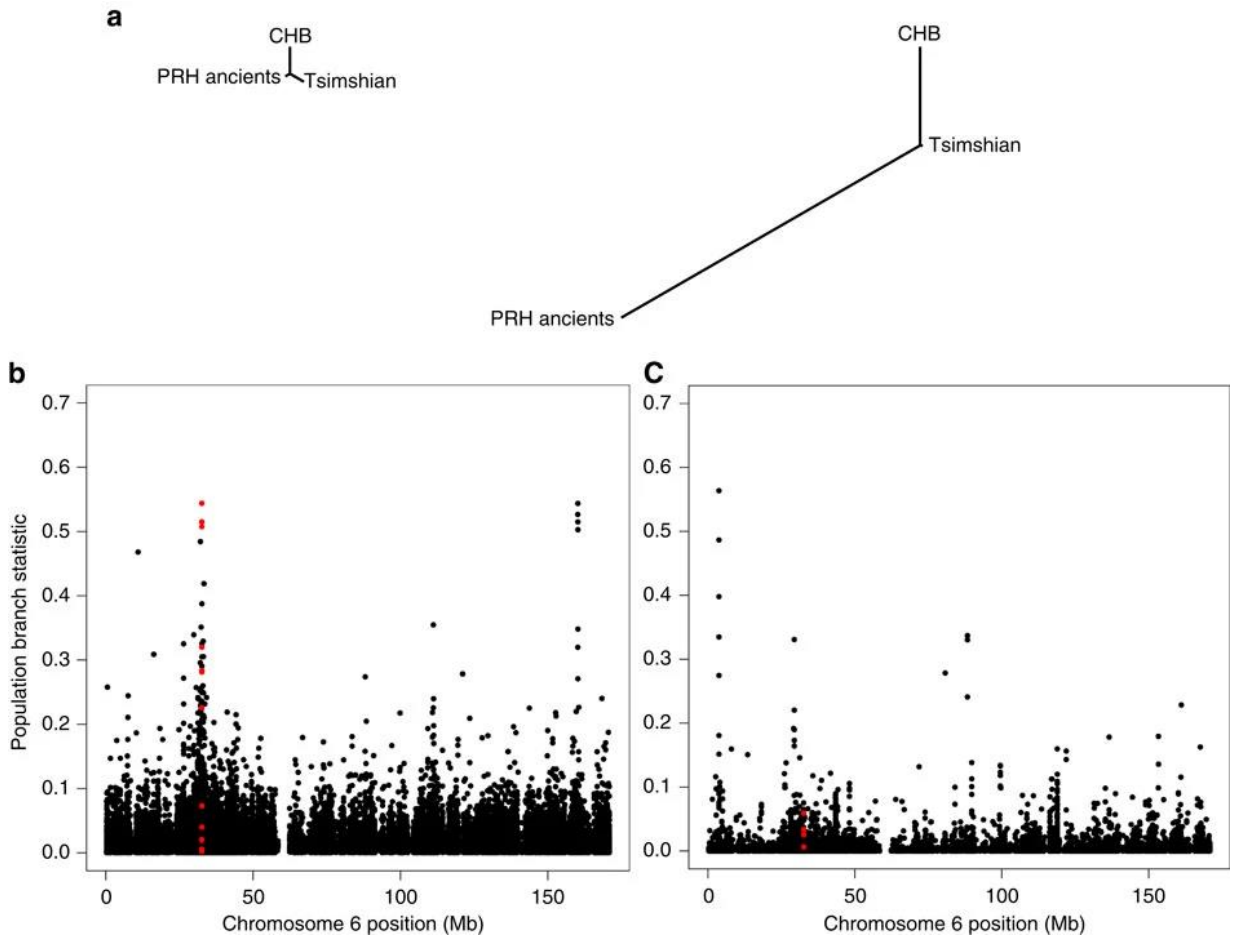
This article is part of the theme issue 'Insights into health and disease from ancient biomolecules'.



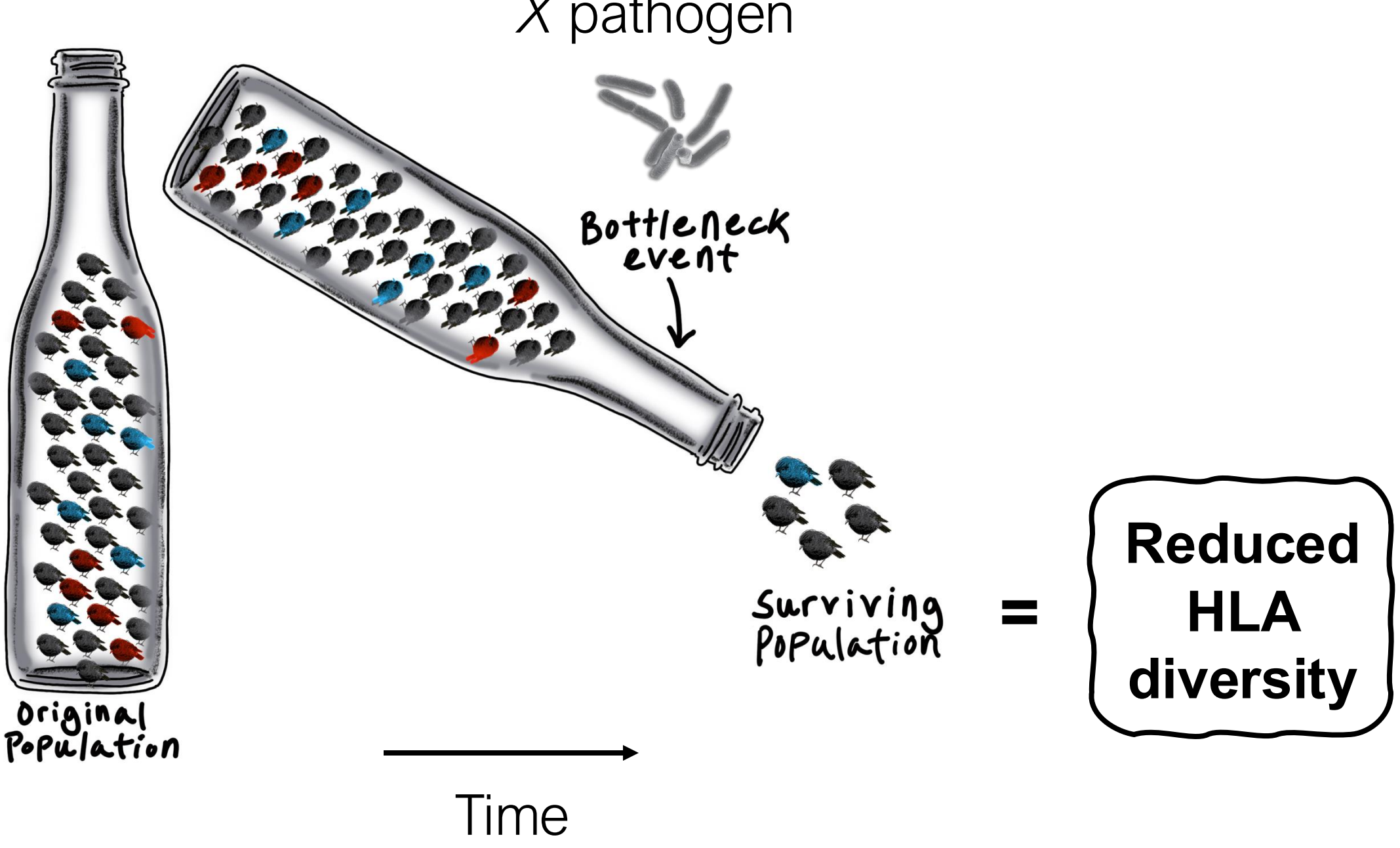
Population Collapse: Identifying bottlenecks after European contact



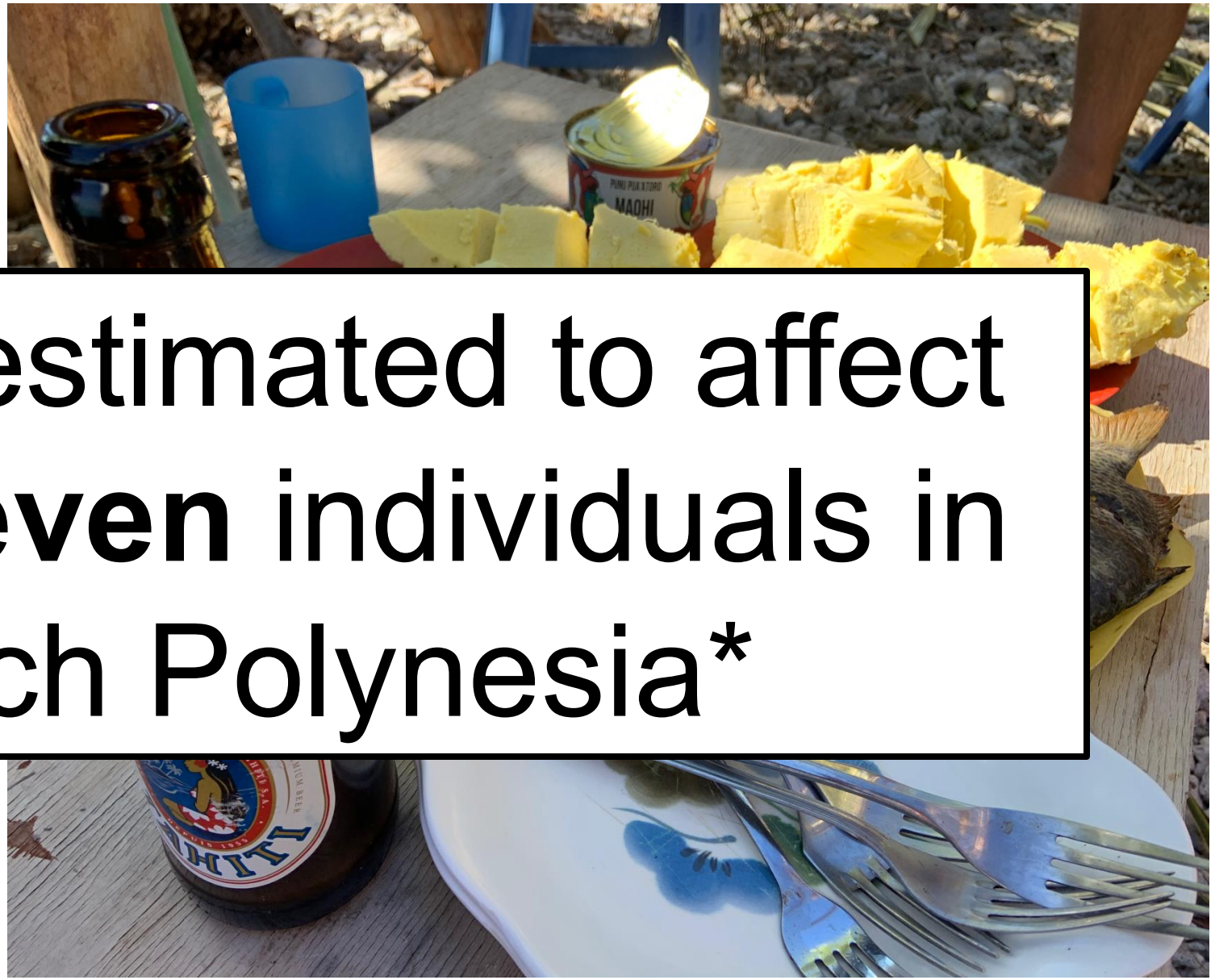
Lindo et al., (2016)



Population branch statistic (PBS) of the *HLA-DQA1* gene

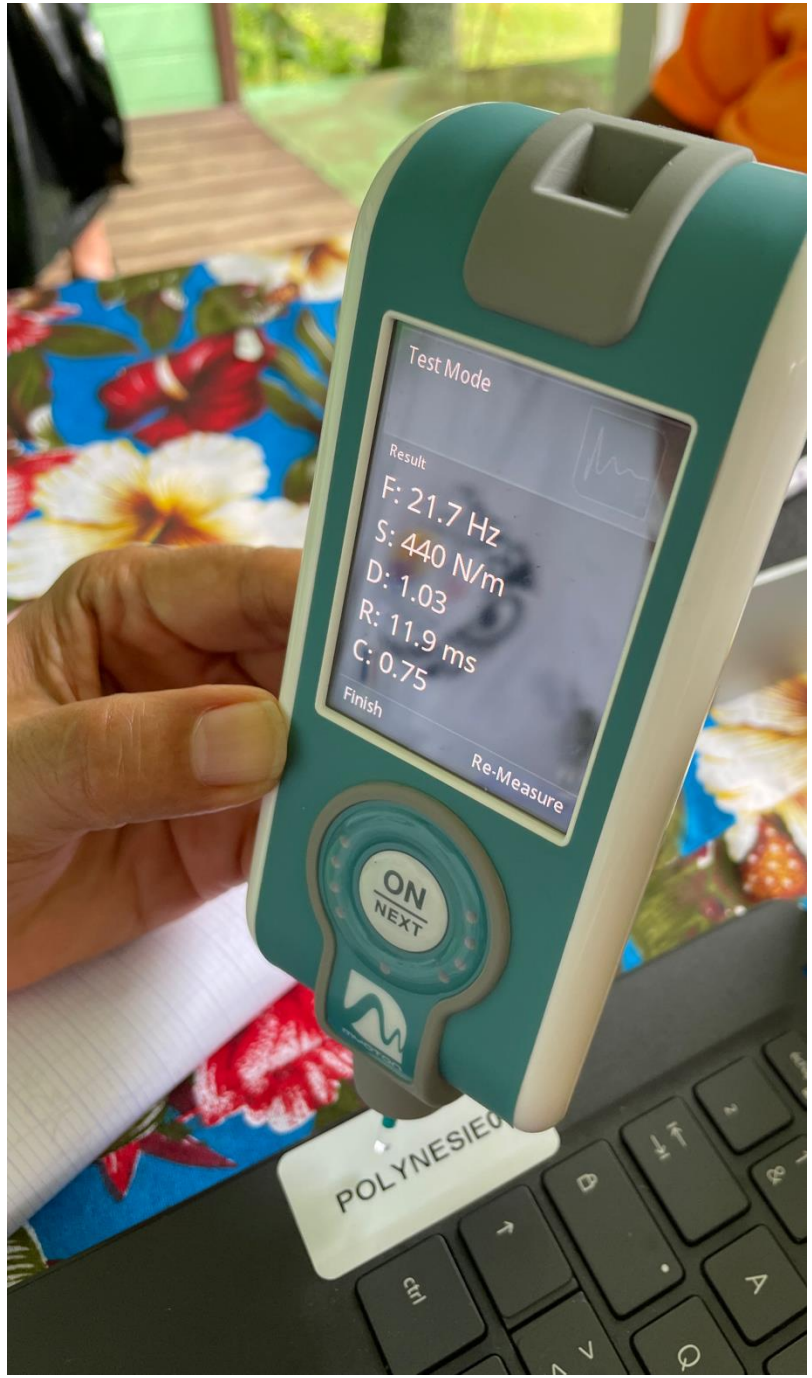

X pathogen
Bottleneck event
Original Population
Surviving Population
=
Reduced HLA diversity
Time


Tahiti



*Gout is estimated to affect **one in seven** individuals in French Polynesia*

Pascart et al., Lancet Global Health (2024)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S: 440 N/m
D: 1.03
R: 11.9 ms
C: 0.75
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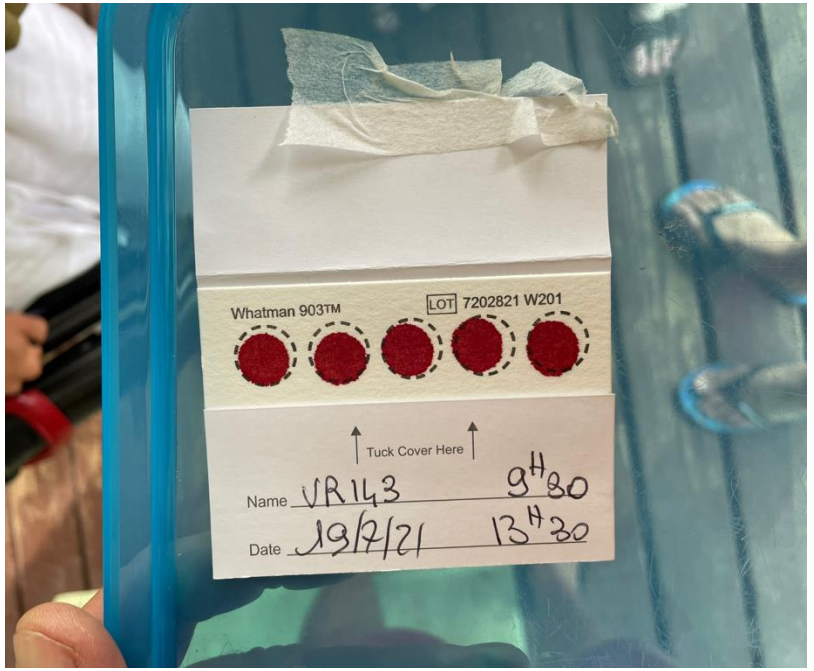
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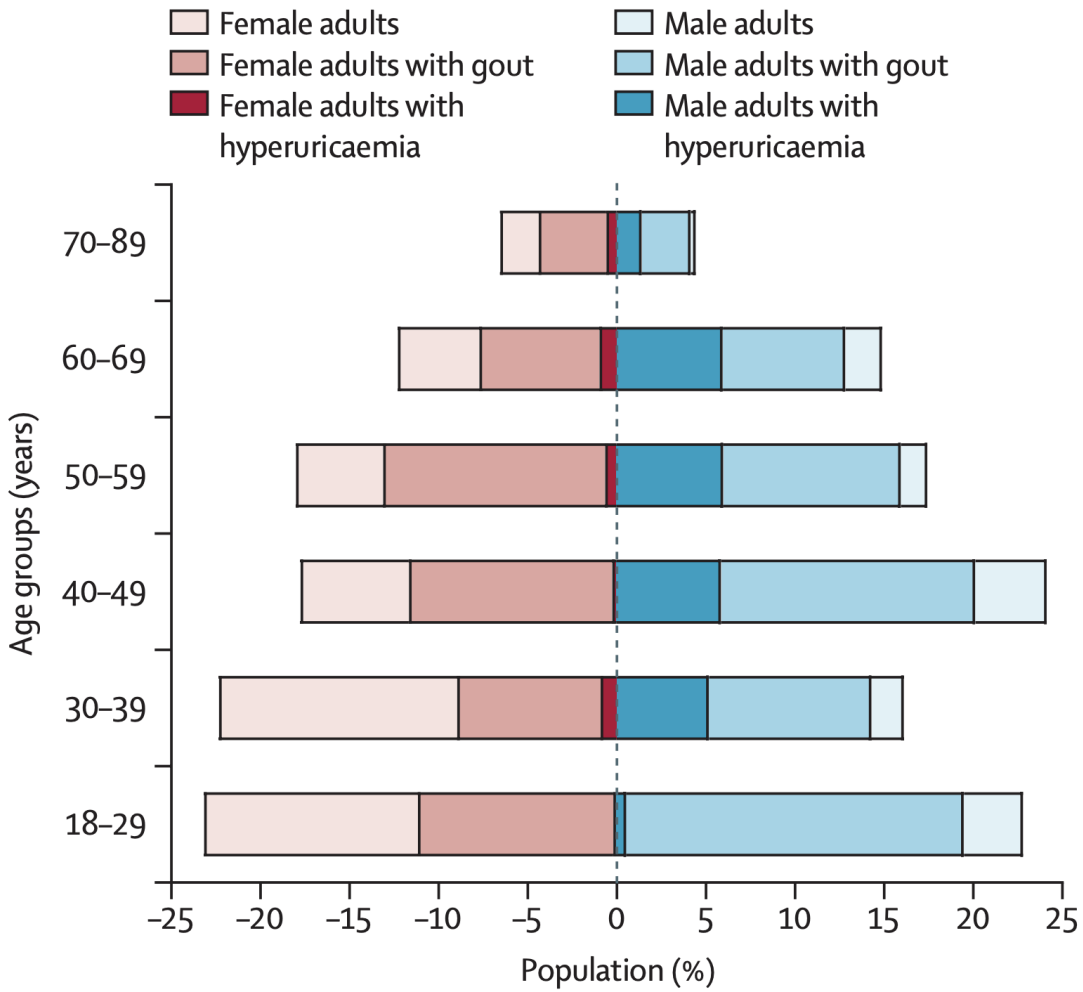
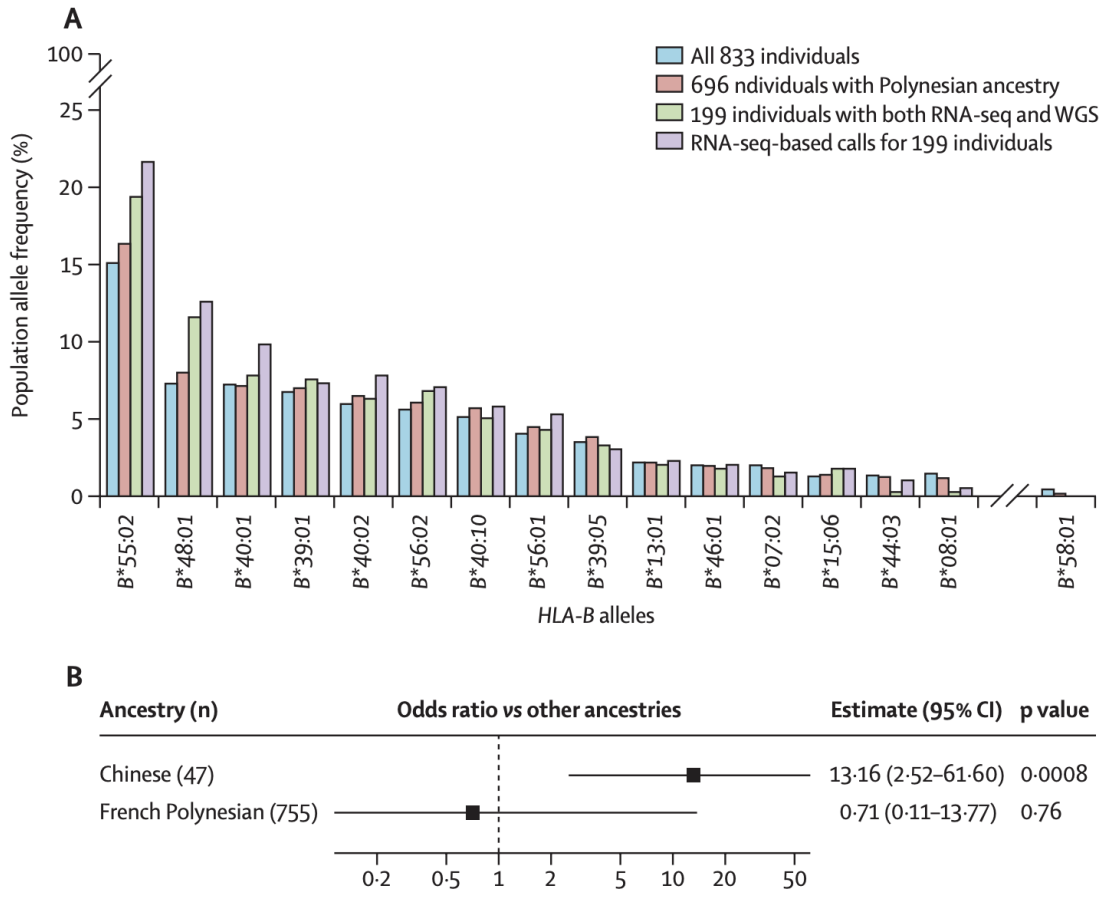
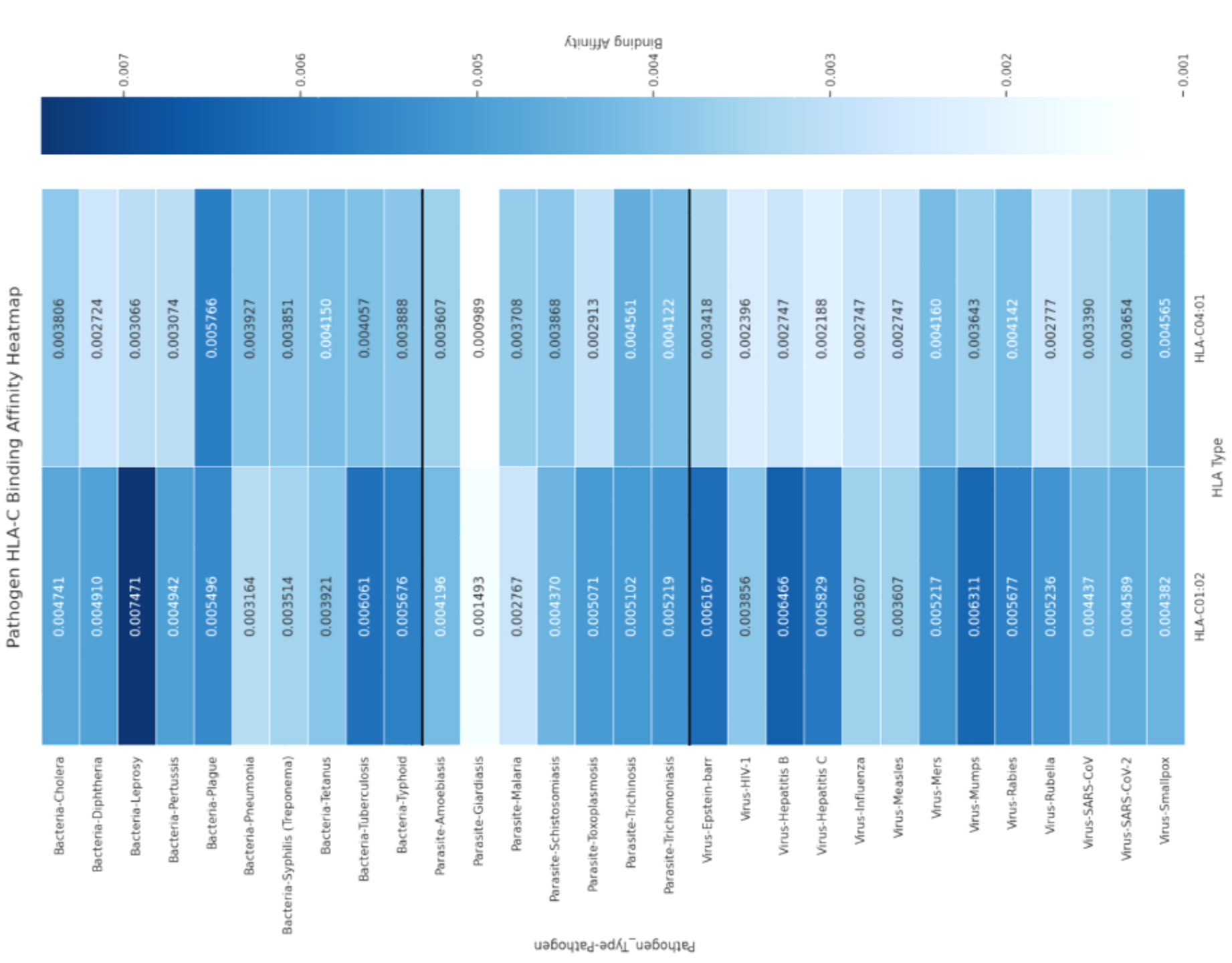
The gout epidemic in French Polynesia:
Results from the *Ma'i u'u* Territorial Survey





Pascart et al., Lancet Global Health (2024)

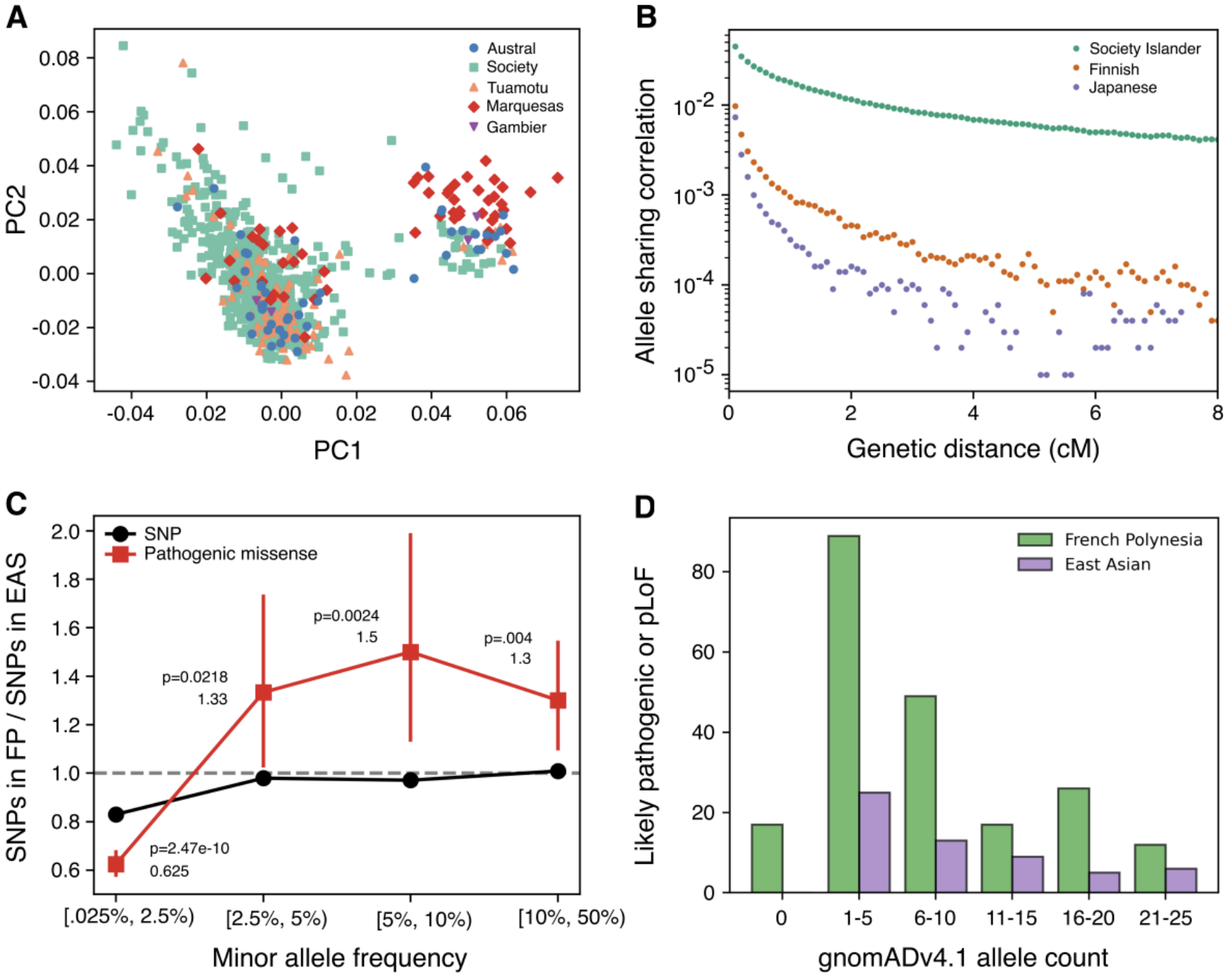
Clinically relevant MHC Calls in Pacific Islander populations:



Shanks et al.,

In Press (2025)

Ancestry-Specific Genetic Variation & Allele Sharing in Polynesian Populations



Shanks et al.,

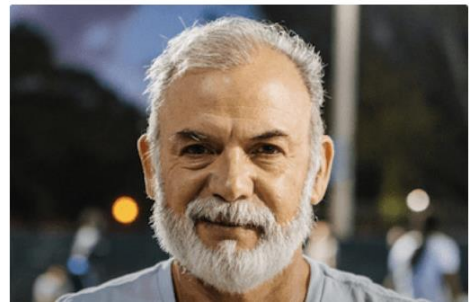
In Press (2025)

PEOPLE-DRIVEN THERAPEUTICS

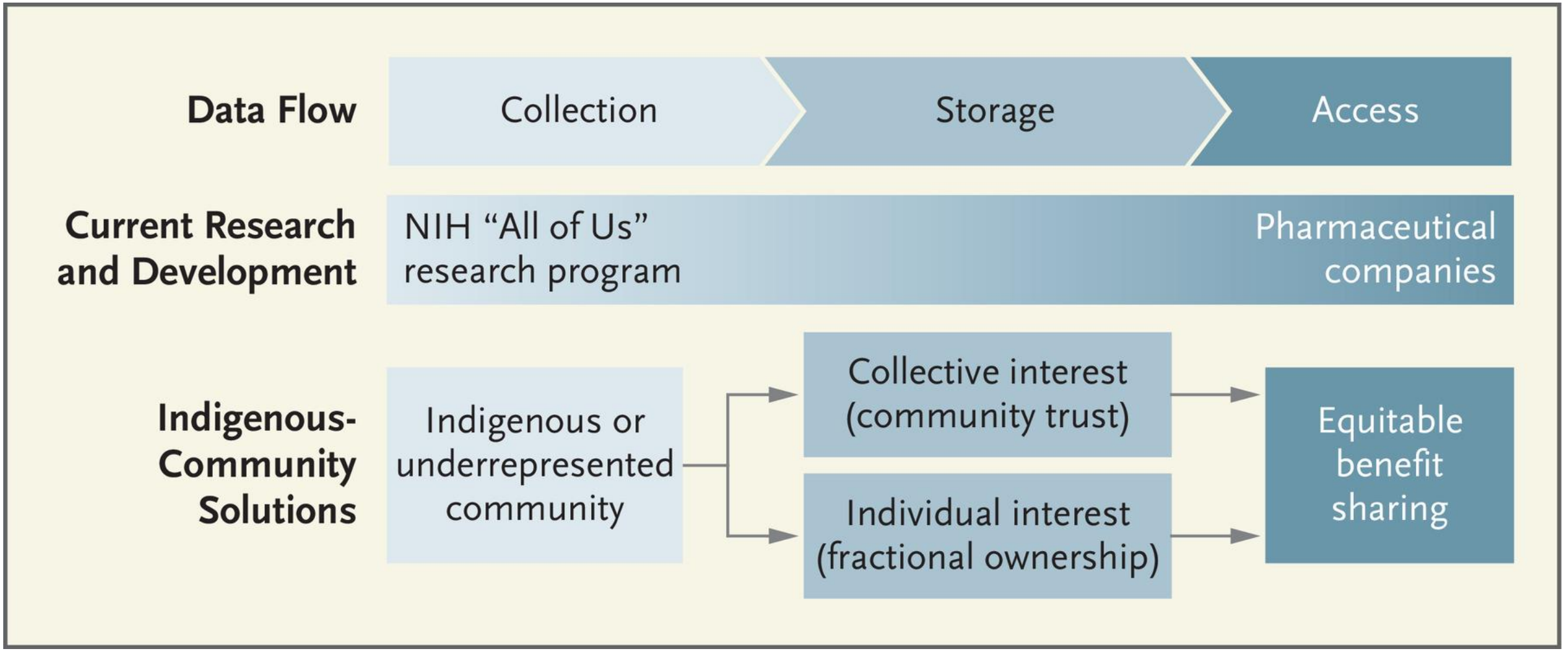
Exceptional Traits Among Us

Variant Bio is developing therapies that will improve global health by studying the genes of people with exceptional health-related traits. These examples are just some of the studies that have inspired us.

Our Approach →



Approaches to Equitable Benefit Sharing



Fox K, NEJM. (2020)

GeekWire NEWS JOBS EVENTS LISTS MEMBERS STUDIOS ABOUT Search

Seattle genomics startup Variant Bio signs deal with Novo Nordisk worth up to $50M

BY LISA STIFFLER on January 7, 2025 at 10:07 am

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Variant Bio Announces Multi-Year Research Partnership with Novo Nordisk to Discover Novel Targets for Metabolic Disease

Variant Bio

NEWS PROVIDED BY
Variant Bio, Inc.
Jan 07, 2025, 07:03 ET

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- *Collaboration leverages Variant Bio's innovative VB-Inference Platform and expertise partnering with global populations*
- *Commercial terms include an upfront payment and additional near-term R&D funding totaling up to $50 million, plus potential option and milestone payments*

SEATTLE, Jan. 7, 2025 /PRNewswire/ -- Variant Bio, a genomics-driven drug discovery company, today announced a multi-year

Drug Company to Share Revenues With Indigenous People Who Donated Their Genes

Variant Bio, a small biotech company based in Seattle, is using genetic information from Indigenous people to develop drugs for obesity and diabetes.

Listen to this article · 7:34 min Learn more

Share full article

Kaja Wasik, a geneticist and co-founder of the biotech company Variant Bio, during a field work community engagement trip to French Polynesia in 2021. Tom Martienssen

By Brendan Borrell

Jan. 7, 2025, 7:03 a.m. ET

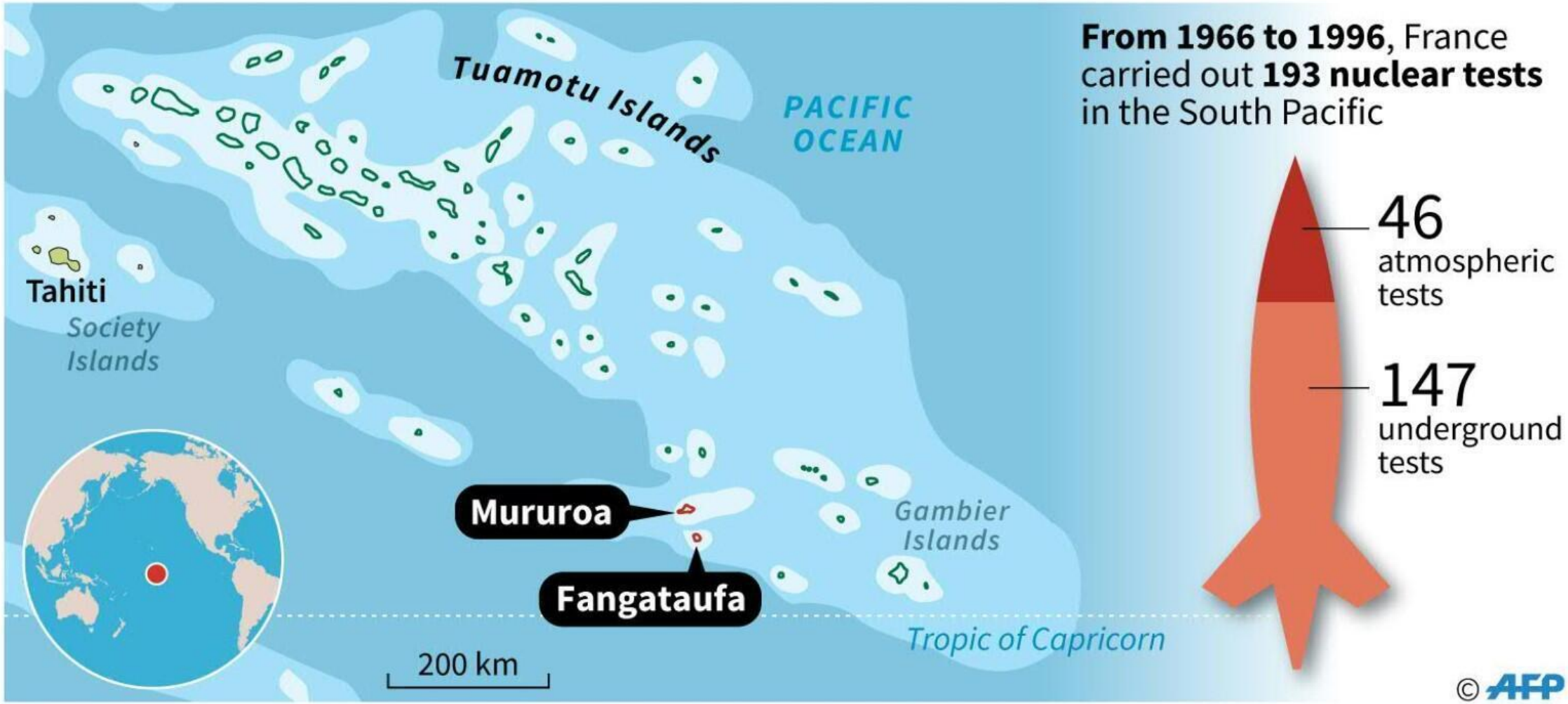

Tahitian Land Trust


Know the big currents.
And the little currents.
‘Ike i ke au nui, me ke au iki
(Said of someone who is very well versed)
–Mary Kawena Pukui
‘Ōlelo No‘eau No. 1209


$116.87
per month
France


$300.00
per month
French
Polynesia

Nuclear tests in French Polynesia




LES DIFFERENTS TYPES
DE CONSTITUTION
COUTUMIERE (NON-ECRITE)
ECRITE (MATERIELLE / FORMELLE)
« RIGIDE »: NE PEUT ÊTRE REVISEE QUE PAR UN ORGANE
DISTINCT OU UNE PROCEDURE DEDIEE
« SOUPLE »: PEUT ÊTRE REVISEE PAR LES MÊMES ORGANES & MEMES PROCEDURES SERVANT A L'ADOPTION DES LOIS ORDINAIRES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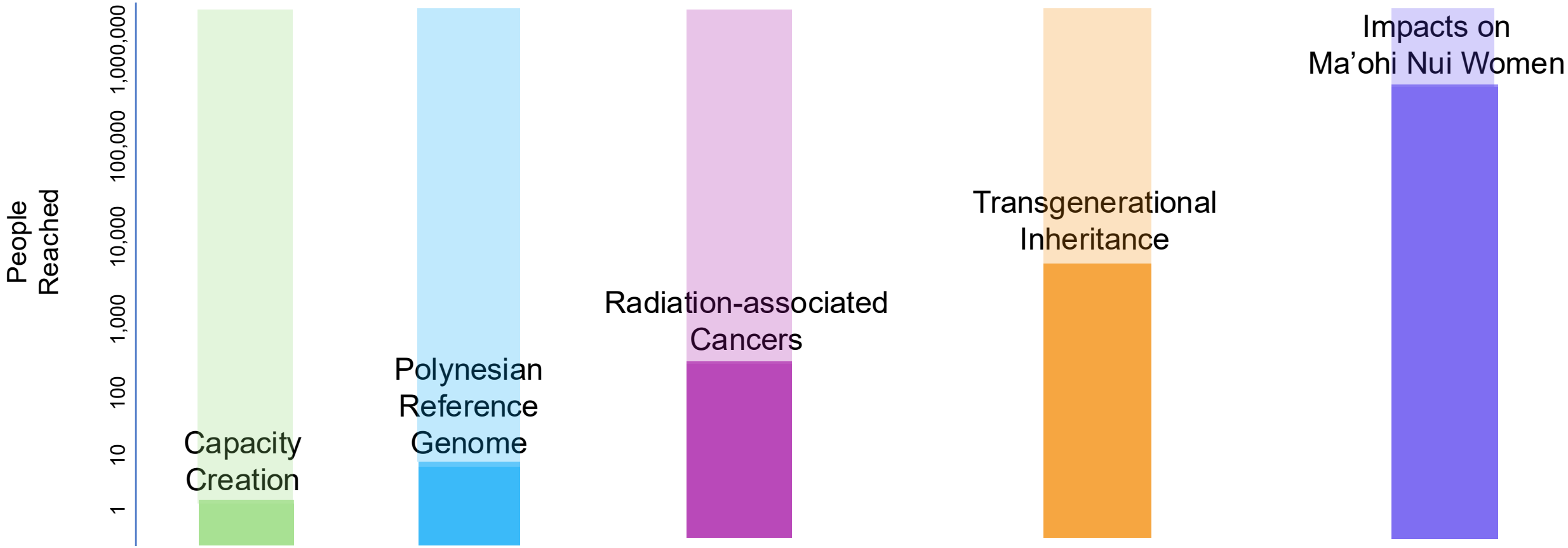
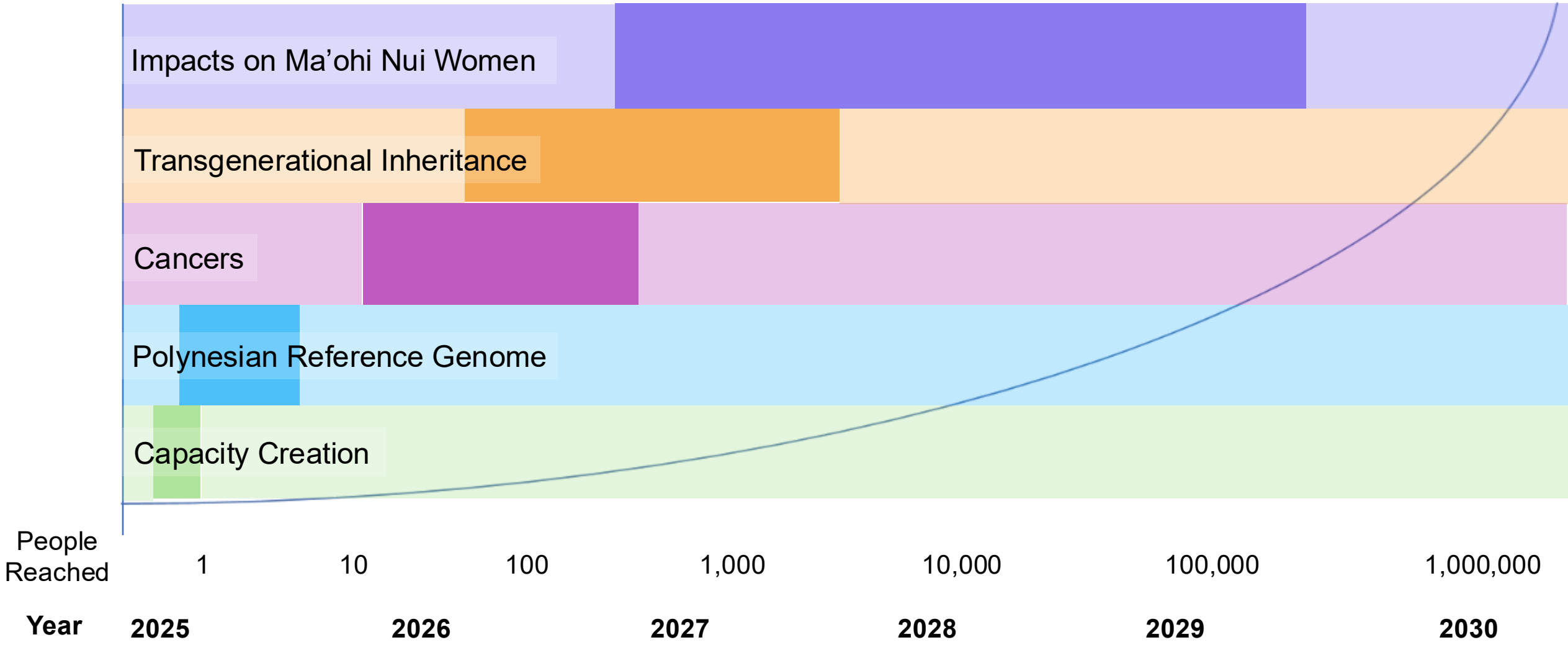
Direct Benefits for the People of French Polynesia & Globally

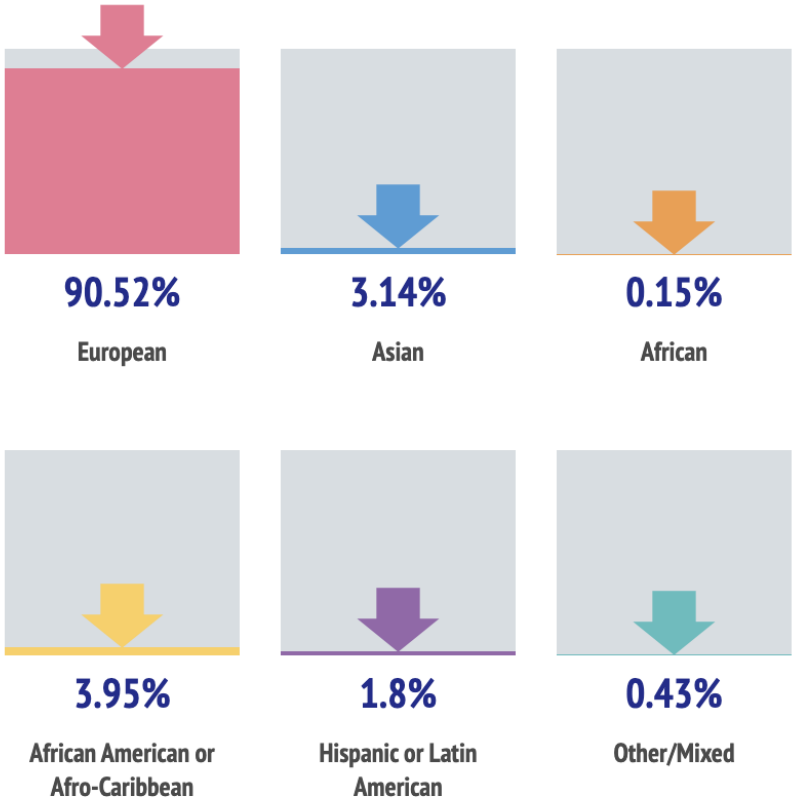


Project Impact & Timelines



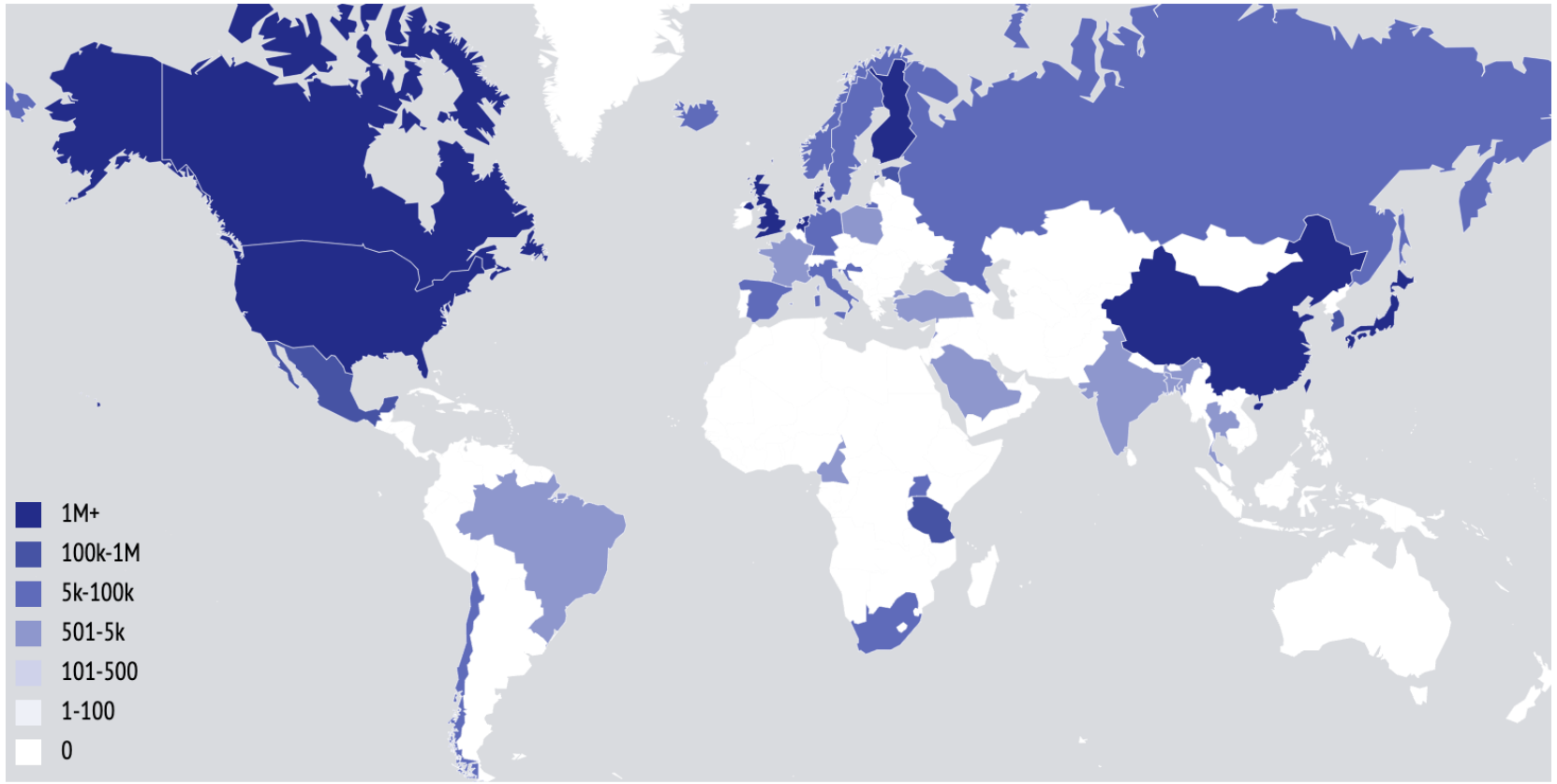
Total GWAS participants diversity

Version 1.0.0. Last check for data: 2025-04-28 00:20:34 .



Participants by country (all parent terms)

Both Stages



https://gwasdiversitymonitor.com/

***72%** of genetic discoveries have taken places in three countries

Illumina HQ, La Jolla, CA 2023

There were approximately **45,000 patents filed worldwide that mention DNA sequencing** or analysis as a significant application or method

Liddicoat & Leachman Nature (2018)


OIL
OIL
OIL
OIL
OIL


Why are we having a boom in data center development in the desert?

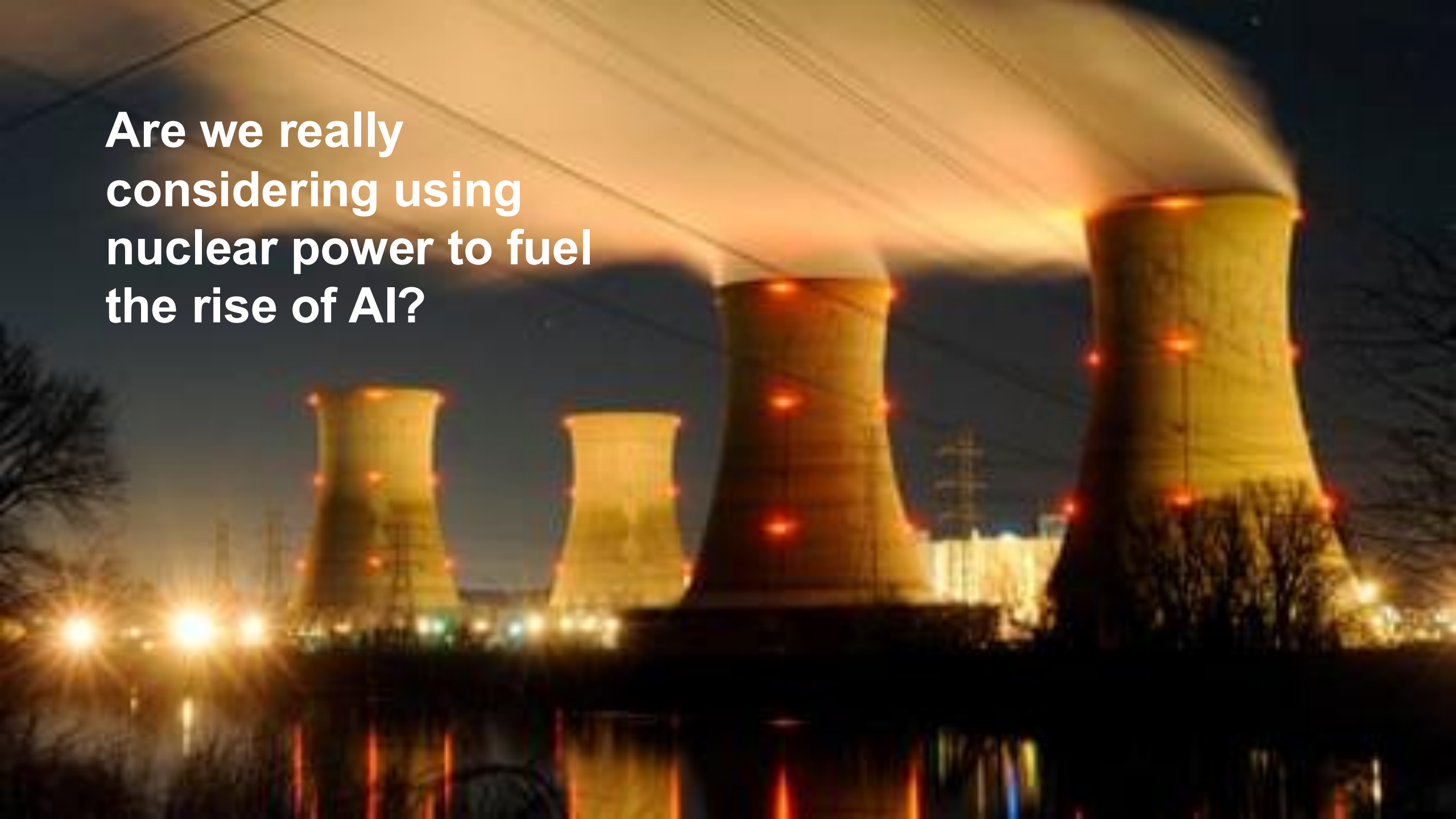
TECH · A.I.

A.I. tools fueled a 34% spike in Microsoft's water consumption, and one city with its data centers is concerned about the effect on residential supply

BY MATT O'BRIEN, HANNAH FINGERHUT AND THE ASSOCIATED PRESS
September 9, 2023 at 8:01 AM PDT

Microsoft CEO Satya Nadella discusses his company's partnership with ChatGPT maker OpenAI.
CHONA KASINGER/BLOOMBERG VIA GETTY IMAGES

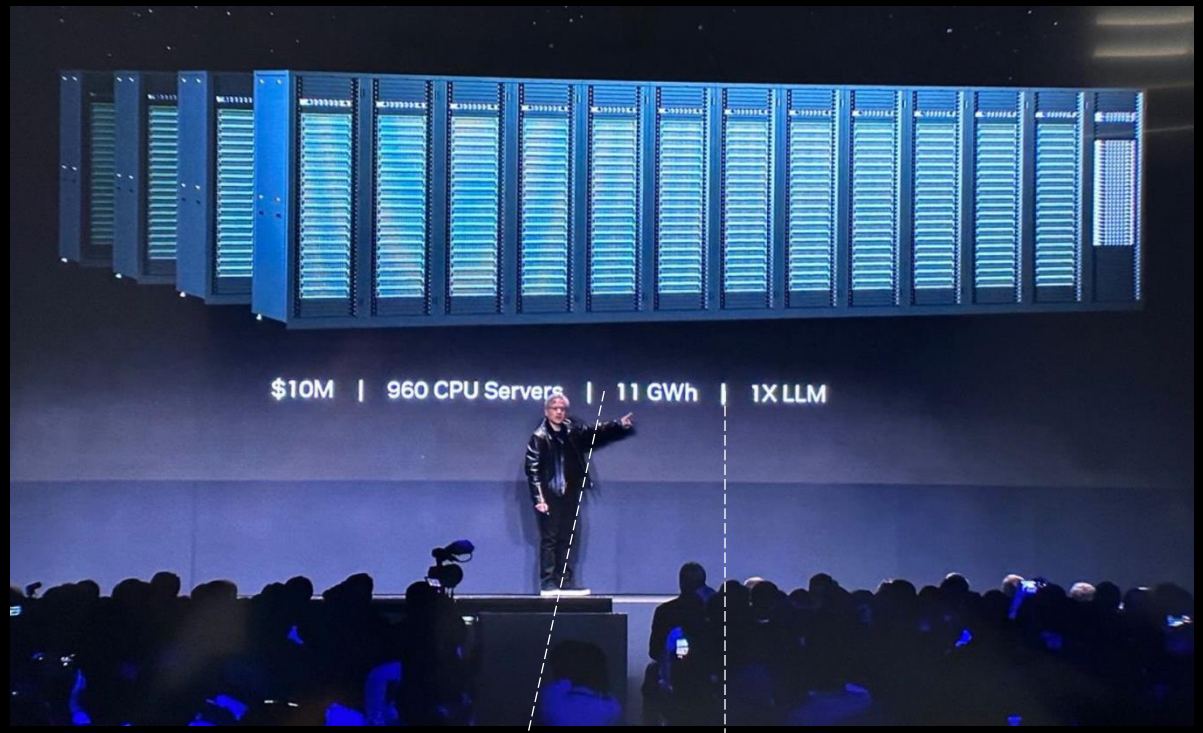
Could AI keep us dependent on natural gas for decades to come?


Are we really considering using nuclear power to fuel the rise of AI?

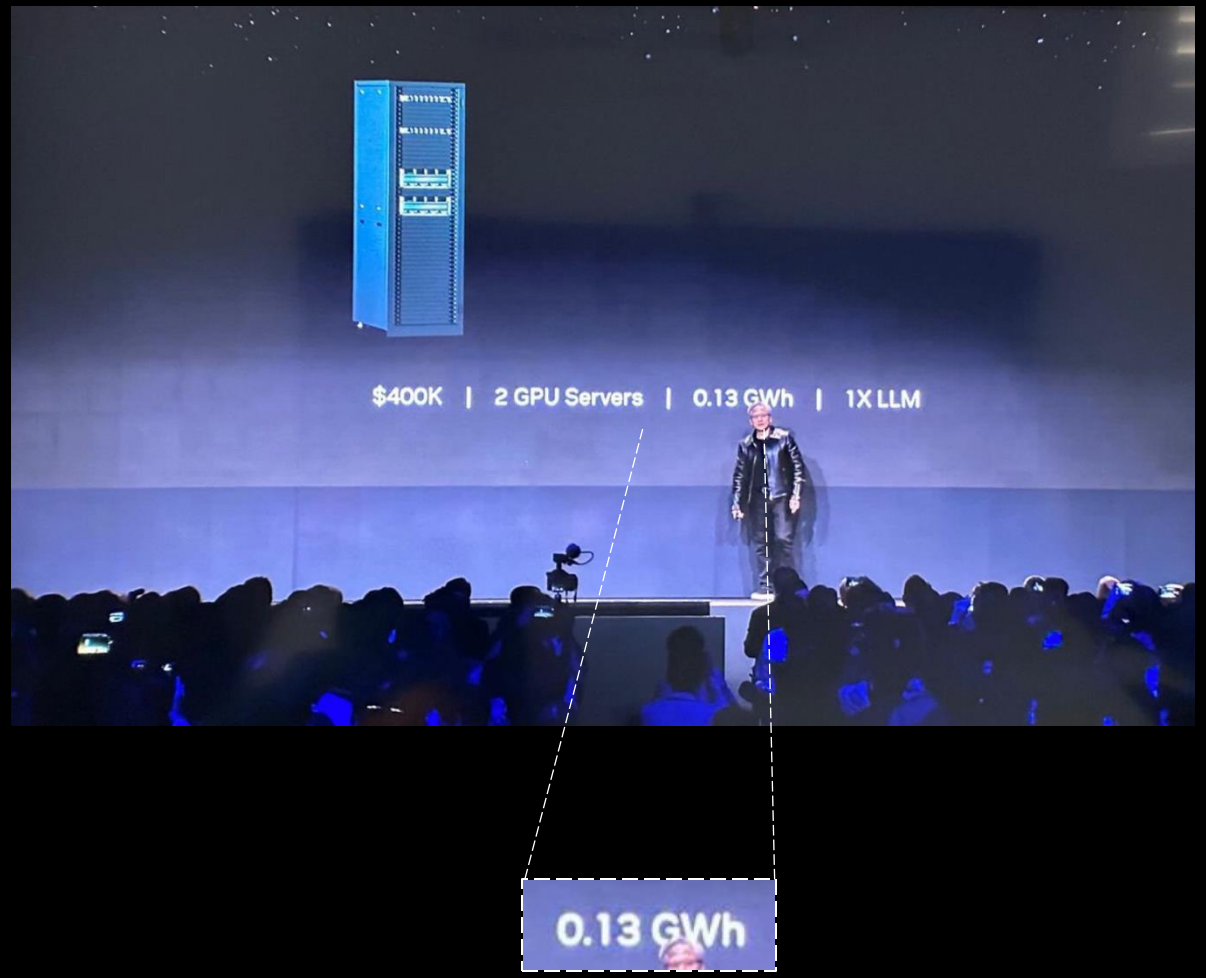
Jevons Paradox:

When improving efficiency in using a resource leads to more overall use of that resource, instead of less.
It happens because using the resource becomes cheaper and easier, which encourages more people to use it.

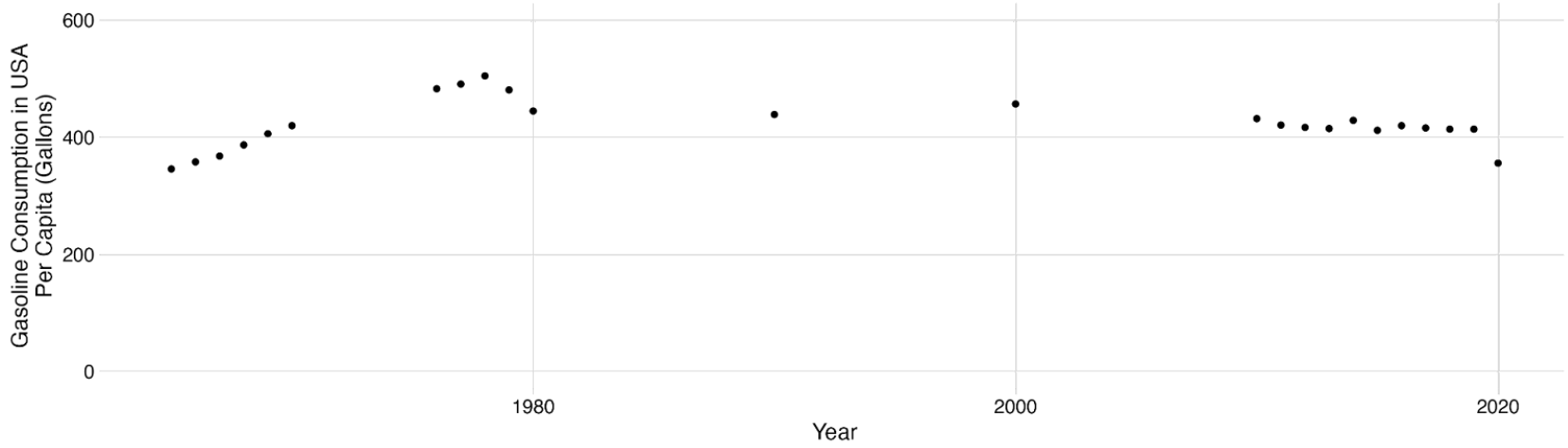
How it started

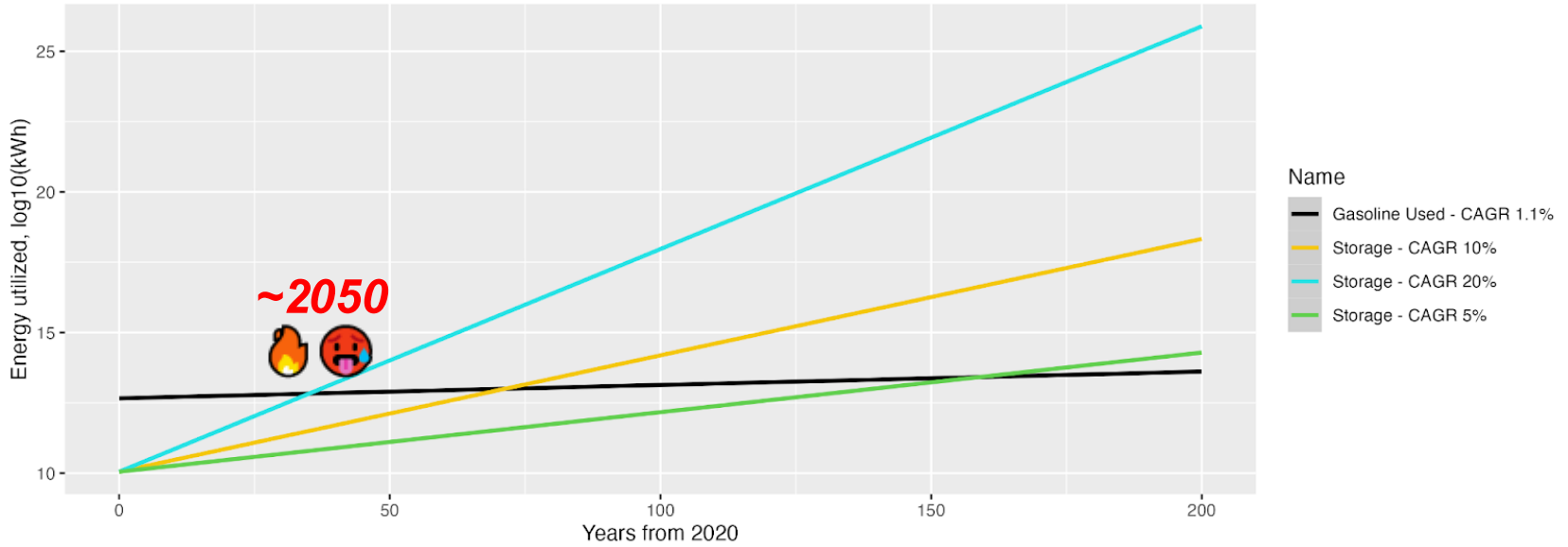


How it’s going



Estimating rates of growth in gasoline consumption + data generation

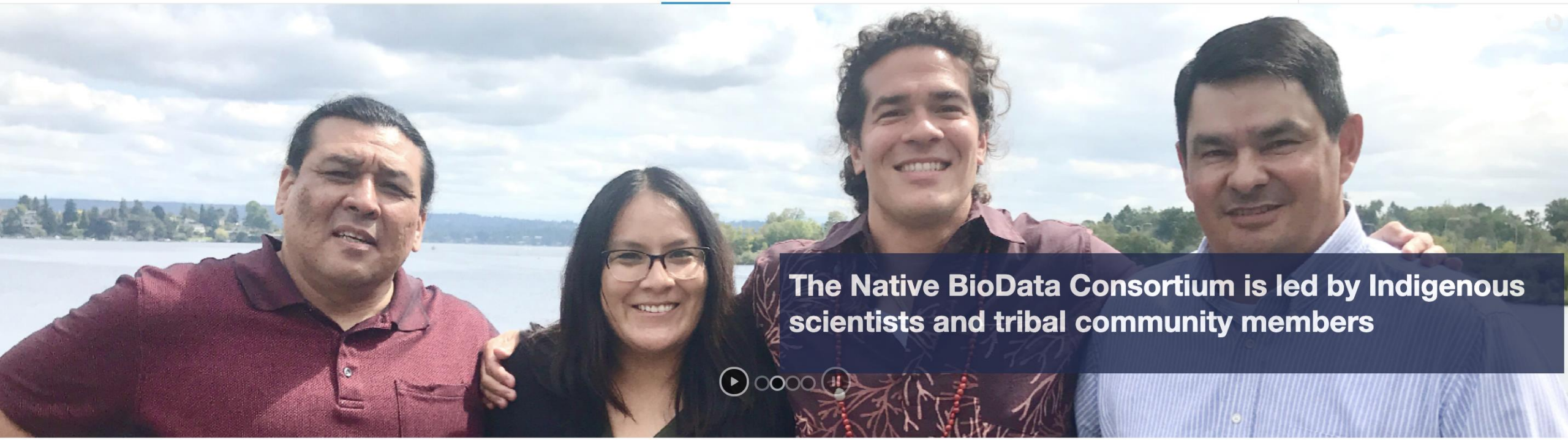




Keolu Fox & Eric Dawson (2023)

Native BioData consortium

MacArthur Foundation



RESEARCH FOR NATIVES, BY NATIVES

The **Native BioData Consortium (NBDC)** is the first 501(c)(3) nonprofit research institute led by Indigenous scientists and tribal members in the United States. As a biorepository (or “biobank”), we ensure that advances in genetics and health research benefit all Indigenous people.

Sovereignty = Sustainability

abundant intelligences

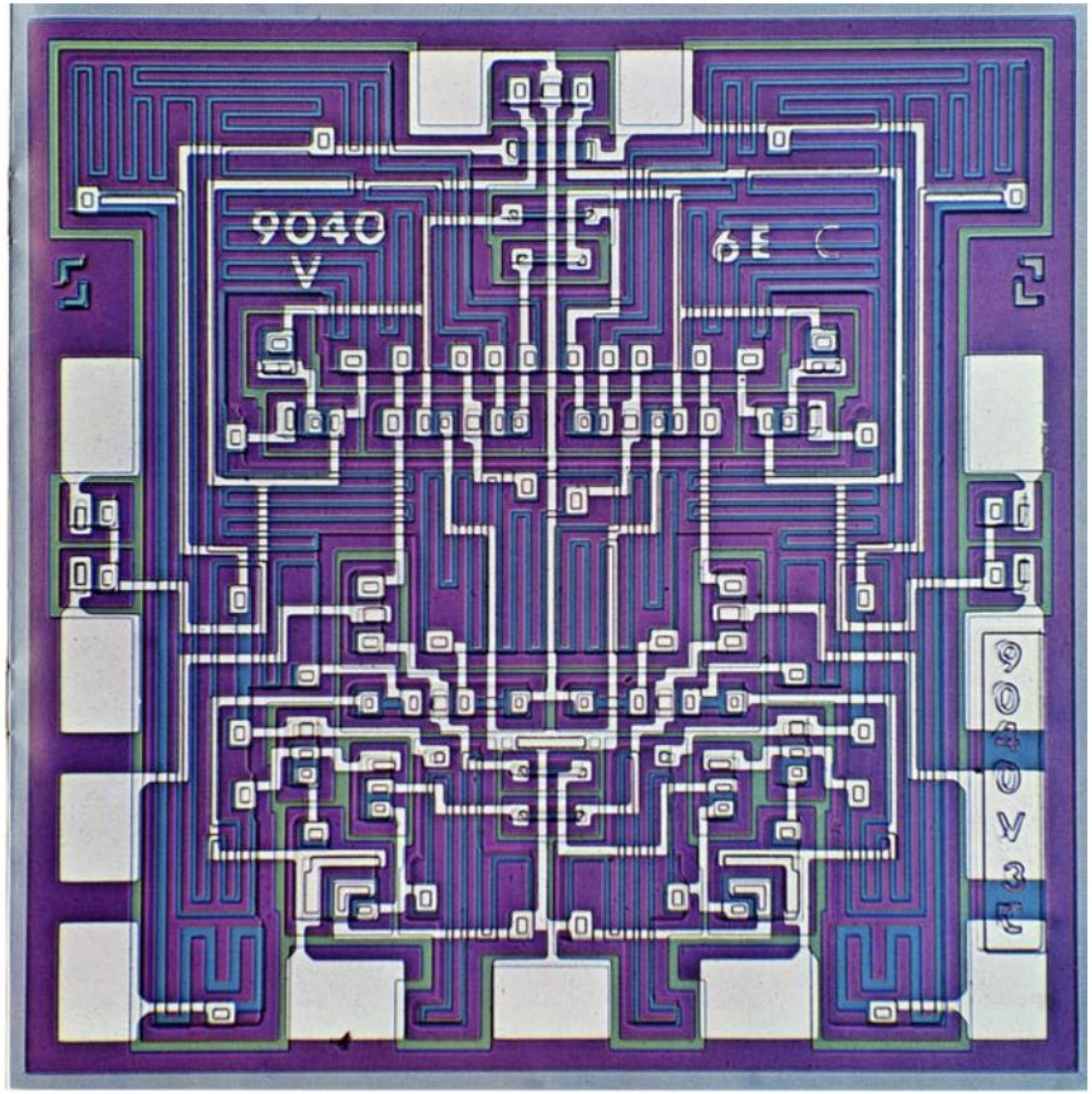
Indigenous Approaches to Artificial Intelligences

↓ Get to know us

Abundant Intelligences is an Indigenous-led research program that conceptualizes, designs, develops, and deploys Artificial Intelligence based on Indigenous Knowledge systems.

A.

B.




FAIRCHILD
SEMICONDUCTOR

We don’t have to accept the narrative that AI must be extractive!

1. **Circularity**: Designing systems where nothing is wasted.

2. **Technology Shocks**: Challenging the status quo and repurposing what already exists.

3. **Community Sovereignty**: Empowering all communities — especially those historically left out — to shape and benefit from AI.

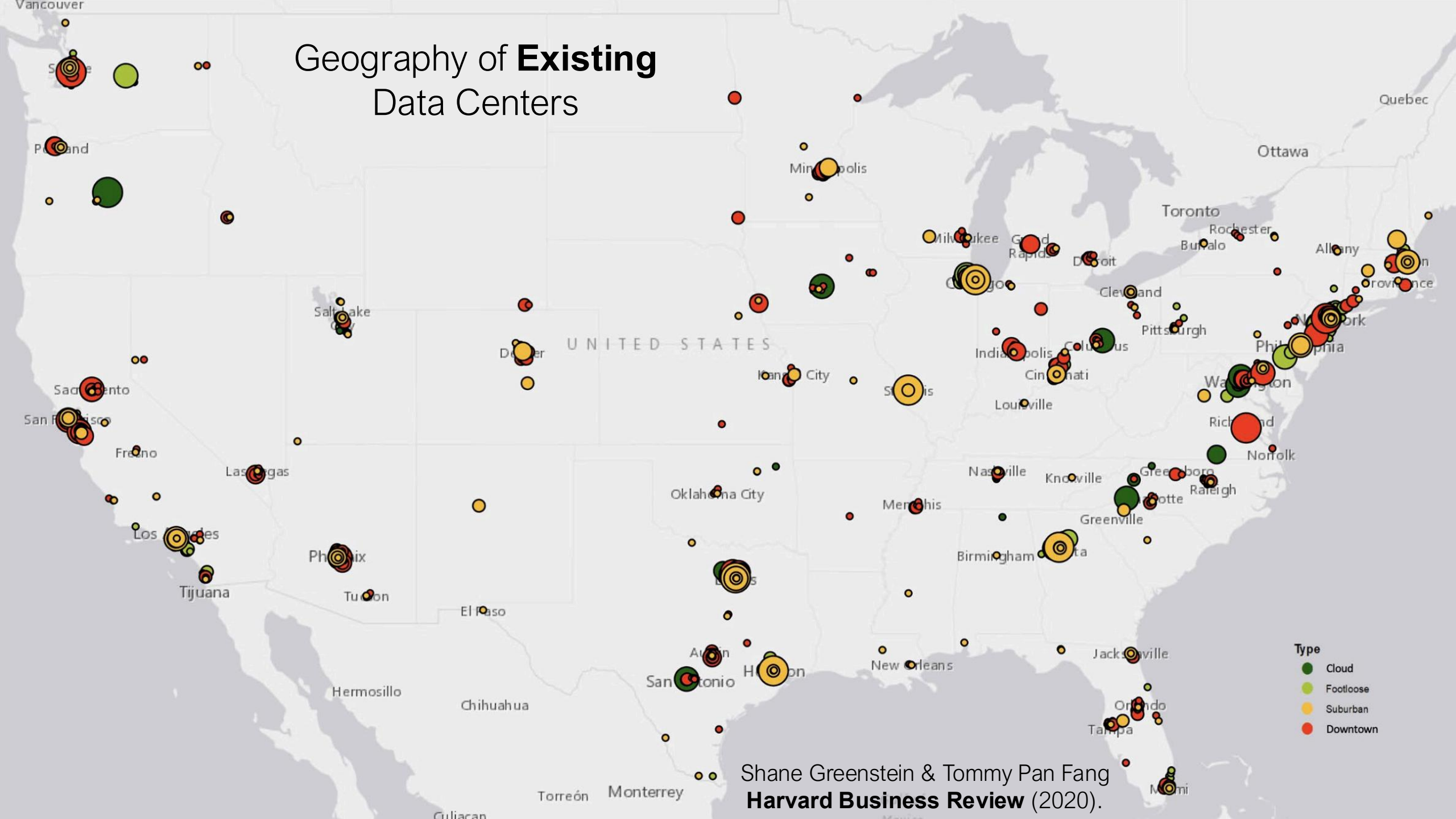

Circularity:
Designing systems where nothing is wasted.

Ahupua'a land management system
National Geographic Magazine, (*Indigenous Futures Issue*)

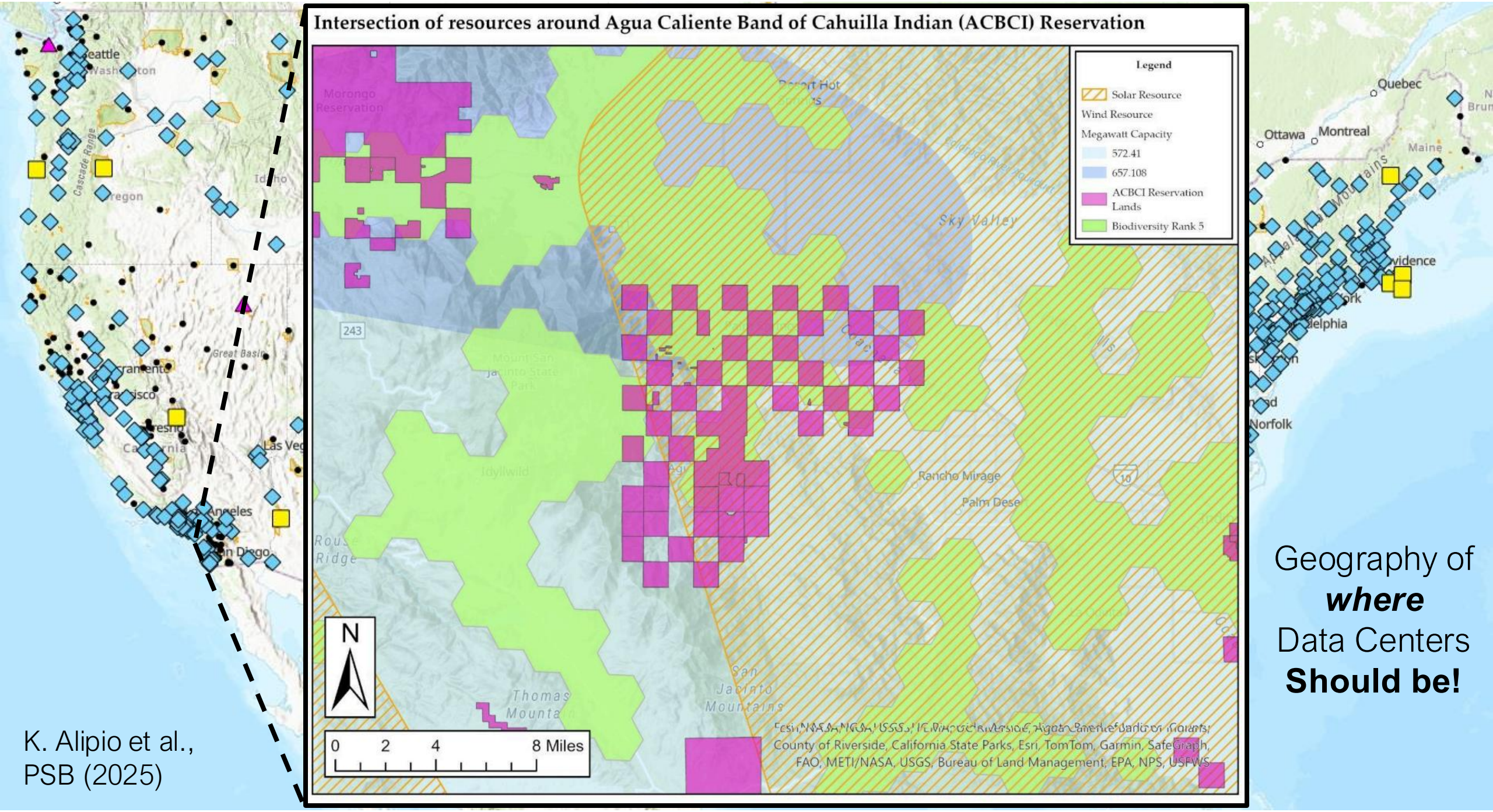
What if we use knowledge from *circular systems* to design data centers?

1. Resource Flow and Reciprocity
2. Self-Sufficiency and Closed-Loop Systems
3. Adaptive Management

Geography of **Existing** Data Centers



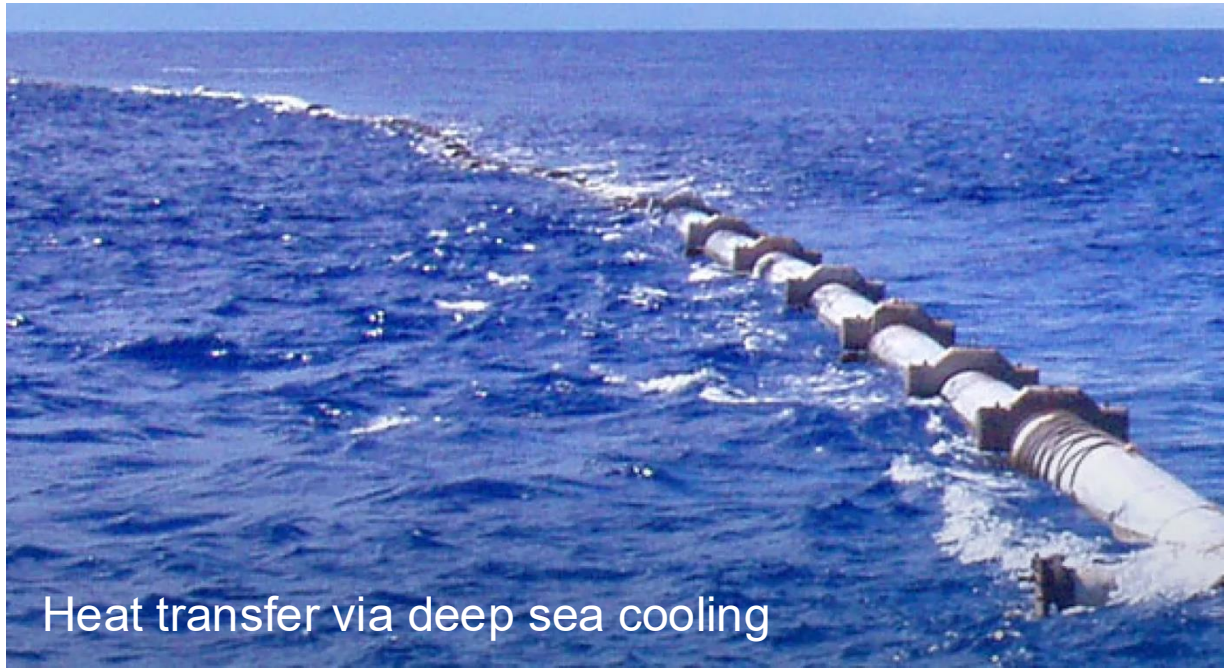
Shane Greenstein & Tommy Pan Fang
Harvard Business Review (2020).

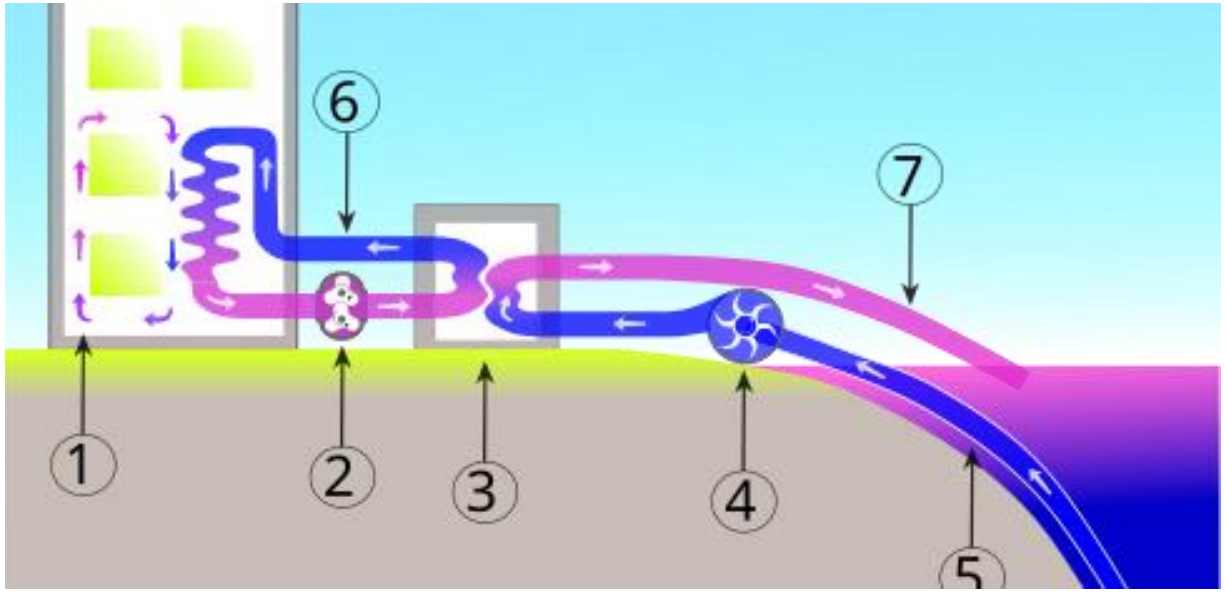


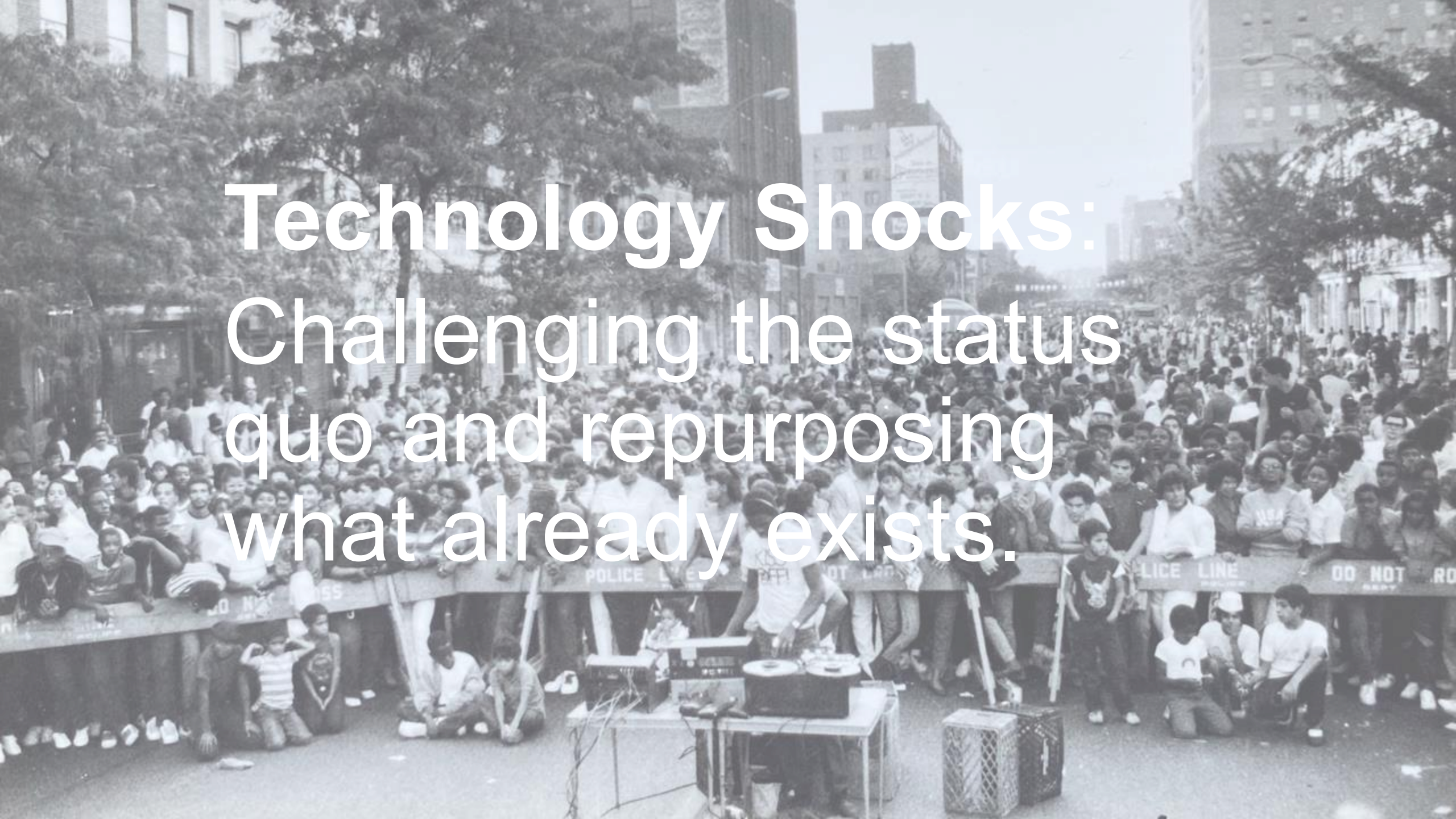
K. Alipio et al.,
PSB (2025)

Geography of
where
Data Centers
Should be!

PROJECT MOANA: *Sea Water Air Conditioning (SWAC) Data Center*







Technology Shocks:

Challenging the status quo and repurposing what already exists.

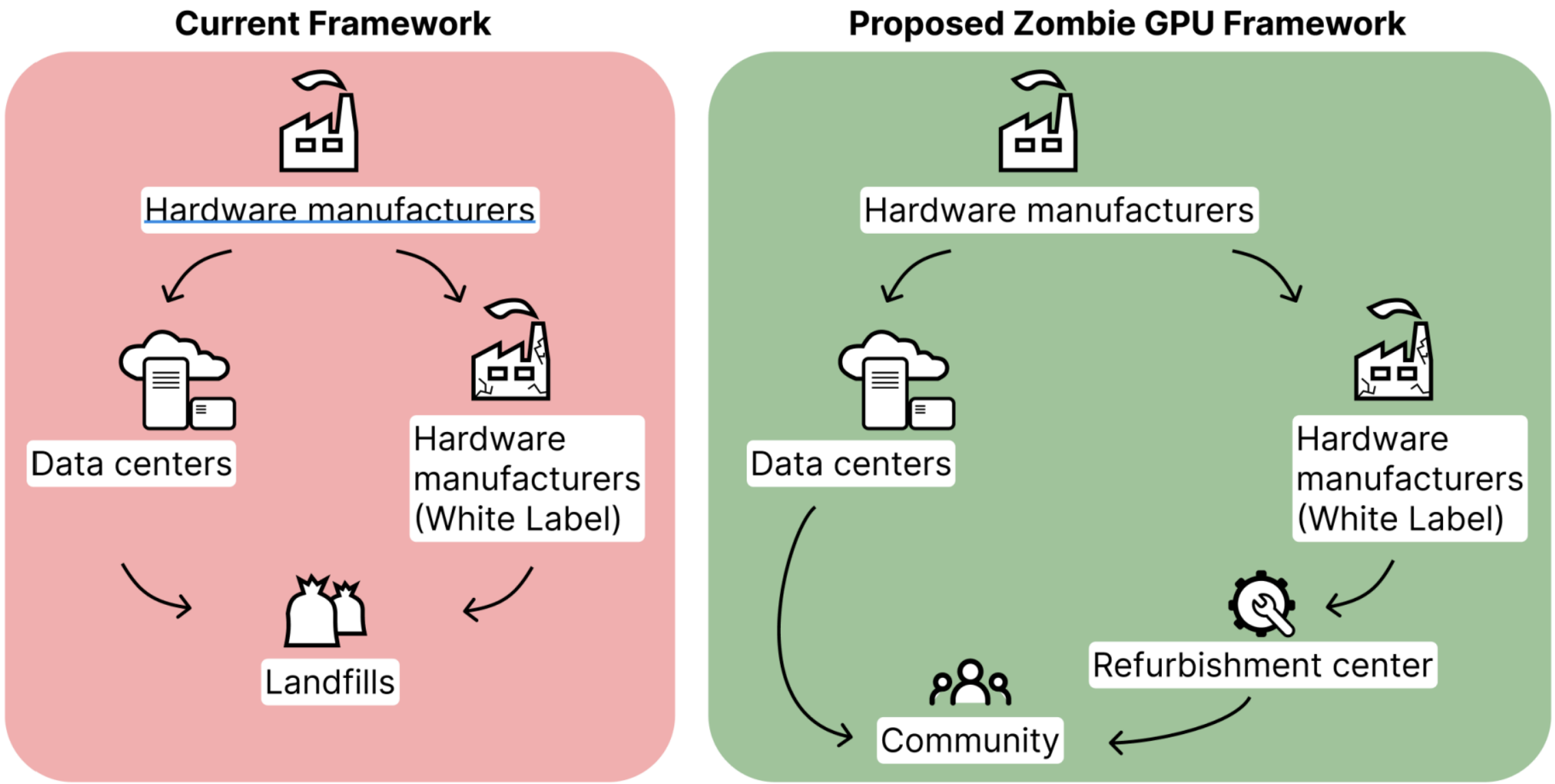
Half Dome in Yosemite National Park — has a mass of around **50 billion to 100 billion kg**

- **62 billion kg** of e-waste generated globally in 2022
- **Since 2010**, the growth of e-waste generation is **outpacing the formal collection and recycling by a factor of 5**

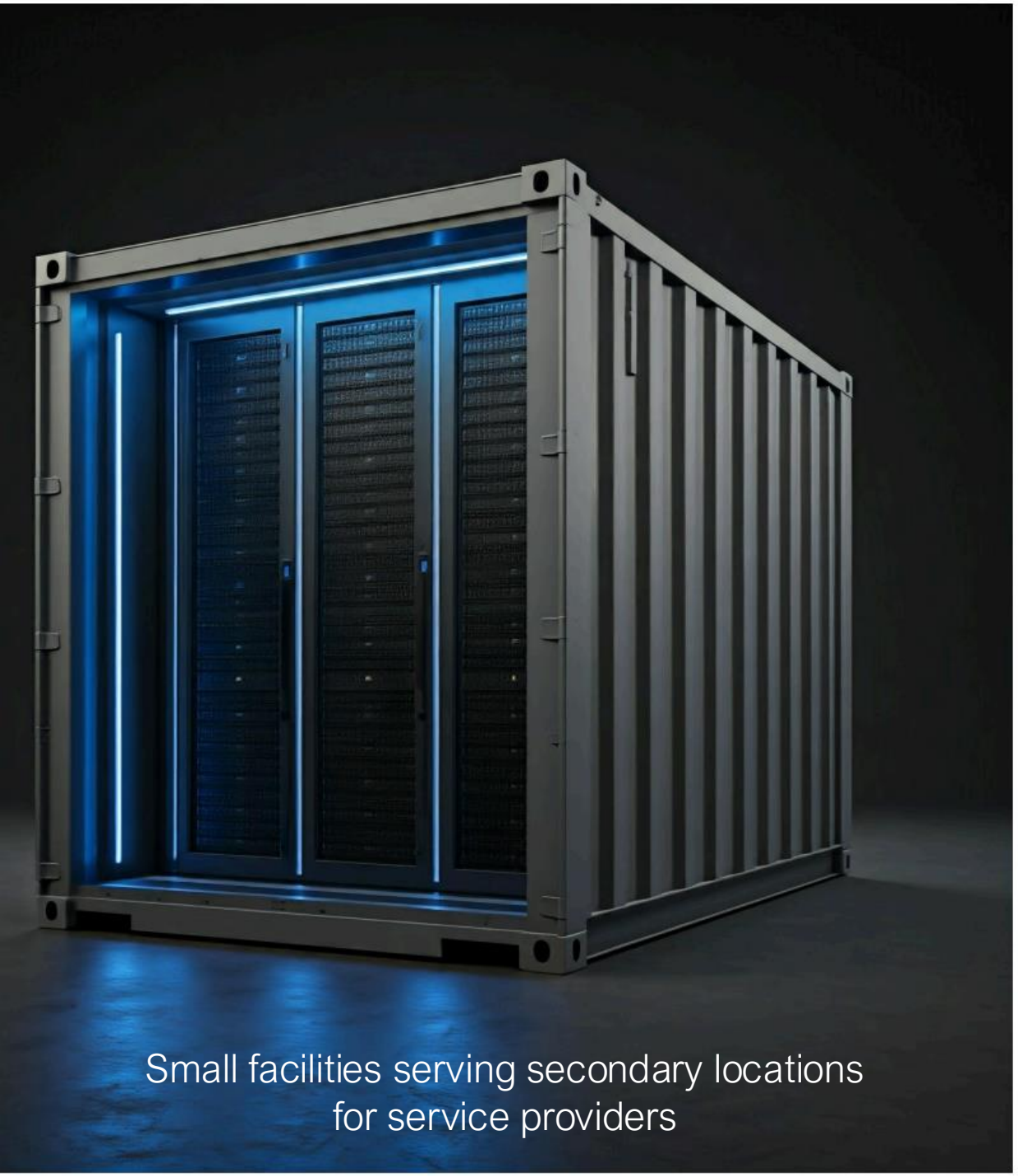
Graveyard of "Zombie GPUs"

Category	Annual Shipments	Relevant Timeframe	Total Units
Consumer Discrete GPUs	50million units	5 years (2019–2023)	250 million units
Data Center GPUs	1 million units	5 years (2019–2023)	5 million units
Total Estimate			***255 million units***

Rajput et al., PSB (2025)



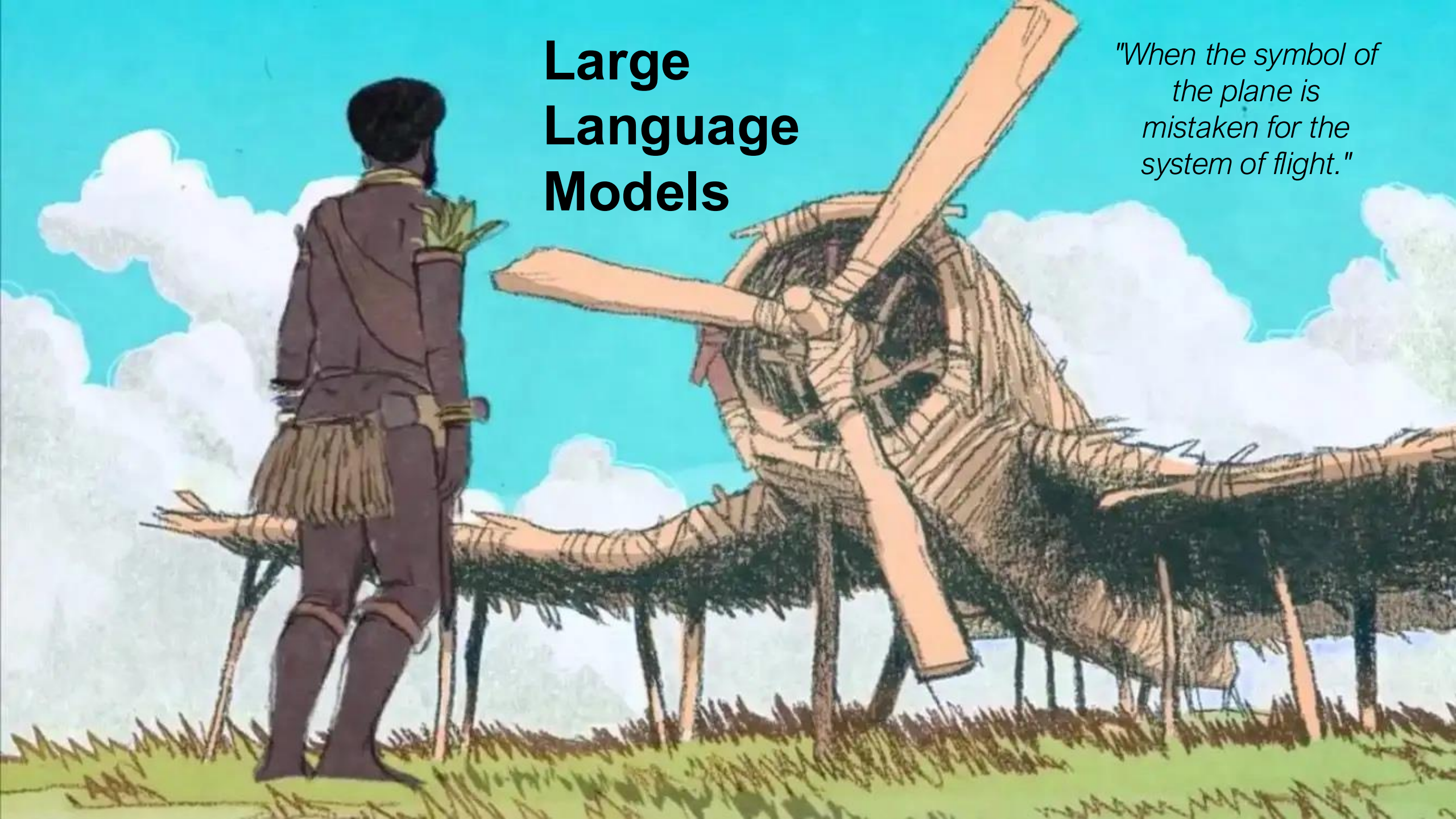
Rajput et al., in prep (2025)

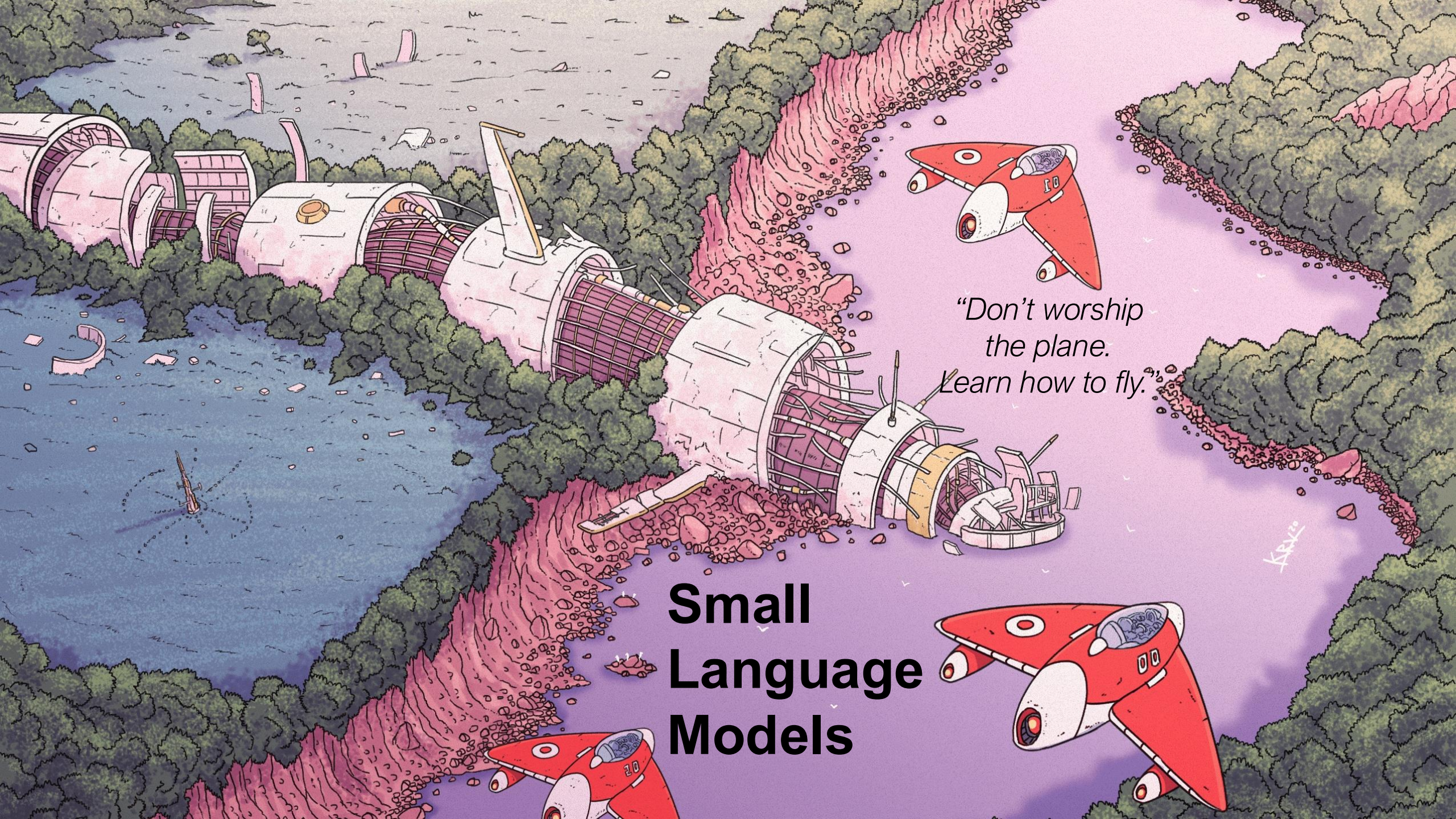


Small facilities serving secondary locations for service providers

Modularized sites near an organization's network edge

Community Sovereignty:
Empowering all communities — especially those historically left out — to shape and benefit from AI.


Large
Language
Models
"When the symbol of the plane is mistaken for the system of flight."


“Don’t worship
the plane.
Learn how to fly.”
Small
Language
Models

We don’t have to accept the narrative that AI must be extractive!

We can choose a trajectory guided by Indigenous values:

1. **Circularity**: Designing systems where nothing is wasted.

2. **Technology Shocks**: Challenging the status quo and repurposing what already exists.

3. **Community Sovereignty**: Empowering all communities — especially those historically left out — to shape and benefit from AI.


1872
2020

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PRESENTED TO

DR. KEOLU FOX

IN RECOGNITION OF

YOUR WORK REGARDING EFC 574 - EMPOWERING FUTURE COMPUTING ACROSS INDIAN COUNTRY

APRIL 28, 2025
DATE

JUAN VARGAS
MEMBER OF CONGRESS
FIFTY-SECOND DISTRICT, CALIFORNIA

NATIONAL ACADEMIES Sciences Engineering Medicine

Proceedings of a Workshop—in Brief

Convened June 4, 2025

Artificial Intelligence for Sustainability: Maximizing Benefits for the United States

Proceedings of a Workshop—in Brief

Mahalo nui ☺ – Questions?