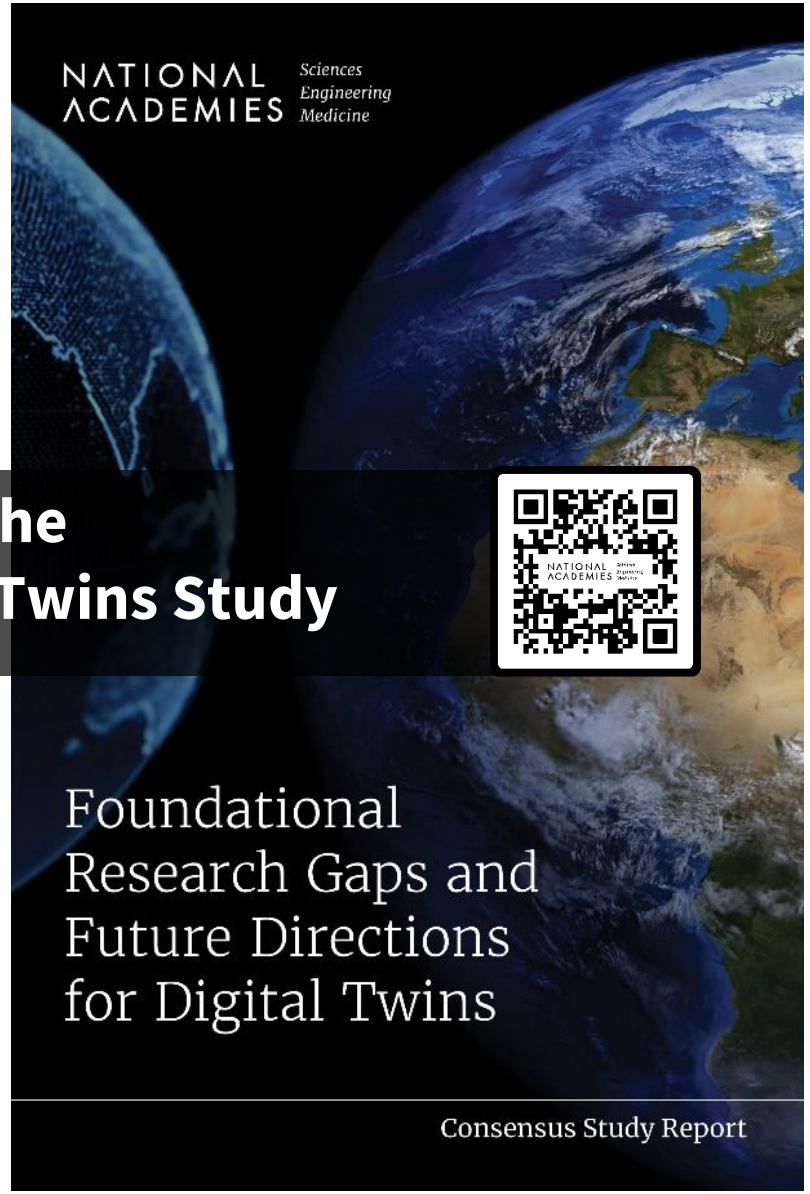
FDA/MDIC Symposium on Computational Modeling and Simulation

Generating Regulatory In Silico Evidence

Foundational Research Gaps and Future Directions for Digital Twins

Conrad Grant

MDIC Medical Device Innovation Consortium



About the Digital Twins Study

Advancing mathematical, statistical, and computational foundations

- How are digital twins defined across different communities?
- Foundational research needs and systemic gaps
- Promising practices across domains and sectors
- Opportunities for translation of best practices across domains
- Use cases for awareness and building confidence
- Key opportunities in research, development, and application

Committee Members

- Karen Willcox (NAE; chair), UT Austin
- Derek Bingham, Simon Fraser University
- Caroline Chung, MD Anderson
- Julianne Chung, Emory
- Carolina Cruz-Neira (NAE), UCF
- Conrad Grant, JHUAPL
- Jim Kinter, George Mason
- Ruby Leung (NAE), PNNL
- Parviz Moin (NAS/NAE), Stanford
- Lucila Ohno-Machodo (NAM), Yale
- Colin Parris (NAE), GE
- Irene Qualters, LANL
- Ines Thiele, Univ. of Galway
- Conrad Tucker, CMU
- Rebecca Willett, Univ. of Chicago
- Xinyue Ye, Texas A&M

Study Director: Brittany Segundo

Information Gathering

10 speakers in 5 information gathering sessions

46 speakers in 3 domain-specific workshops

Recordings and proceedings are available on the study webpage: https://www.nationalacademies.org/digital-twins

- Three public workshops
  - Biomedical Sciences (Jan 30, 2023)
  - Atmospheric, Climate, and Sustainability Sciences (Feb 1-2, 2023)
  - Engineering Domains (Feb 7 & 9, 2023)

Report Snapshot

0. Summary
1. Introduction
2. The Digital Twin Landscape
3. Virtual Representation
4. The Physical Counterpart
5. Feedback Flow from Physical to Virtual
6. Feedback Flow from Virtual to Physical
7. Towards Scalable and Sustainable Digital Twins
8. Summary of Findings, Conclusions, and Recommendations

48	22	19	8
Gaps	Findings	Conclusions	Recommendations

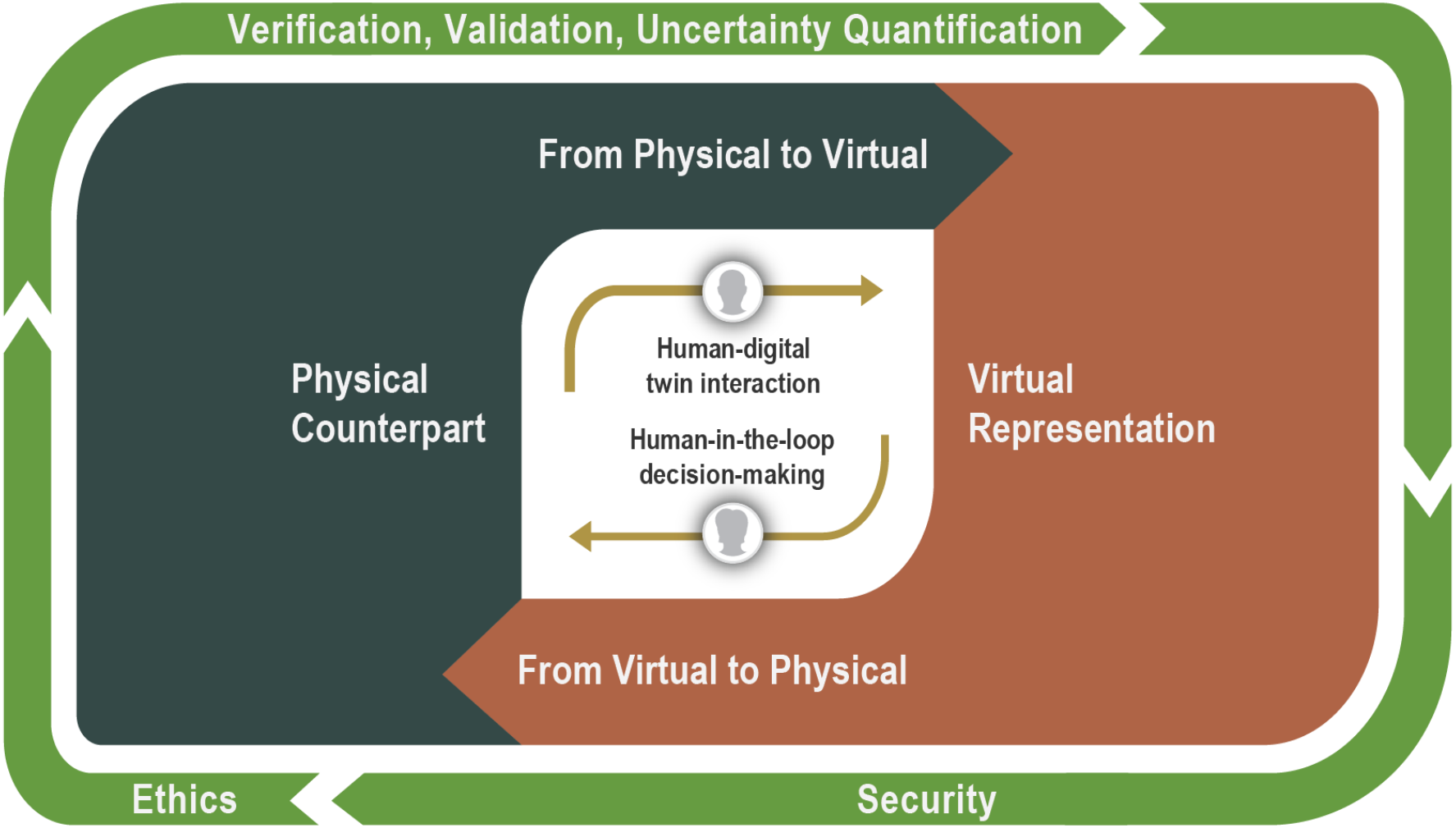
Digital twins hold immense promise in accelerating scientific discovery and revolutionizing industries, and they can be a critical tool for decision-making based on a synergistic combination of models and data.

Definition of a Digital Twin

> *A digital twin is a set of virtual information constructs that mimics the structure, context, and behavior of a natural, engineered, or social system (or system-of-systems), is dynamically updated with data from its physical twin, has a predictive capability, and informs decisions that realize value. The bidirectional interaction between the virtual and the physical is central to the digital twin.*

Committee's definition builds on a definition from an AIAA and AIA Position Paper (2020)

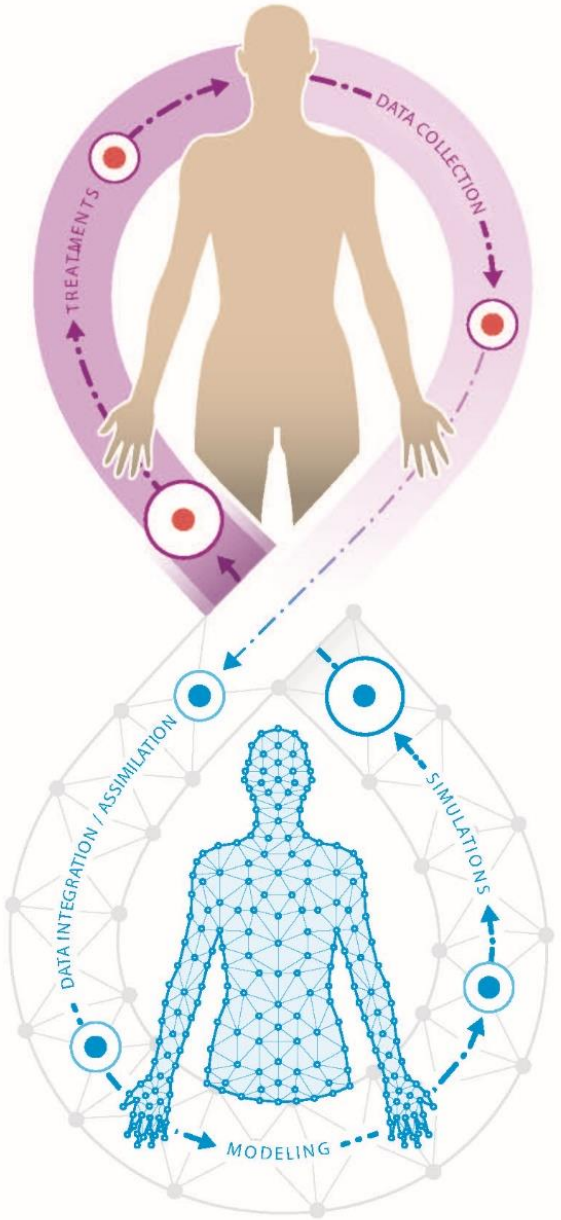
A Digital Twin is More Than Just Simulation and Modeling



Digital Twin Elements

A Cancer Patient Example

- **Virtual representation**: Mechanistic and empirical models representing tumor growth, patient response, etc.
- **Physical counterpart**: Patient data collected from imaging studies, blood tests, and other clinical assessments
- **Bidirectional interaction**
  - updates the virtual representation to reflect characteristics of the individual patient
  - informs clinical decisions: treatments and clinical assessments
  - new clinical assessments inform and update the digital twin



What has been realized and what remains aspirational?

The **publicity** around digital twins currently **outweighs the evidence** base of success.

Cutting through the hype

Digital twins have the capacity to revolutionize scientific and industrial growth, but…

Important to separate the aspirational from the actual to **strengthen the credibility** of digital twin research and to **recognize that serious research questions remain.**

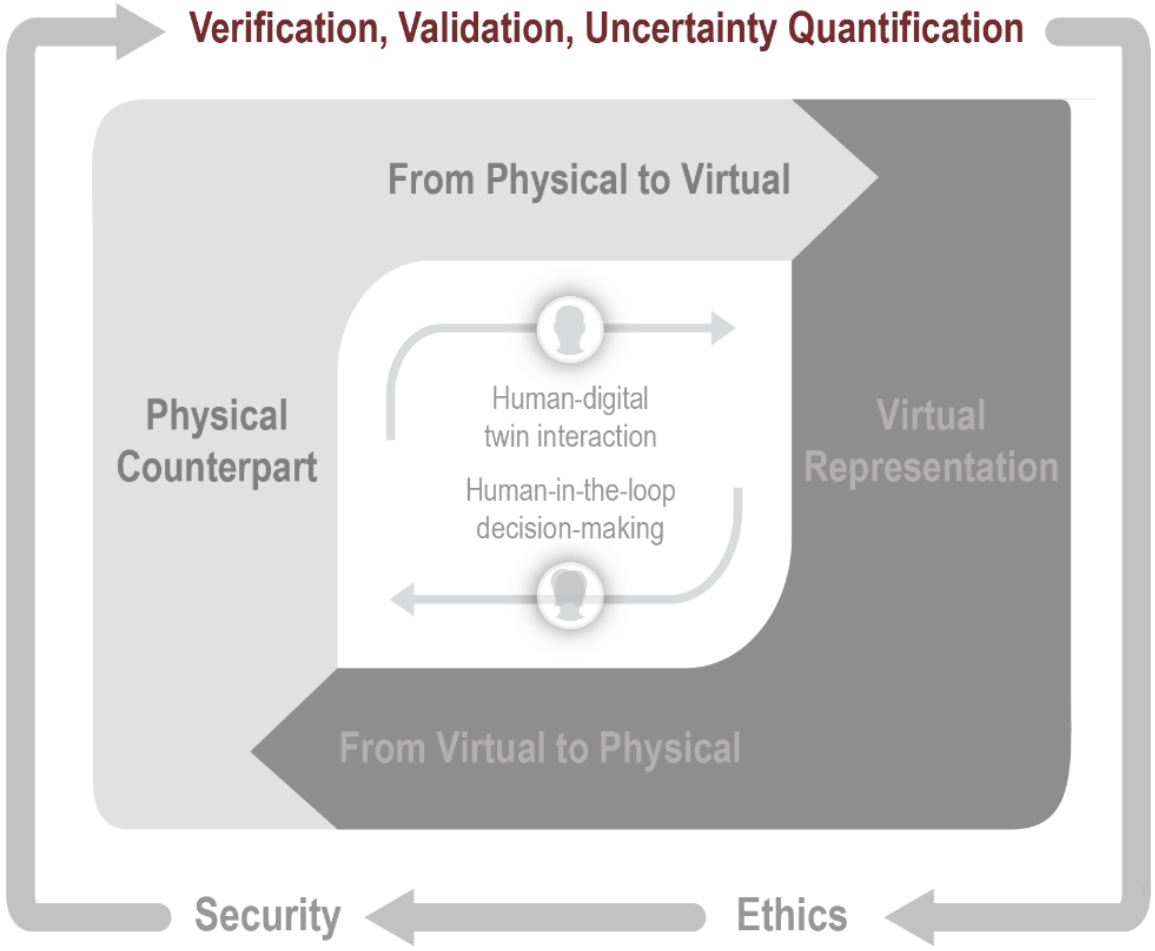
RECOMMENDATION 1

An Integrated Research Agenda

- Need an integrated research agenda that includes foundational needs as well as domain-specific needs
- Recommend that federal agencies launch crosscutting programs to advance the foundations
- An interagency working group may be helpful to ensure coordination

Verification, Validation & Uncertainty Quantification (VVUQ)

Methods for continual VVUQ and monitoring of digital twins are required to establish trust.



Verification. Does a computer program correctly solve the equations of the mathematical model?

Validation. To what degree is a model an accurate representation of the real world, from the perspective of the intended model uses?

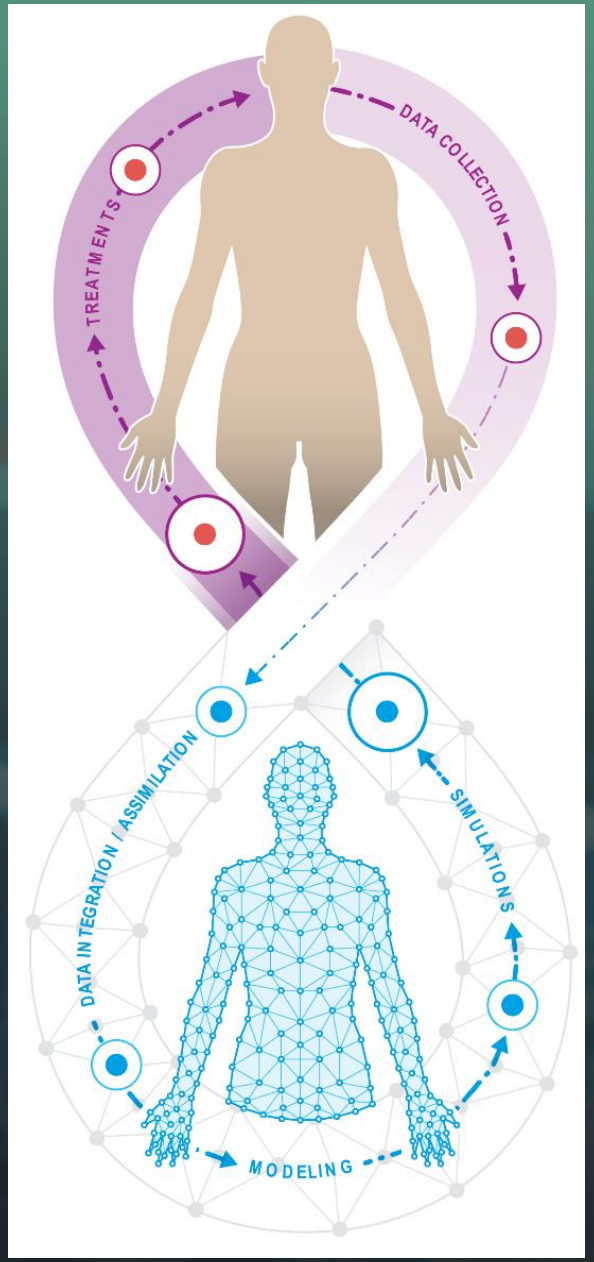
Uncertainty Quantification. What are uncertainties in model calculations of quantities of interest?

RECOMMENDATION 2

VVUQ is Critical to the Success of Digital Twins

- VVUQ must be deeply embedded in the design, creation, and deployment of digital twins
- Need new methods for continual VVUQ that adapt to changes in models, data, and decision contexts
- AI, machine learning, and empirical models pose particular VVUQ challenges
- In future digital twin research developments, VVUQ should play a core role and tight integration should be emphasized

The Department of Energy Predictive Science Academic Alliance Program is a possible model to emulate.



CONCLUSION 3-1

A Digital Twin should be Fit for Purpose

Balancing required fidelity for prediction, available resources, and acceptable costs

- Different digital twin purposes drive different fitness requirements related to modeling fidelity, data availability, visualization, time-to-solution, etc.
- For many potential use cases, achieving fitness-for-purpose is currently intractable

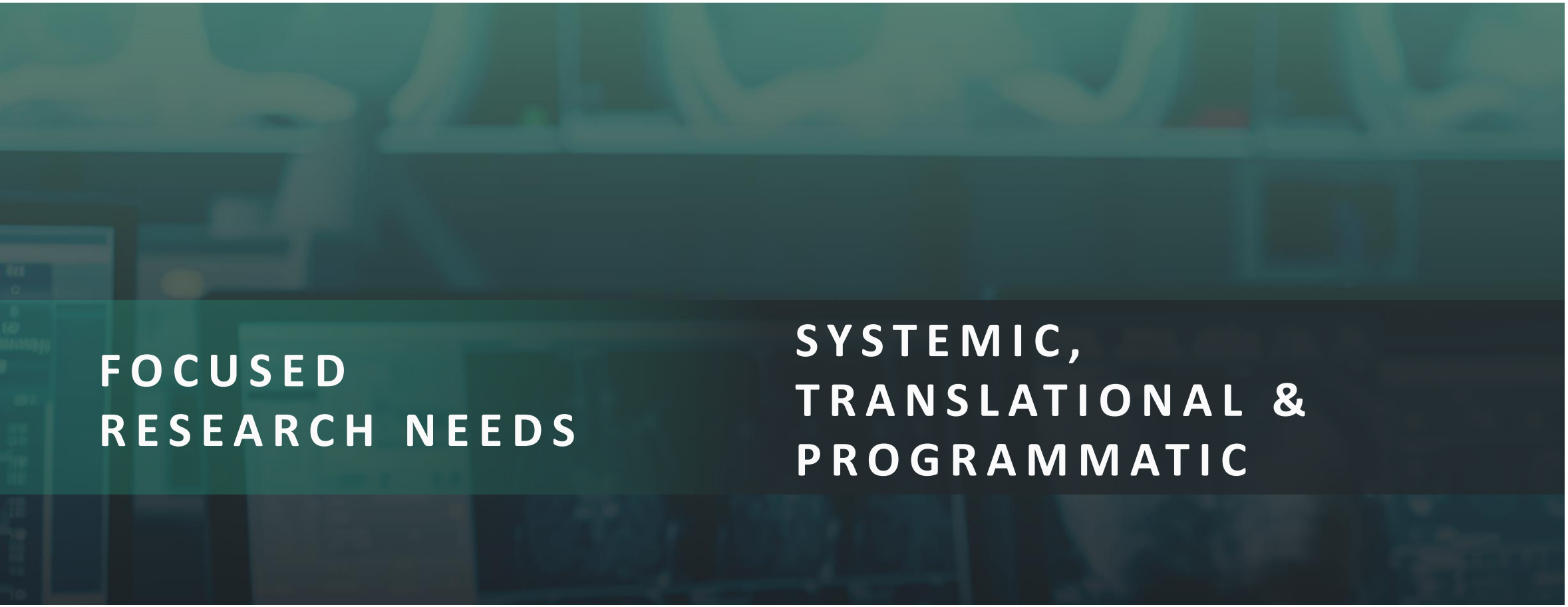
RECOMMENDATION 3

Need mechanisms to provide digital twin researchers with computational resources

FINDING 3-4

Need advances in mathematical theory and algorithms to reduce computational needs

A Range of Research Gaps and Opportunities



FOCUSED RESEARCH NEEDS

SYSTEMIC, TRANSLATIONAL & PROGRAMMATIC

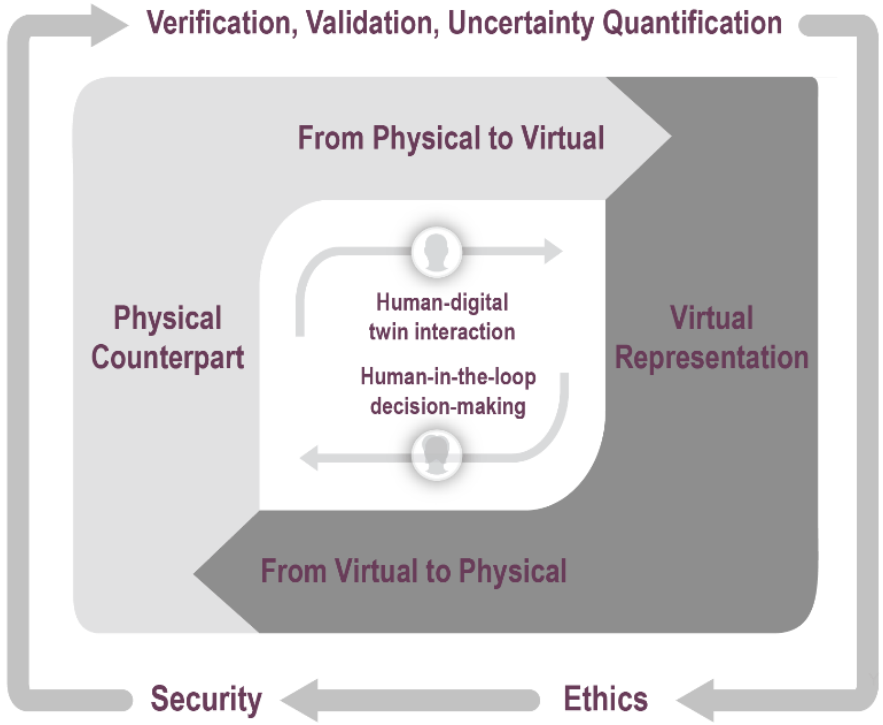
Virtual Representation
multiscale modeling, machine learning & hybrid modeling, surrogates, coupling, system integration, validation, …

Physical Counterpart
data acquisition, imputation, integration, interoperability, …

Physical-to-Virtual
scalable data assimilation, Bayesian inversion, UQ, …

Virtual-to-Physical
scalable optimization under uncertainty, quantifying risk, optimal experimental design, human-in-the-loop decision making, …

Human–digital twin interactions
user-centered digital twin design, ethics, privacy, communicating UQ, …



FOCUSED RESEARCH NEEDS

SYSTEMIC, TRANSLATIONAL & PROGRAMMATIC

Digital twin sustainability

Translational & collaborative research

Fostering model & data collaborations

Interdisciplinary education

RECOMMENDATION 4

Planning for Digital Twin Sustainability

- The virtual representation should be thought of as an asset
- Virtual elements of a digital twin (models, workflows) should receive investment and sustainment, paralleling sustainment of physical counterparts
- Sustaining, maintaining, and managing the life-cycle of digital twins is critical to realizing the value of upstream investments

RECOMMENDATIONS 5,6,7

Collaborations are Imperative

- Digital twin challenges crosscut domains
- Many advances in modeling, data assimilation, VVUQ, and decision-making have evolved within disciplines
- Need a concerted effort to examine formally which advances in methods and workflows might translate across disciplines
- Model and data collaborations are essential, including collaboration and coordination with international bodies
- Need for cross-agency and cross-sector collaborations

RECOMMENDATION 8

Preparing an Interdisciplinary Workforce

Interdisciplinary degrees

that span computational, data, mathematical, and domain sciences are foundational to creating a workforce to advance development and use of digital twins

Digital twins hold immense potential to accelerate scientific discovery and progress across sectors, but an integrated agenda is needed to harmonize research across sectors and focus efforts on realistic applications.

For More Information

https://www.nationalacademies.org/digital-twins