AI and Biodesign:
NASEM in silico workshop

Lynda Stuart, MD PhD

CEO, Fund for Science and Technology

Former Executive Director, Institute for Protein Design, University of Washington

Co-chair, NASEM Consensus Study: “The Age of AI in the Life Sciences”

Our New Report

Committee on Assessing and Navigating Biosecurity Concerns and Benefits of Artificial Intelligence Use in the Life Sciences

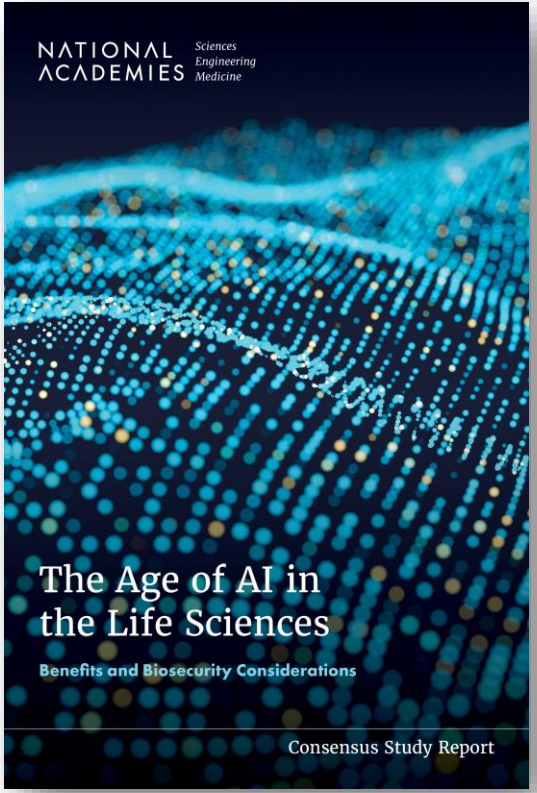
Sponsor:

The Department of Defense (DoD)

Board on Life Sciences

Computer Science and Telecommunications Board

Committee on International Security and Arms Control



Report available to the public on Friday, March 14 @ 11am ET.

Convergence of AI and Life Sciences

- Computer and information sciences have been evolving for decades to meet the needs of the life sciences

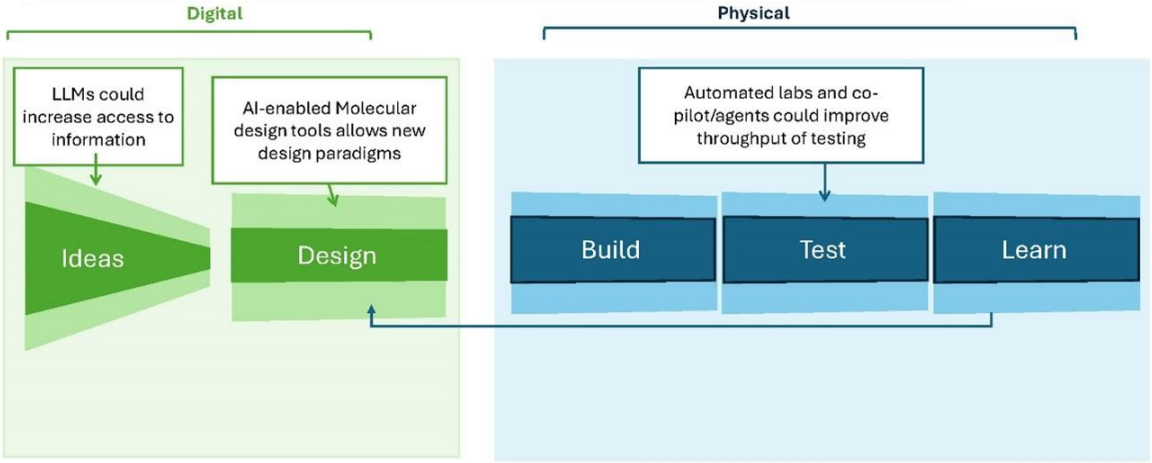
- The past four years have witnessed rapid advances in the development of AI models for biological applications

- Promising applications
  - Drug discovery
  - Precision medicine
  - Medical imaging interpretation
  - Synthetic biology

- Security concerns
  - Engineer biological agents: design, build, and deploy
  - Lower barriers to entry: expertise, resources

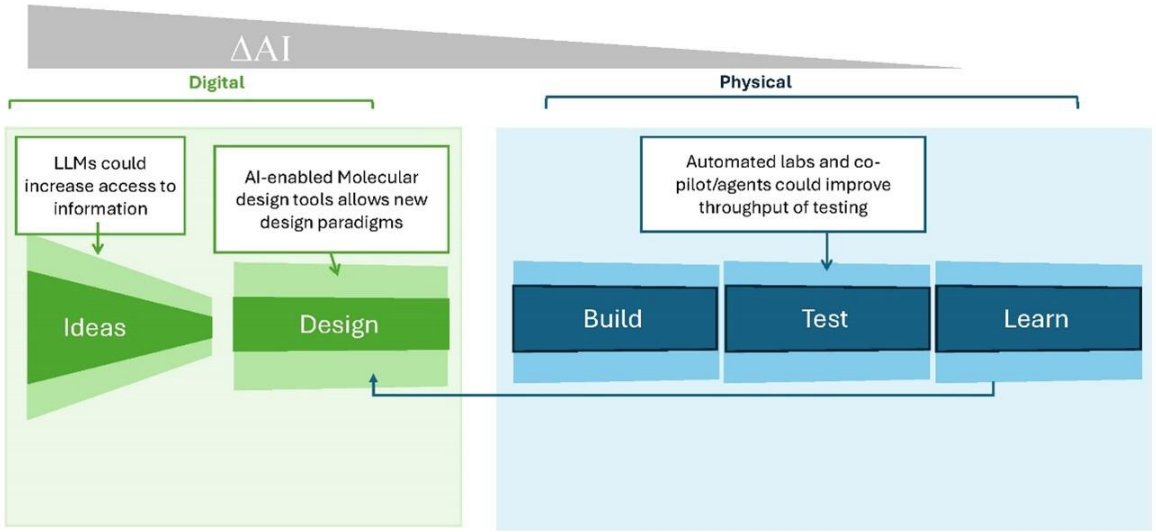
Nobel Prize in Chemistry 2024

AI-Enabled Biological Design



- Synthetic Biology: concepts, approaches, and tools that enable the modification or creation of biological organisms

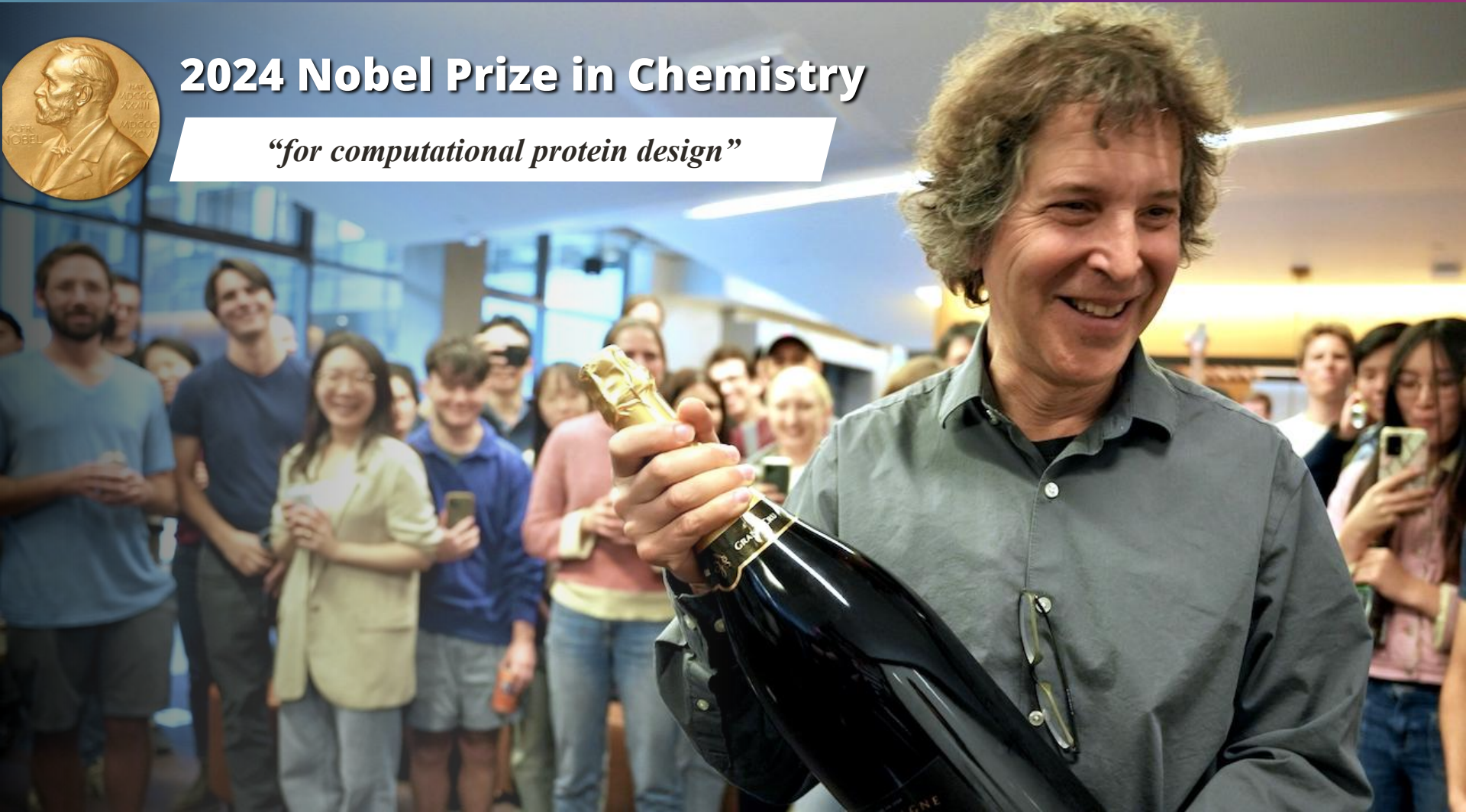
AI-Enabled Biological Design



- Synthetic Biology: concepts, approaches, and tools that enable the modification or creation of biological organisms
- **ΔAI: What is the capability uplift in synthetic biology?**

Summary

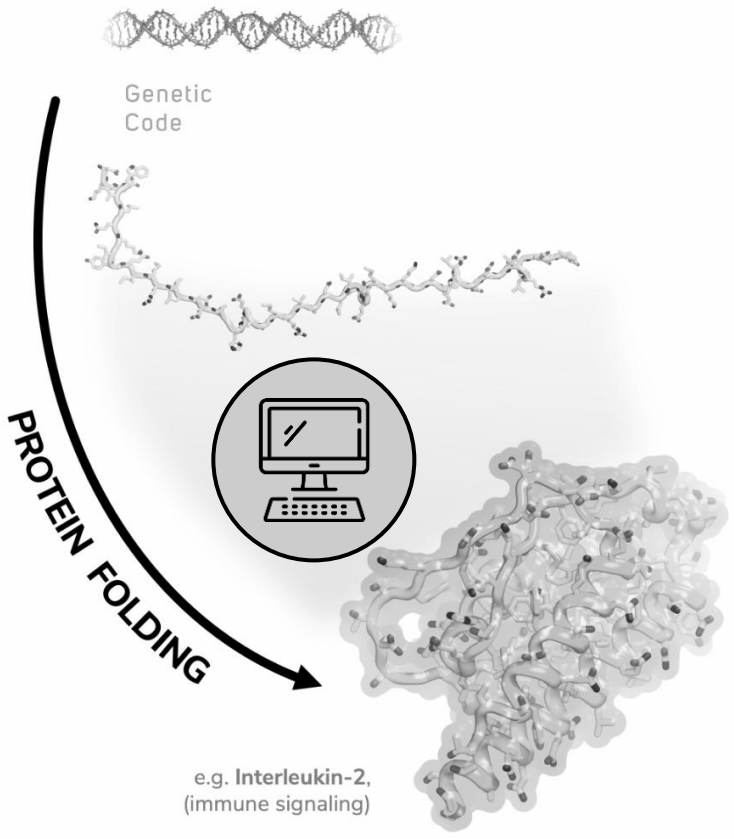
- AI applications in the life sciences is a dynamic area of development
- Capabilities are limited by the biological complexity of tasks, availability of biological data for training models, and need for experimental validation
- High-quality biological data is crucial for training models and innovation
- Balance of beneficial applications in biosecurity against potential risks by investing in research and infrastructure with risk assessment
- **Capability uplift of current AI biological tools most significant for design**
- **AI tools for developing vaccines and medical countermeasure could contribute to biosecurity by accelerating the response to microbial threats, irrespective of their origin**



2024 Nobel Prize in Chemistry

“for computational protein design”

I. Protein Structure Prediction

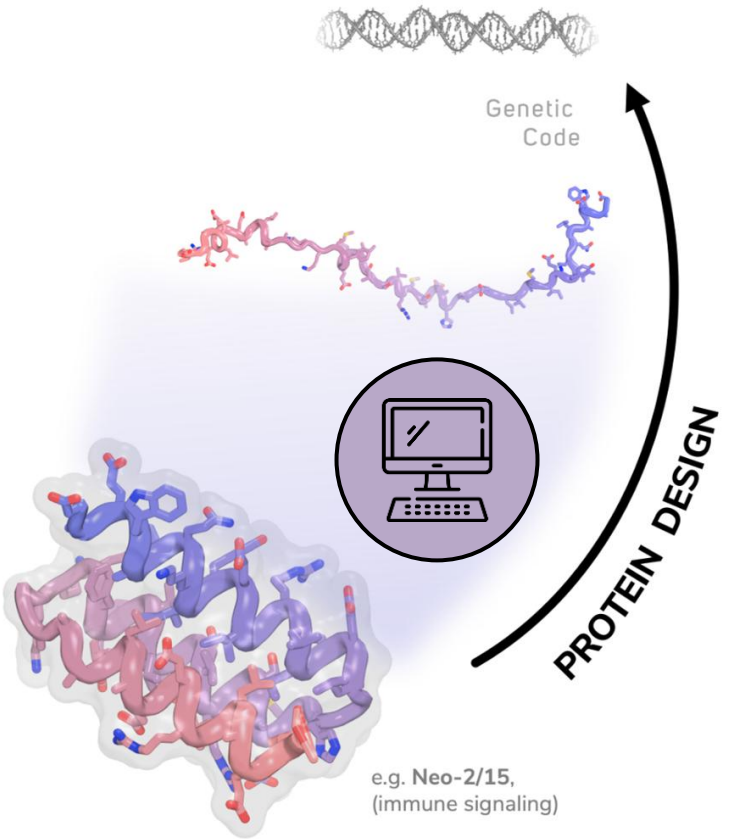


Gene sequence

Amino acid sequence

3D protein structure

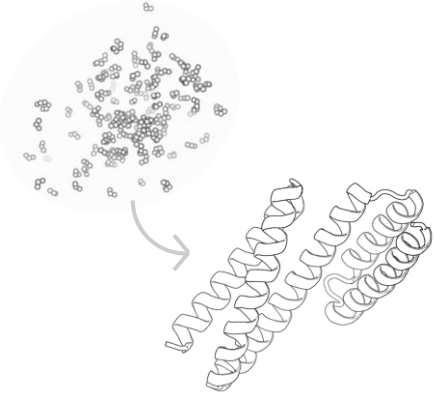
II. Protein Design



New AI tools unlock a universe of new possibilities

RFdiffusion

Generates new protein structures

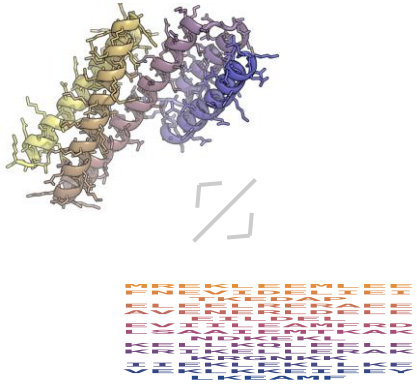


Original: Watson et al, **Nature**. 2023

All-Atom: Krishna et al, **Science**. 2024

ProteinMPNN

Assigns amino acids to protein structures

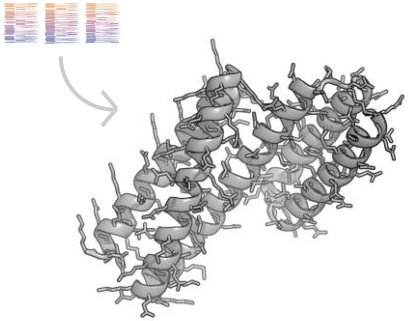


Original: Dauparas et al, **Science**. 2022

All-Atom: *in development*

RoseTTAFold

Predicts structures from sequence



Original: Baek et al, **Science**. 2021

All-Atom: Krishna et al, **Science**. 2024

2021 **BREAKTHROUGH OF THE YEAR** *Science*
2021 **METHOD OF THE YEAR** *Nature Methods*

Generative AI for protein design

IMAGE DIFFUSION

inject noise

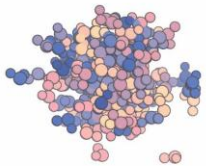
- **Trained on real photos**
- **Generates new images**

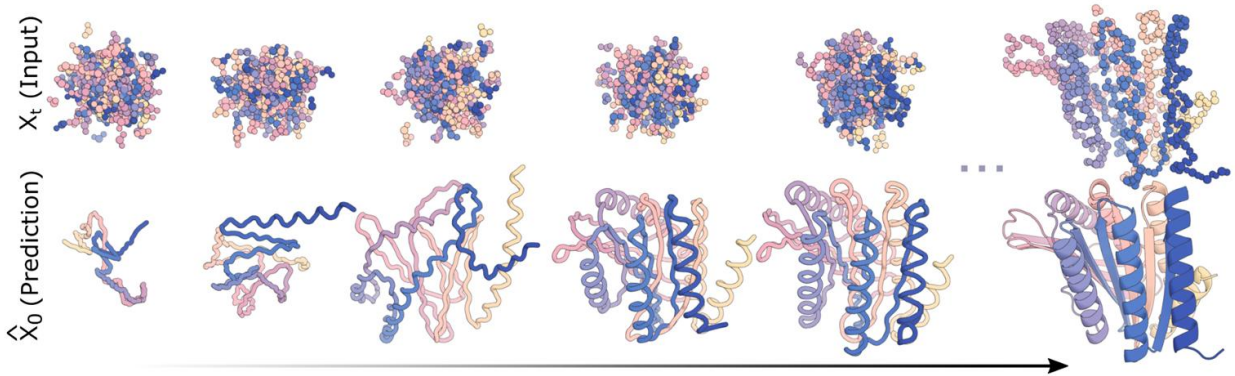
e.g. DALL-E, Midjourney, Stable Diffusion

Image trajectory by NVIDIA

PROTEIN DIFFUSION

remove noise



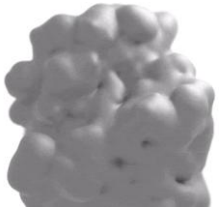


RFdiffusion Watson et al, Nature, 2023

With new protein design tools we can create…

BIOLOGICS

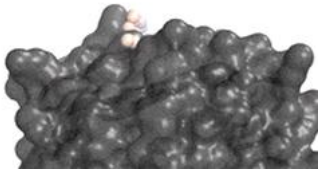
Peptides



e.g. BCL2

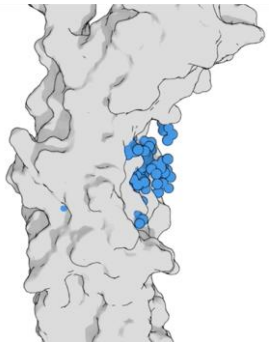
Minibinders

≤65AA



e.g. insulin receptor

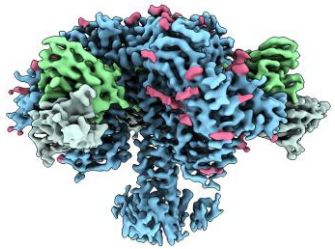
Antibodies



e.g. influenza HA

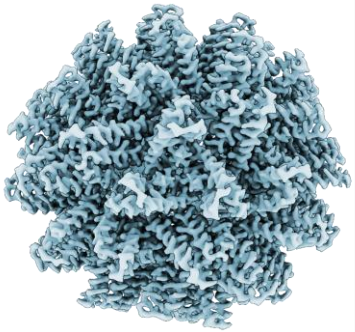
VACCINES

Immunogens



e.g. HIV envelope

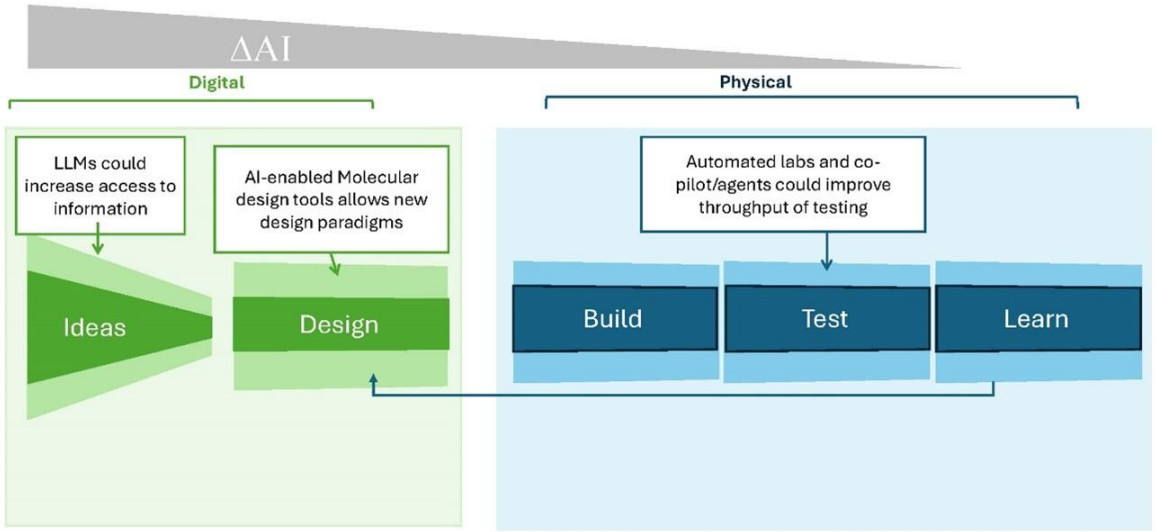
Nanoparticles



e.g. class 1 viral fusion proteins

SIZE (amino acids)

AI-Enabled Biological Design



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The in silico benefits and risk (1)

- Synthetic Biology and now bio-design is a promising area for research and scientific investment
- US is currently the leader in this field (evidenced by the Nobel)
- Opportunities for Impact will continue to increase in the wake of the next generation of AI-enabled bio-design tools
- Benefits currently outweigh risk and innovation should be supported to realize the potential impact
- Risks can be managed by adopting an adaptive “if-then framing” to monitor new advances in this area (see NASEM report for detailed recommendations)

The in silico benefits and risk (2)

- AI tools can generate vast numbers of hypotheses
- **Risks for synthetic biology do not manifest in the design phase but only after they move from the digital to physical world**
- Currently wet lab experimentation is required to validate design to confirm function
- It is possible to imagine, at some point in the future, that both design and filtering (the final step) reaches a level of accuracy that wet lab testing is not required but currently that is not the case.
- Could propose to adopt an “if-then” solution for evaluating how or what to publish based on: 1) the proposed function being designed and 2) the state of the accuracy of design models and need for wet lab testing