PRO-MICROBE

Predictions for Real-time Optimization of MICRObiomes of Built Environments

Advanced Research Projects Agency for Health (ARPA-H)

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What if we could discover probiotics in buildings?

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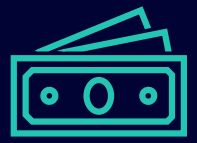
Healthy buildings are critical – especially now

Indoor microbial exposures can lead to disease transmission, health complications, and death.

- Up to **18x** higher transmission rate of respiratory disease indoors.[1]
- Lower respiratory infections are **8th leading cause of death** pre-COVID; 4th leading cause globally.[2]
- **345M** globally suffer from asthma[3] and **400M** from allergic rhinitus annually (impacting 30-40% of Americans).[4]
- **2.8M** antimicrobial-resistant infections occur annually in US[5], costing **35K** lives.[5]

The disease burden from unhealthy microbial exposures comes at significant cost.



- **>$45B** US healthcare spending for respiratory infections.[6]
- **> $39B** US healthcare spending for allergic rhinitis and asthma.[6,7]
- **$55B** US healthcare spending for antimicrobial-resistant infections.[8]

Health risks due to microbial exposures are increasing.

- **68%** of the world's population in cities by 2050.
- **58%** human pathogen diseases aggravated by climate change.[9]
- **20 day** increase in pollen season.[10]
- **20%** increase in hospital-onset resistant infections in the U.S since the COVID-19 pandemic.[5]

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[1] Bulfone et al., 2021, [2] Kochanek et al., 2019, [3] Safiri et al., 2022, [4] Dykewicz et al., 2020, [5] CDC 2024, [6] Duan et al., 2023, [7] Mudarri 2016, [8] Dadgostar 2019, [9] Mora et al., 2022, [10] Anderegg et al., 2021

Buildings are not optimized for microbial health.
PRO-MICROBE will bridge this gap.

Current State

- Insights confined to known pathogens and allergens.
- Lacking community- and systems-level understanding of microbial exposure.
- No standardized and cost-effective way to classify the microbial health of a building.

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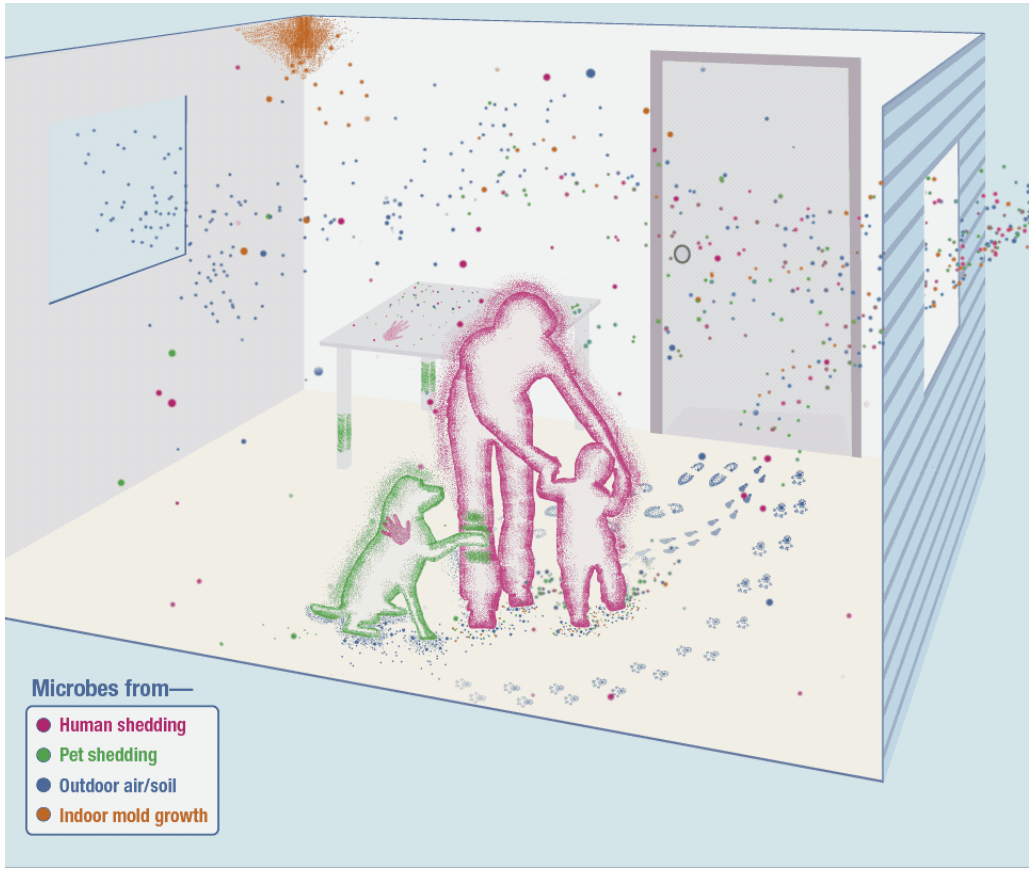
- Discover healthy and beneficial microbes.
- Healthy building strategies informed by developing Microbiome of the Built Environment (MoBE) Index.
- Promotion indoor environmental quality through microbial "rewilding" and probiotic transformation.



https://www.epa.gov/indoor-air-quality-iaq/indoor-microbiome

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PRO-MICROBE

Radically reimagines how indoor spaces can promote health.

Microbiome of the Built Environment Index

PRO-MICROBE aims to create a **healthy building index** that can score the **microbial health** of any indoor environment.

PRO-MICROBE will involve:

- Microbial sample collection and processing in buildings that are classified as “healthy” or “unhealthy”
- Model development to deliver robust predictive tools based on complex data from multiple streams

Performer Expectations at Kickoff

Access to health outcome data. Additional data can be collected or supplemented early-on.

“Healthy" versus "unhealthy" building types should be clearly defined using the health outcome data.

Definitions should include attributes like the **prevalence of chronic diseases** among occupants or **beneficial health outcomes** above a normalized baseline.

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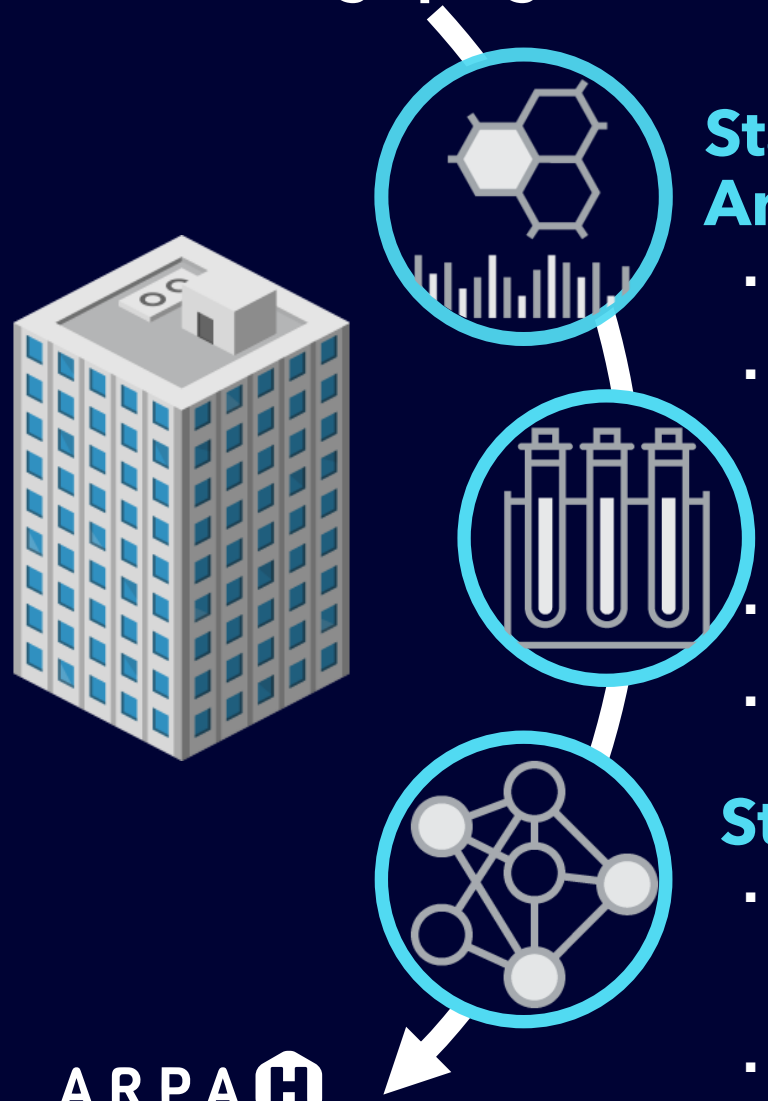
PRO-MICROBE: predicting health of indoor environments

A multi-stage program for microbial sampling, analysis, and predictive modeling



Stage I.I: Broad-Brush Sampling and Correlation Analysis

- **Goal:** Identify microbial indicators and environmental metadata that can be consistently collected across facilities and that relate to building health.
- **Example Approaches:** Microbiome sample data with relatively shallow breadth/depth of coverage, incorporating a priori hypotheses (e.g. microbial taxa & functional genes); air quality, GPS, street view and facility operations data

Stage I.II: In-Depth Sampling and Data Collection

- **Goal:** Build on Stage I.I insights to develop a robust and comprehensive dataset that accurately correlates microbiome composition and environmental metadata with building health.
- **Example Approaches:** Deep Genomic Sequencing, Transcriptomics, Proteomics, and/or Metabolomics

Stage II: Model Building and Validation

- **Goal:** Create a reliable index that predicts building health by integrating microbial and environmental data, while also developing tools that leverage environmental data to predict MoBE health indices. These tools will reduce reliance on intensive microbial sampling, making the assessment process more efficient and scalable.
- **Example Approaches:** Machine Learning models (Gradient Boosting Machines, Support Vector Machines, Neural Networks)

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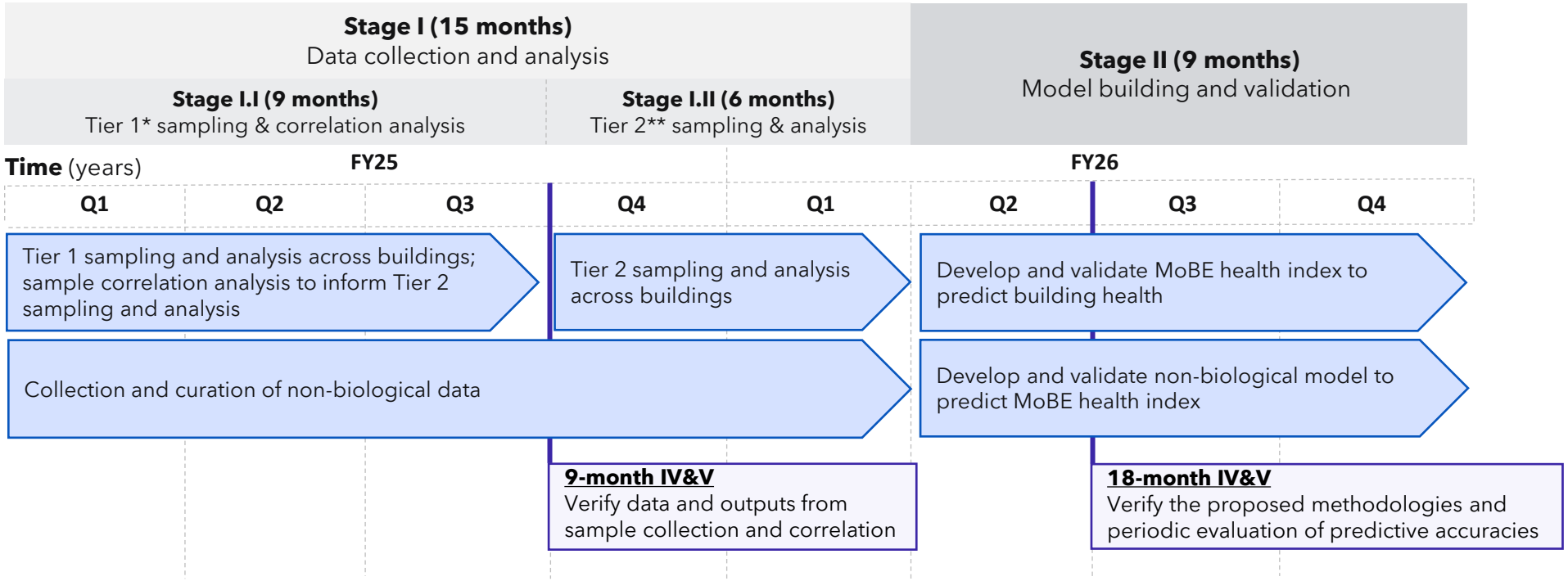
Program Timeline & Deliverables



Key Program Deliverables

Stage I.I: Correlation dashboard and reporting tool for MoBE features

Stage I.II: Tier 2 Sampling and Analysis Tools and Reporting

Stage II: MoBE Health Index and Non-Biological Data Model Developments

**Tier 1 sampling*: broad, shallow survey of microbial samples, covering a wide range of locations or conditions.
*** Tier 2 sampling*: intensive sampling and analysis, employing advanced techniques like deep genomic sequencing, and transcriptomics.

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Key Metrics for Success

		Stage I.I		Stage I.II	Stage II
Metrics	Description	End of 6 months	End of 9 months	End of 15 months	End of 24 months
Sample Correlation	Correlation of MoBE features or groups of features (e.g., abundance, composition, and/or diversity) with building health classification	Set target	≥95% of target	n/a	n/a
MoBE Health Index Predictive Accuracy	MoBE health index scores are consistent with validation sources (i.e., building health classification)	n/a	n/a	Set accuracy target	≥95% of target
Dimensionality	MoBE index utilizes the minimal, yet most influential MoBE features or combinations of features, as determined by feature importance scores	n/a	n/a	Set target	100% of target
Non-biological Model Predictive Accuracy	Model accuracy is consistent with validation sources (i.e., MoBE health index)	n/a	n/a	Set accuracy target	≥95% of target

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BREATHE is focused on pathogen and allergens

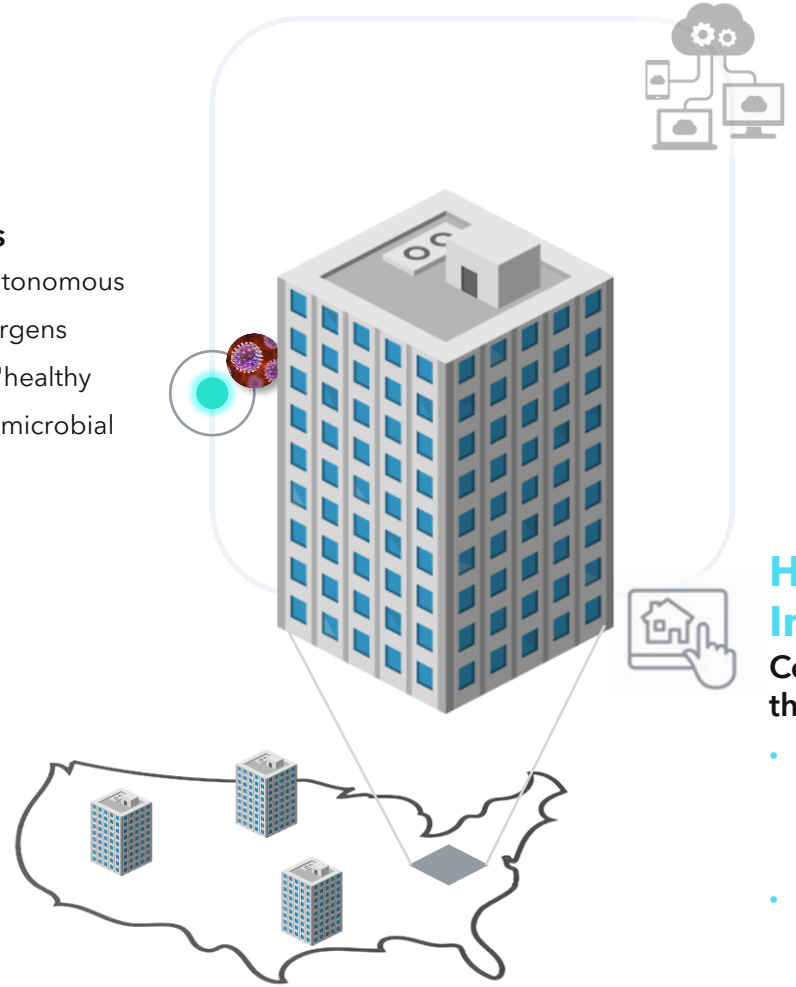
PRO-MICROBE will expand indoor environmental quality to include "healthy microbiomes"

BREATHE Technical Areas outlined below are detailed here

Indoor Air Biosensors

Rapidly detect airborne biothreats

- **BREATHE** is developing cost-effect autonomous sensors for known pathogens and allergens
- **PRO-MICROBE** will enable targeting "healthy microbiomes" and currently unknown microbial indicators of building health



Respiratory Risk Assessment Software

Determine whether health impacts are likely

- **BREATHE** is assessing indoor exposure risk for known pathogens and allergens
- **PRO-MICROBE** data insights will expand risk algorithms to include "healthy microbiomes" and the MoBE Health Index

Real-word testing and evidence

Conduct nation-wide efficacy trial

- **BREATHE** is demonstrating a reduction indoor respiratory incidence by at least 25% by directly measuring occupant health outcomes
- **PRO-MICROBE** is generating a MoBE Health Index tha can be leveraged to assess BREATHE system efficacy

Healthy Building Controls and System Integration

Cost-optimize use of building interventions to mitigate threats

- **BREATHE** is demonstrating real-time response to exposure risk using interventions (e.g. ventilation, filtration and disinfection) by directly measuring occupant health outcomes
- **PRO-MICROBE** is generating a MoBE Health Index that can be leveraged to assess intervention efficacy

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PRO-MICROBE Will Synergize with BREATHE Systems

PRO-MICROBE Insights		BREATHE Program Areas
Identify molecules, genes, taxa and microbiomes indicative of building health	*Expand/inform biosensor targets*	TA1: Biosensor Development (multiplexed autonomous air sampling)
Develop MOBE health index and predictive models	*Improve predictions via microbiome-informed risk assessment*	TA2: Risk Assessment Modeling
	Test effect of interventions on MOBE health index	TA3: Building Interventions
Real world microbial sampling and association with occupant health	*Contribute to 25% reduction in a respiratory illness with 10% ROI*	Field efficacy trials in buildings across the country

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Exploration Topic: PRO-MICROBE (Predictions for Real-time Optimization of MICRObiomes of Built Environments)

Technology focus area:

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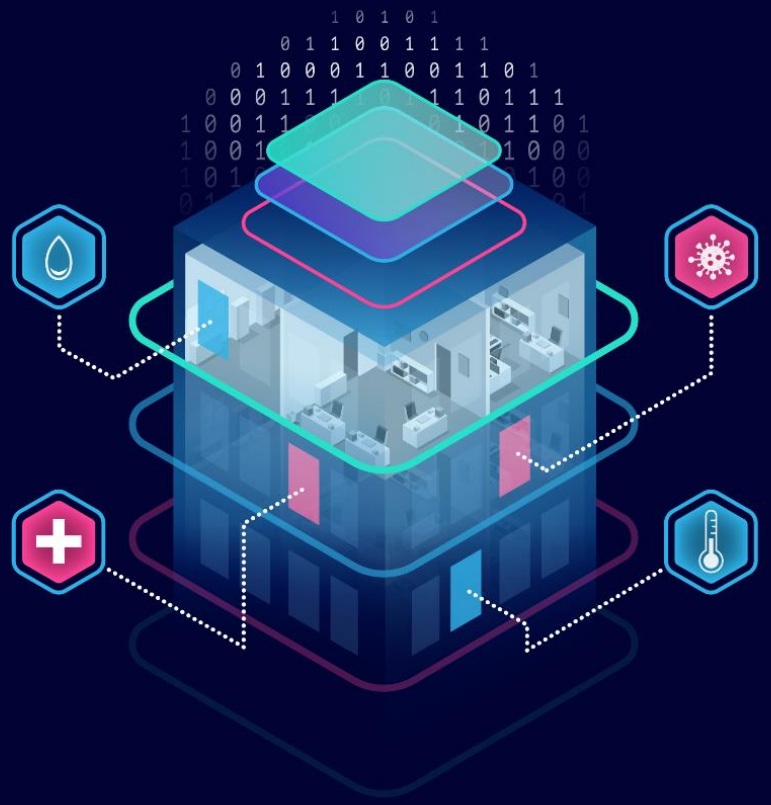

Key Information:

- PRO-MICROBE proposals are due on **November 4th, 2024**.
- View the final program solicitation on sam.gov: https://sam.gov/opp/06679fafce184ee784bdcabee9624a22/view
- View the ARPA-H announcement (and Q&As as they are posted): https://arpa-h.gov/news-and-events/arpa-h-launches-exploration-topic-develop-novel-healthy-building-index

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