BTO BIOLOGICAL TECHNOLOGIES OFFICE

Michael Koeris, Office Director

Briefing prepared for George Mason University

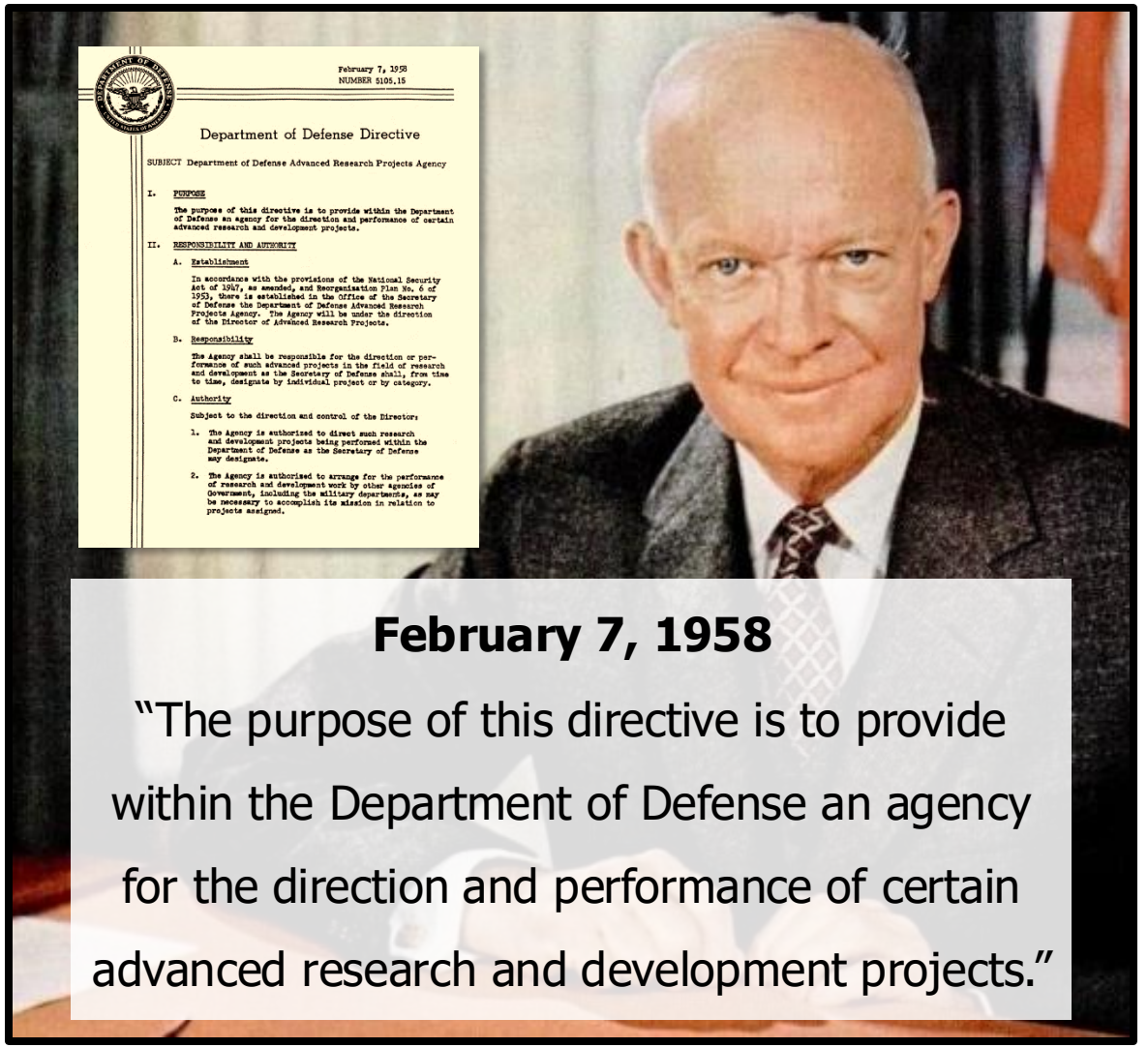
November 13th , 2024

DARPA

Origins

October 4, 1957

U.S.S.R. beats U.S. to space with Sputnik satellite; U.S. should never again be surprised by technology.



February 7, 1958
NUMBER 5105.15

Department of Defense Directive

SUBJECT Department of Defense Advanced Research Projects Agency

I. PURPOSE

The purpose of this directive is to provide within the Department of Defense an agency for the direction and performance of certain advanced research and development projects.

II. RESPONSIBILITY AND AUTHORITY

A. Establishment

In accordance with the provisions of the National Security Act of 1947, as amended, and Reorganization Plan No. 6 of 1953, there is established in the Office of the Secretary of Defense the Department of Defense Advanced Research Projects Agency. The Agency will be under the direction of the Director of Advanced Research Projects.

B. Responsibility

The Agency shall be responsible for the direction or performance of such advanced projects in the field of research and development as the Secretary of Defense shall, from time to time, designate by individual project or by category.

C. Authority

Subject to the direction and control of the Director:

1. The Agency is authorized to direct such research and development projects being performed within the Department of Defense as the Secretary of Defense may designate.

2. The Agency is authorized to arrange for the performance of research and development work by other Agencies of Government, including the military departments, as may be necessary to accomplish its mission in relation to projects assigned.

February 7, 1958

"The purpose of this directive is to provide within the Department of Defense an agency for the direction and performance of certain advanced research and development projects."

Breakthrough Technologies and Capabilities

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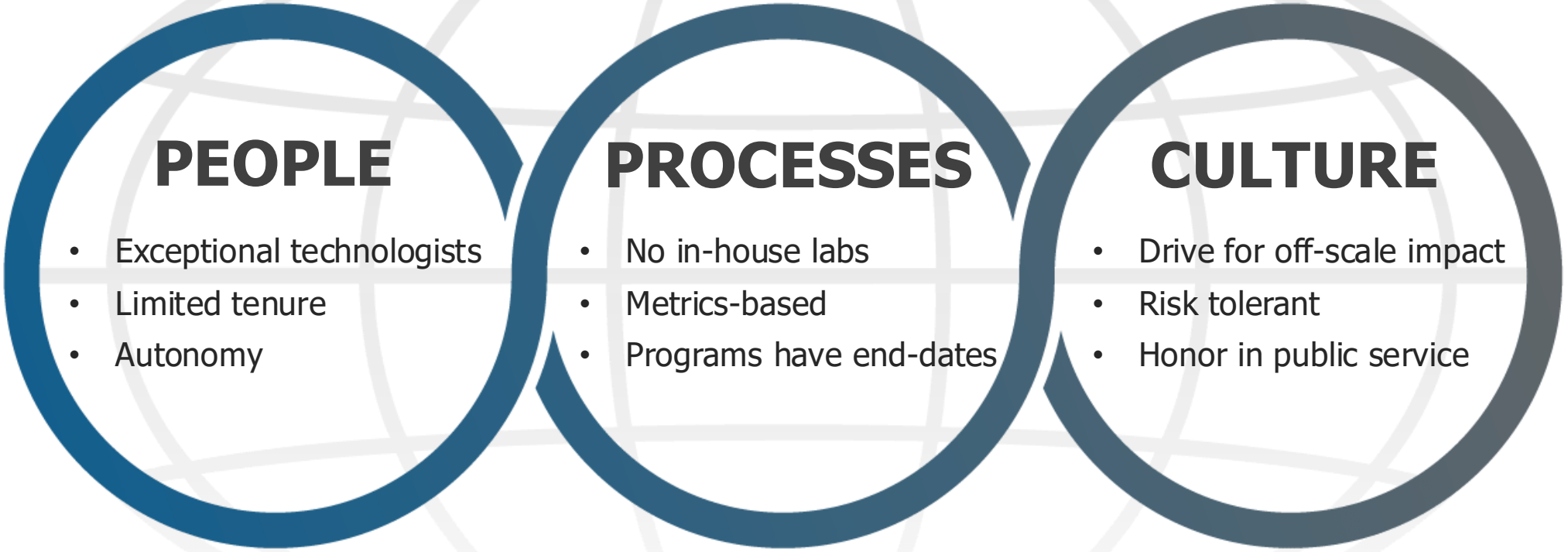

DARPA's culture persists and the agency delivers

Role in S&T ecosystem

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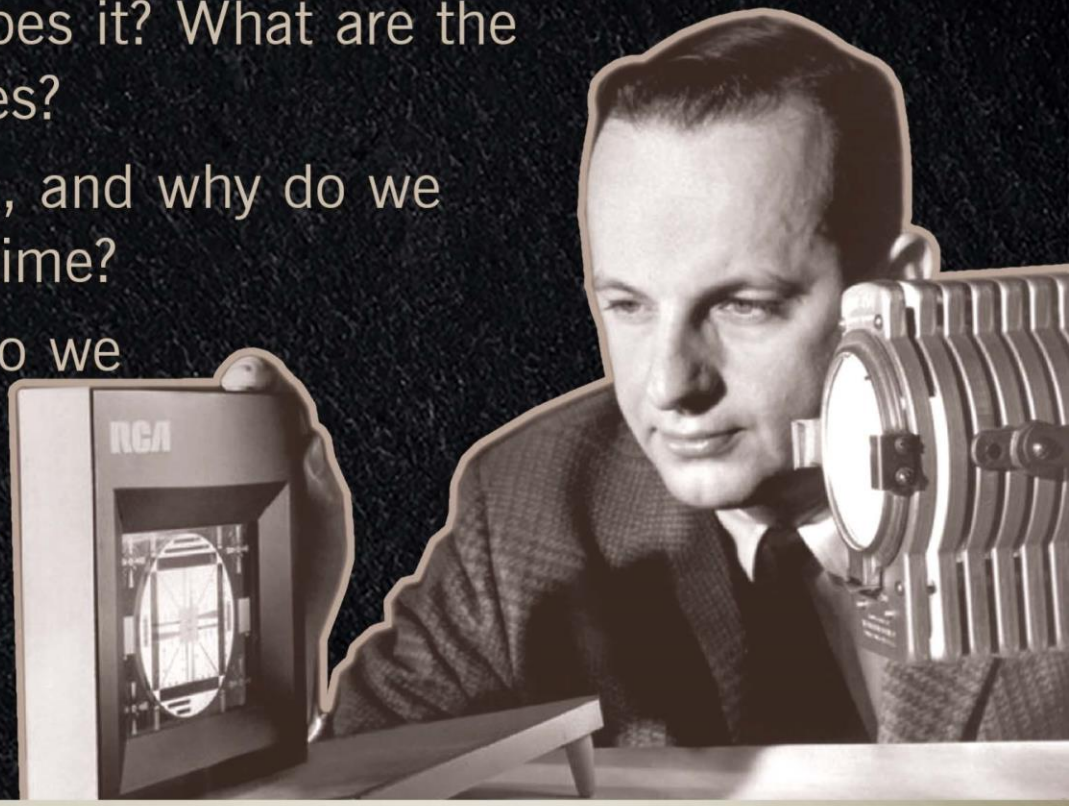
- **Create breakthrough, paradigm-shifting solutions.**
- **Accept and manage significant technology risk.**
- **Disrupt or massively accelerate technology roadmaps.**





The Heilmeier Catechism

1. What are we trying to do?
2. How is it done today and who does it? What are the limitations of the present approaches?
3. What is new about our approach, and why do we think we can be successful at this time?
4. If we succeed, what difference do we think it will make?
5. How long do we think it will take, and what are our mid-term and final exams? How much will it cost?



DARPA

George Heilmeier
DARPA Director 1975-1977

DARPA's Mission: Breakthrough Technologies for National Security

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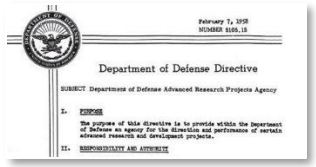
Department of Defense Directive

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I. PURPOSE

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1958: DARPA Founded

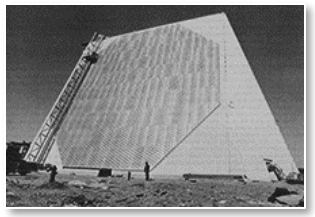
1963: Arecibo Observatory

1977: Stealth Technology

1988: UAVs

2004: Autonomous Vehicle Grand Challenge

2014: mRNA Vaccine



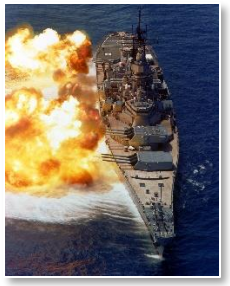
1959: Phased Array RADAR

1969: ARPANET

1984: X-29 Aircraft

2013: Blast Gauge

1960s	1970s	1980s	1990s	2000s	2010s	2020s



Early Research Investments: DARPA Pioneered Nucleic Acid Technologies

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2011

ADEPT Program Kick-Off
Next-generation vaccines and protective treatments

2013

Moderna First Funded
DARPA provides seedling funding for Moderna to pursue modified mRNA therapeutics

2014

Ebola Outbreak
ADEPT produces DNA vaccine for Ebola, >95% test subjects achieved protective immunity response

2019

Moderna Chikungunya Antibody
Moderna Announces Positive Phase 1 Results for the First Systemic Messenger RNA Therapeutic Encoding a Secreted Protein

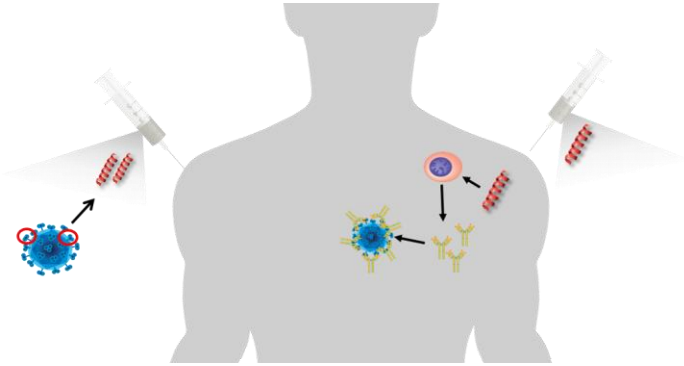
First demonstration of safety and expression in people for a gene-encoded antibody

2020

COVID Response
In July 2020, Moderna RNA vaccine entered phase 3 clinical trials

2021

COVID Response
Moderna received EUA for widespread mRNA vaccine usage



2022

COVID Response
Moderna mRNA vaccine receives full FDA approval

BTO Drives Ethical, Legal, and Social Issue (ELSI) Engagement to Ensure Responsible Technology Development

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Goal: Flexible ELSI framework to accommodate changing technical & policy landscape

Expert Analysis and Perspective

On Neurotechnology


Review

October 17, 2019

Ethical Challenges of Risk, Informed Consent, and Posttrial Responsibilities in Human Research With Neural Devices

A Review

Saskia Hendriks, MD, PhD[1,2]; Christine Grady, RN, PhD[1]; Khara M. Ramos, PhD[2]; et al

On Gene Drives


Neuroethics Guiding Principles for the NIH BRAIN Initiative

Henry T. Greely, Christine Grady, Khara M. Ramos, Winston Chiong, James Eberwine, Nita A. Farahany, L. Syd M Johnson, Bradley T. Hyman, Steven E. Hyman, Karen S. Rommelfanger, and Elba E. Serrano

Journal of Neuroscience 12 December 2018, 38 (50) 10586-10588; DOI: https://doi.org/10.1523/JNEUROSCI.2077-18.2018

Responsible Media Engagement


DARPA DEFENSE ADVANCED RESEARCH PROJECTS AGENCY ABOUT US / OUR RESEARCH /

Defense Advanced Research Projects Agency › News And Events › Setting a Safe Course for Gene Editing Research

Setting a Safe Course for Gene Editing Research

Safe Genes program aims to build a biosafety and biosecurity toolkit to reduce potential risks and encourage innovation in the field of genome editing

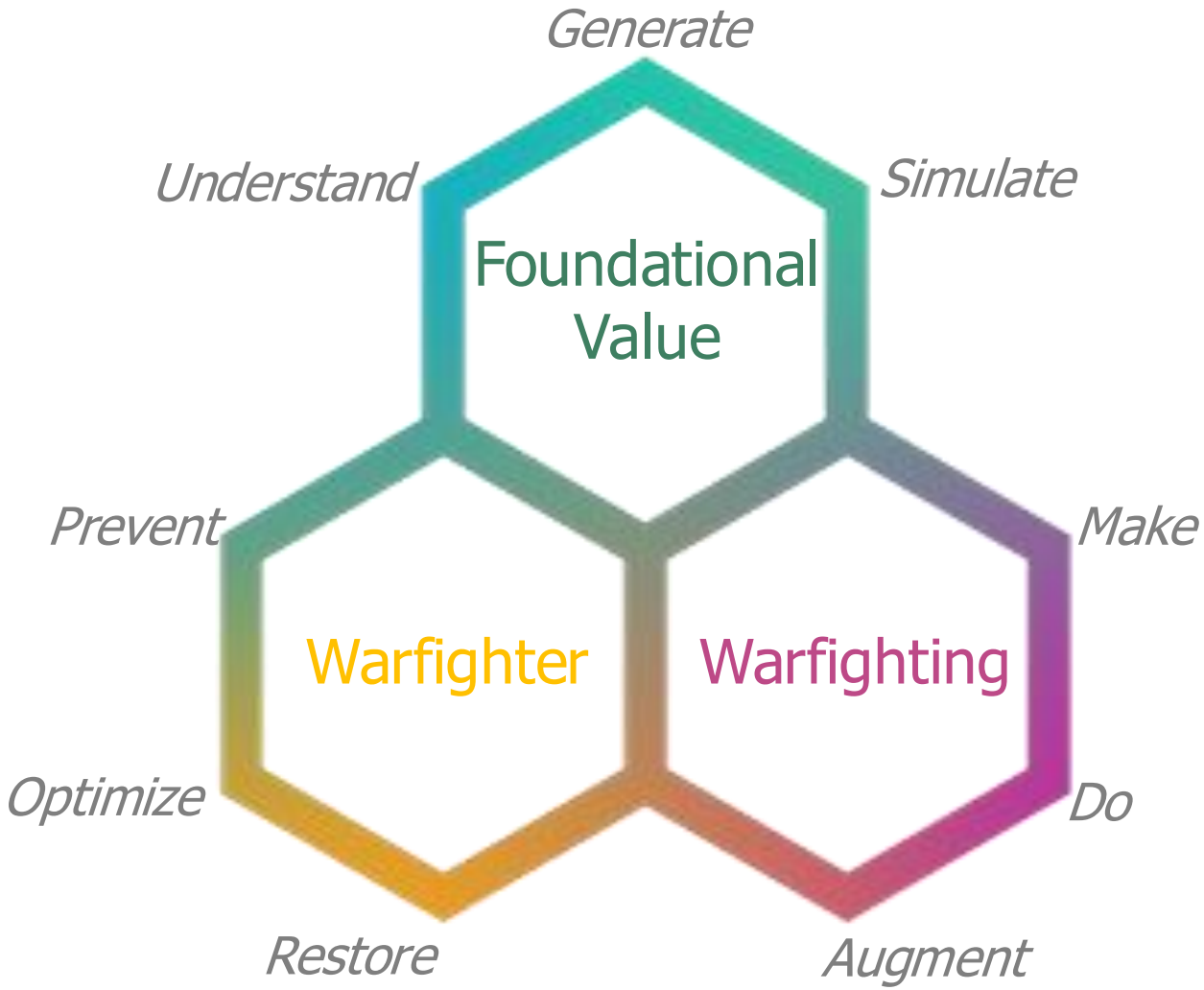
OUTREACH@DARPA.MIL
9/7/2016

Regular ELSI Meetings – Opportunity for Comment on Ongoing Efforts

Issue and Stakeholder Communication → Program Integration → Responsiveness and Transition

- New Start Discussion
- Ad Hoc Discussion
- Event Driven Interaction
- Meeting Participation

Data Factories



Combat Casualty Care

Logistics

Optimize

Ensuring peak warfighter performance throughout all phases of a mission, both physical and cognitive.

Prevent

Protecting warfighters from any threat and advancing capabilities on the battlefield for immediate injury treatment.

Restore

Creating biotechnological approaches to provide tactical care and restore function to injured warfighters.

Do

Creating solutions that increase operational resilience and logistic security

Make

Utilize the advantages of biology to enable point of need production or strengthen existing supply chains for critical commodities.

Augment

Providing technologies that harden operations against disruption and expand capabilities in the field.

Foundational Value

Generate

Vastly improve the quality and quantity of biological data, while reducing costs. Increased speed and automation of cloud labs.

Understand

Explore the state of the art and enlist stakeholders to construct necessary research portfolio.

Simulate

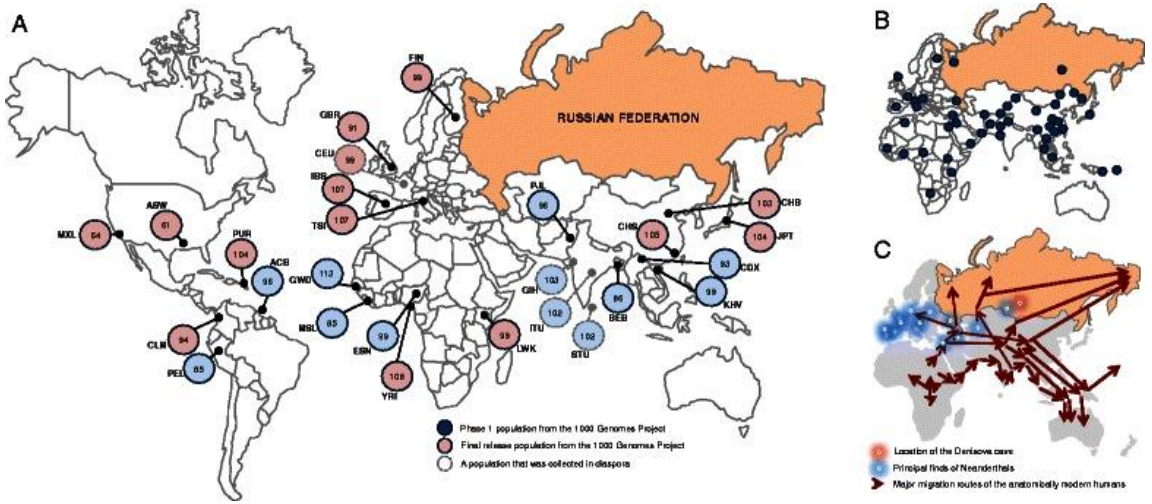
Sequence to function and function to sequence that can enable whole cell modeling and cell-cell interactions.

Modern Day Data Race

https://www.dni.gov/files/NCSC/documents/SafeguardingOurFuture/NCSC_China_Genomics_Fact_Sheet_2021revision20210203.pdf

U.S. Warns of Efforts by China to Collect Genetic Data

https://www.nytimes.com/2021/10/22/us/politics/china-genetic-data-collection.html

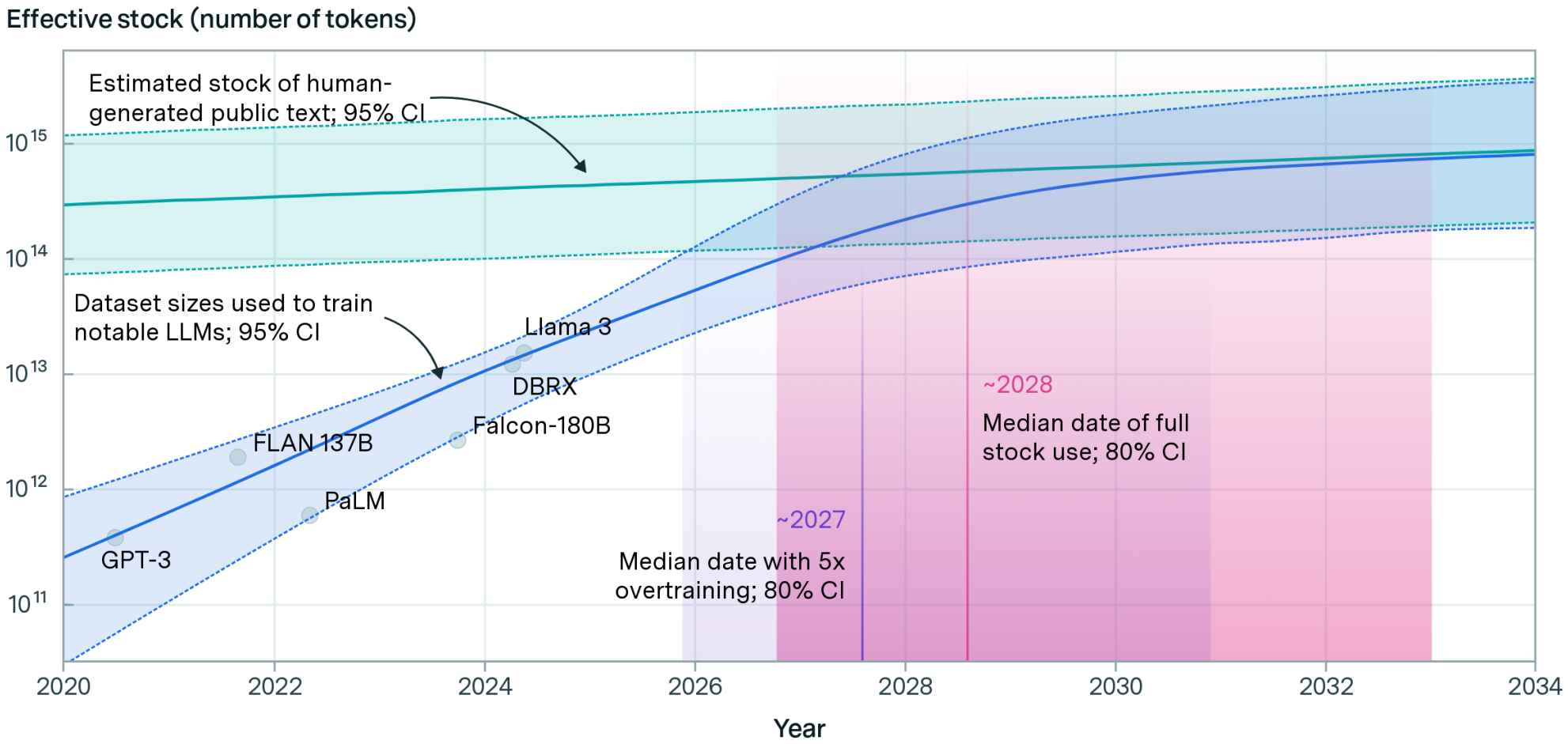


https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4644275/

Data Scarcity and Scaling Models/Laws

Projections of the stock of public text and data usage

EPOCH AI



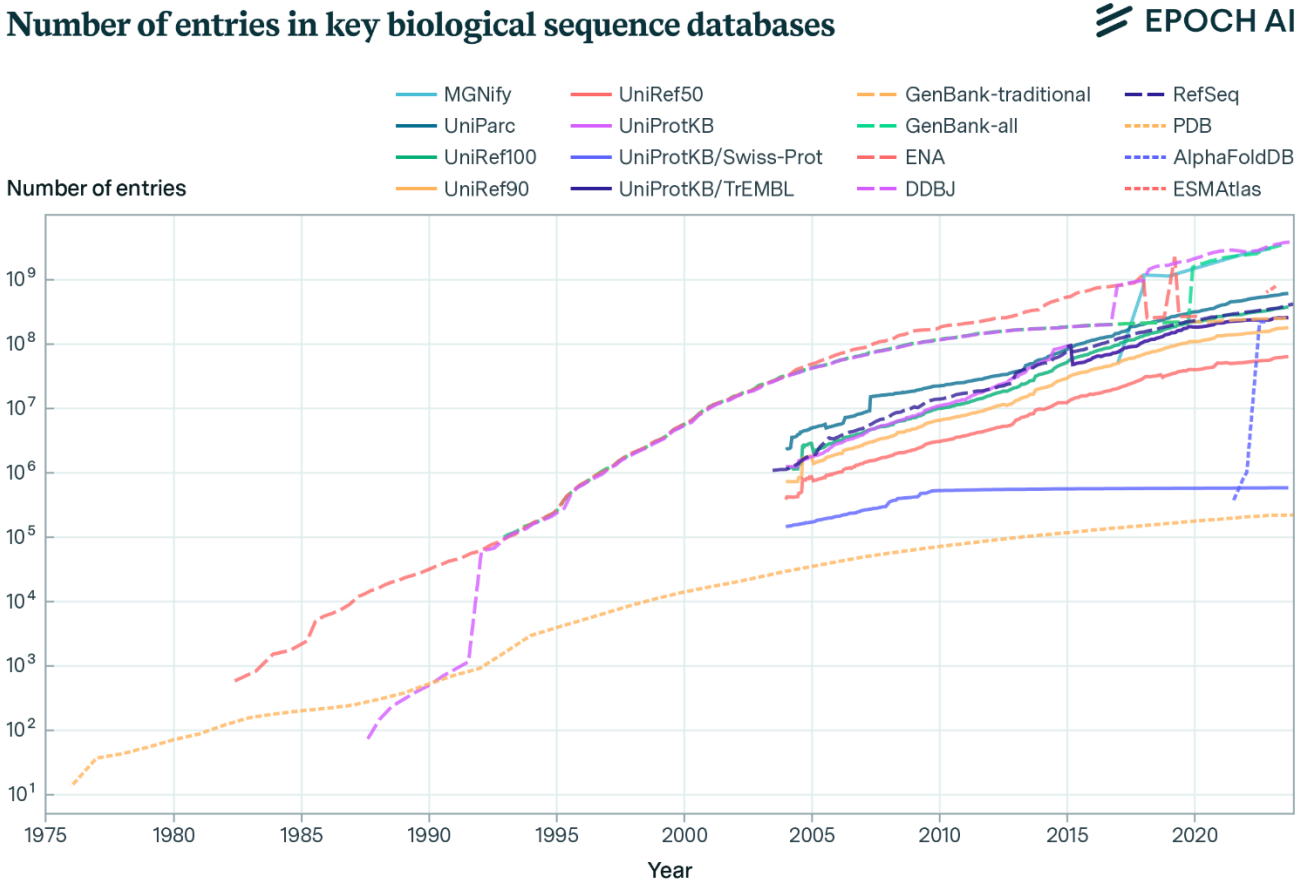
Pablo Villalobos, Anson Ho, Jaime Sevilla, Tamay Besiroglu, Lennart Heim, and Marius Hobbhahn. 'Will we run out of data? Limits of LLM scaling based on human-generated data'. *Published online at epochai.org.*

Biological Data Scarcity and Scaling Models/Laws

Current estimated state of biological sequence data is 7 billion protein sequences, which represents 1.4 trillion tokens (unique identifier).

State-of-the-art Large Language Models are typically trained on the order of 10T tokens.

We are biological sequence data limited for training foundational biological models.



Nicole Maug, Aidan O'Gara and Tamay Besiroglu (2024), "Biological Sequence Models in the Context of the AI Directives". *Published online at epochai.org.*

Data vs Software vs Hardware Tipping Points

Current limitation is we don't have enough biological data to test Foundational Biological Models

Solutions to Scaling Biological Data Generation

- Human (low scale / high flexibility / low reproducibility)
- Automation (moderate scale / low flexibility / high reproducibility)
- Pooling (high scale, less flexibility / depth)
- Gap analysis & synesthetic data generation

BTO AI Focus Areas

- Prediction and Health
- Autonomous Science
- Bio-Manufacturing/ Synthetic Biology
- Challenges with Scale
- Exciting Frontiers

Recently Approved Programs (~ last 6 months)

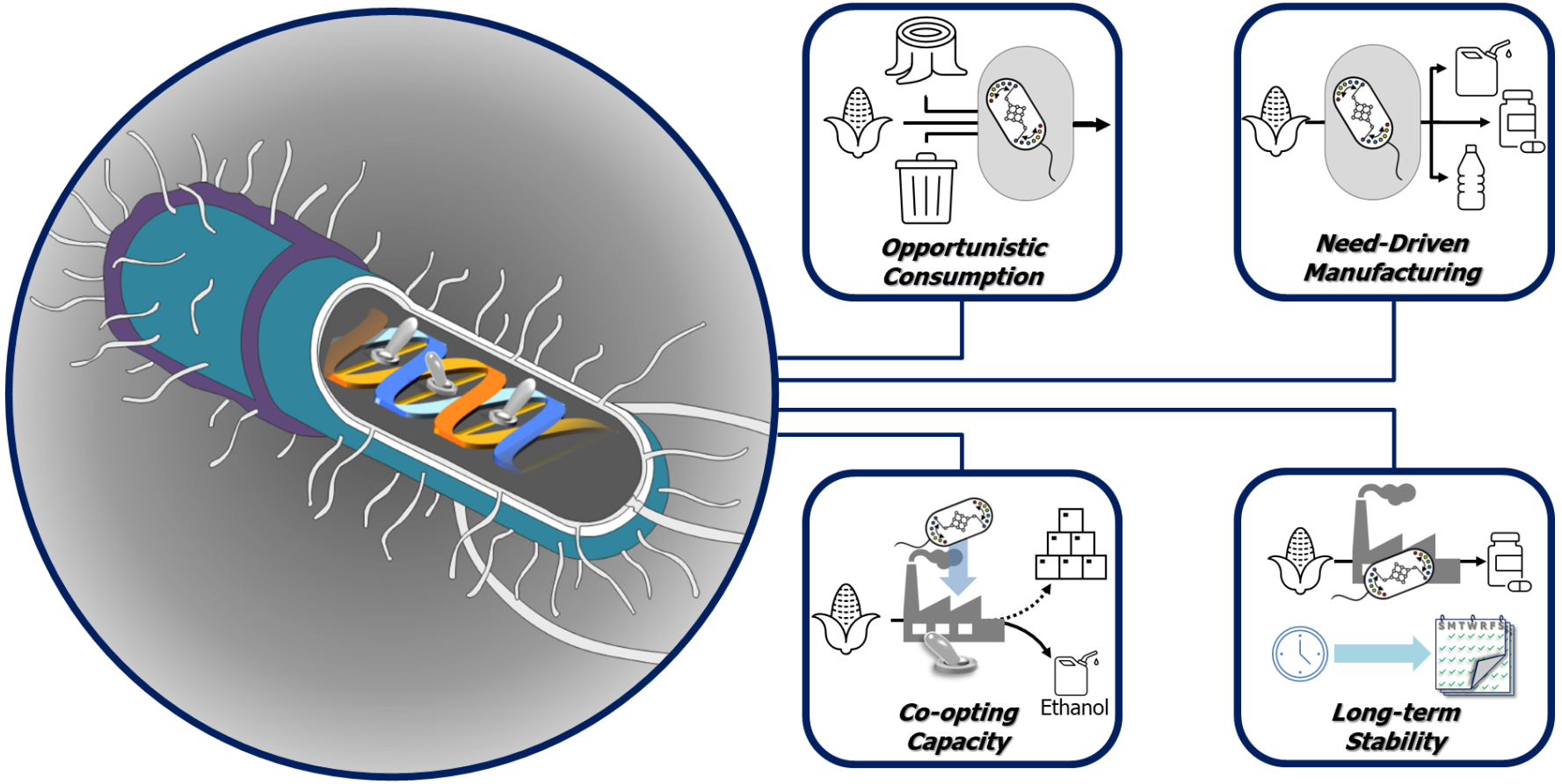
Alert WARfighter Enablement (AWARE)

DoD Problem: Active duty conditions lead to sleep loss, which impairs warfighter alertness and performance

Program Vision: Rapidly achieve peak cognitive function following sleep loss through targeted neuromodulation

Switch

DoD Problem: DoD needs commodity organic chemical/material manufacturing capacity that can be turned on in a crisis, but this will be limited by access to raw materials/natural products



Vision: Improve commercial tractability of biomanufacturing by enabling new CONOPS that afford flexible chemical synthesis

Simulating Microbial Systems (SMS)

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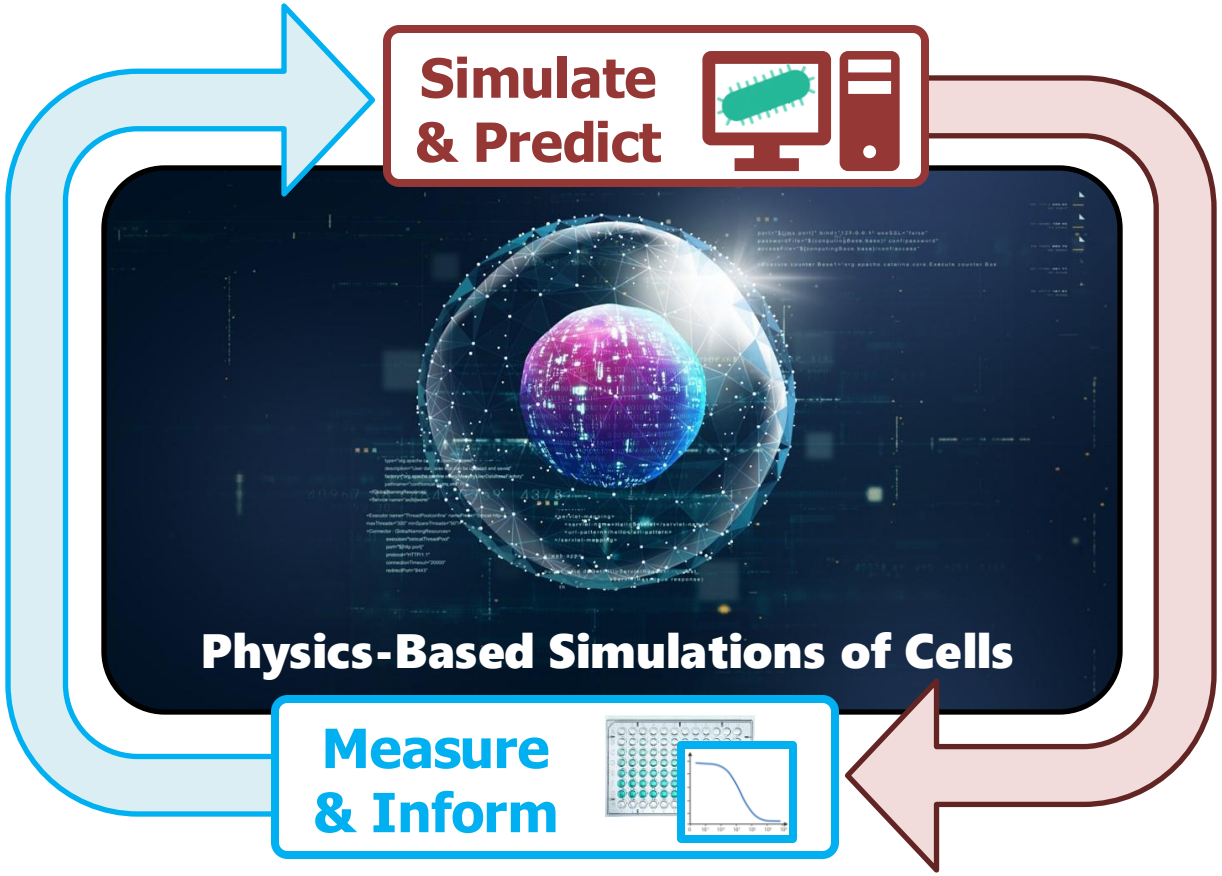
DoD Problem: Need general capability to simulate cell function at all classification levels to predict chem/bio threats and prevent surprise



Simulations will be a valuable tool for…

Biosecurity & Threat Assessment

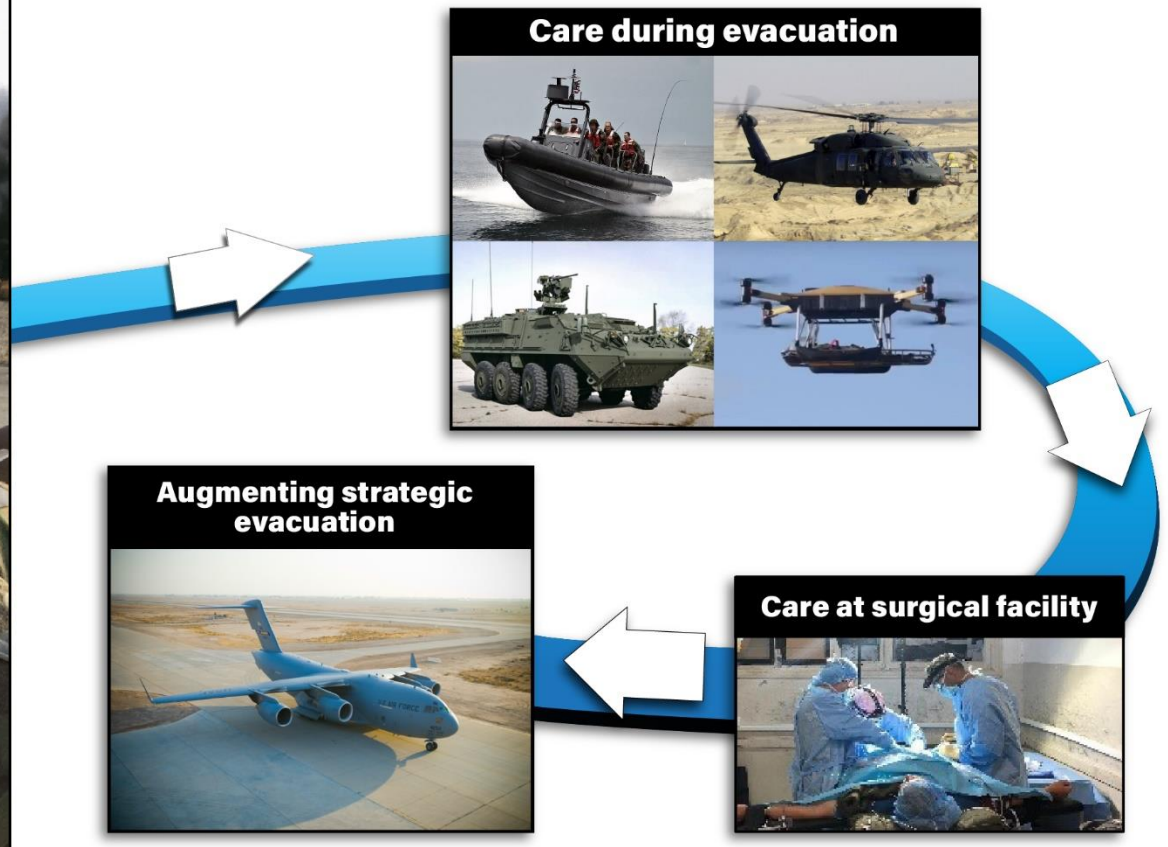
Accelerate Medical Countermeasure R&D

Biomanufacturing (Robust Supply Chain)

Program Vision: Create physics-based simulations to predict the behavior of cells

GOLDen hour extended EVACuation (GOLDEVAC)

DoD Problem: Current "golden hour" operations for medical evacuation of injured service members will not function for future conflicts in all theaters



Program vision: Provide expert level care – from point of injury through entire evacuation process

www.darpa.mil