U.S. DEPARTMENT OF ENERGY | Office of Science

Foundational Science for Biopreparedness and Response

DOE-SC Roundtable

Report to BESAC December 7th 2022

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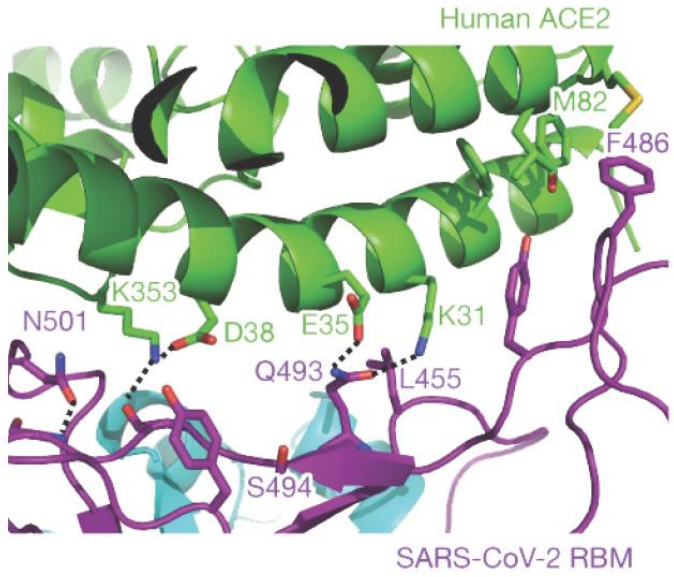
Charter and goals

- Chartered by the Office of the Deputy Director for Science Programs, in collaboration with ASCR, BES and BER
- Motivated by the impact of NVBL on COVID-19 response
- Convened to gather information on the unique roles DOE-SC could play in addressing future pandemics and related crises
- Identify Priority Research Opportunities and specialized capabilities to support biopreparedness studies at user facilites

Roundtable process

- Charter launched activities
- "Technical Document" written – current status of capabilities (Cindy Bruckner-Lea lead author)
- 5 panels formed with 2 panel-leads and 5 members each
- Roundtable held (kick off meeting, check in and report-out over 2 weeks) – March 2022
- Brochure (Executive Summary) published June 2022
- Report published Oct 2022



SARS-CoV-2 Spike protein bound with human ACE2

Five panels met to determine the PROs

Panel 1: Surveillance, testing and diagnostics

- Kristin Omberg (PNNL)
- Monica Boruki (LLNL)

Panel 2: Molecular mechanisms, systems biology and therapeutics

- Ben Brown (LBNL)
- Marti Head (ORNL)

Panel 3: Epidemiology and modeling

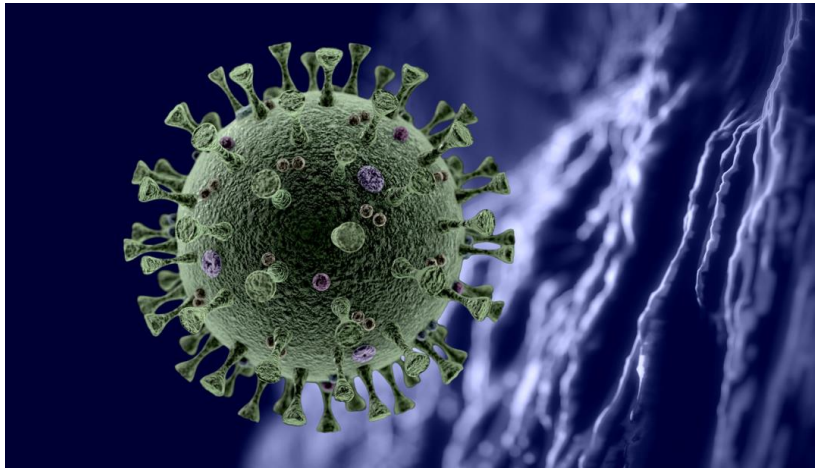
- Sara Del Valle (LANL)
- Budhu Bhadhuri (ORNL)

Panel 4: Materials and Manufacturing

- Ilke Arslan (ANL)
- Brett Helms (LBNL)

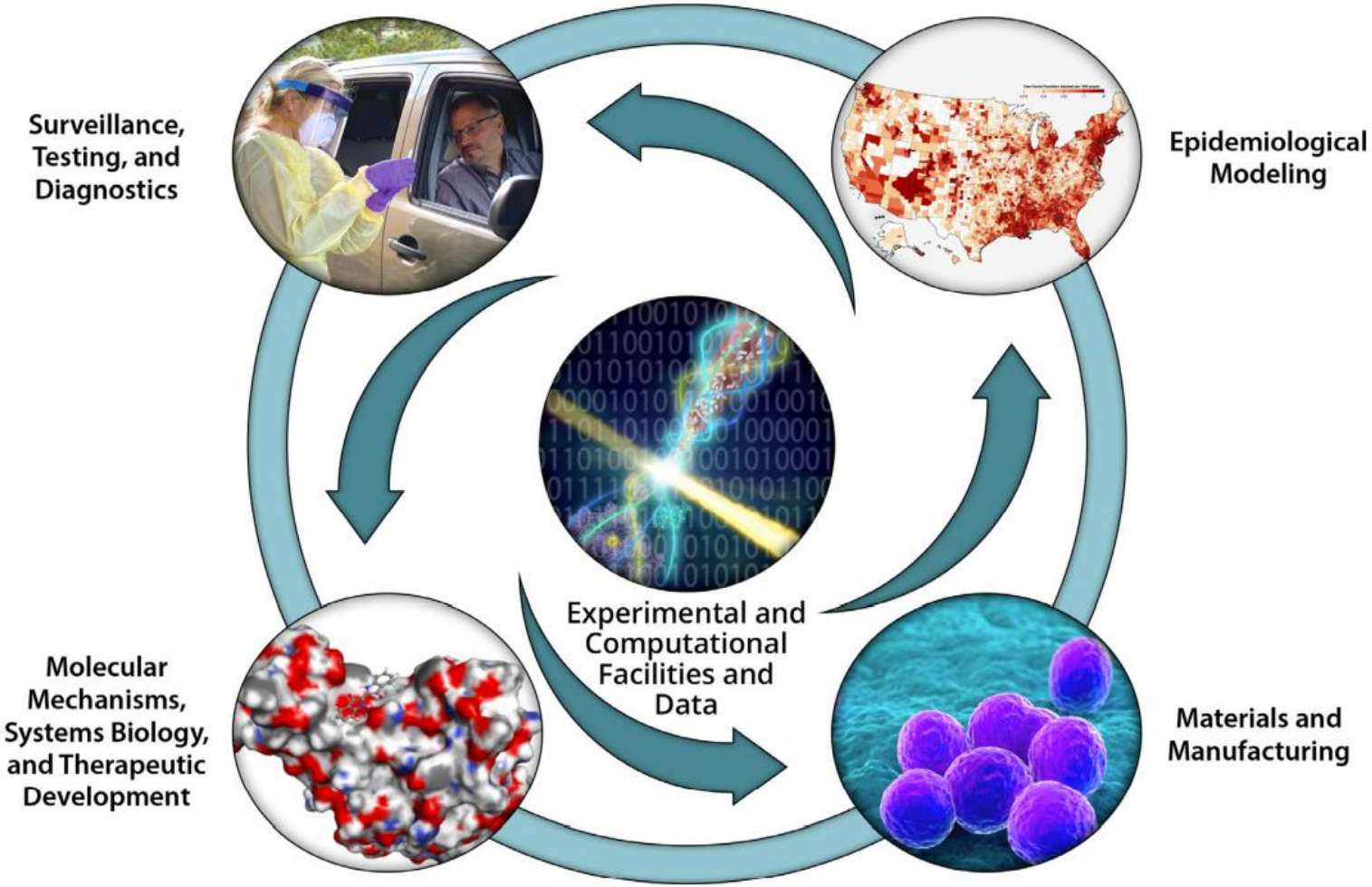
Panel 5: Cross Cutting

- Jim Brase (LLNL)
- Soichi Wakatsuki (SLAC)



User Facilities are key to biopreparedness

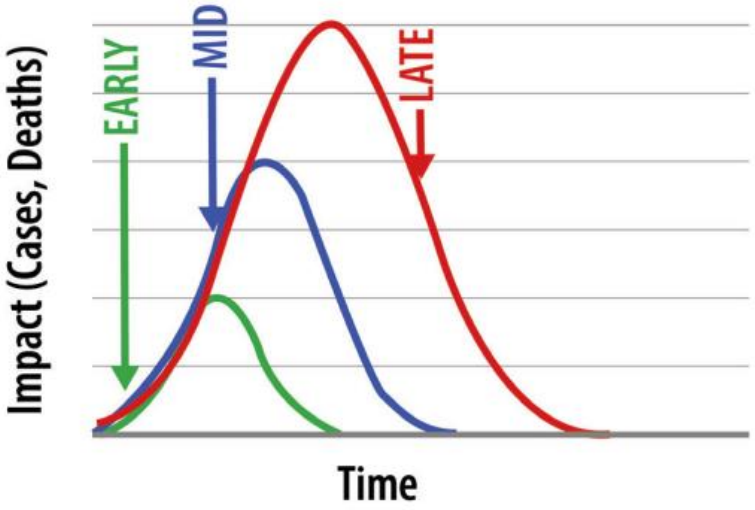
DOE Office of Science experimental and computational user facilities are uniquely positioned to advance the foundational research for biopreparedness in the four key areas of roundtable.



Priority Research Opportunities

PRO1: Decode pathogen emergence, evolution, and host-pathogen dynamics in real time

Early intervention is crucial:



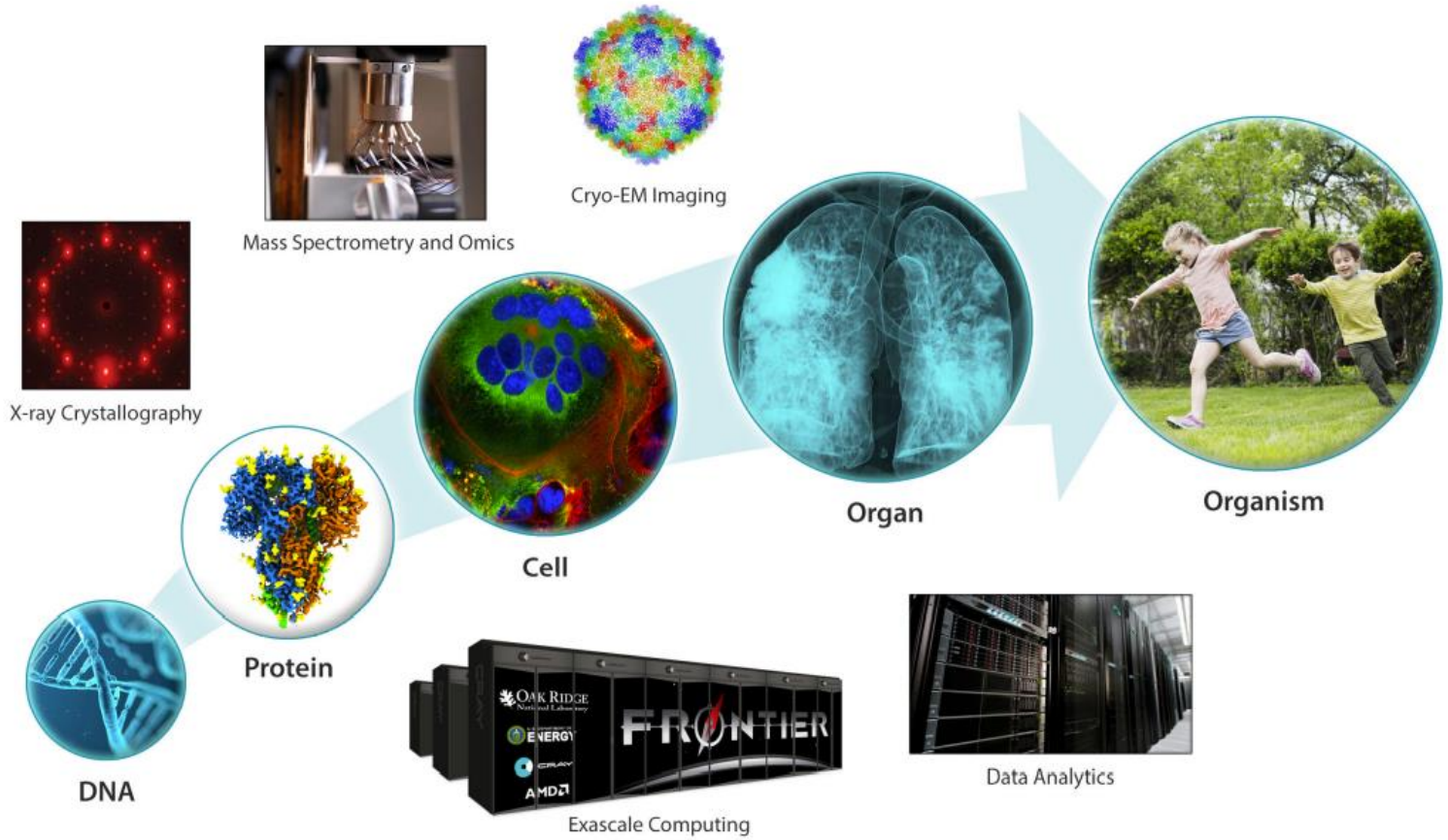
Key Question: How do complex and dynamic biological systems interact with a host?

Characterization of the susceptibility of a host requires understanding of the full ecosystem and its interactions

PRO2:Build a multiscale understanding of biomolecular interactions to catalyze design of targeted interventions

Key Question: How do molecular interactions and vast biological networks give rise to cellular functions on physiological scales and co-evolution on ecological scales?

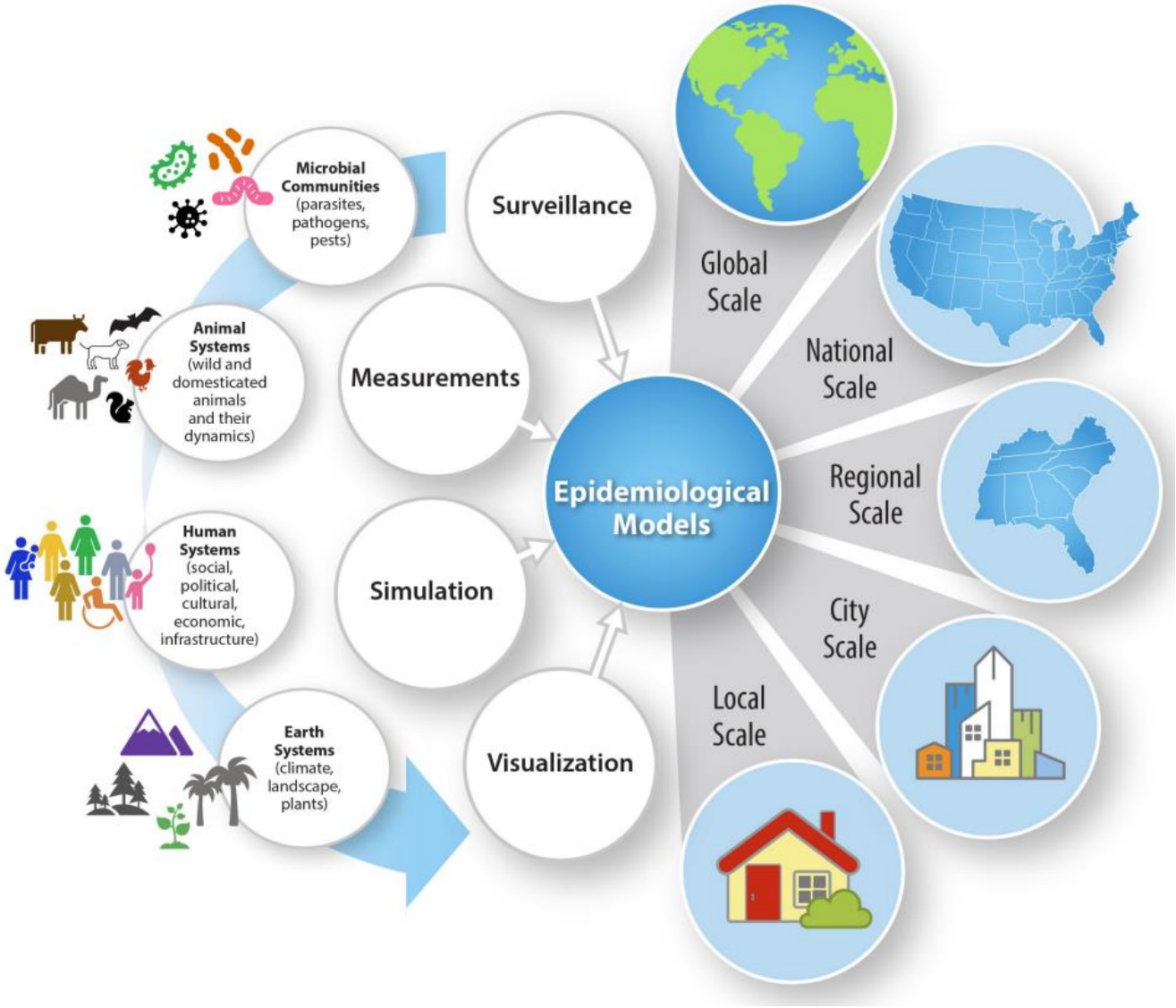
Future biopreparedness will rely on advanced computing capabilities and integration of experimental data across spatiotemporal scales to create an understanding of biomolecular interactions



PRO3:Elucidate multiscale ecosystem complexities for robust epidemiological modeling

Key Question: How can complex and dynamic ecosystem interactions be captured in a framework of multiscale models?

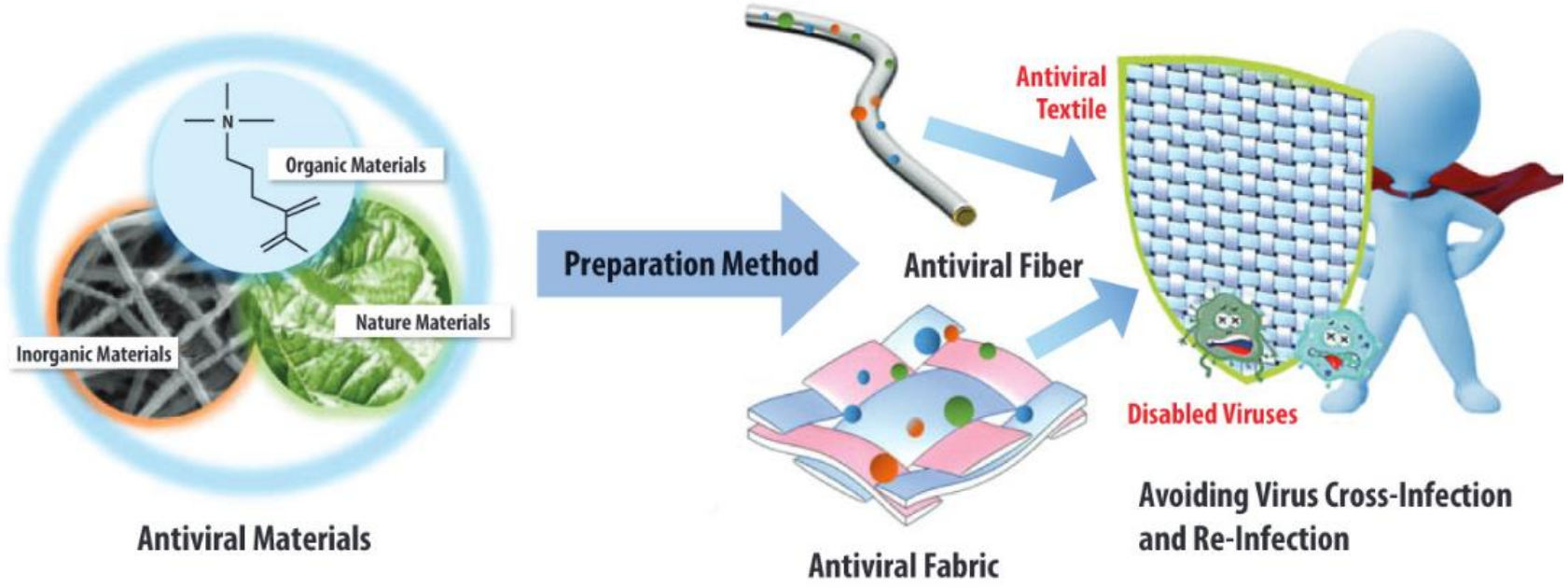
Integrated models that represent the interrelationships and behavioral responses of the four key ecosystem components across space, time and disciplines are necessary to accurately represent and quantify disease impacts



PRO4:Exploit biotic–abiotic interfaces to accelerate design, discovery, and manufacturing of materials

Key Question: How do we understand, predict, and control biotic-abiotic interfaces in ambient conditions and across time scales?

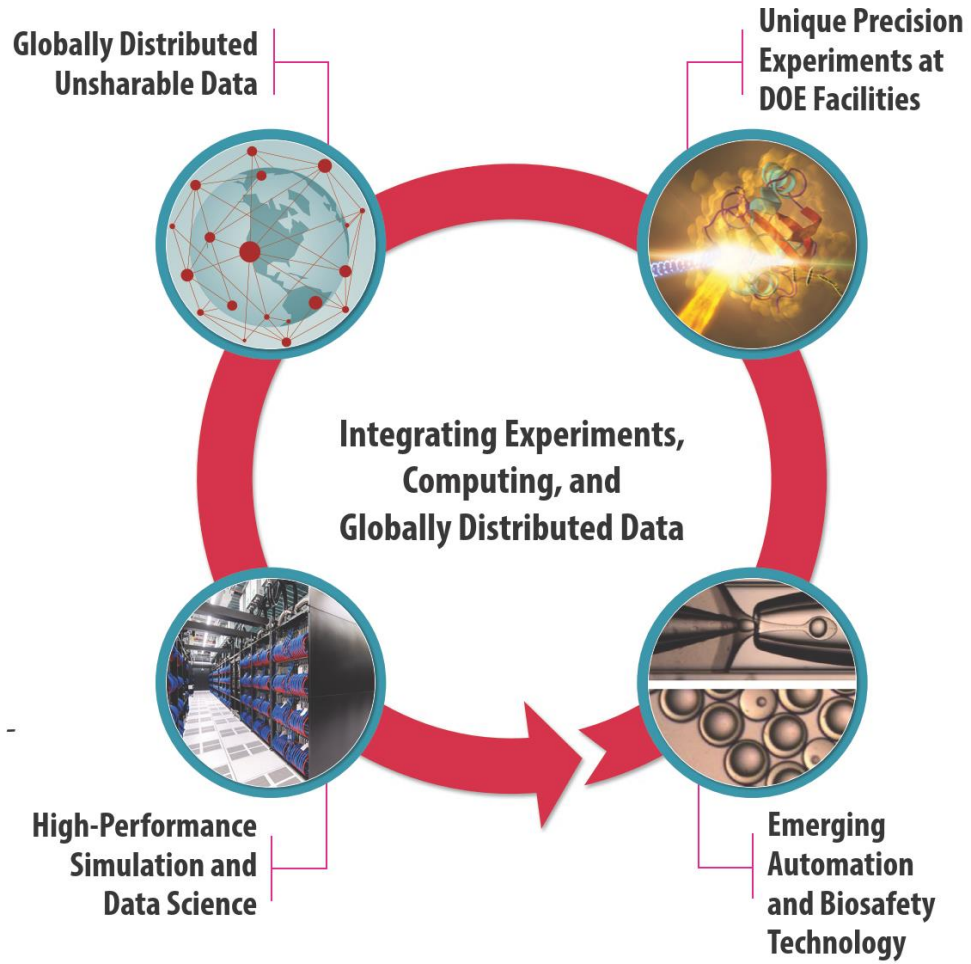
Functional organic and inorganic materials can be used to control pathogen interactions, such as those occurring in the porous materials used to manufacture personal protective equipment.



PRO5:Accelerate biopreparedness by integrating experimentation, computing, and globally distributed data

Key Question: How do we support innovative scientific research with integrated experimental, computational, and data capabilities?

Accelerating the iterative experiment-compute cycle and supporting access to globally shared and distributed data will significantly increase automation of the analytical process and result in more timely insights.



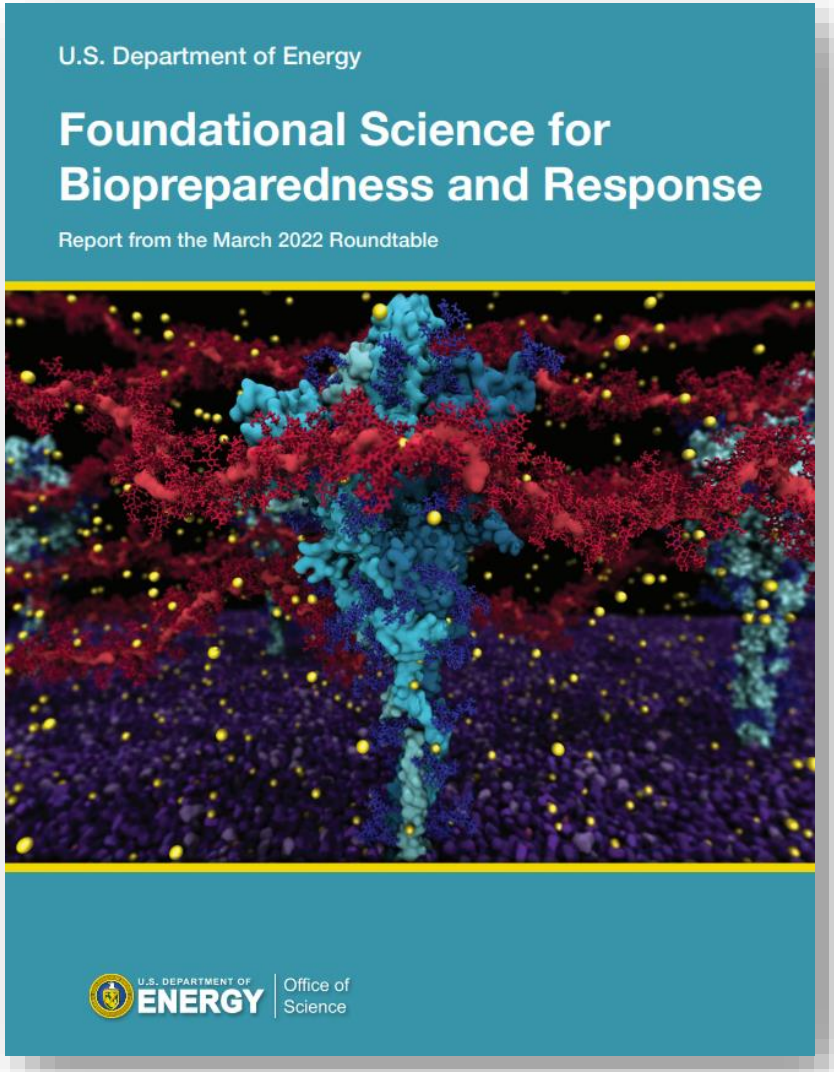
Report

Report contains:

1) Executive Summary
2) Detailed discussion of the 5 PROs
   - Scientific challenges
   - Scientific impact
   - Biopreparedness impact
3) Technical document
4) Thank you to Holly Haun and ORISE for editing!

Published October 6th 2022

https://science.osti.gov/Initiatives/Biopreparedness/Community-Resources



Conclusion

- Basic research, uniquely carried out in DOE-BES, ASCR and BER mission space and supported by the SC user facilities, can address scientific questions with impact on the Nation's biopreparedness.
- Further, capabilities developed for this research will be able to pivot to directly address future bio-crises
- We identified 5 PROs to better position the Nation in this work
- BRaVE act funding in FY23 and beyond will enable some of this work
- DOE-BES, ASCR and BER research can help make the Nation safer in future crises

Backup slides

Team

Chair

John Hill
Brookhaven
National Laboratory

Co-Chairs

Patrick Fitch
Los Alamos
National Laboratory

Deborah Gracio
Pacific Northwest
National Laboratory

Office of Science Team

Michelle Buchanan
Office of Science

Natalia Melcer
Office of Science

Katie Runkles
Office of Science

Joseph Graber
Biological and
Environmental Research

Margaret Lentz
Advanced Scientific
Computing Research

Thomas Russell
Basic Energy Sciences

Plenary program provided input from other agencies

- Susan Gregurik (National Institutes of Health)
- Ron Hann (US Dept. of Defense)
- Joann Andreadis (Centers for Disease Control)
- Stephen Streiffer (Stanford, NVBL)




Decode pathogen emergence, evolution, and host-pathogen dynamics in real time

Scientific challenges

- Our ability to measure and understand baselines in real-time, *in situ*, is insufficient to allow comprehensive surveillance and identify pandemic-relevant anomalies

Summary of research direction

- Develop analytical methods that reveal, monitor and (real-time) report on correlative signals that define host-pathogen interactions, pathogen-environment interactions, and pathogen evolution

Potential scientific impact

- Discovery of novel scientific principles and phenomena that define pathogens, host response and host-pathogen interactions

Potential impact on bio preparedness

- Enables pathogen-agnostic and OneHealth biosurveillance (human, animal, plant, environment)

Build a multiscale understanding of biomolecular interactions to catalyze design of targeted interventions

Scientific challenges

- **Characterize molecular systems in context**: Delineate interactions of subcellular components within organisms and at molecular interfaces between organisms and their abiotic contexts

Summary of research direction

- **Molecules in context**: Determine structures and interactions of complex native macromolecular subsystems; build dynamical models of structures in metabolic contexts to give rise to sub-system behaviors

Potential scientific impact

- Comprehensive cell models from molecular level to phenotype scale

Potential impact on bio preparedness

Identify rapidly:

- Integrate biological data, systems modeling workflows that leverage AI/ML and mechanistic models for resilient response to future threats

Elucidate Multi-scale Ecosystem Complexities for Robust Epidemiological Modeling

Scientific challenges

- **Integration** of human, animal, and climate interactions in epidemiology models

Summary of research direction

- Approaches to **link models** at multiple scales and **model reduction** methods

Potential scientific impact

- **Accurate representation** of human-environment interactions and responses in disease models

Potential impact on bio preparedness

- **Anticipate** and reduce human, economic, and infrastructure **impacts**

Exploit Biotic–Abiotic Interfaces to Accelerate Design, Discovery, and Manufacturing of Materials for Bio-Preparedness

Scientific challenges

- Understand interactions of pathogens, therapeutics, and vaccines at interfaces with hard and soft materials, particularly at the molecular scale and across time scales

Summary of research direction

- Design and discover new materials providing protection, sensing, therapeutic, or immunological benefits through characterization and understanding of structure and dynamics of biotic–abiotic interfaces under realistic conditions

Potential scientific impact

- Biologically robust multimodal and *operando* capabilities for non-destructive and multiscale characterization of biotic–abiotic interfaces

Potential impact on bio preparedness

- Improved materials with anti-viral/microbial properties for filtration (PPE, air filters) and surfaces (doors, walls, floors, desks, etc.)