MULTISCALE REASONING FOR HUMAN PHYSIOLOGY
Request For Information (RFI) – DARPA-SN-26-100
Responses due August 10, 2026, 5:00 PM ET
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URL: https://www.darpa.mil/about/offices/bto#opportunities

I. Introduction

The Defense Advanced Research Projects Agency (DARPA) Biological Technologies Office (BTO) is issuing this Request for Information (RFI) to solicit input from industry, academia, government laboratories, healthcare organizations, and non-traditional performers regarding emerging technologies, datasets, computational frameworks, artificial intelligence systems, and foundation models that enable multiscale reasoning across human physiology.

This RFI seeks to identify existing capabilities, foundational datasets, and critical scientific gaps in connecting biological and physiological processes across molecular, cellular, tissue, organ, whole-body, and clinical scales. While the primary focus of this RFI is on advancing military medicine, specifically prediction, diagnosis, intervention, and recovery in combat and prolonged casualty care (CCC and PCC), we encourage non-military applications that boldly highlight the core scientific challenges of multi-scale biological reasoning.

This RFI is issued solely for information-gathering and planning purposes. It does not constitute a solicitation for proposals, abstracts, or quotations.

II. Background

Human biology operates across an extraordinary range of spatial and temporal scales, spanning molecules, cells, tissues, organs, and whole-body physiology. Biological processes unfold over many orders of magnitude, from microseconds associated with molecular interactions to years associated with disease progression and recovery, and from nanometer-scale molecular structures to meter-scale human systems. These scales are tightly coupled; changes at one scale can propagate through multiple intermediate levels to influence physiological function, clinical outcomes, and therapeutic response.

Recent advances in artificial intelligence, foundation models, computational physiology, multimodal sensing, imaging, and digital twins have created new opportunities to model human health and disease across these scales. However, despite substantial progress within individual domains, our understanding of how biological information, mechanisms, and interventions propagate across scales remains limited. Significant challenges remain in connecting observations, mechanisms, predictions, and interventions in a manner that is scientifically grounded, computationally tractable, and clinically actionable.

DARPA seeks to understand the current state of the art in multiscale reasoning and identify technologies, directly rooted in and applicable to multi-scale biology, that can enable:

- Integration of heterogeneous data spanning molecular, cellular, physiological, imaging, and clinical domains.
- Prediction of physiological trajectories under injury, disease, stress, and intervention.
- Mechanistic understanding of disease progression, recovery, and therapeutic response.
- Translation of observations at one biological scale into predictions and interventions at another.
- Robust operation under sparse-data, denied, degraded, and disrupted environments.
- Identification, characterization, and utilization of datasets capable of supporting multiscale reasoning across human physiology.

III. Areas of Interest
DARPA is seeking information on technologies, models, and datasets relevant to multiscale reasoning in human physiology. The list includes, but is not limited to:

1. Multiscale Computational Models
Particular interest is placed on approaches that connect biological scales that are widely separated in space, time, or modality.

- Mechanistic physiological models
- Computational medicine and digital twins
- Scientific machine learning
- Coupling mechanisms and operators for cross-scale model integration
- Reduced-order models
- Hybrid mechanistic-AI systems
- Causal and intervention-aware models
- Models connecting molecular, cellular, tissue, organ, and clinical outcomes

2. Foundation Models for Multi-scale Biology and Medicine

- Multimodal foundation models
- Biological foundation models
- Physiological foundation models
- Models integrating omics, imaging, waveforms, laboratory data, and clinical records
- Reasoning architectures that connect multiple biological scales
- Foundation models supporting mechanistic discovery or intervention prediction

3. Multi-scale Human Physiology Data Resources
DARPA is particularly interested in identifying existing datasets capable of supporting multiscale reasoning.

- Longitudinal human physiology datasets
- Multimodal physiological monitoring datasets
- Imaging repositories
- Genomic, transcriptomic, proteomic, metabolomic, and spatial biology datasets
- Critical care and operational medicine datasets
- Datasets containing linked measurements across multiple biological scales
- Datasets containing interventions and longitudinal outcomes

4. Prediction and Intervention Across Scales of Biology and Medicine

- Physiological forecasting
- Treatment-response prediction
- Counterfactual reasoning
- Closed-loop medical systems
- Decision-support systems
- Intervention planning and optimization
- Human-machine teaming for medical decision-making

5. Military and Operational Medicine Applications Leveraging Multi-Scale Modeling Solutions

- Combat casualty care
- Acute Chemical, Biological, Radiological, Nuclear, and high-yield Explosives (CBRNE) Exposure, including acute toxic industrial chemical/material exposure
- Hemorrhage and shock
- Traumatic brain injury
- Airway and respiratory compromise
- Multi-organ dysfunction

- Sepsis and infection
- Prolonged casualty care
- Recovery and rehabilitation
- Human performance and resilience

IV. Requested Information
Respondents are invited to provide the following:

A. Technology Description
- Current capability and maturity (TRL, if applicable)
- Biological scales represented
- Underlying modeling approach
- Role of AI, foundation models, and mechanistic models
- Evidence of cross-scale reasoning capability

B. Scale Integration
- Which biological scales are directly measured versus inferred?
- How are scales mathematically or computationally coupled?
- What mechanisms link observations across scales? How are interventions represented and propagated through the model?
- What scales constitute the largest demonstrated separation between inputs and outputs?
- How do critical changes in small-scale dynamics influence non-linearly disproportionate changes in macro-scale dynamics?

C. Human Physiology Data Assets
For each dataset, please include: Dataset name, number of subjects, data modalities, biological scales represented, longitudinal duration, accessibility and military relevance

Particular interest is placed on datasets containing linked measurements across molecular, cellular, tissue, organ, physiological, and clinical scales, as well as datasets containing interventions and outcomes.

D. Validation and Evidence
If applicable, please include: Publications, demonstrations, clinical validation, pre-clinical biological model studies, benchmarking approaches, evidence supporting mechanistic validity across scales

E. Performance Metrics
Examples may include but not limited to: Cross-scale prediction accuracy, forecast horizon, intervention prediction accuracy, mechanistic fidelity, robustness to sparse data, uncertainty calibration

F. Key Gaps & Risks
- Missing datasets
- Missing biological measurements
- Missing links between scales
- Barriers to multiscale reasoning
- Critical scientific and technical challenges
- Opportunities for DARPA investment

V. Response Guidelines

- While there is no page limit for responses to this RFI, DARPA strongly encourages submissions that are focused and concise. Brevity and clarity are preferred.
- Respondents are encouraged to include references, demonstrations, datasets, benchmarks, and publicly available resources where applicable.
- Submissions should be delivered electronically in PDF format to bioreasoning@darpa.mil.
- Responses must clearly mark any proprietary or sensitive information.

VI. Disclaimer

This is an RFI issued solely for information and new program planning purposes; it does not constitute a formal solicitation for proposals. In accordance with FAR 15.201(e), responses to this notice are not offers and cannot be accepted by the Government to form a binding contract. Submission is voluntary and is not required to propose to a subsequent Broad Agency Announcement (BAA), Program Solicitation (PS), or other research opportunity on this topic.

DARPA will NOT provide reimbursement for costs incurred in responding to this RFI. NO CLASSIFIED INFORMATION SHOULD BE INCLUDED IN THE RFI RESPONSE.

It is the submitter's responsibility to clearly define to the Government what is considered proprietary data. Any proprietary information should be clearly labeled as "proprietary." DARPA will disclose submission contents only for the purpose of review and evaluation. Respondents are advised that DARPA is under no obligation to acknowledge receipt of the information received or provide feedback with respect to any information submitted under this RFI.