Biosecurity:
Escalating Technological, Geopolitical and National Security Complexities

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BioSecurity and Pandemic Resilience: Winter 2025

BIOE 122, EMED 122/222, PUBLPOL 122/222

Stanford University School of Medicine, January 22, 2025

Slides available @ https://casi.asu.edu/presentations/

Albrecht Dürer, 1498

The Four Horsemen of the Apocalypse

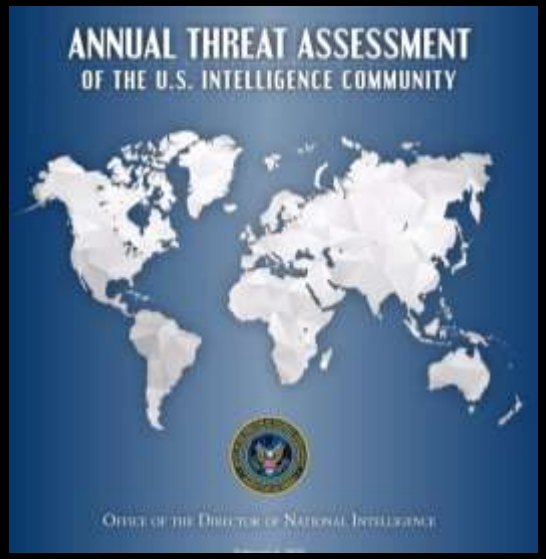
- pestilence
- war
- famine
- death

Albrecht Dürer, 1498

The Horsemen of the Apocalypse

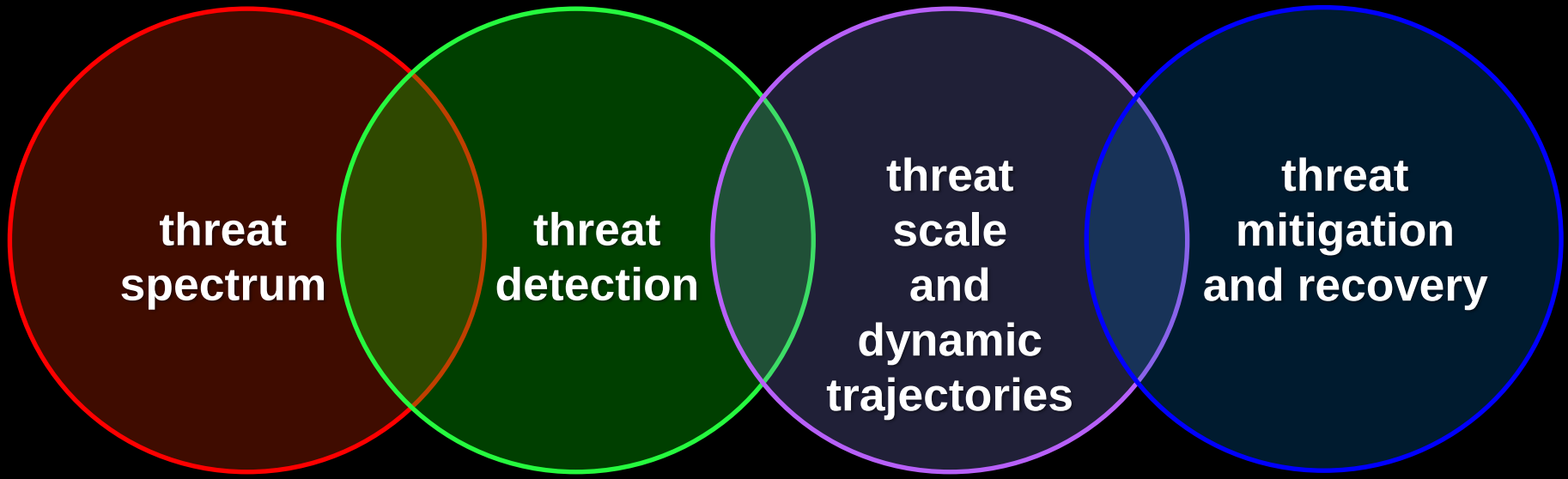
- pestilence
- war
- famine
- death
- (social media will arrive later five centuries)

Biosecurity



- more than protection against infectious diseases (natural or engineered)
- a complex spectrum of multi-dimensional events with potential to cause major disruptions in societal stability and/or increase risk of global conflict
- escalating complexity driven by global connectivities and acceleration of technology innovation
- substantial expansion of theoretical dual-use applications from convergence of advances in biotechnology, synthetic biology and AI
- parallel strategic importance for national economic competitiveness and military advantage of the industrial bioeconomy
- increased importance of biosecurity and the bioeconomy in global trade, foreign policy and military strategy

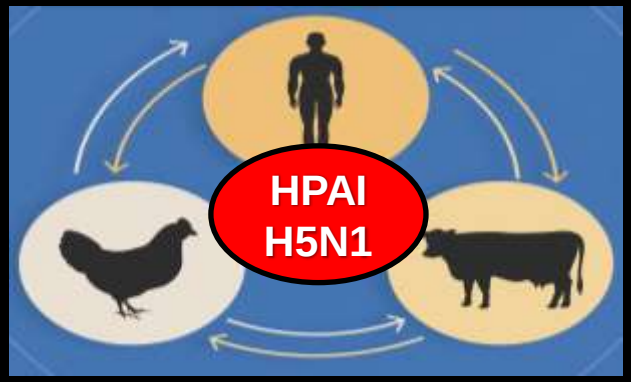
Biosecurity:
Preparedness, Response, Resiliency & Recovery (PR3) Capabilities



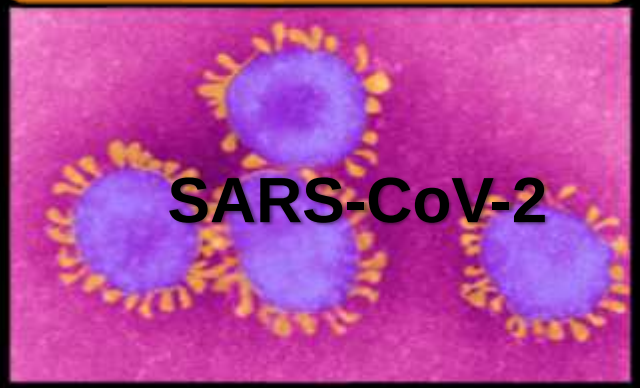
The Relentless Ever-Changing Dynamics of Infectious Diseases

old foes resurgent: Rx – resistance

omnipresent pandemic threats

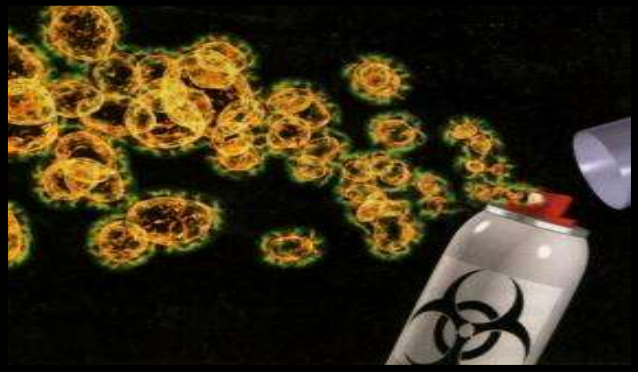


new foes: emerging infectious diseases



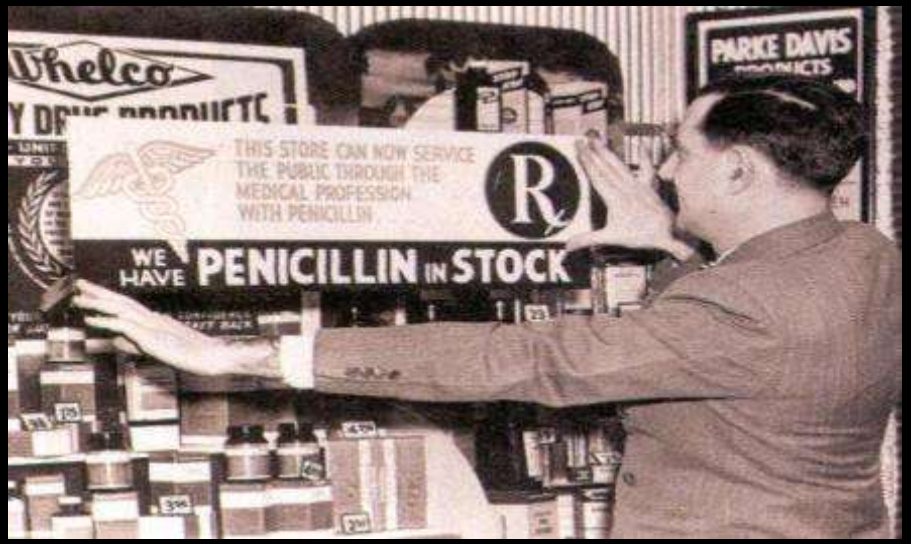
climate change and new vector ranges

bioterrorism and bioweapons

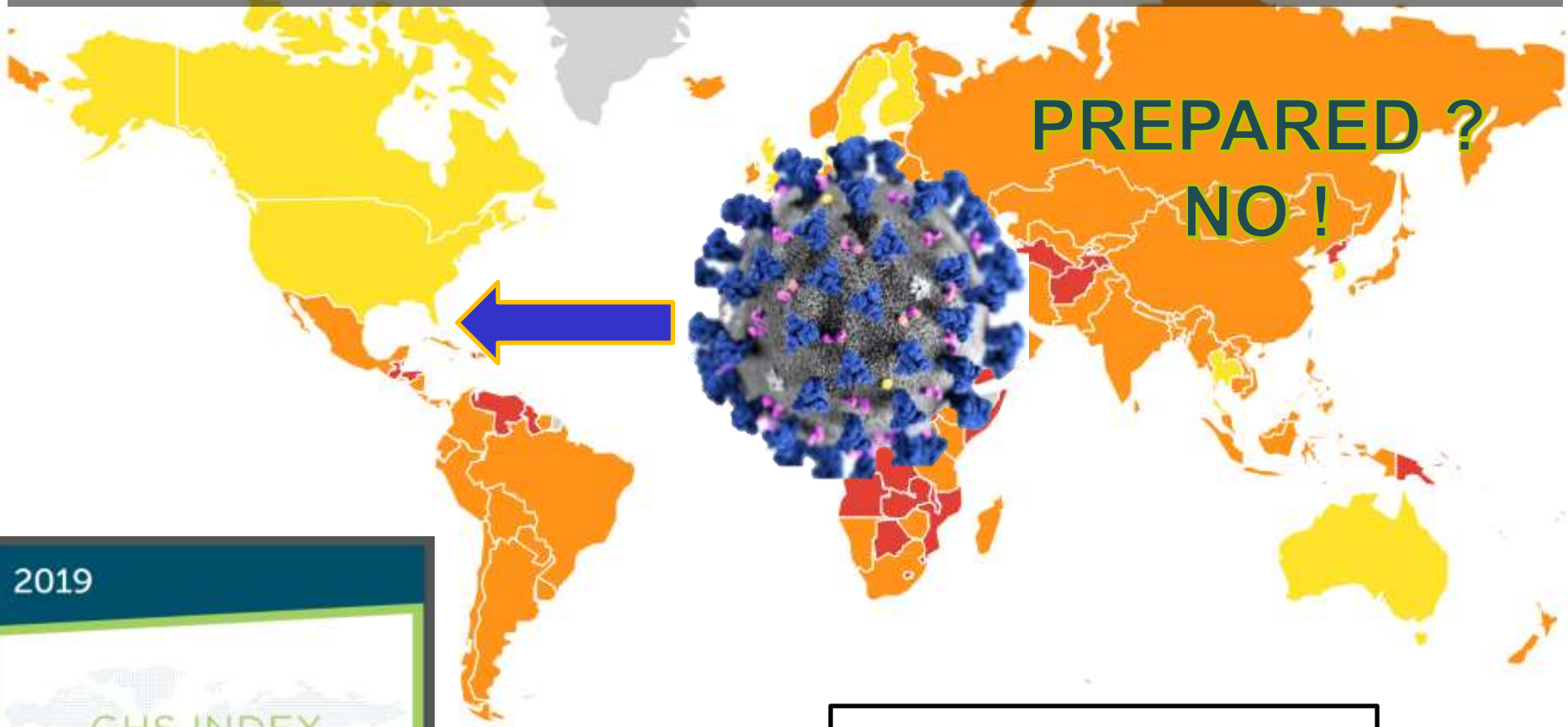


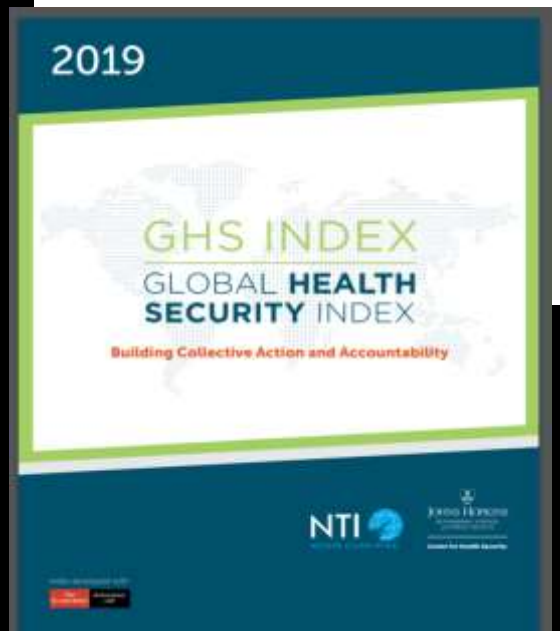
dual-use research of concern

Comfort and Complacency: The Enemies of Vigilance and Preparedness



SARS-CoV-2 Revealed Major Shortcomings in US Public Health Capabilities and Fragility of Healthcare Delivery Systems



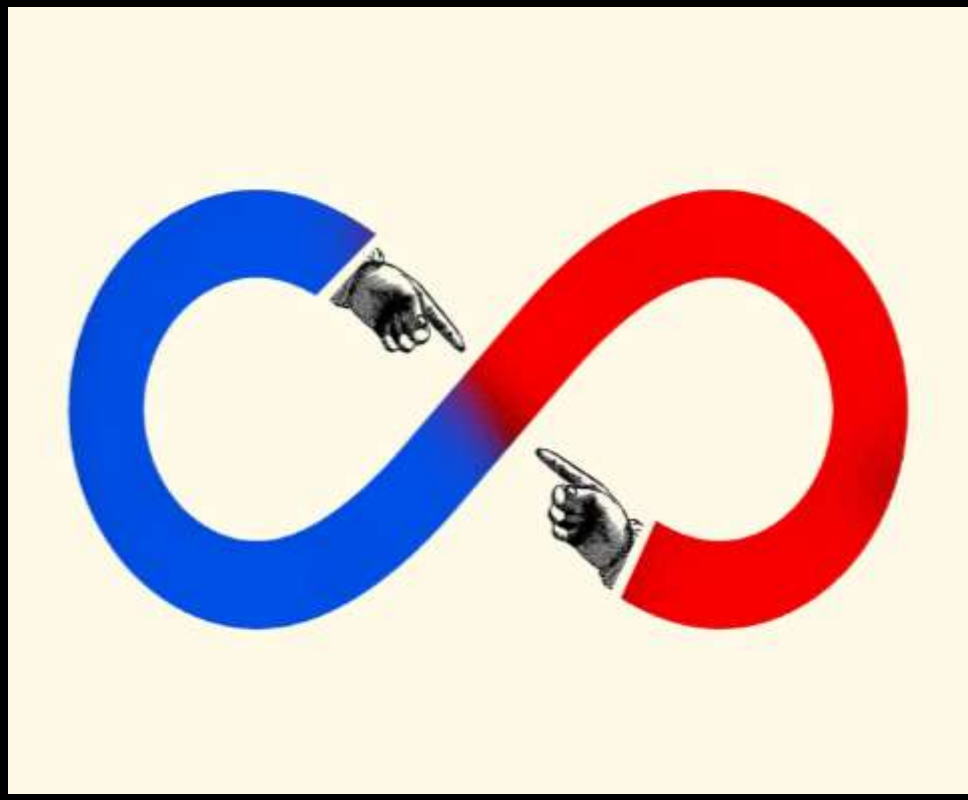


- **1,219,487 deaths**
- **111,820,000 cases**
- **estimated $14 trillion economic impact**

The (False) Comfort and Complacency in the COVID Pandemic: Rude Shocks

- epidemics are something that happens over there!
- out-of-sight/out-of-mind
- unvoiced but persistent belief of American exceptionalism
  - money, resources, sophisticated research capabilities and superior health will stop disease in its tracks
  - delusion rudely shattered by COVID-19
- chronic neglect of public health investment in an era of globalization of commerce and transport
- risk warnings long ignored
- COVID just latest episode in repeated historical cycles of neglect-panic-fund-forget again in preparedness, response, resilience and recovery (PR3) against the threat of infectious/parasitic diseases

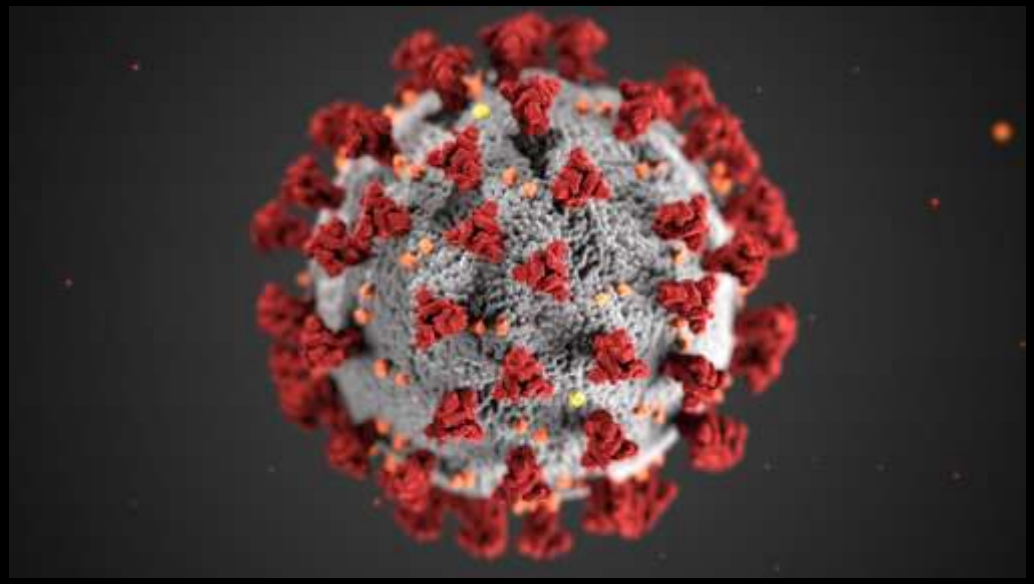
A Critique of the US Response to COVID-19



- mix politics and public health then politics always wins
- technological illiteracy of the legislative and executive branches
- divisive partisan politics
- ever changing messaging
- media sensationalism and ‘gotcha’ journalism
- proliferation of disinformation on social media
- public confusion and mistrust

Countering Disinformation: A Growing Challenge in Public Health Communications and Sustaining Public Trust

- unchecked dissemination of inaccurate information on social media
- controversy and extremism drives clicks=revenue
- manipulate public opinion, increase socio-political tensions and erode trust in authorities/decisions
- active role of PRC and Russia in COVID-19 pandemic



If we knew then what we know now,
what would we have done differently?

Seven Overarching Requirements for Proficient Preparedness, Response, Resilience and Recovery (PR3)

- pathogen agnostic capabilities
- detection (surveillance, diagnostics:Dx)
- countermeasures (Dx, Rx and vaccines)
- speed, scale up, stockpiles and supply chains (private sector engagement)
- data (real-time situational awareness)
- coordination (national, international)
- decisions (policy, transparency, messaging, public trust)
- equity (resources, training)

Preparedness, Response, Resiliency and Recovery (PR3) Capabilities

- epidemics can be as devastating as pandemics at the local level
  - dengue, yellow fever, Marburg, Ebola, Zika, Chikungunya
- next major epi-pandemic (Agent-X) may have very different features to COVID-19
  - transmissibility; symptomatic: asymptomatic ratio; duration of fomite shedding
  - lethality; organ morbidity patterns; and post-infection sequelae
  - different high-risk cohorts (children vs adults)
  - GI vs respiratory spread vs vector-borne
  - contaminated surfaces risk vs aerosols
  - environmental persistence and decontamination needs
  - zoonotic source(s) and reverse zoonoses risk

Silos Subvert Solutions! The Imperative for Integrated, Systems-Based Coordination of PR3 Capabilities

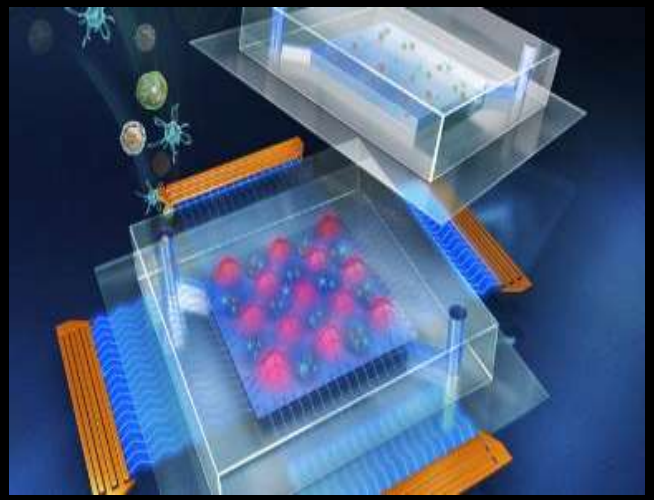
December 2024

https://www.mckinsey.com/capabilities/risk-and-resilience/our-insights/the-six-habits-of-highly-successful-chief-risk-officers

The Primacy of Pathogen-Agnostic Diagnostics and Real-Time Data in Biosurveillance and Rapid Response

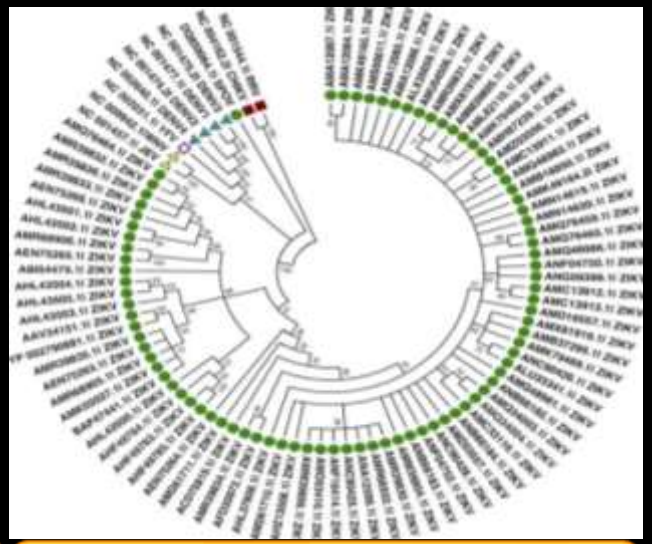
Profile:
signatures of threat agents

Detect:
rapid automated PON/POC diagnostics



Act:
real-time situation awareness, decisions

global surveillance



genomics of
pathogen evolution

dual-use research and
engineered biothreats

New Technologies for Rapid Detection of Biothreats

- waste-water surveillance and pathogen detection

Flying Blind!
The Dangerous Void Created by Lack of Comprehensive Diagnostic Infrastructure for Pathogen Detection

- massive gaps in real-time spatio-temporal epidemiological data in early stages of COVID-19 pandemic
  - inadequate availability of diagnostic tests to map infection prevalence and distribution
  - underappreciation of asymptomatic infections
- negative impact on accuracy of computational forecast modeling of pandemic trajectory
  - influence on national policy decisions
  - ‘lock downs’, school/work closures, travel bans, employment
  - multibillion USG emergency financing to support the economy

The Dangers of Intellectual Arrogance: Public Sector Failings as a Major Vulnerability in Limiting COVID Detection

CDC Advisory Committee to the Director (ACD)

Laboratory Workgroup (LW)

Review of the Shortcomings of CDC's First COVID-19 Test and Recommendations for the Policies, Practices, and Systems to Mitigate Future Issues

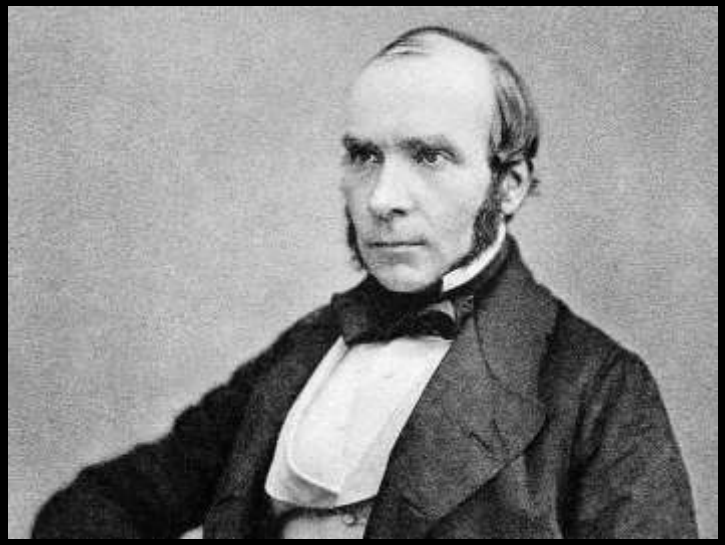
ADOPTED BY ACD VOTE ON FEBURARY 7, 2023

World Health Organization

Abbott

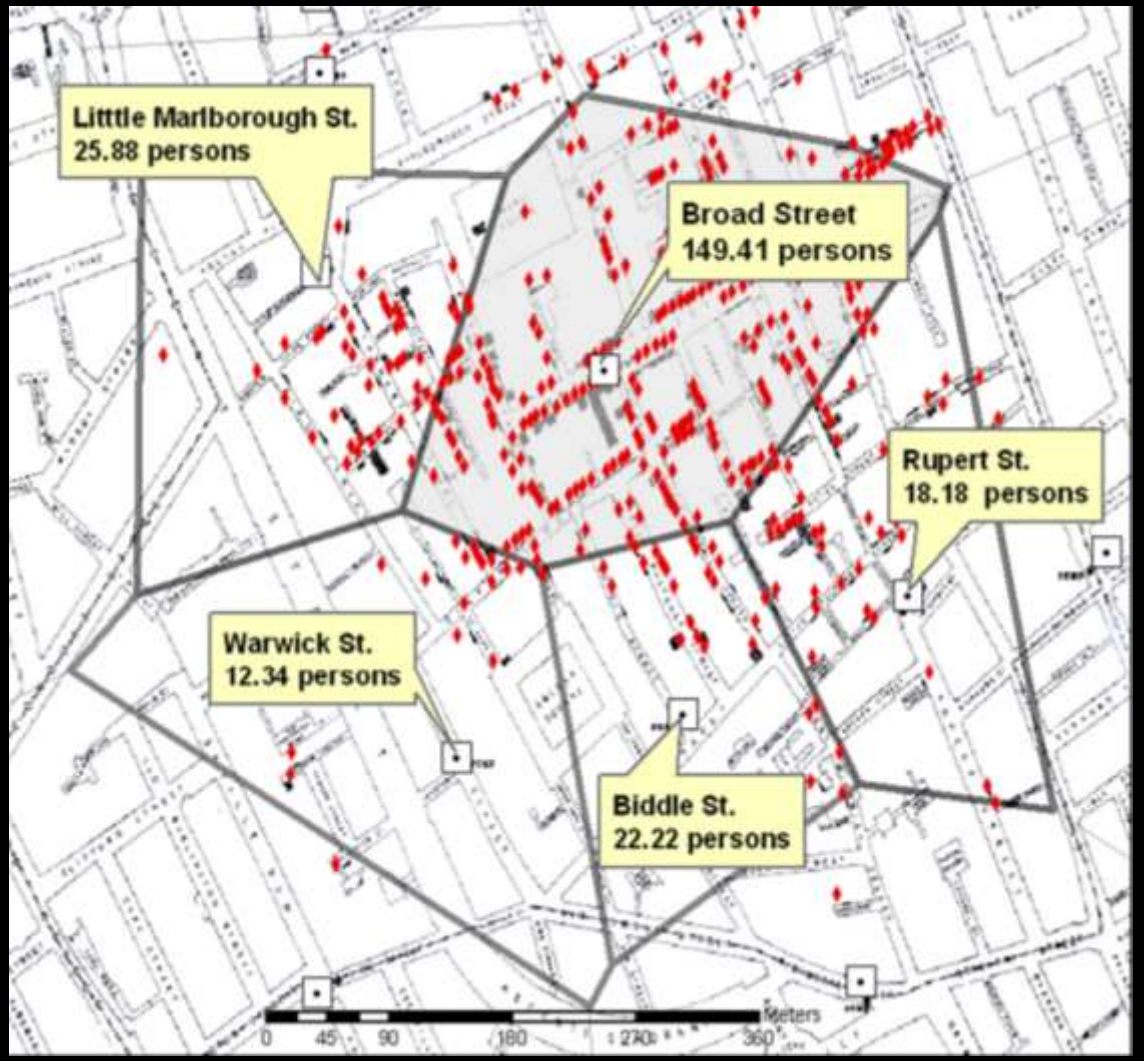
- WHO turned down Abbott's application to join WHO's outbreak alert network
  - "discomfort with the industry connection"
  - "free from concerns which are primarily of a commercial or profit-making nature"

Data:
The Foundation of Epidemiology and Informed Decisions



Dr. John Snow, 1855

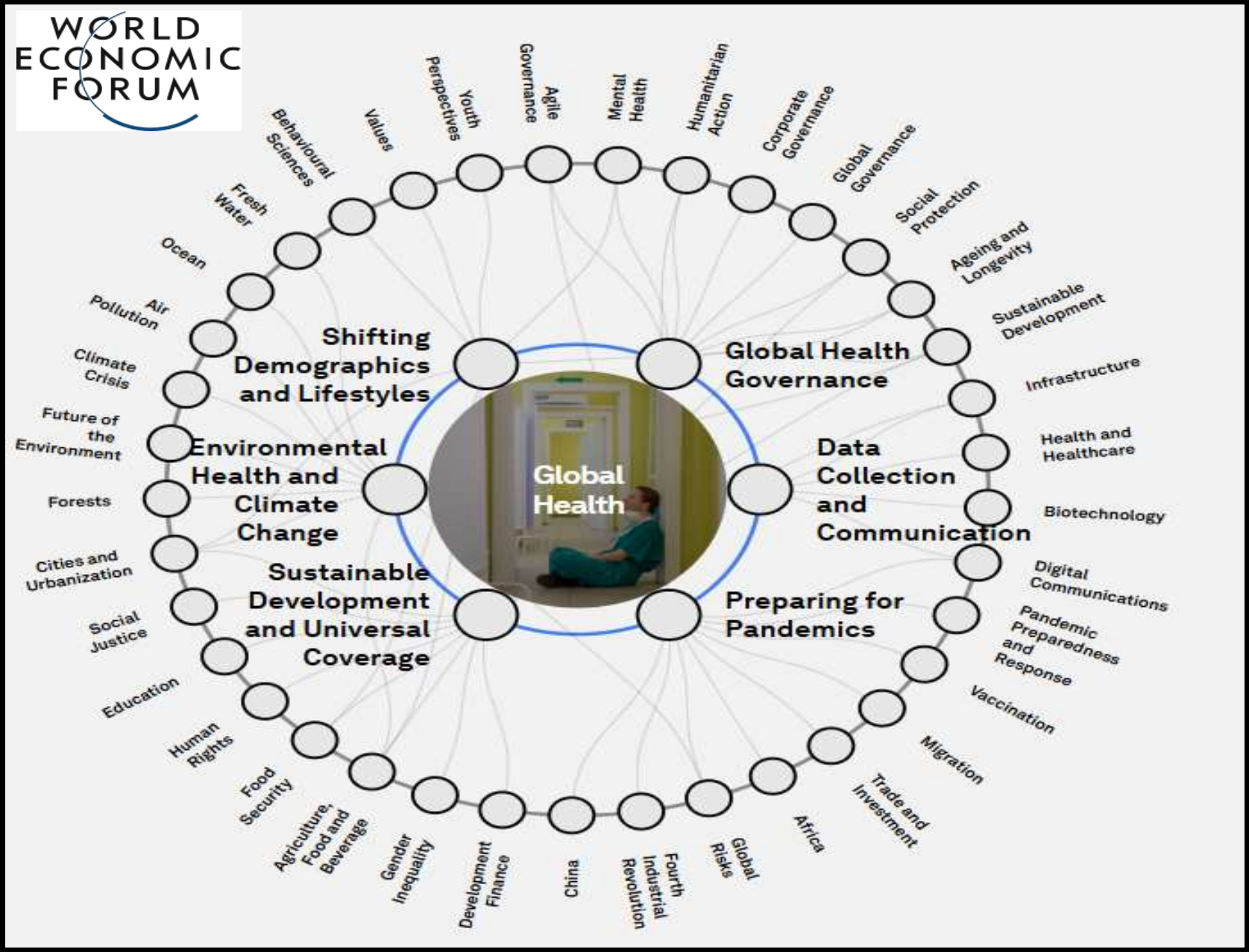
- cholera deaths per 1,000 population



Biosecurity and BIOINT:
Capture of Threat-Agnostic Multi-Modal Data

- global to local
- threat tracking (known, suspected, theoretical)
- population demographics
- public health, syndromic surveillance
- geospatial (environmental, meteorological, ecological)
- travel and trade patterns
- social media and behavioral patterns

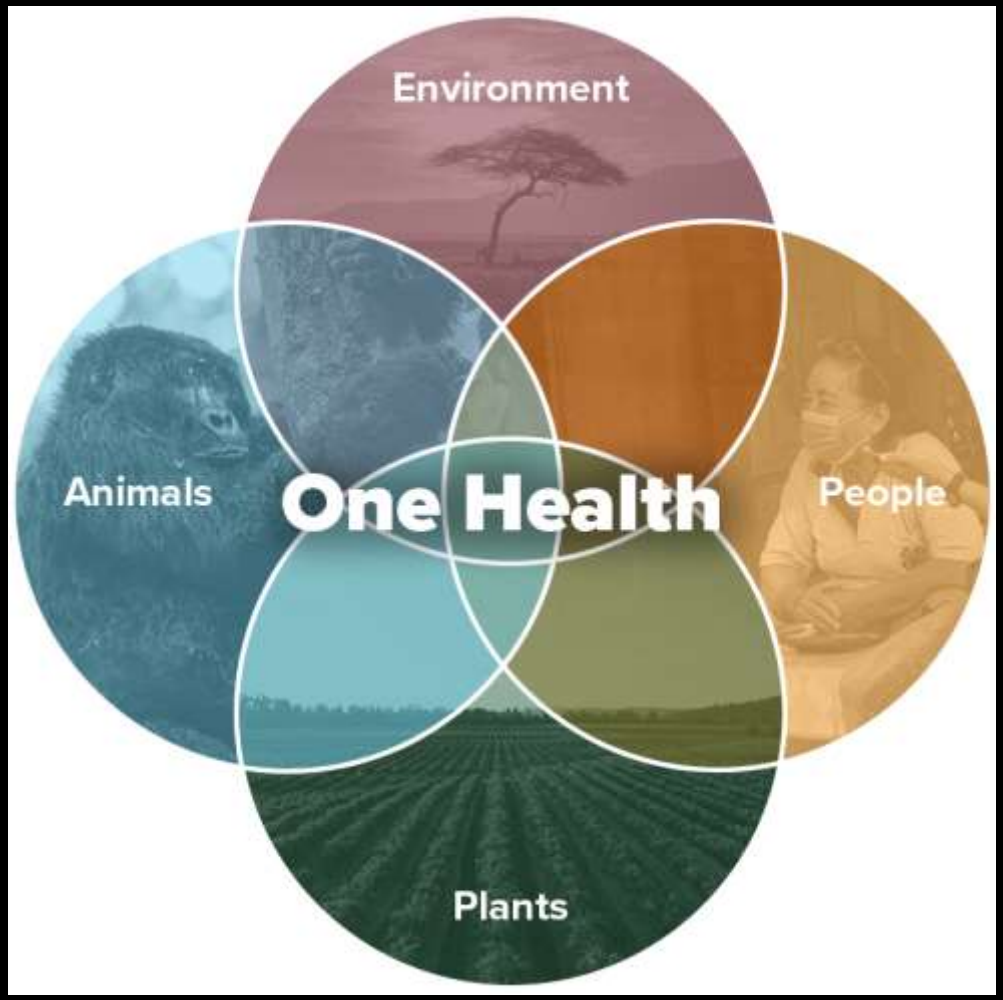
Biosecurity: Everything Connects



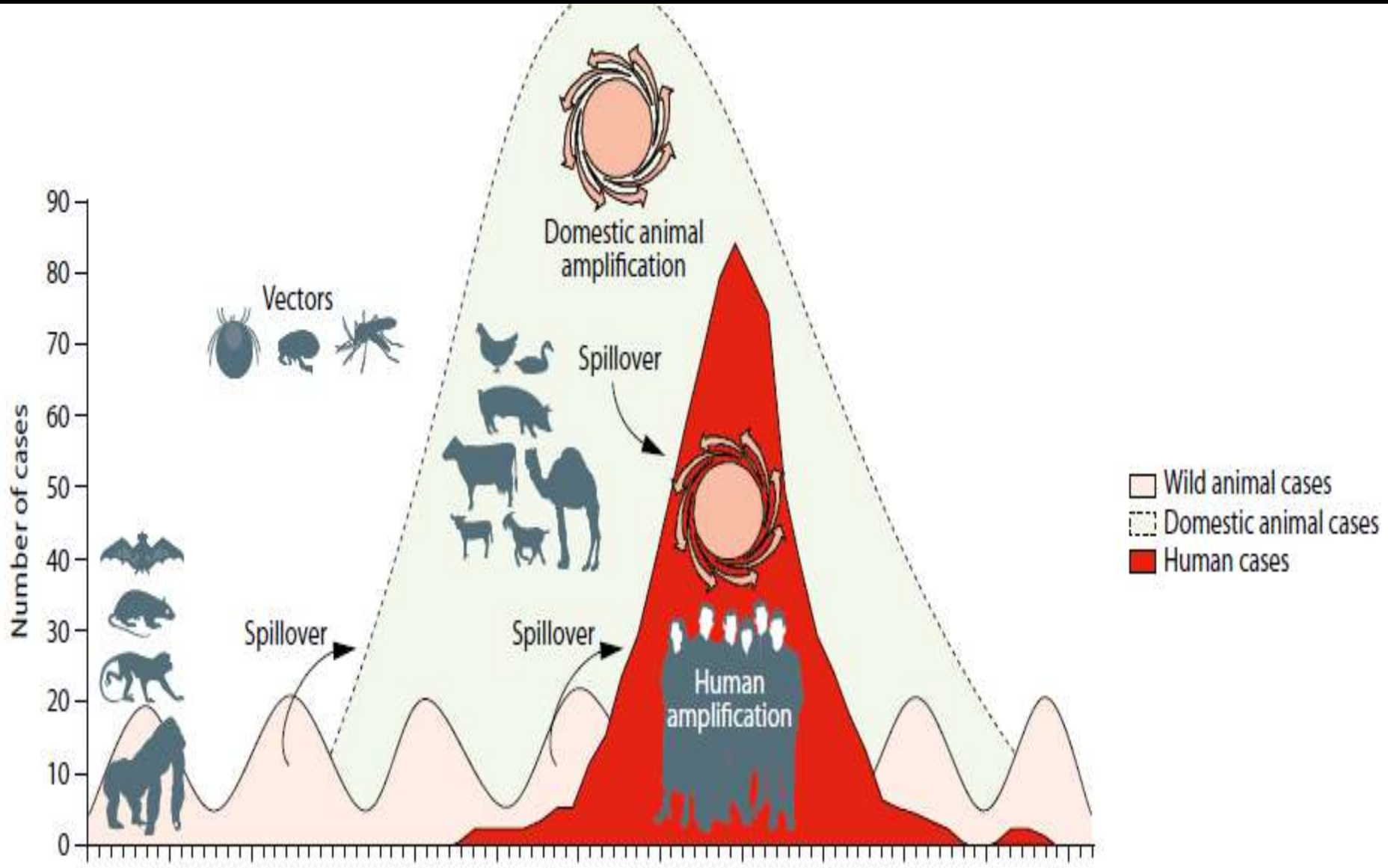
August 2024 International Journal for Research Publication and Seminars 15(3):153-165 DOI:10.36676/jrps.v15.i3.1464

One Health and Global Biosecurity

- an integrated, systems-based approach to optimize the health of people and animals, ensure availability of crucial food chains and sustainable environmental ecosystems

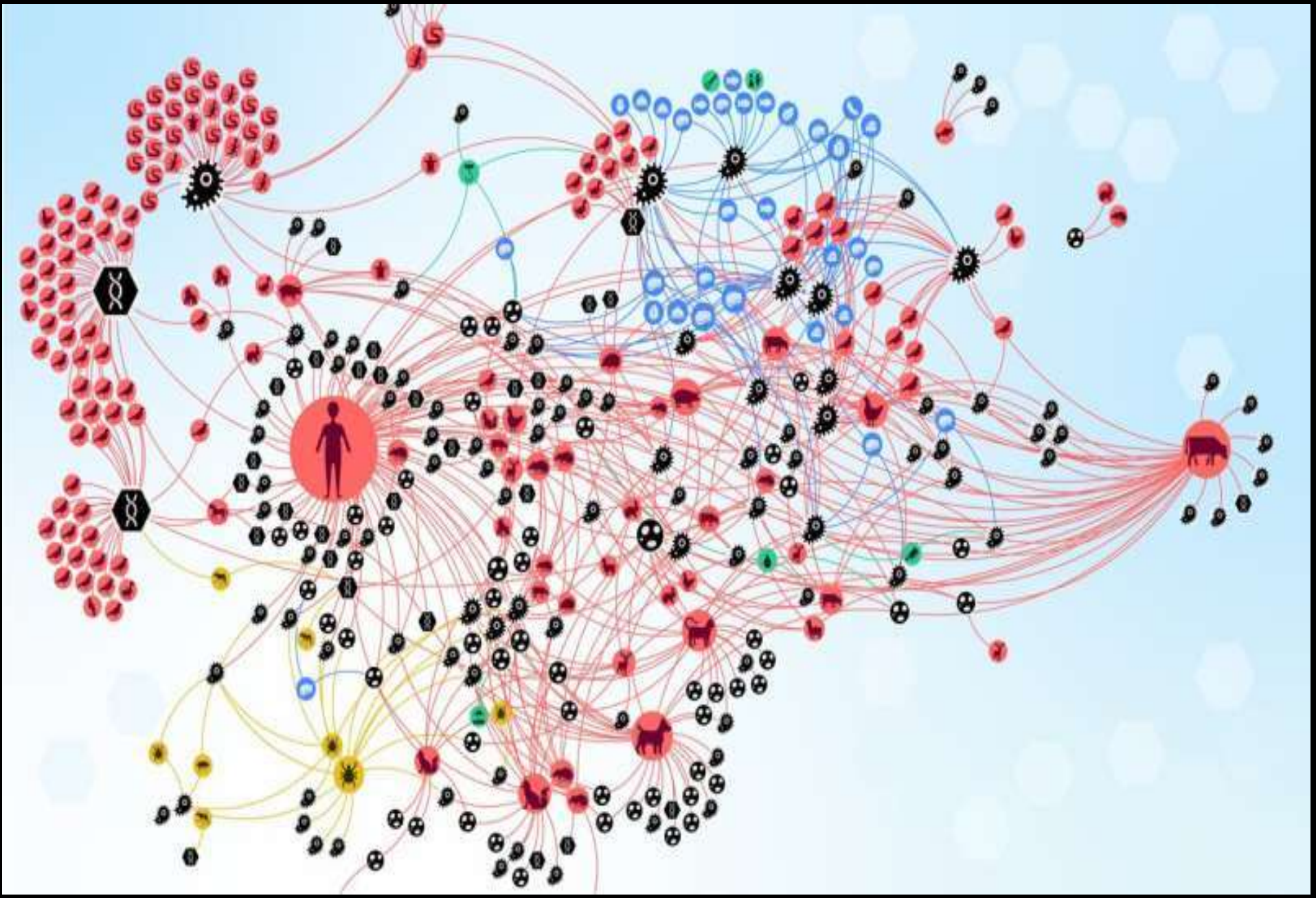


Dynamics of Cross-Species Zoonotic Pathogen Risk Spillover



W. Karesh et. al. (2012) Lancet 380, 1942

Complexity of Zoonotic Transmission Chains



Complexity Science Hub Vienna https://phys.org/news/2024-07-unveils-complexity-zoonotic-transmission-chains.html#google_vignette

RNA Viruses as Major EID Threats

- 45-50% of EIDs
- error-prone replication cycles
- faster evolutionary rates and emergence of variants
  - higher risk of ‘species-jump’
  - immune evasion mutations
  - altered tissue tropism
- genetic reassortment between avian, mammalian and human viruses

Dissecting Pandemic-Prone Viral Families

JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH | Center for Health Security

December 2023 Author: Amesh A. Adalja, MD

https://centerforhealthsecurity.org/sites/default/files/2023-12/231222-viral-families-report.pdf

Urbanization and Mega-Cities in LMICs

Urbanization and Mega-Cities in LMICs and the Increased Threat of Zoonotic EIDs

High Population Density With Inadequate Biosurveillance

Expanded Footprint and New Zoonotic Exposures/Risks

Major Gaps in Health Infrastructure and Rapid Disease Reporting

Anthropogenic Forces That Increase Exposure of Human and Livestock to Feral Animal Zoonotic Reservoirs

Habitat Destruction for Expansion of Urban Food Supply Chains

Concentrated Animal Feeding Operations (CAFOs)

Science 380, 6640 Apr 2023

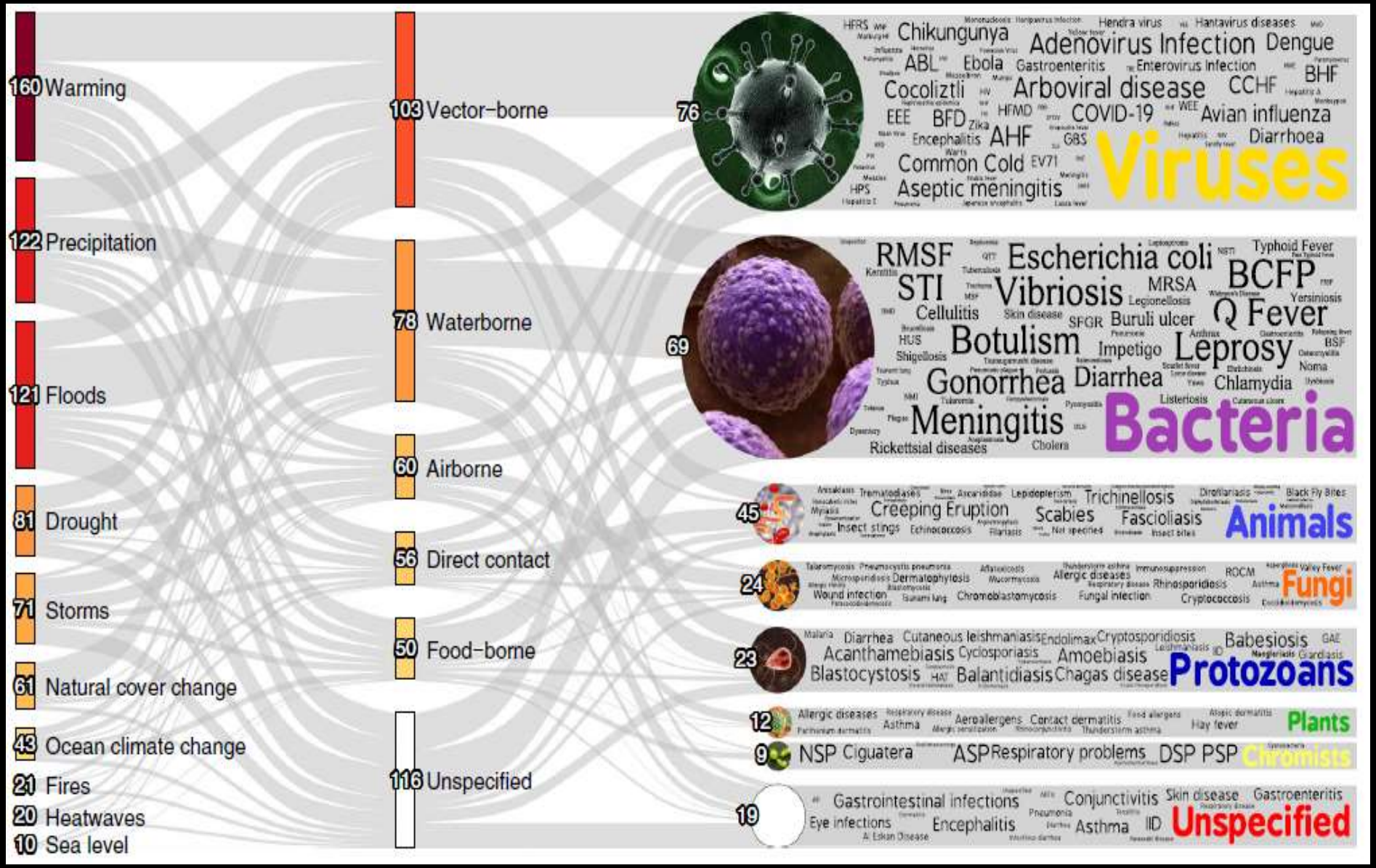
February 2020. Photo: Feature China/Barcroft Media via Getty Images

Aggressive Actions to Contain Highly Pathogenic Avian Influenza as Potential Human Pandemic Agent






Over Half of Known Human Pathogenic Diseases Can Be Aggravated By Changing Weather Patterns



The Convergence of Biotechnology, Synthetic Biology and Artificial Intelligence (BIOxAI)

Dramatic Expansion of the Dual-Use Dilemma

Oversight Mechanisms for Biosafety and Biosecurity

- dual-use research of concern (DURC)
- pathogens with pandemic potential (PPP)
  - enhanced PPP (ePPP)
- gain-of-function (GOF)
  - “research with pandemic potential risks”

- understandable but narrow historical focus on microbial pathogens and toxins
- bias towards anthropocentric risk versus panzootics, crop infestations and ecosystem disruption
- pace of rapid technological change outstripping oversight and regulatory revisions

Increased Public and Legislative Concerns Regarding Adequacy of Oversight

Global Expansion of High Biosafety Level (BSL-3/4) Laboratories

- COVID-19 pandemic highlighted gaps in preparedness resources for handling high-risk pathogens
  - conventional public health (BSL-3)
  - expanded capabilities for translational research (Rx, vaccines)
- plans announced to build 27 new BSL-4 facilities
  - Russia (15), PRC (4), India (4), Kazakhstan, Singapore, Philippines, US (1)
- long lead times for construction and certification
- high operational costs ($15-20M/year)
  - maintenance, air handling, security
- staff training and (re)certification in stringent-biohazard containment protocols to limit risk of biosecurity breach

Discovery of Illicit Chinese Laboratory: Reedley, California

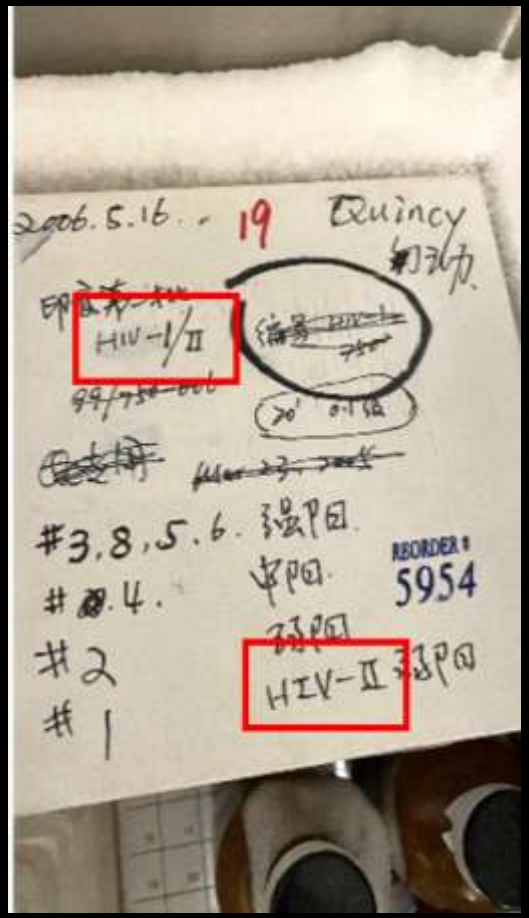

Figure A.

Figure B.

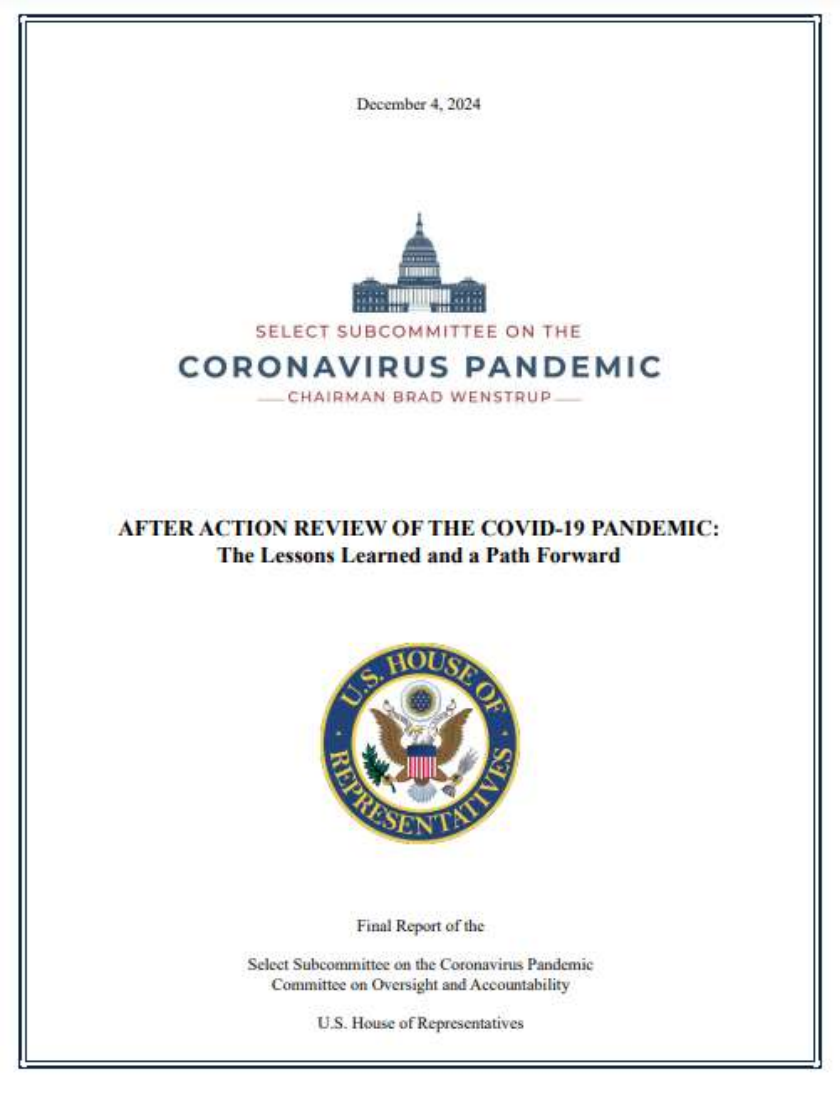
THE SELECT COMMITTEE ON THE
CHINESE COMMUNIST PARTY
FREEDOM IS THE VICTOR

INVESTIGATION INTO THE
REEDLEY BIOLAB

UNITED STATES CONGRESS



Predictable and Destructive Partisanship: Ideology Matters More than Facts- A Poor Prognosis for Addressing Future Escalating Complexity



December 4, 2024

SELECT SUBCOMMITTEE ON THE

CORONAVIRUS PANDEMIC

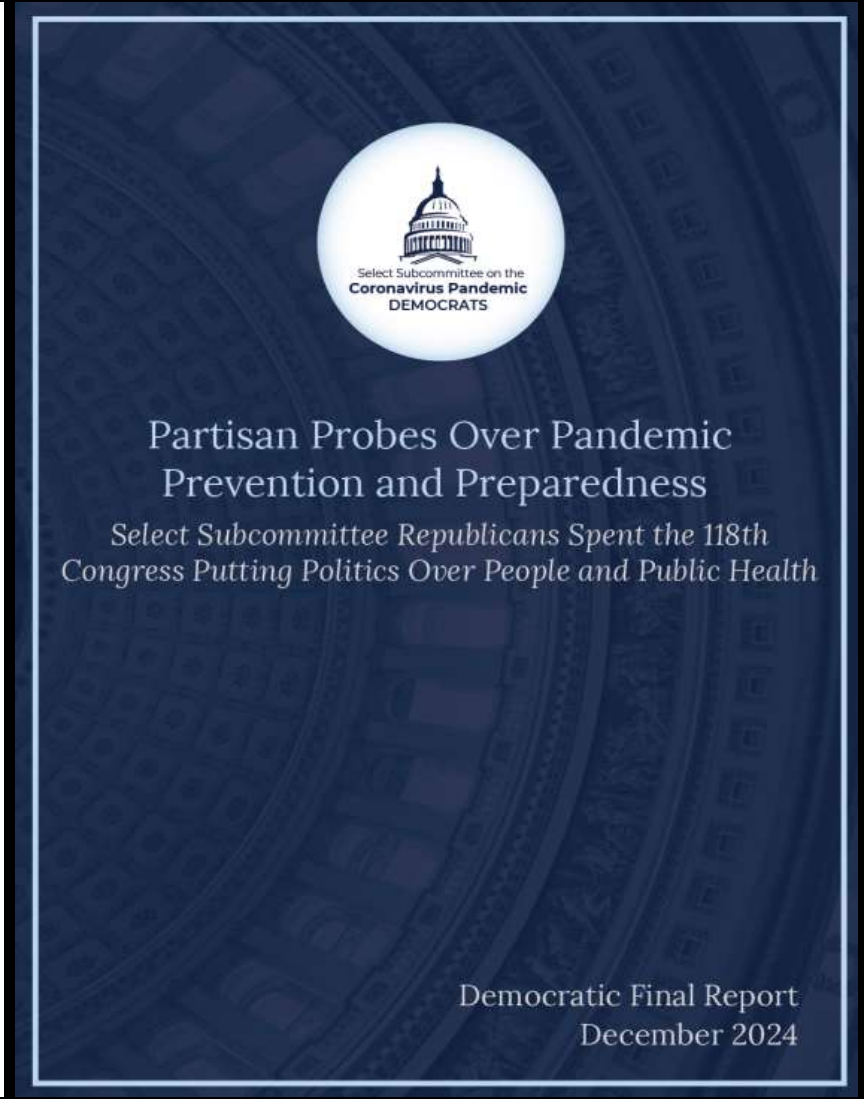
CHAIRMAN BRAD WENSTRUP

AFTER ACTION REVIEW OF THE COVID-19 PANDEMIC:
The Lessons Learned and a Path Forward

Final Report of the

Select Subcommittee on the Coronavirus Pandemic
Committee on Oversight and Accountability

U.S. House of Representatives



Select Subcommittee on the
Coronavirus Pandemic
DEMOCRATS

Partisan Probes Over Pandemic Prevention and Preparedness

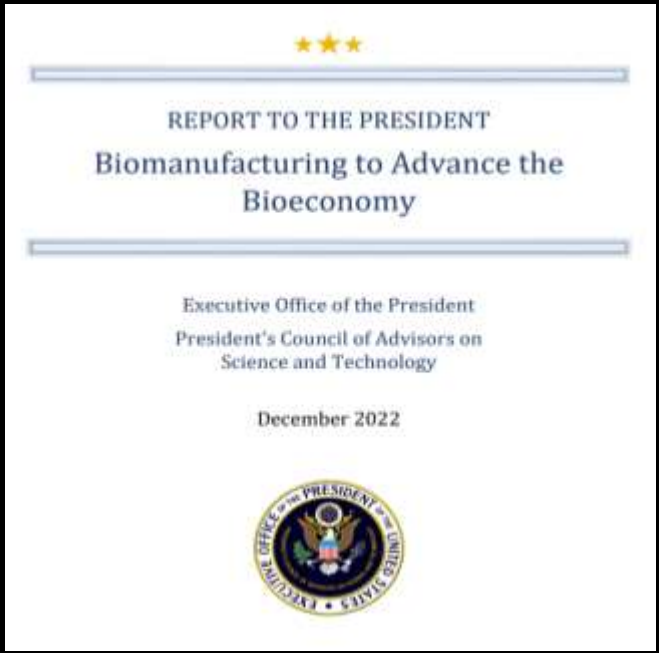
Select Subcommittee Republicans Spent the 118th Congress Putting Politics Over People and Public Health

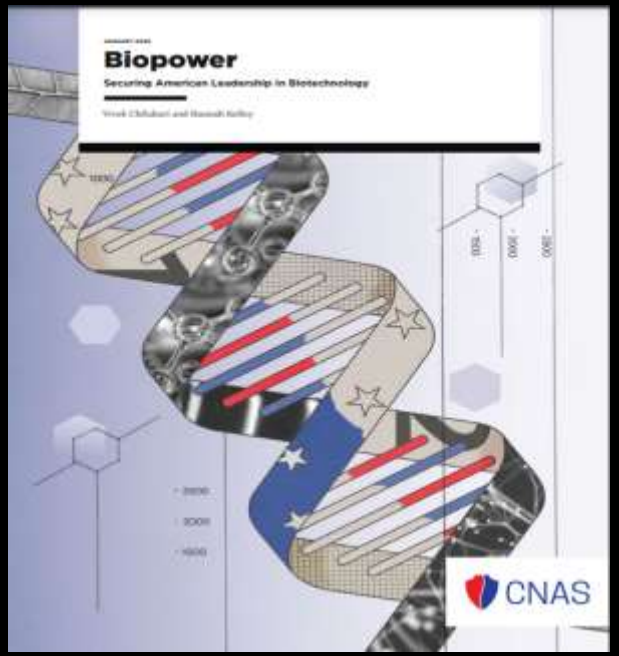
Democratic Final Report
December 2024

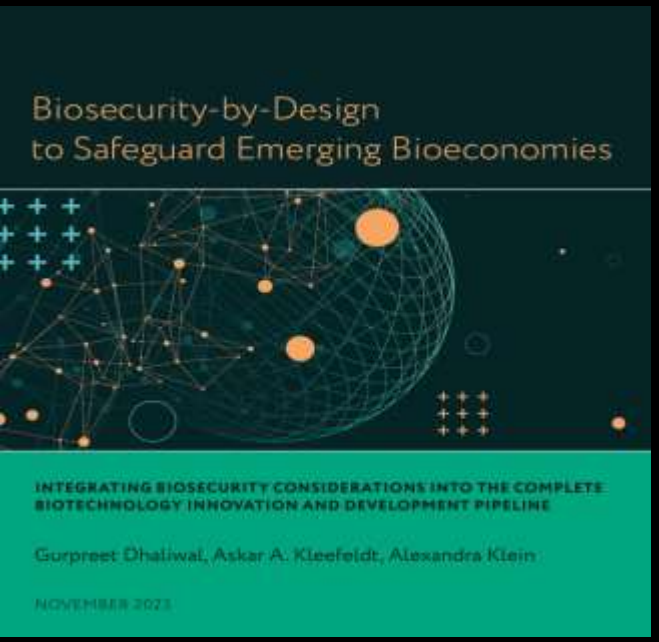
The Eroding Commitment to International Coordination in Public Health

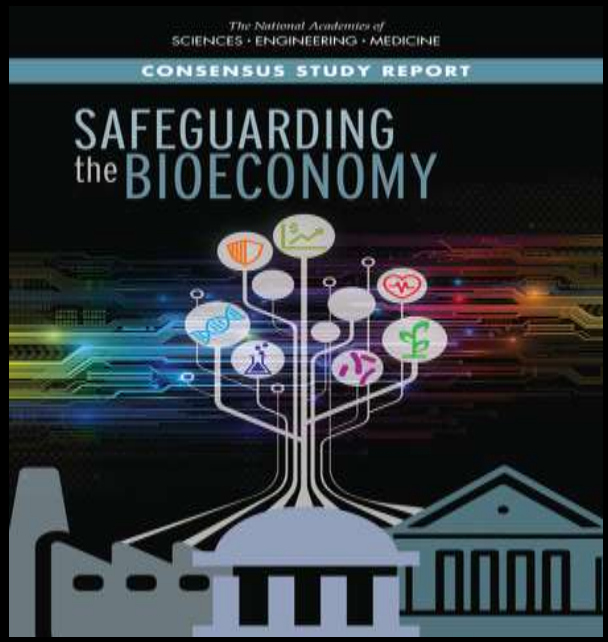
Dangerous Times Ahead: The International Competition for Commercial and Military Dominance of BIOxAI

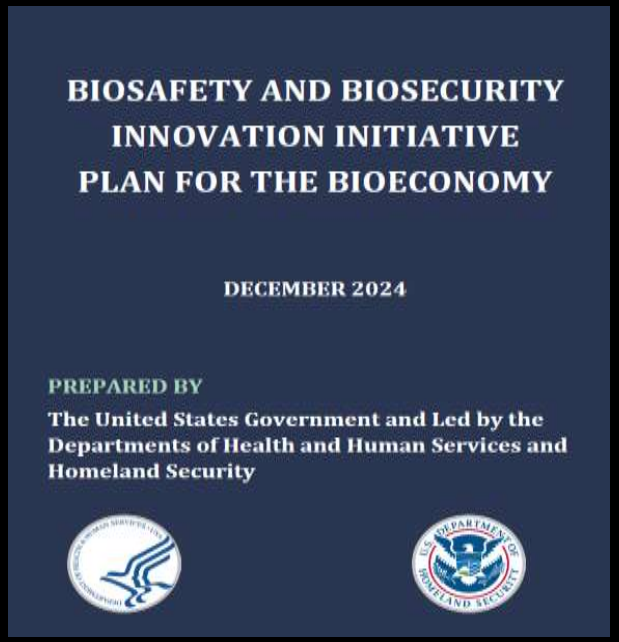
The Geopolitical Race for Commercial and Military Superiority in Applications of Biotechnology, Synthetic Biology and Artificial Intelligence







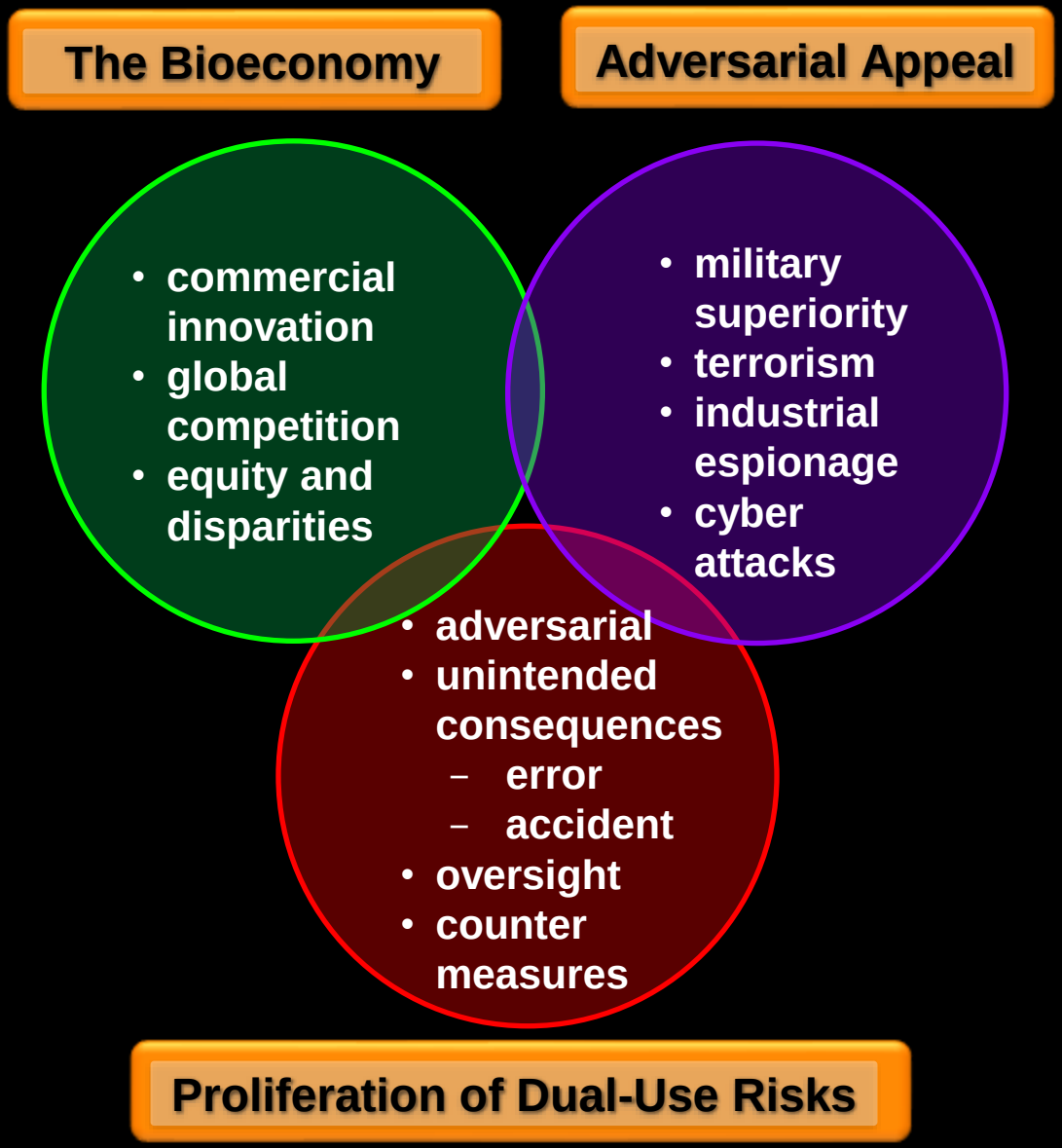




Global Problems Require Global Solutions

- balancing growing tension between nation-focused economic and military competitiveness in advanced technologies with global cooperation in mitigation of shared threats

New Biosecurity Challenges Posed by the BIOxAI Convergence and the Escalating Complexity of Oversight and Governance



The Changing Dimensions of Big Data

2024 Nobel Prizes Reflect Two Pathways in AI

the science of AI

Physics

John J. Hopfield
Princeton University, NJ, USA

Geoffrey Hinton
University of Toronto, Canada

applications of AI

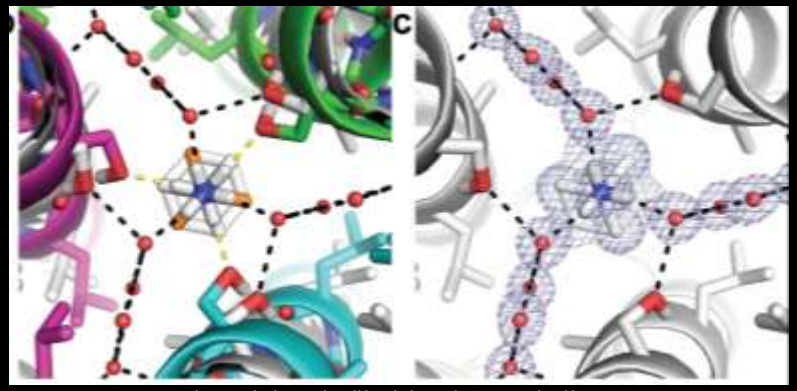
Chemistry

David Baker
University of Washington, USA

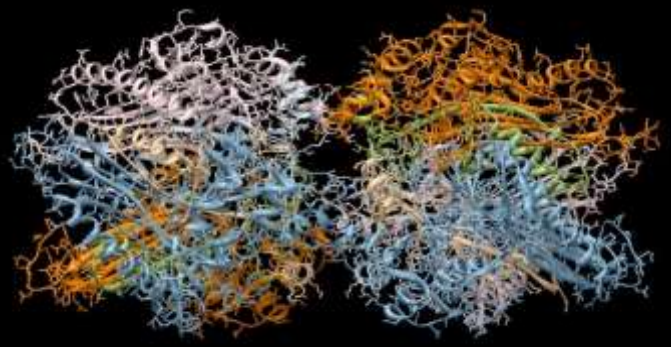
Demis Hassabis
Google DeepMind, UK

John M. Jumper
Google DeepMind, UK

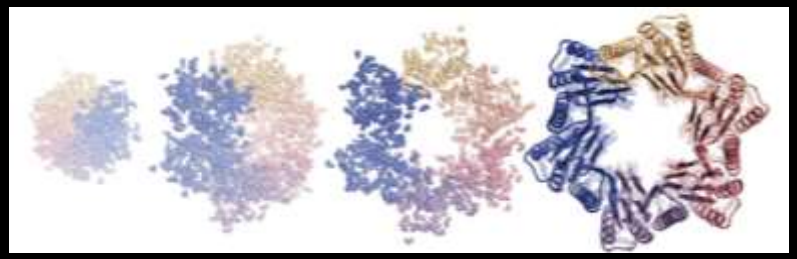
Use of ML-AI in Protein Design in Drug Discovery and Synthetic Biology



J. Park et. al. (2019) Elife doi.org/10.7554/eLife.47839



https://www.cnet.com/science/biology/googles-deepmind-ai-predicts-3d-structure-of-nearly-every-protein-known-to-science/



E. Callaway (2023) Nature 619:236-238; doi.org/10.1038/d41586-023-02227-y

- **Expanded Inventory of Novel Protein Structures**
- **Improved Drug-Pocket Affinities and Allosteric Sites**
- **Design of Protein-Protein Interactions**
- **Drugging the Undruggable**
- **Designer ADME, Targeting Systems for Drug Delivery and Cellular Therapy**

AI-Enabled Protein Design: A Strategic Asset for Global Health and Biosecurity

By Lynda M. Stuart, Rick A. Bright, and Eric Horvitz

October 28, 2024 | Commentary https://doi.org/10.31478/202410d

DAVID BAKER AND GEORGE CHURCH Authors Info & Affiliations

SCIENCE
25 Jan 2024
Vol 383, Issue 6681
p. 349
DOI: 10.1126/science.ado1671

Protein design meets biosecurity

PAPER — Nov 14, 2024

Developing Guardrails for AI Biodesign Tools

NTI

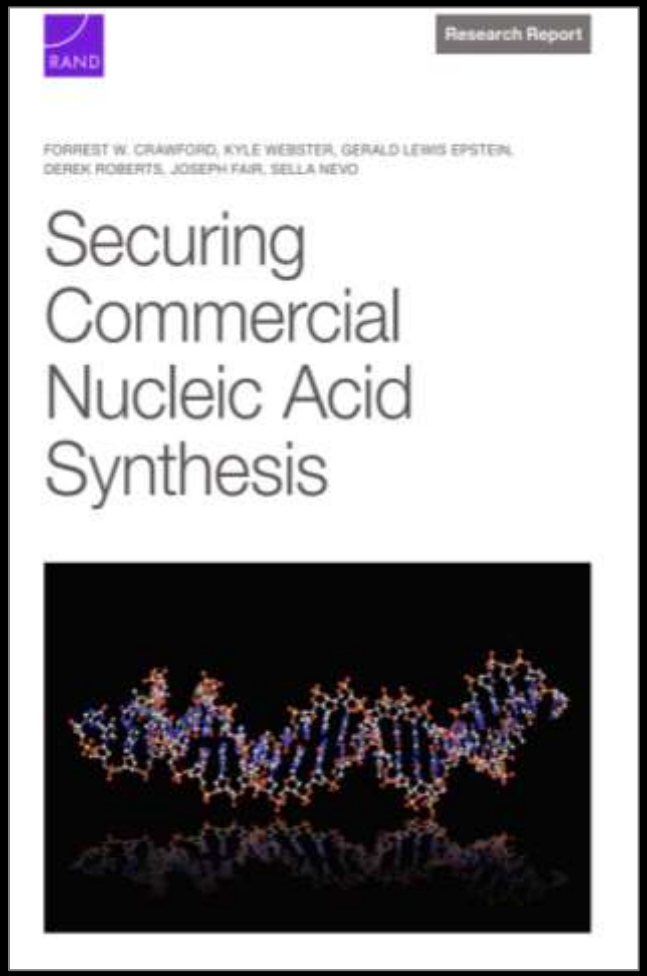
The Dual-Use/High Risk Triad

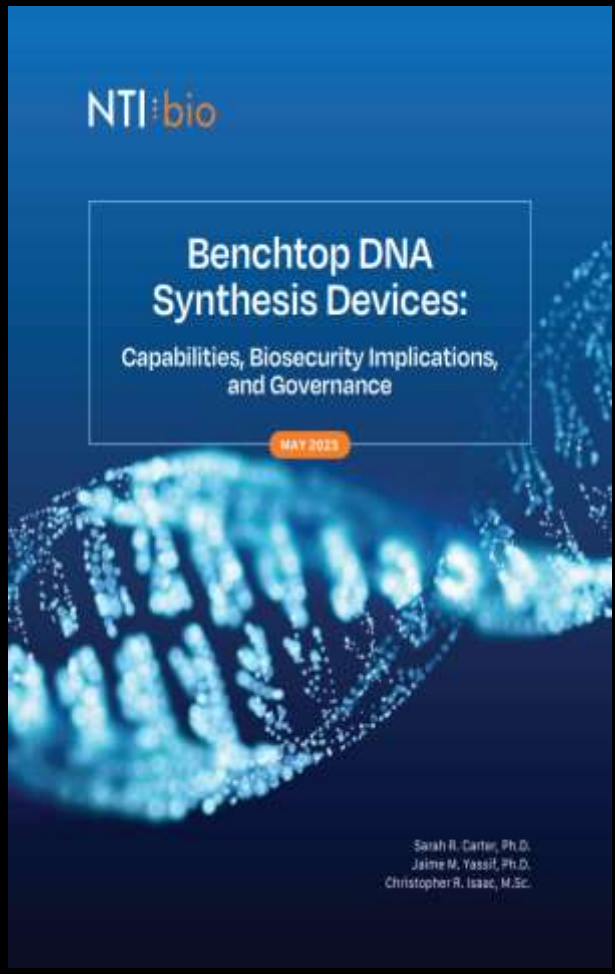
- risk: benefit assessment
- alternative methods
- cost
- classification level
- within/outside current regulations
- organizational safety pre-commitments

- credentialed expertise
- biosafety protocols
- facilities
- cybersecurity
- oversight and audit
- red teaming and penetration

- original envisaged confirmed
- unexpected outcomes/ implications
- open vs. controlled data dissemination
- cybersecurity
- post-deployment monitoring

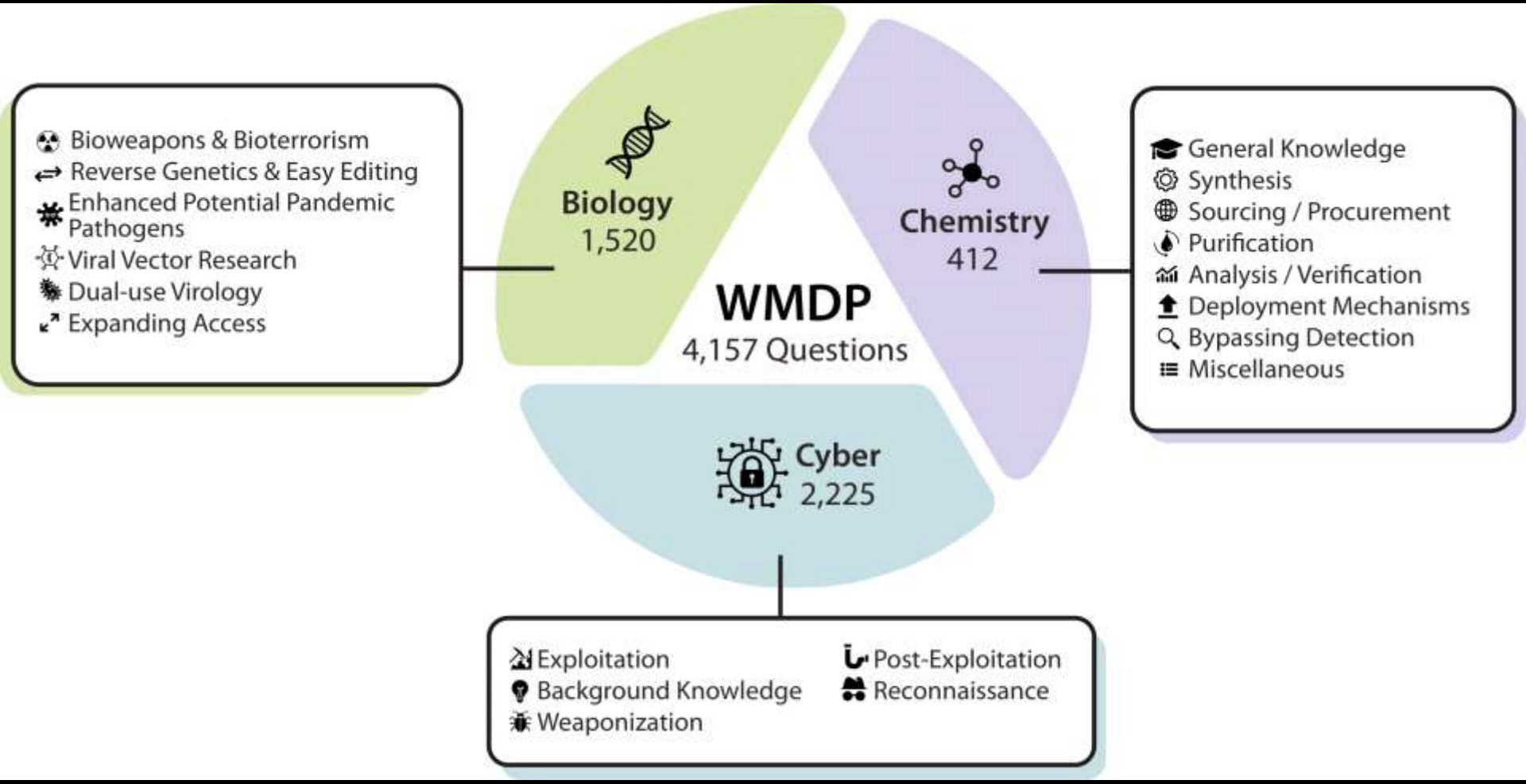
Secure Screens for Synthesis of Sequences of Concern (SOCs)





- all viruses described as potential pandemic pathogens
- all known viruses capable to human-to-human transmission

Technology Convergence, Rapid Global Diffusion and Proliferation of Dual-Use Risk: The Challenge for Biosafety Professionals and Credentialling



Weapons of Mass Destruction Proxy (WMDP) Model

From: Center for AI Safety (2024) https://www.wmdp.ai/

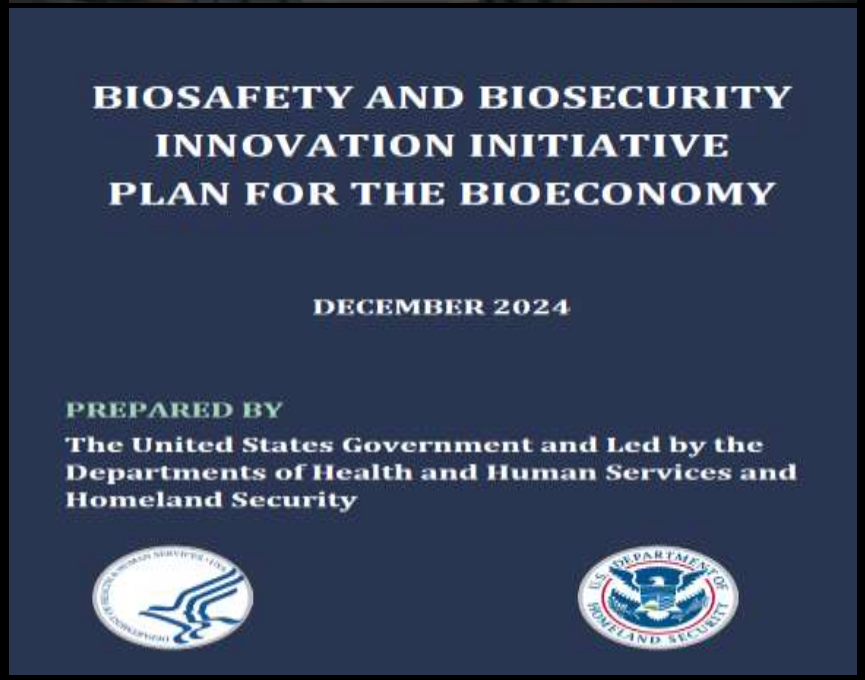
PRC and Targeted Biotechnology and Pharmaceutical Espionage*

- PRC ‘military-civil’ fusion merges the military and pharmaceutical sector
- US House Committee on Oversight and Accountability (2024)
  - escalation of PLA industrial espionage “to weaponize genomic and medical data”
- 2022 CuckooBees multiyear cyberespionage campaign sponsored by PLA Winnti APT (APT41) hackers
  - exfiltration of estimated hundreds of gigabytes of research innovation and IP

*Epoch Times (2024) 17 July 2024

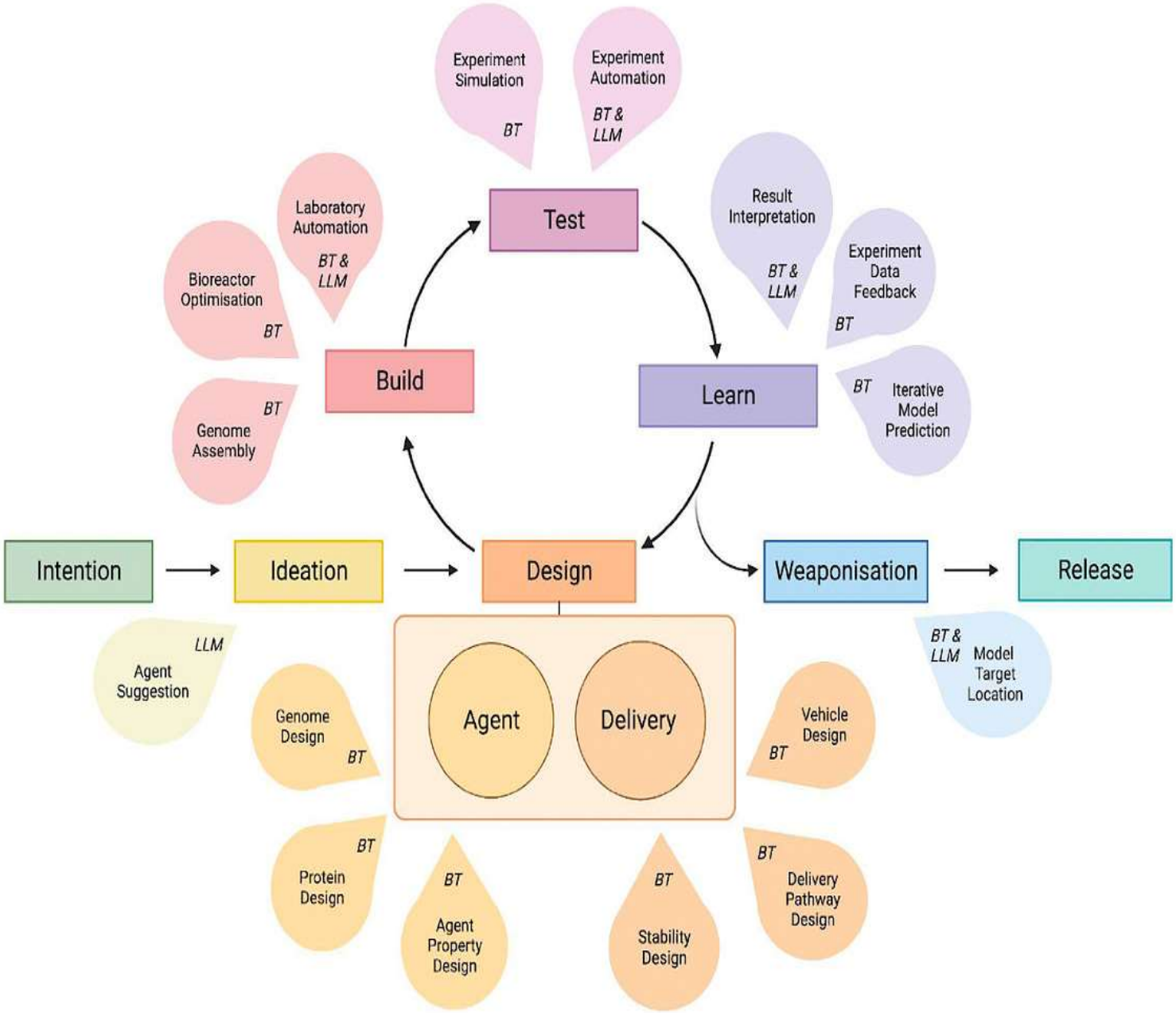

MAY 2023
Optimizing Export Controls for Critical and Emerging Technologies
Semiconductors, Quantum Technology, AI, and Biotechnology
AUTHORS
William A. Reinsch
Emily Benson
Thibault Denamiel
Margot Putnam
A Report of the CSIS Scholl Chair in International Business
CSIS | CENTER FOR STRATEGIC & INTERNATIONAL STUDIES


Department of Commerce Export Controls for Biological Equipment and Technology
U.S. DEPARTMENT OF COMMERCE
BUREAU OF INDUSTRY AND SECURITY
Chemical and Biological Controls Division
Office of Nonproliferation & Treaty Compliance


BIOSAFETY AND BIOSECURITY INNOVATION INITIATIVE PLAN FOR THE BIOECONOMY
DECEMBER 2024
PREPARED BY
The United States Government and Led by the Departments of Health and Human Services and Homeland Security


GOVERNMENT OPERATIONS AND POLITICS
BIOSECURE Act
House Bill 7085

Risk Chain Analysis in Biological Weapon Development



Large-Scale Automation of Biomedical Laboratory Research

Building an AI Scientist.

Our 10-year mission is to build semi-autonomous AIs that can scale scientific research, to accelerate the pace of discovery and to provide world-wide access to cutting-edge scientific, medical, and engineering expertise.

WikiCrow: Automating Synthesis of Human Scientific Knowledge

FutureHouse

New Biosecurity Challenges from Cloud Laboratories

Robust Biosecurity Measures Should Be Standardized at Scientific Cloud Labs

RAND

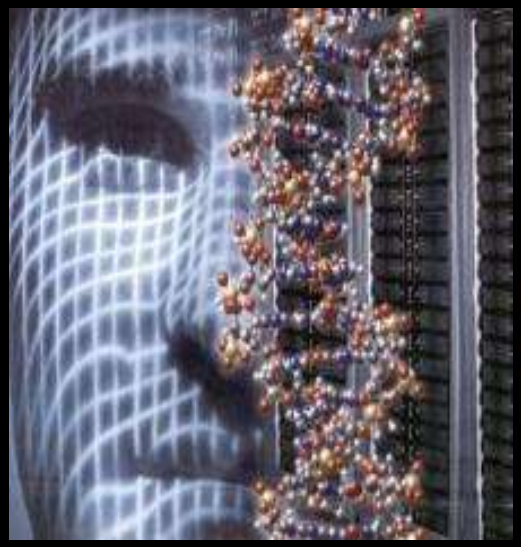
COMMENTARY — Nov 8, 2024

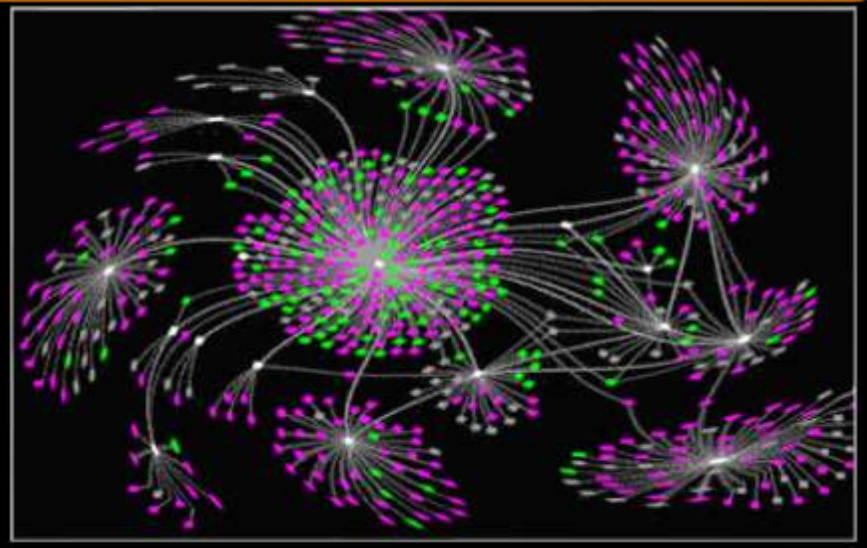
Scale and The Facilities “Forensic Footprint”

https://www.genengnews.com/topics/bioprocessing/increasing-vaccine-efficacy-with-novel-adjuvants/

Precision Health

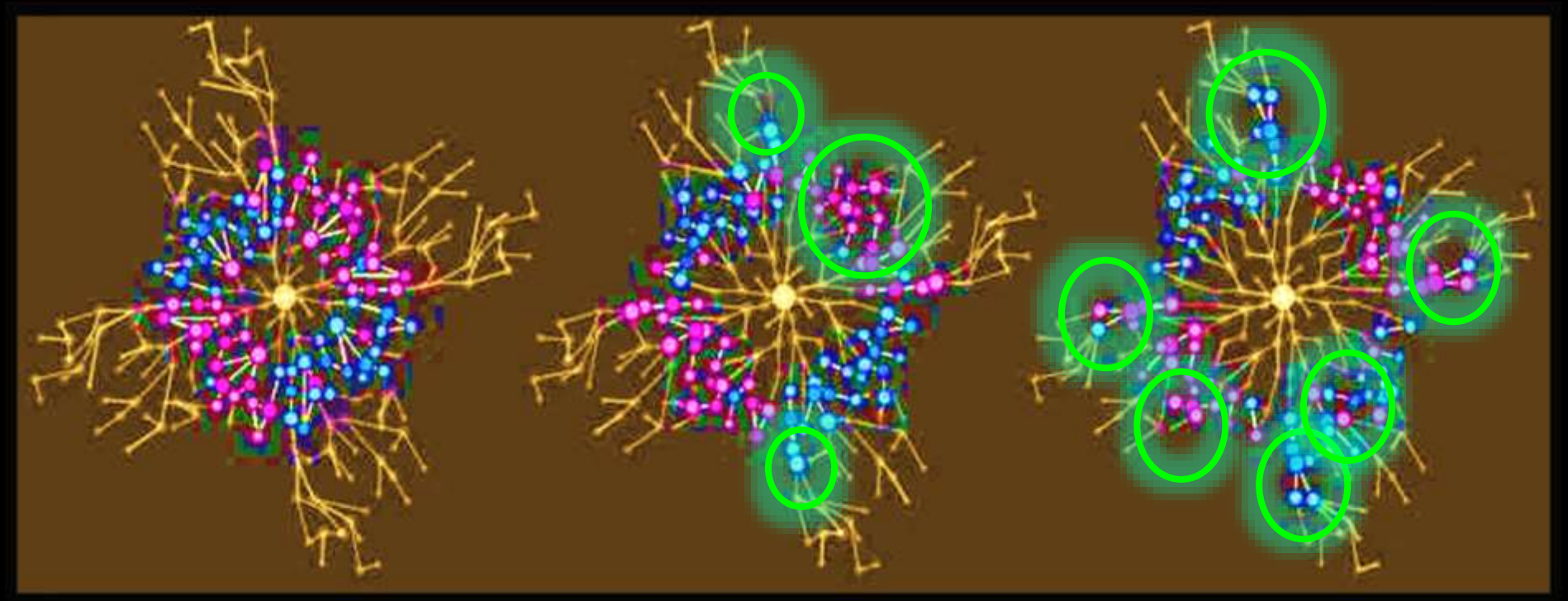
**Detection of Altered Molecular Signaling Networks in Disease:
A New Taxonomy of Disease and Subtype Classification**





**MDx Signatures of Disease Predisposition and Subtyping
of Overt Disease for Optimum Rx Selection**

Precision Health:
Mapping System State Shifts (Phenomes) and Cumulative Perturbations in Molecular Signaling Networks in the Health to Disease Continuum



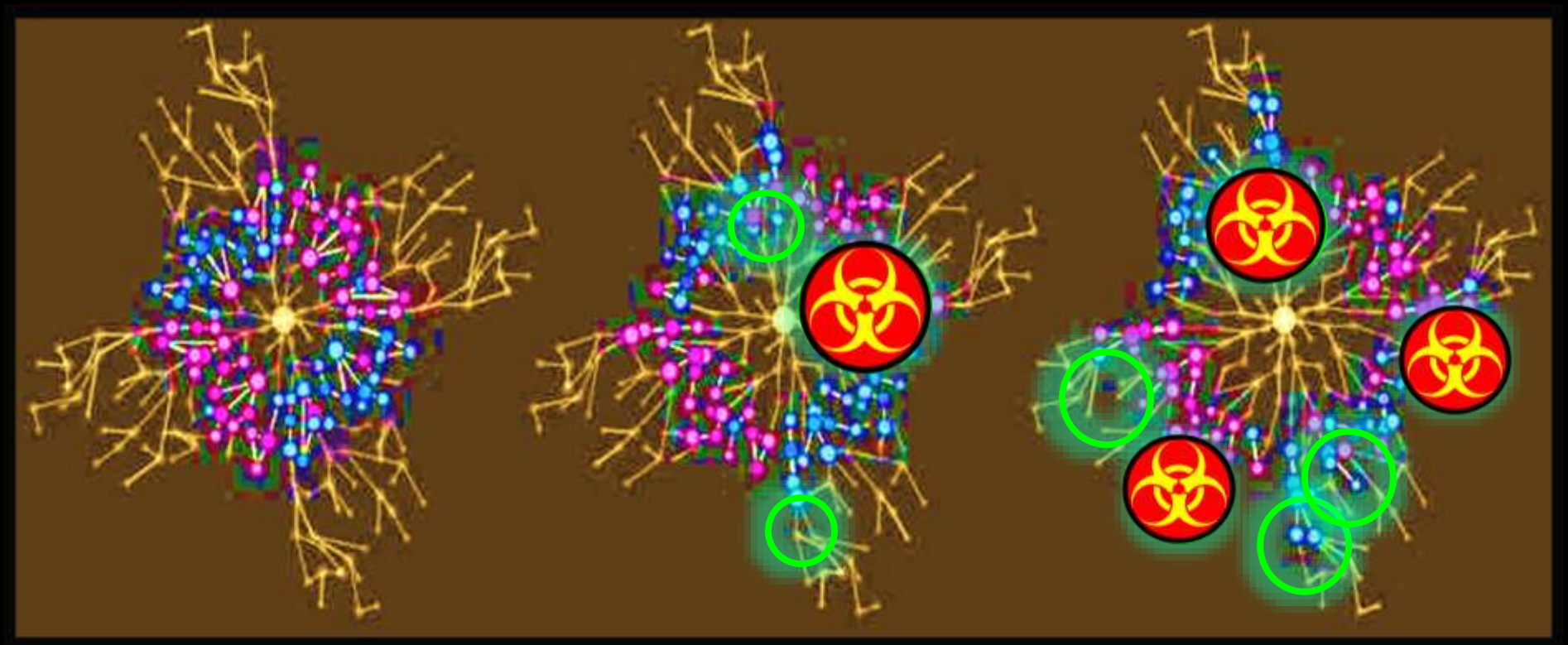
$T_{1(n)}$ health

$T_{2(n)}$ subclinical disease

$T_{3(n)}$ overt disease

- identification of biomarkers/diagnostics and therapeutic targets in dysregulated networks
- DrugMechDB (2023) 4583 Rx indications, 5666 pathways
  32,249 molecular interaction networks across 14 biological parameters

Molecular Information Networks: a Limitless Range of Targets for Nefarious Dual-Use Activities

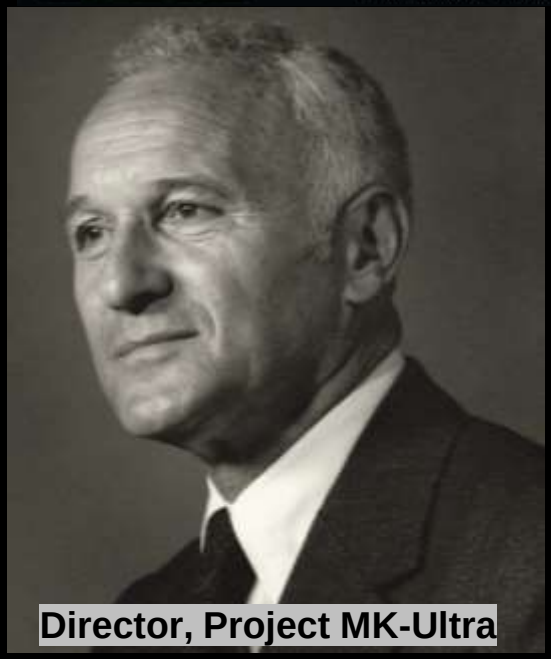


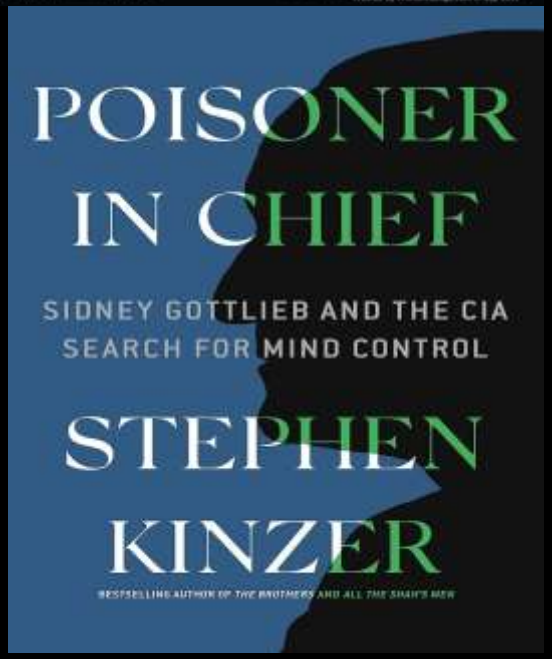
health	acute disease: single-target	chronic disease: multi-target pleiotropic

- next-generation chemical weapons
- more complex viral targeting including latent agents

Targeting of Biological Signaling Networks

- immune systems


Director, Project MK-Ultra



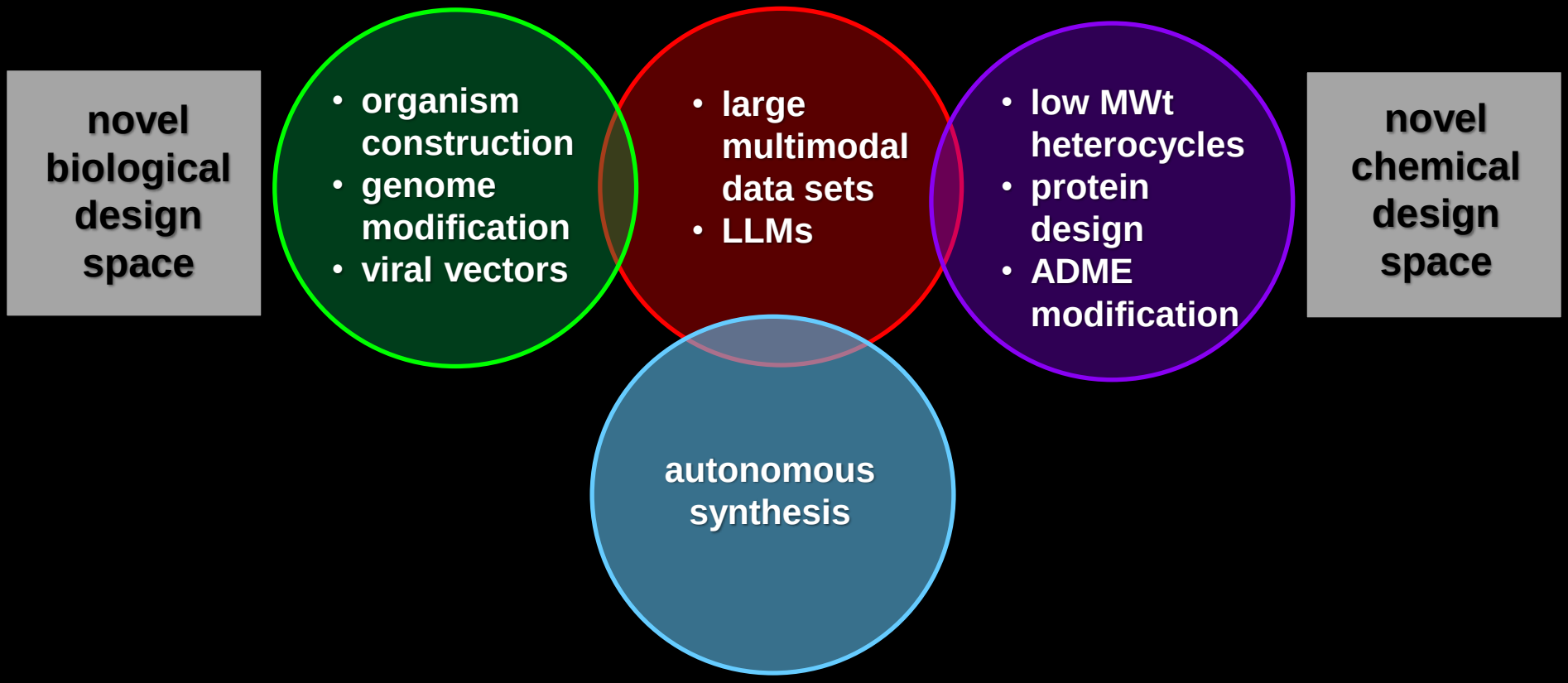
- neuromodulation

Technical Report on Mirror Bacteria: Feasibility and Risks

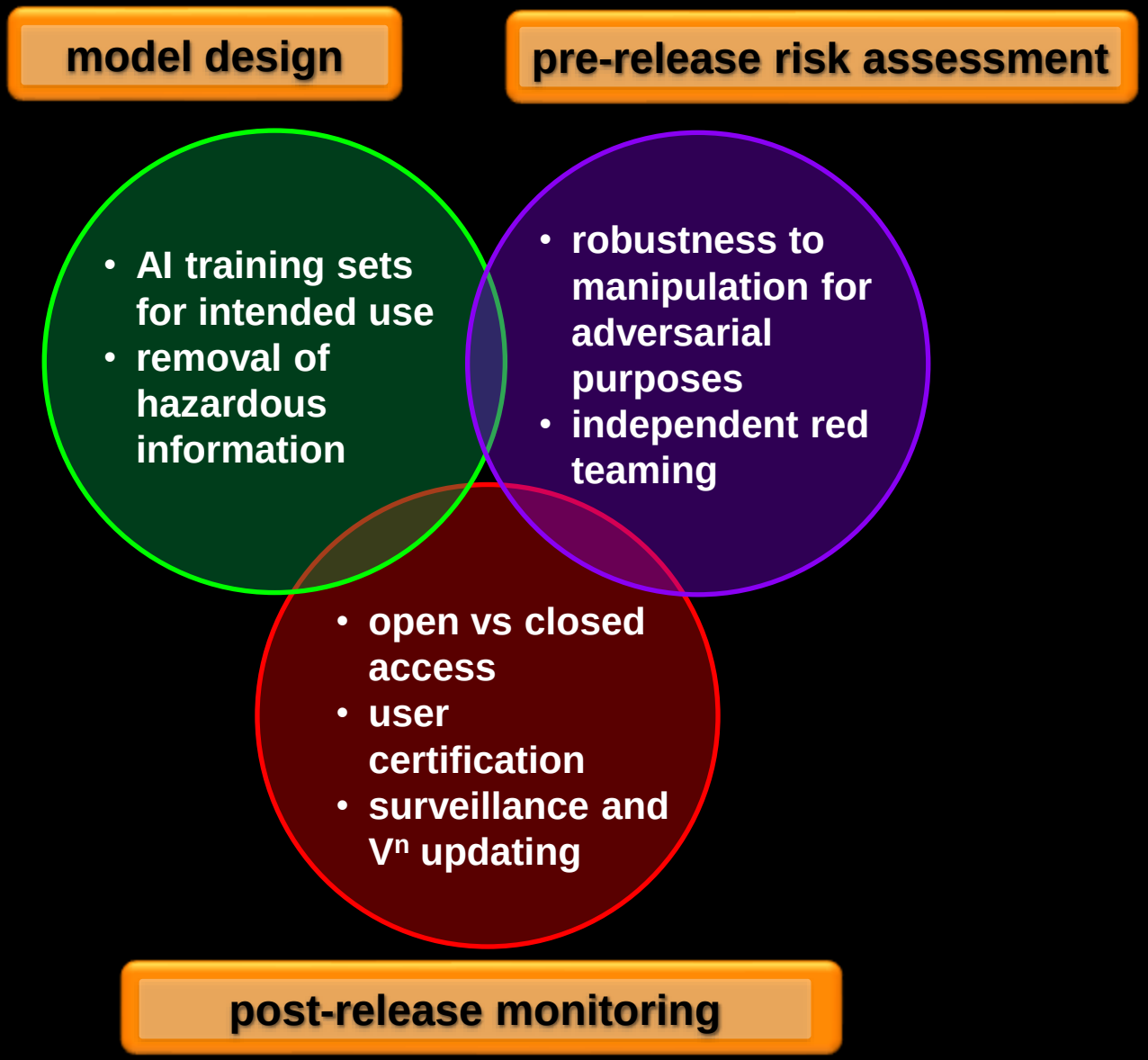
K. P. Adamala et al., “Technical report on mirror bacteria: Feasibility and risks” (Stanford Digital Repository, 2024); https://doi.org/10.25740/cv716pj4036.

December, 2024

The Quartet of BIOxAI Platforms



Guardrails for Limiting Dual-Risk Threats from the BIOxAI Convergence and LLMs



Open AI Models:
Democratization of Innovation or National Security Threat?

Proponents of Open Source of AI Models

- transparency and accessibility as catalysts to accelerate AI research and democratized innovation
- public release of model weights allows greater scrutiny, enhancing safety and security by ID and mitigation of flaws and biases
- US restrictions versus PRC open-source models might encourage more countries to adopt PRC standards/tools that will not align with liberal democratic values

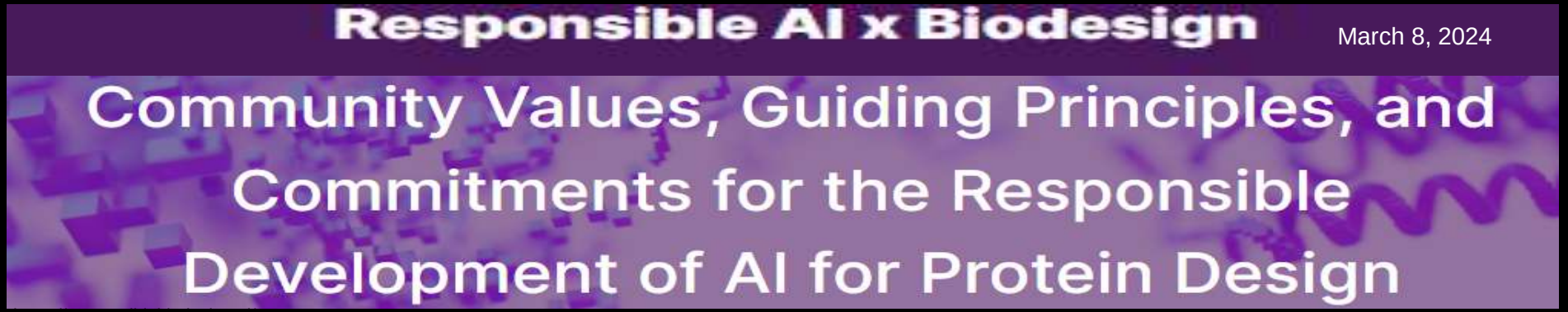
Critics of Open AI

- use for disinformation campaigns
- enhance cyberattacks
- development of military capabilities by adversarial state and non-state actors

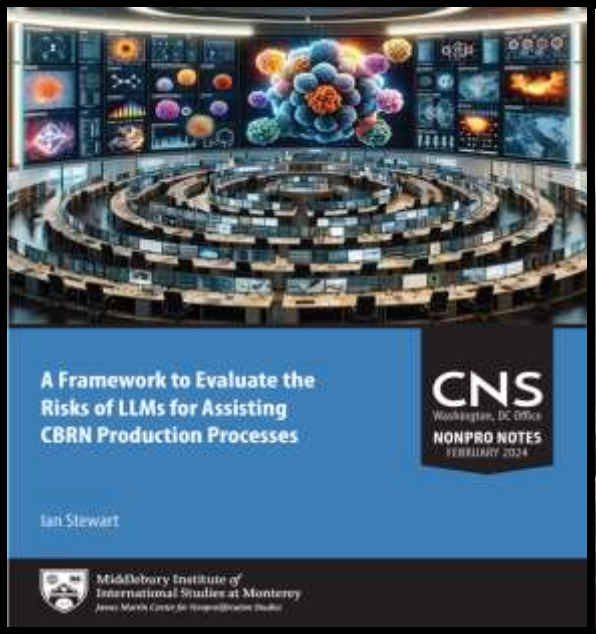
Codes of Conduct

Asilomar, February 1975

AI and Protein Design



International Cooperation in Countering the Proliferation of Weapons of Mass Destruction



Compliance With Biological Weapons Convention

- 4 signatory nations assessed as likely to have active offensive BW programs (the CRINK axis)




Satellite Images Show Major Expansion At Russian Site With Secret Bioweapons Past

https://www.washingtonpost.com/national-security/interactive/2024/russia-biological-chemical-weapons-laboratory-expansion/

A Study in Contrasts

Chemical Weapons Convention

- robust international treaty with mandated declarations, inspections and member state compliance
- comprehensive verification scheme enforced by the Organization for the Prohibition of Chemical Weapons

Biological Weapons Convention

- lack of comparable robust verification and inspections
- reliance more on voluntary compliance and transparency

International Health Regulations

- WHO oversight and major gaps revealed by COVID-19 pandemic and lack of cooperation by nation states
- do not address laboratory accidents or DURC activities and no inclusion in draft still unratified pandemic treaty draft

Biosecurity

- historical and current policies dominated by reactive responses to threats versus proactive mitigation
- expanded conceptual landscape to identify and mitigate societal instabilities posed by a broad spectrum of human interactions with diverse biological ecologies
- communicable and non-communicable diseases
- complex interactions of ecological, socio-economic, cultural, technological, commercial and political factors
  - global to local
- 'One Health' concept: the inter-dependencies (and vulnerabilities) of human, animal, plant health and ecosystem (in)stability
- the challenge of international harmonization

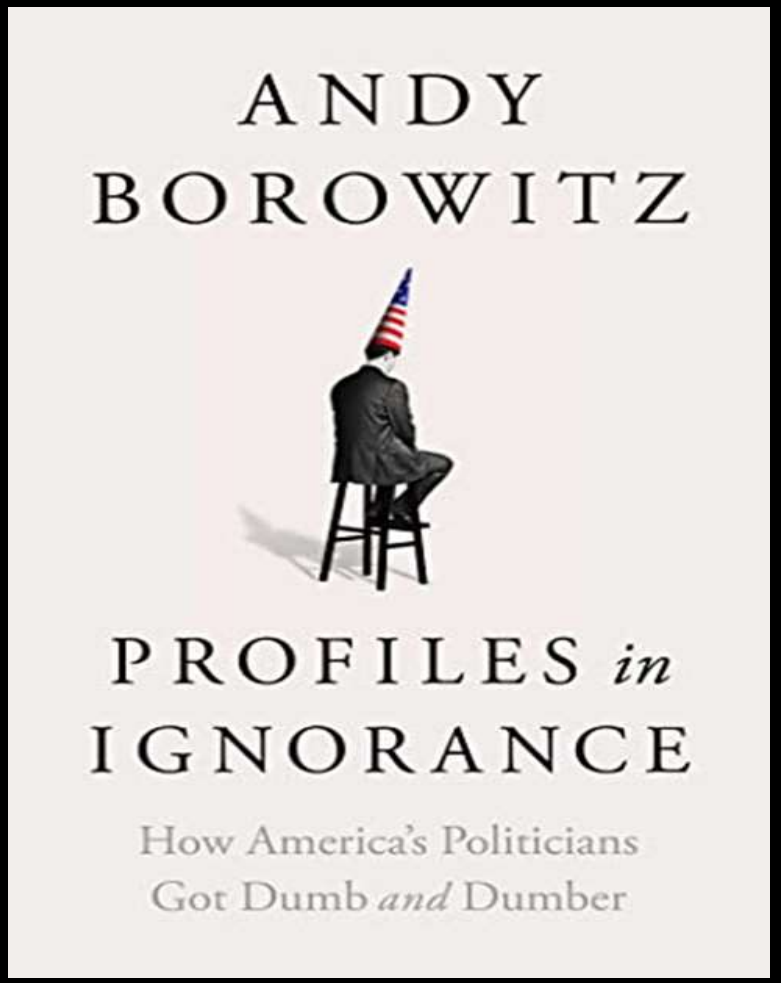
Mobilization of Whole-of-Government Capabilities to Counter Existential Threats

- the Cold War brought a sense of urgency to government decision making and whole of society engagement
  - USG (and allies), academia, industry
- similar engagement for biosecurity has not yet taken hold
- proactive inventory of known and potential threats to provide decision makers with requisite information/options to mobilize proactive actions
- many future threats are not the kind that can be defeated, only managed
  - microbes, climate, genes, digits

Napoleon Bonaparte
"In politics, stupidity is not a handicap."

"There's nothing more frightening than ignorance in action."

Goethe (1826)



The Burden of Leadership

- transcending short-termism and kicking the problem down the road
- forceful advocacy of the consequences of continued neglect and failure to act
- moving beyond the current media gotcha circus that drives political timidity an adoption of adults-in-the-room policies
- acknowledge complexity(ies) and where uncertainties exist
- communicate the unavoidable need for painful choices

“Politicians the world over known what needs to be done, just not how to get re-elected having done it.”

Jean-Claude Juncker
Former EU Commissioner
The Economist 7 Sept. 2024

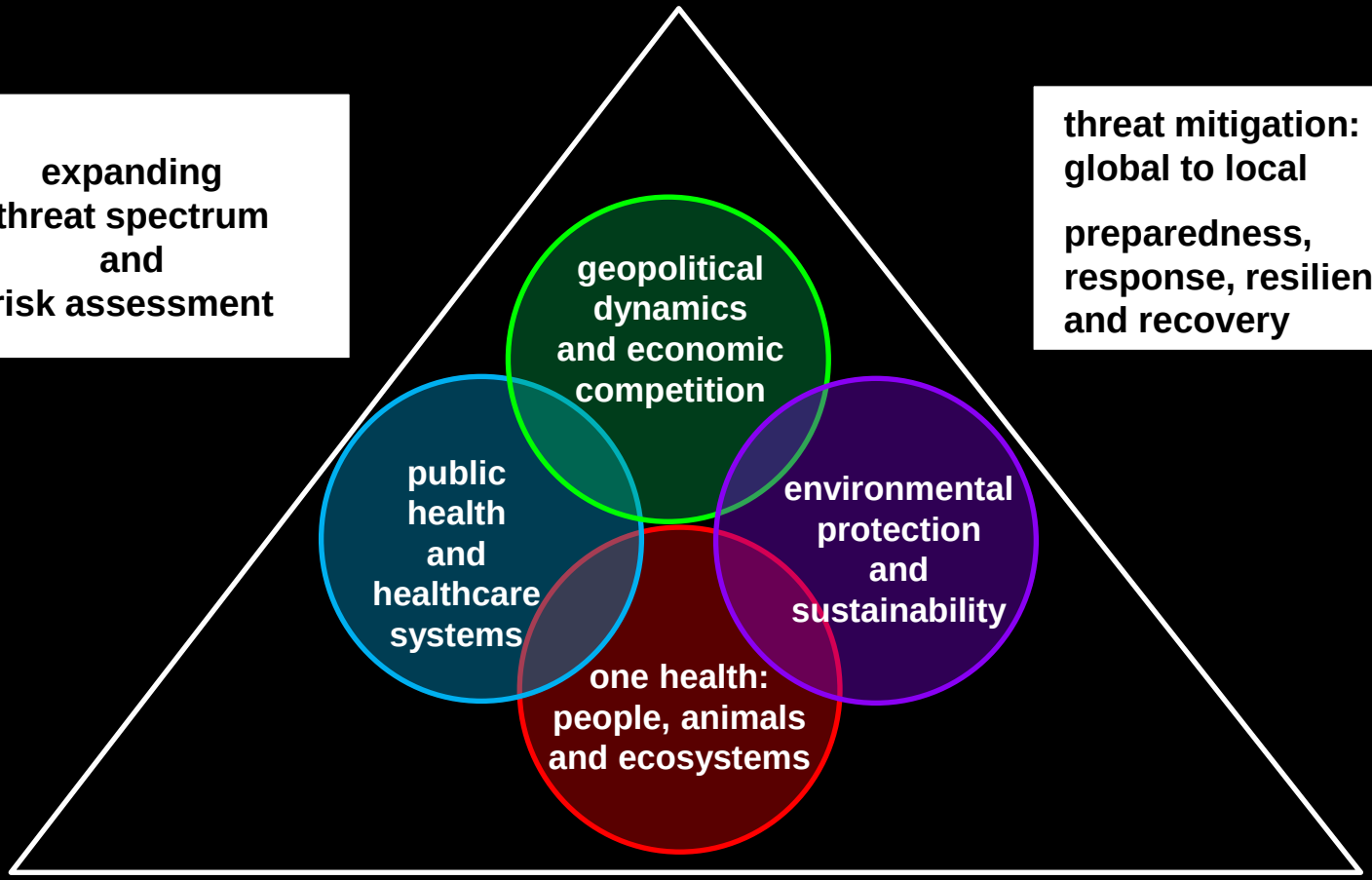
Biosecurity:

international harmonization

expanding
threat spectrum
and
risk assessment

threat mitigation:
global to local

preparedness,
response, resiliency
and recovery



technology acceleration
and
cross-disciplinary
convergence

rapid global
diffusion of
technology innovation

expansion
of
dual-risk
technologies

“Politics is the art of the possible,
the calculated science of survival”

Prince Otto von Bismarck

“Survival owes little to the art of politics,
but everything to the calculated application
of science”.

Professor Rudolph Virchow
(in reply)

“Politics is the art of the possible,
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Slides available @ https://casi.asu.edu/presentations/

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(in reply)